

Inequalities in COVID-19 healthcare and research affecting women

Edited by

Vijay Kumar Chattu, Hamid Allahverdipour, Kelly Jane Thompson, Sanni Yaya and Lakshmi Surya Prabha Manem

Published in

Frontiers in Global Women's Health



FRONTIERS EBOOK COPYRIGHT STATEMENT

The copyright in the text of individual articles in this ebook is the property of their respective authors or their respective institutions or funders. The copyright in graphics and images within each article may be subject to copyright of other parties. In both cases this is subject to a license granted to Frontiers.

The compilation of articles constituting this ebook is the property of Frontiers.

Each article within this ebook, and the ebook itself, are published under the most recent version of the Creative Commons CC-BY licence. The version current at the date of publication of this ebook is CC-BY 4.0. If the CC-BY licence is updated, the licence granted by Frontiers is automatically updated to the new version.

When exercising any right under the CC-BY licence, Frontiers must be attributed as the original publisher of the article or ebook, as applicable.

Authors have the responsibility of ensuring that any graphics or other materials which are the property of others may be included in the CC-BY licence, but this should be checked before relying on the CC-BY licence to reproduce those materials. Any copyright notices relating to those materials must be complied with.

Copyright and source acknowledgement notices may not be removed and must be displayed in any copy, derivative work or partial copy which includes the elements in question.

All copyright, and all rights therein, are protected by national and international copyright laws. The above represents a summary only. For further information please read Frontiers' Conditions for Website Use and Copyright Statement, and the applicable CC-BY licence.

ISSN 1664-8714
ISBN 978-2-8325-2493-0
DOI 10.3389/978-2-8325-2493-0

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Inequalities in COVID-19 healthcare and research affecting women

Topic editors

Vijay Kumar Chattu — University of Toronto, Canada

Hamid Allahverdipour — Tabriz University of Medical Sciences, Iran

Kelly Jane Thompson — University of New South Wales, Australia

Sanni Yaya — University of Ottawa, Canada

Lakshmi Surya Prabha Manem — Dr. NTR University of Health Sciences, India

Citation

Chattu, V. K., Allahverdipour, H., Thompson, K. J., Yaya, S., Manem, L. S. P., eds. (2023). *Inequalities in COVID-19 healthcare and research affecting women*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-2493-0

Table of contents

- 05 **Editorial: Inequalities in COVID-19 healthcare and research affecting women**
Vijay Kumar Chattu, Lakshmi Surya Prabha Manem, Behdin Nowrouzi-Kia, Kelly Jane Thompson, Hamid Allahverdipour and Sanni Yaya
- 08 **COVID-19 Pandemic Worsening Gender Inequalities for Women and Girls in Sub-Saharan Africa**
Bright Opoku Ahinkorah, John Elvis Hagan Jr., Edward Kwabena Ameyaw, Abdul-Aziz Seidu and Thomas Schack
- 14 **Sex and Gender in COVID-19 Vaccine Research: Substantial Evidence Gaps Remain**
Amy Vassallo, Sultana Shajahan, Katie Harris, Laura Hallam, Carinna Hockham, Kate Womersley, Mark Woodward and Meru Sheel
- 26 **Sex and Gender Bias in Covid-19 Clinical Case Reports**
Aysha E. Salter-Volz, Abigail Oyasu, Chen Yeh, Lutfiyya N. Muhammad and Nicole C. Woitowich
- 32 **A Perspective on Intimate Partner Violence Since COVID-19**
Raveed Khan and Syriah David
- 35 **Isolation in COVID, and COVID in Isolation—Exacerbated Shortfalls in Provision for Women's Health and Well-Being Among Marginalized Urban Communities in India**
Lakshmi K. Josyula, Shrutika Murthy, Himabindu Karampudi and Surekha Garimella
- 42 **"Worn-out but happy": Postpartum Women's Mental Health and Well-Being During COVID-19 Restrictions in Australia**
Hannah E. Christie, Kassia Beetham, Elizabeth Stratton and Monique E. Francois
- 52 **Molecular and Physiological Aspects of SARS-CoV-2 Infection in Women and Pregnancy**
Anna Liu, Janet Raja xavier, Yogesh Singh, Sara Y. Brucker and Madhuri S. Salker
- 71 **Accessing Maternal Health Care in the Midst of the COVID-19 Pandemic: A Study in Two Districts of Assam, India**
Rashmi Padhye, Anusha Purushotham, Maitrayee Paul, Nilangi Sardeshpande, Ramnath Ballala, Shelley Dhar, Sunil Kaul and Renu Khanna
- 80 **Effects of the COVID-19 Pandemic and Telehealth on Antenatal Screening and Services, Including for Mental Health and Domestic Violence: An Australian Mixed-Methods Study**
Amanda Henry, Jennifer Yang, Sarah Grattan, Lynne Roberts, Anne Lainchbury, Janani Shanthosh, Patricia Cullen and Louise Everitt

- 92 **Maternal self-conception and mental wellbeing during the first wave of the COVID-19 pandemic. A qualitative interview study through the lens of “intensive mothering” and “ideal worker” ideology**
Stephanie Batram-Zantvoort, Lisa Wandschneider, Vera Niehues, Oliver Razum and Céline Miani
- 108 **Intimate partner violence against women of reproductive age and associated factors during COVID-19 pandemic in Northern Ethiopia, 2021: A community-based cross-sectional study**
Mekasha Getnet Demeke and Ehtemariam Tefera Shibeshi



OPEN ACCESS

EDITED AND REVIEWED BY
Sanne Peters,
University Medical Center Utrecht, Netherlands

*CORRESPONDENCE
Vijay Kumar Chattu
✉ drvkumar.ch@gmail.com

SPECIALTY SECTION
This article was submitted to Sex and Gender Differences in Disease, a section of the journal Frontiers in Global Women's Health

RECEIVED 23 January 2023
ACCEPTED 24 February 2023
PUBLISHED 10 March 2023

CITATION
Chattu VK, Manem LSP, Nowrouzi-Kia B, Thompson KJ, Allahverdipour H and Yaya S (2023) Editorial: Inequalities in COVID-19 healthcare and research affecting women. *Front. Glob. Womens Health* 4:1150186. doi: 10.3389/fgwh.2023.1150186

COPYRIGHT
© 2023 Chattu, Manem, Nowrouzi-Kia, Thompson, Allahverdipour and Yaya. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](#). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Editorial: Inequalities in COVID-19 healthcare and research affecting women

Vijay Kumar Chattu^{1,2,3*}, Lakshmi Surya Prabha Manem⁴,
Behdin Nowrouzi-Kia¹, Kelly Jane Thompson^{5,6},
Hamid Allahverdipour^{7,8} and Sanni Yaya^{9,10}

¹Department of Occupational Science & Occupational Therapy, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada, ²Center for Interdisciplinary Research, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, (SIMATS), Saveetha University, Chennai, India, ³Department of Community Medicine, Faculty of Medicine, Datta Meghe Institute of Medical Sciences, Wardha, India, ⁴Research & Development, Dr. NTR University of Health Sciences, Vijayawada, India, ⁵George Institute for Global Health, University of New South Wales, Newtown, NSW, Australia, ⁶Research & Development, Nepean and Blue Mountains Local Health District, Sydney, NSW, Australia, ⁷Research Center of Psychiatry and Behavioral Sciences, Tabriz University of Medical Sciences, Tabriz, Iran, ⁸Department of Health Education and Promotion, Tabriz University of Medical Sciences, Tabriz, Iran, ⁹School of International Development and Global Studies, University of Ottawa, Ottawa, ON, Canada, ¹⁰The George Institute for Global Health, Imperial College London, London, United Kingdom

KEYWORDS

gender, equity, inequalities, women, COVID-19, mental health, research, sexual and reproductive health (SRH)

Editorial on the Research Topic Inequalities in COVID-19 healthcare and research affecting women

This Research Topic, *Inequalities in COVID-19 Healthcare and Research Affecting Women*, presents a rich collection of articles from all over, including Africa, Asia, Australia, North America, and Europe. The Topic is a compilation of various articles addressing diverse topics such as gender gaps, violence against women, gender bias in research, postpartum care, accessibility to services, and so on, with a basket of policy options and recommendations.

The current COVID-19 pandemic is no exception, as women are disproportionately affected by the global crisis. Therefore, building fair, sustainable, and healthy societies requires understanding and attention to the impacts of both sex and gender on health outcomes. Although the lockdowns and stay-at-home orders are critical in limiting and preventing COVID-19 spread, they devastate vulnerable groups such as women and girls for gender-based violence (GBV). Besides, preventive confinement practices exacerbate many causes of or contributors to violence against women and girls (1). Additionally, COVID-19 has revealed that women are underrepresented in ongoing COVID-19 research publications, in the governance of epidemic management, and as authors of COVID research (2). In the same context, it was also highlighted that women are generally underrepresented as research participants in COVID research, and pregnant women were frequently excluded from research (3).

Despite the World Health Organization's (WHO) Executive Board recognizing the need of including women in decision-making for pandemic planning and response, women's representation is inadequate in COVID-19 policy domains at both national and global platforms. COVID-19 policy domains (4). The COVID-19 pandemic has disrupted

especially the sexual and reproductive health services globally, resulting in many unwanted pregnancies, stillbirths, and maternal and neonatal deaths with negative impacts on mental health outcomes for women. Chattu et al. have highlighted that digital health equity must be included in health policies, particularly in remote areas to address equity, access, and affordability (5). Therefore, as argued by Singh et al. achieving equity and equality remains a bigger challenge (6), highlighting the pursuit of the WHO's principle, "No one is safe until everyone is safe" (7). Given this context, this Research Topic contains a total of 11 articles has 4 original articles, 2 brief research reports, 3 reviews, one opinion piece and one perspective, which are summarized below.

A study by Ahinkorah et al. highlighted the alarming statistics of gender inequalities in Sub-Saharan Africa and discussed various strategies to mitigate them and improve services for women and girls. To overcome household, educational, work/employment, and housing inequities, the authors emphasized that these interconnected disparities require broader policy actions to improve the current burden faced by many women. The review concludes to avoid/discourage attending mass gatherings and ensure face-masking with non-medical cloth-like masks, which are low-cost preventive measures to prevent the virus's spread among women.

Another study from northeast India by Padhye et al. addressed the challenges of accessing maternal health care amid the COVID-19 pandemic. In this explorative study through purposive sampling, the data was collected through telephonic interviews among pregnant women, health care providers, and the members of the village health sanitation and nutrition committees. The study found that women were spending out-of-pocket for some essential services despite accessing public health facilities. They further concluded that the major challenges, such as lack of transport facilities and medicines, resulted in a high proportion of Caesarian section deliveries and stillbirths. This study emphasized health systems' preparedness and strengthening of community health centers to ensure affordable and quality, uninterrupted maternal health care services.

Similarly, another Indian study by Josyula et al. highlighted their work through the global consortium "Accountability for Informal Urban Equity" (ARISE). This study explored participants' lived experiences of health-seeking behaviour, healthcare recourse, and the well-being aspects among the women waste pickers who belong to a marginalized community in urban India. The study highlighted the intersectionality of various factors such as gender, socioeconomic factors, cultural contexts, and other potential occupational hazards these women may face and provided specific recommendations to ensure healthcare access, safety and security.

Khan and David have addressed the growing rates of intimate partner violence in Trinidad and Tobago, a twin island in the Caribbean region. The paper highlighted that the COVID-19 pandemic created a milieu which is conducive to domestic violence surge as there is already an existing high prevalence rate aggravated due to confinement and possibly other lifestyle factors such as increased consumption of alcoholic products and other drugs by the males at home. Besides, they also cited that women

suffering from domestic violence or abuse may be less inclined to seek care at a hospital because of fear of COVID-19 infection. Eventually, a social distancing strategy, albeit essential to prevent virus spread, may exacerbate the violence and keep it hidden. The authors emphasized that health care providers must tactfully screen for domestic violence during virtual encounters/telemedicine platforms by using safe words and trying to dissuade perpetrators by creating a supportive environment for women.

Salter-Volz et al. from the United States, have reported on the sex and gender bias in research related to COVID-19 clinical case reports during the pandemic. Their bibliometric analysis concluded that the majority (61%) had male first authors, and the case reports with male last authors were more likely to describe male patients. However, the reports with female last authors were more likely to include both sexes, highlighting potential biases in disseminating clinical information *via* case reports. This study also explores the inextricable influences of both sex and gender biases within the domain of biomedicine.

Another interesting German study by Liu et al. on the molecular and physiological aspects of the SARS-CoV-2 infection among pregnant women highlighted the possibility of in-utero transmission of the virus based on the evidence from placental infection and expression of viral entry receptors at the maternal-fetal interface. The researchers added that SARS-CoV-2 could further damage the placenta, cause maternal systemic inflammation, and hinder access to healthcare services during the pandemic.

This Research Topic also included the role of sex and gender in vaccine research and, in this context, the review by Vassallo et al. has highlighted the failure to recognize important sex and gender implications on the efficacy, safety, and implementation are detrimental for the global vaccine rollout in controlling the COVID-19 pandemic. The review concluded that there were missed opportunities to apply a sex and/or gender-sensitive lens in developing COVID-19 vaccines. Further, they emphasized improving data reliability, fostering public trust in immunization programs, reducing vaccination hesitancy, and boosting coverage. They further recommended that public health data collected through routine disease surveillance be sex/gender-disaggregated and be made available to the general public.

An Australian study on mental health and well-being of postpartum women by Christie et al. has explored mothers' mental health, well-being, and health behaviors up to 12 months postpartum under COVID-19 level III and level IV restrictions in Australia. The research suggested that most postpartum mothers have normal mental health symptoms, and most of them are happy, at least for a good amount of the time, despite being worn out. Further, the study highlighted the critical role of health values in maintaining physical activity during leisure and promoting mental health through participation in virtual group exercises, community programs, and socializing with friends.

Another Australian mixed methods study by Henry et al. investigated the local maternity service providers about the impact of COVID-19 on domestic and family violence (DFV), mental health screening, and broader health service provision. Half the respondents felt the pandemic negatively affected the

delivery of services, timeliness and quality of services to pregnant women, DFV and screening and management of mental health issues. The study also concluded that women who were at high risk due to their physical health, mental health, DFV, or other social issues were considered unsuitable for telehealth services.

In the same context, [Demeke and Shibeshi](#) have also assessed and discussed the intimate partner violence against women of reproductive age and associated factors in Northern Ethiopia. The results showed an alarming rate of psychological (35%), physical (15%), and sexual violence (15%) among the respondents. The study concluded the high rates of IPV were due to multiple factors such as level of education, smoking habits, and alcoholism among male counterparts and highlighted the role of empowering women and simultaneously educating and sensitizing the male partners through tailor-made programs.

Another qualitative research study from Germany by [Batram-Zantvoort et al.](#) explored the first wave of the COVID-19 pandemic on maternal self-conception and mental well-being. The study investigated how women referred to and made sense of the dominant gender norms in their arrangements of daily life during the pandemic and how these beliefs have impacted their maternal self-conception. The interviews were analyzed and were seen through the lens of “intensive mothering” ideology and “ideal workers” norms. They found that mothers’ notions of guilt and their decrease in health link to dominant discourses on motherhood intersect with “ideal worker” norms which further amplify the burden of gendered health inequalities.

In conclusion, the pandemic has also shown an increase in gender-based violence and domestic abuse. There is a lack of attention to sex and gender in COVID prevention and treatment research. The impact on women, particularly the immediate risks that are associated with their roles on the front line of healthcare, social care and secondary impacts, such as intimate partner violence risks during the extended periods of social isolation/distancing. The pandemic has disrupted SRH services globally and impacted women’s mental health and well-being. Therefore, this Research Topic addressing the inequalities of COVID-19 healthcare and research affecting women is a valuable

addition to the existing knowledge base with some exceptional original research studies (including qualitative, quantitative, and mixed-methods), review articles, and evidence-based policy recommendations from different geographical regions.

Author contributions

VC wrote the first draft. LM, BK, KT, HA, and SY read the initial draft and provided feedback. All authors discussed the results and contributed their inputs to the final manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgments

We thank all the authors, reviewers, and editorial members for their contributions and excellent services in bringing out this special issue.

Publisher’s note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- United Nations. Addressing the impact of the COVID-19 pandemic on violence against women and girls (2020). Available at: <https://www.un.org/en/addressing-impact-covid-19-pandemic-violence-against-women-and-girls> (Accessed November 16, 2022).
- Pinho-Gomes AC, Peters S, Thompson K, Hockham C, Ripullone K, Woodward M, et al. Where are the women? Gender inequalities in COVID-19 research authorship. *BMJ Global Health*. (2020) 5:e002922. doi: 10.1136/bmjgh-2020-002922
- Taylor MM, Kobeissi L, Kim C, Amin A, Thorson AE, Bellare NB, et al. Inclusion of pregnant women in COVID-19 treatment trials: a review and global call to action. *Lancet Glob Health*. (2021) 9(3):e366–71. doi: 10.1016/S2214-109X(20)30484-8
- WHO. Executive board EB146/Conf/17: strengthening preparedness for health emergencies; implementation of international health regulations, IHR (2005). Geneva: World Health Organization (2020).
- Chattu VK, Lopes CA, Javed S, Yaya S. Fulfilling the promise of digital health interventions (DHI) to promote women’s sexual, reproductive and mental health in the aftermath of COVID-19. *Reprod Health*. (2021) 18:112. doi: 10.1186/s12978-021-01168-x
- Singh B, Chattu VK. Prioritizing ‘equity’ in COVID-19 vaccine distribution through global health diplomacy. *Health Promot Perspect*. (2021) 11(3):281. doi: 10.34172/hpp.2021.36
- World Health Organization. A global pandemic requires a world effort to end it – none of us will be safe until everyone is safe (2020). Available at: <https://www.who.int/news-room/commentaries/detail/a-global-pandemic-requires-a-world-effort-to-end-it-none-of-us-will-be-safe-until-everyone-is-safe> (Accessed June 16, 2021).



COVID-19 Pandemic Worsening Gender Inequalities for Women and Girls in Sub-Saharan Africa

Bright Opoku Ahinkorah¹, John Elvis Hagan Jr.^{2,3*}, Edward Kwabena Ameyaw^{1,4}, Abdul-Aziz Seidu^{5,6} and Thomas Schack³

¹ Faculty of Health, School of Public Health, University of Technology Sydney, Sydney, NSW, Australia, ² Department of Health, Physical Education, and Recreation, University of Cape Coast, Cape Coast, Ghana, ³ Neurocognition and Action-Biomechanics-Research Group, Faculty of Psychology and Sport Sciences, Bielefeld University, Bielefeld, Germany, ⁴ L & E Research Consult, Wa, Ghana, ⁵ Department of Population and Health, University of Cape Coast, Cape Coast, Ghana, ⁶ College of Public Health, Medical and Veterinary Services, James Cook University, Townsville, QLD, Australia

OPEN ACCESS

Edited by:

Lakshmi Surya Prabha Manem,
Dr. NTR University of Health
Sciences, India

Reviewed by:

Indranil Mukhopadhyay,
O.P. Jindal Global University, India
Paula Munoz Venturelli,
Universidad del Desarrollo, Chile

*Correspondence:

John Elvis Hagan Jr.
elvis.hagan@ucc.edu.gh

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 28 March 2021

Accepted: 30 June 2021

Published: 29 July 2021

Citation:

Ahinkorah BO, Hagan JE Jr, Ameyaw EK, Seidu A-A and Schack T (2021) COVID-19 Pandemic Worsening Gender Inequalities for Women and Girls in Sub-Saharan Africa.
Front. Glob. Womens Health 2:686984.
doi: 10.3389/fgwh.2021.686984

Pandemics such as COVID-19 have often resulted in international, national and sub-regional crises, with considerable inequities across many societies. With the already existing structural and socio-economic inequalities in sub-Saharan Africa, the stay-at-home orders, lockdowns, and shutdowns across the sub-regional states could worsen and have a tremendous impact on vulnerable groups. Numerous studies across a variety of contexts have well-documented gender, and cultures on varied health outcomes. However, these have not been contextualized in sub-Saharan Africa in the light of the COVID-19 pandemic. This mini review discusses the ways by which COVID-19 has impacted the lives of girls and women across sub-Saharan Africa and the strategies that can help mitigate these challenges. The mini review specifically shares light on a wide array of dimensions where the inequities exist. These include the disproportionate areas affected by COVID-19; household inequities; educational inequalities; work/employment inequalities; disparities related to healthcare, sexual and reproductive health as well as housing inequities. Conclusively, the review accentuates the need for sub-Saharan African countries to adopt low-cost preventive measures such as discouraging mass gatherings (e.g., local community gatherings), and face masking with non-medical cloth like masks for the local populace as these are crucial in managing the spread of the virus among disproportionate women population. For localities with limited access to handwashing facilities, alternative strategies like alcohol-based hand rub solutions could be deployed. The complex interrelated disparities require a broad set of policy actions to lessen the current burden faced by many women in sub-Saharan Africa.

Keywords: COVID-19, girls, inequity, sub-Saharan Africa, women

INTRODUCTION

Pandemics have often resulted in international, national and sub-regional crises, with considerable inequities across many societies. The novel COVID-19 disease, till date, has placed enormous burden on individuals due to stringent mitigating interventions (e.g., lockdowns, social/physical distancing measures) and causing further inequities in many vulnerable populations (e.g., low socioeconomic backgrounds) (1).

Literature on racial, gender, and social class disparities suggest that individuals from vulnerable or marginalized backgrounds often experience marginalization and discrimination across many social systems (e.g., education, health, labor) (1, 2). According to Kantamneni, challenges associated with COVID-19 could reinforce and exacerbate disparities (e.g., health, unemployment) because of limited resources (3).

With the already existing structural and socio-economic inequalities in sub-Saharan Africa, the stay-at-home orders, lockdowns, and shutdowns across the sub-regional states could worsen and have a tremendous impact on vulnerable groups such as women (3). Considering that numerous studies [e.g., (4–7)] across a variety of contexts have well-documented gender, and cultures on varied health outcomes, this mini review discusses the ways through which COVID-19 have disproportionately impacted the lives of vulnerable girls and women across sub-Saharan Africa and the strategies that can help mitigate these challenges.

Disproportionate Areas Affected by COVID-19

Social determinants of health such as gender or sex uniquely presents inequalities or disparities along which COVID-19 may widen existing challenges in sub-Saharan Africa (8, 9). For instance, various separate reports from the pandemic suggest that young girls and women commonly report more physical and mental unhealthy period of the year despite using more preventive health care services compared to men (10). Available statistics reveal that women of diverse ethnic backgrounds (e.g., Canada, US) experience negative health conditions including asthma (10), diabetes (11), and myocardial infarctions (12). According to Kantamneni (1), these health inequalities are worsened in young girls and/or women from low socioeconomic background (SES), those with no or low education, and those in rural geographic locations. Therefore, COVID-19 pandemic could further widen existing inequalities (e.g., healthcare, income, education) within sub-Saharan African societies with serious repercussions.

Household Inequities

The COVID-19 pandemic has already shown unequal gender roles and household inequities across many societies (13). According to Haynes, the burden of household care has been an enormous barrier against women's socioeconomic development universally. Although parents have been affected by school closures, job losses, and primarily working from home to observe social/physical distancing measures, women, especially mothers, have been saddled with multiple responsibilities for work (i.e., formal/informal), domestic work, and childcare compared to men and/or fathers (14). Available records show that while fathers have also seen increased childcare responsibilities during the pandemic, women's childcare related tasks during lockdown have increased to more than 3 extra h per day than the reported 2 h for men averagely (15). For example, the American Time Use Survey investigated household labor divisions across gender and revealed that a higher percentage of women (84%) spent more hours (2.6 h) per day on household activities when compared to

men (69%) who spent averagely (2.0 h) on domestic activities (16). The survey also showed that women spent nearly two times the period for offering child care at home than men (16). Given that patriarchal and socio-cultural norms and structural inequalities favor men, including household responsibilities in many parts of sub-Saharan Africa, the COVID-19 pandemic may place additional burden of household work and childcare on young girls and women. Although sub-regional specific data is not readily available, other customarily roles may create additional burden of elder care and care of the sick, relatives and the vulnerable during the pandemic may exacerbate the already household burden for young girls and women compared to men (17). With sub-Saharan Africa noted as one of the regions with the highest prevalence of intimate partner violence globally (18–20), these household inequalities (i.e., domestic family responsibilities) during the pandemic could create multiple role conflicts that could trigger domestic violence (e.g., physical, sexual and emotional abuse) against women, and create potential lasting mental health consequences in the region (18, 19, 21).

Educational Inequalities

The academic environment for learning has been acknowledged to have long-lasting implications on the educational outcomes of children (22). However, the current pandemic has caused substantial interruptions to the educational settings worldwide. Since the outbreak of the COVID-19, day care centers, schools, colleges, and universities have had to be closed by various governments as a preventive strategy to control the spread of COVID-19. These school closures have affected nearly 90% of students across all levels, with the highest proportion, over 800 million being girls and young women (23). Significantly, majority of these vulnerable girls live in least developed nations where access to education is already problematic so COVID-19 could worsen the existing inequities (24). With the already existing socio-cultural and structural barriers to girls/women's education and other limited empowerment opportunities in sub-Saharan Africa, COVID-19 may cause disproportionate drop out of school by teenage girls and young women for varied socio-economic reasons (e.g., unwanted pregnancies, manual labor). Experiences from the past Ebola outbreak show that school closures led to increases in teenage pregnancies after resumption (25). These young girls were subsequently barred from returning to school, according to Elston and colleagues. It is more likely that the current pandemic could cause similar challenges with female drop-outs in sub-Saharan Africa, where adolescent pregnancy prevalence rate is reportedly higher than other regions (26, 27). From a socio-cultural perspective, adolescent or teenage girls and women may have limited time studying than male counterparts because of increased domestic responsibilities during the pandemic (23). Socio-cultural norms in many parts of sub-Saharan Africa devalue girl child education and rather favor a boy child educational training (28, 29). Therefore, it is more likely that more teenage girls and young women could be encouraged by parents and family to choose alternate arrangements (e.g., job placement, early marriage) at the expense of their education upon school resumption. Therefore, the current COVID-19 pandemic could cause more females than

males serving at home, with limited studying opportunities, and dropping out of school if necessary interventions are not implemented by various sub-regional governments and educational institutions.

Work/Employment Inequalities

According to the International Labor Organization, approximately 2.7 billion people, 81% of the world's working population have been seriously affected by COVID-19 related lockdown interventions (e.g., social/physical distancing protocols). Of this proportion, nearly 61% of these workers are reportedly from the informal sector, of whom 90% are in low-income and middle-income countries, including sub-Saharan Africa (30). With unemployment and low income rates already high in the sub-Saharan region (31), the intervention protocols associated with the pandemic could further widen and cause disproportionate number of employee challenges. Available evidence shows that majority of women in sub-Saharan Africa live on the fringes of the peripheral sectors of the African economy, with common economic engagements such as small-scale farming, petty trading, small enterprises, and domestic tasks with minimal financial rewards (32–34). Besides, among several groups of workers that have been deemed “essential” and required to be physically present at work are health care professionals (35). These health care workers are considered as frontline staff against COVID-19 who are not only at higher risk of infection but are also under significant psychological stress due to enormous work schedules (36, 37). COVID-19 institutional actions have inadvertently deepen the vulnerability of workers, especially among women who form the largest proportion of the nursing staff in many health facilities in the region (38–40). As health care professionals, women multiple role conflict between work schedules and family life (i.e., more household and caretaking responsibilities) during the pandemic may expose them to heightened risk and enormous pressure compared to men (1). Again, due to workplace expectations, and sociocultural norms associated with parenting and household responsibilities in sub-Saharan Africa, women are likely to experience additional strain during COVID-19 to manage and/or balance these multiple roles. Therefore, women are likely to prioritize their increased domestic responsibilities over their professional roles and minimize professional responsibilities because of the demanding nature of undertaking both schedules (1, 16).

This perspective of gender exclusion in the region demonstrates low socio-economic welfare experience of women because of the somehow limited opportunities in the formal labor market and further mirrors the inequality burden (32). These existing inequities have been exacerbated by the pandemic which might lead to disproportionate impacts on women's well-being and their economic growth (35). Some of these marginalized women who are extremely burdened by the harsh living conditions at home (e.g., living crowded rooms, poor social amenities- housing, poor drinking water, limited electricity supply, no or poor internet access) will suffer more from the fallout (e.g., shuttering of small businesses, loss of income) of the current pandemic if some drastic interventions (e.g.,

setting micro-finance schemes) to alleviate their burdens are not implemented. According to some scholars [e.g., (32, 33, 41)], the increasing growth of inequities decrease the response of poverty reduction to socio-economic growth, with this gender inclusion likely to affect the achievement of the SDGs related to extreme poverty reduction across the continent. Therefore, work institutions should implement measures (e.g., provide incentives or rewards, psychological support) that keenly promote the well-being of women (35). Future empirical research is required to explore what structural barriers hinder young girls and women's access to employment during the COVID-19 pandemic. These studies could consider the short-term and long-term socioeconomic, vocational, and psychological consequences for this vulnerable group regarding access to basic needs, survival, and the disparity rates caused by COVID-19 (1).

Disparities Related to Healthcare, Sexual and Reproductive Health

Previous history suggests that pandemics create limited access to the healthcare, particularly with preventative and reproductive healthcare (42, 43). Experiences of previous pandemics (e.g., SARS, Ebola) and the current COVID-19 have shown increases in existing gender health inequalities in reproductive health care across many societies, with many compromised healthcare systems (42). For example, there have been reported increases in cesarean rates among SARS-CoV-2 positive patients, which also heighten the risk of maternal and neonatal complications (44, 45). With already disproportionate individual (e.g., no or low education, low income) and contextual barriers (e.g., transportation, geographical location, system organizational challenges, limited availability of healthcare services, health information, health infrastructure) in sub-Saharan Africa obstructing women's access to healthcare in the region (46, 47), the current pandemic will further worsen the existing poor obstetric and neonatal health conditions and increase rates of maternal and child morbidity as well as mortality in the region (48). It has been well-documented that gaps in access to and utilization of healthcare services, healthcare provider and institutional biases contribute to these negative outcomes during pandemics [(15, 49, 50)]. Further, the pandemic could cause inadequate suitable antenatal and postnatal care, which can seriously impact on the health of women's families, thus increasing children's probability of developing comorbidities and possible mortalities in disadvantaged settings (51, 52).

Healthcare obstacles peculiar to women are not always physical barriers in sub-Saharan Africa, but also cultural barriers (e.g., power distances, masculinity-femininity orientation) connected with gender usually discourage women from seeking access to healthcare. These cultural barriers could worsen access to healthcare during the pandemic, especially in populations where traditional practices are deeply rooted in everyday life of the people. Breaking these socio-cultural barriers require novel guidance through strategies like persuasive communication and adequate information to minimize or eliminate gendered cultural norms associated with health seeking behaviors and mainstream health services to manage the spread of the virus.

Housing Inequities

Majority of women in sub-Saharan Africa live in deprived areas (53, 54). Whereas, substandard and inadequate housing conditions affect the general population in Africa, women are more disadvantaged than men (55). These unpleasant housing conditions have enormous effects for women (56). With these substandard and inadequate housing conditions, the burden of COVID-19 could be noticeable in these unstable housed populations often occupied by women and their children. Some scholars have reiterated that living in poor housing conditions (e.g., shelters, crowded areas, access to clean water) make social distancing measures difficult and restricts one's capacity to conform with hand washing and other hygiene protocols to prevent the virus infection and local transmission (57, 58). Therefore, women living in these areas have increased risk for severe complications from virus infection. With the current happenings in the sub-region, gender responsive planning and interventions that are safe and inclusive for women need to be provided by responsible governments (59, 60).

This mini review has some limitations. First, COVID-19 inequities may vary from country to country, hence the current circumstances surrounding the pandemic makes it difficult to gather within and between country specific trends and enormity of the challenge based on empirical data. Second, because of sparse empirical information of the theme, this write-up is restricted in scope and may lack research accuracy. Additionally, data regarding gendered related variations during Covid-19 are limited. Despite these shortcomings, this conceptualized article has research, public, and policy relevance. Future empirical work could investigate within and between country trends and magnitude of COVID-19 related inequities affecting women in sub-Saharan Africa.

CONCLUSIONS

With limited resources across many sub-Saharan member states, adopting and complying with context-specific low-cost preventive measures such as discouraging mass gatherings (e.g., local community gatherings), and face masking with non-medical cloth as masks for the local populace would be crucial in managing the spread of the virus among disproportionate women population. Other complimentary strategies are effective health education and promotion campaigns for personal hygiene, and hand washing, including cultural barriers to healthcare. For localities with limited access to handwashing facilities, alternative strategies like alcohol-based hand rub solutions could be

deployed. Mandatory use of local-made or other protective nose masks by people in public places should be encouraged. The idea is that these local productions could help reduce antimicrobial resistance and other upper respiratory tract infections in low- and middle-income countries (LMICs) often worsened by poor hygiene, and overcrowded living conditions, and lack of adequate infrastructure [see (40, 61) for details]. Women leadership groups should be seen wearing these masks in public places to serve as an example for the local populace. Outreach programmes could incorporate local community leaders to emphasize women citizenry adherence to the preventive measures against the spread of the virus. Protecting local jobs and other small enterprises for women should also be a priority. Leveraging on the current pandemic to develop infrastructural deficit and other opportunities to accommodate the existing disparities of the identified sectors of various economies by African governments will protect livelihoods.

Summarily, it is clear that the COVID-19 pandemic could exacerbate existing inequities (i.e., household, educational, employment, healthcare, housing) and requires a well-planned policy response strategies for these inequalities from worsening more. COVID-19 happenings should make public healthcare and social care drive national goals in the fight against the pandemic. Understanding the role of how COVID-19 can exacerbate these identified areas and inherent challenging experiences related to inequities is crucial if such inequalities are to be addressed appreciably. These barriers provide increased susceptibility for women in the sub-region. Overall, the somehow complex interrelated disparities also require a broad set of multi-sectoral policy actions by individual governments and other stakeholders to lessen the current burden faced by many women in sub-Saharan Africa. Empirical research to investigate gender-racial-ethnic disparities on COVID-19 outcomes in the region is needed.

AUTHOR CONTRIBUTIONS

JH and BA conceived the idea. JH, BA, EA, A-AS, and TS prepared the initial draft of the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

The authors sincerely thank Bielefeld University, Germany for providing financial support through the Open Access Publication Fund for the article processing charge.

REFERENCES

- Kantamneni N. The impact of the COVID-19 pandemic on marginalized populations in the United States: a research agenda. *J Vocat Behav.* (2020) 119:103439. doi: 10.1016/j.jvb.2020.103439
- Flores LY, Martinez LD, McGillen GG, Milord J. Something old and something new: future directions in vocational research with people of color in the United States. *J Career Assess.* (2019) 27:187–208. doi: 10.1177/1069072718822461
- Hagan JE Jr, Ahinkorah BO, Seidu AA, Ameyaw EK, Schack T. Africa's COVID-19 situation in focus and recent happenings: a mini review. *Front Public Health.* (2020) 8:573636. doi: 10.3389/fpubh.2020.573636
- Savage A, McConnell D, Emerson E, Llewellyn G. Disability-based inequity in youth subjective well-being: current findings and future directions. *Disabil Soc.* (2014) 29:877–92. doi: 10.1080/09687599.2014.880331
- Schneider SM. Income inequality and subjective wellbeing: trends, challenges, and research directions. *J Happiness Stud.* (2016) 17:1719–39. doi: 10.1007/s10902-015-9655-3

6. Slopen N, Lewis TT, Williams DR. Discrimination and sleep: a systematic review. *Sleep Med.* (2016) 18:88–95. doi: 10.1016/j.sleep.2015.01.012
7. Azzopardi PS, Hearps SJC, Francis KL, Kennedy EC, Mokdad AH, Kassebaum NJ, et al. Progress in adolescent health and wellbeing: tracking 12 headline indicators for 195 countries and territories, 1990–2016. *Lancet.* (2019) 393:1101–18. doi: 10.1016/S01406736(18)32427-9
8. Springer KW, Mager Stellman J, Jordan-Young RM. Beyond a catalogue of differences: a theoretical frame and good practice guidelines for researching sex/ gender in human health. *Soc Sci Med.* (2012) 74:1817–24. doi: 10.1016/j.socscimed.2011.05.033
9. Rich-Edwards JW, Kaiser UB, Chen GL, Manson JE, Goldstein JM. Sex and gender differences research design for basic, clinical, and population studies: essentials for investigators. *Endocr Rev.* (2018) 39:424–39. doi: 10.1210/er.2017-00246
10. Centers for Disease Control Prevention (CDC). CDC health disparities and inequalities report — United States, 2013. *Morb Mortal Wkly Rep.* (2013) 62 (Suppl. 3):85–154.
11. Roche MM, Wang PP. Sex differences in all-cause and cardiovascular mortality, hospitalization for individuals with and without diabetes, and patients with diabetes diagnosed early and late. *Diabetes Care.* (2013) 36:2582–90. doi: 10.2337/dc12-1272
12. Mehta L, Beckie T, DeVon H, Grines C, Krumholz H, Johnson M, et al. Acute myocardial infarction in women. *Circulation.* (2016) 133:916–47. doi: 10.1161/CIRC.0000000000000351
13. Haynes K. Structural inequalities exposed by COVID-19 in the UK: the need for an accounting for care. *J Account Org Change.* (2020) 4:637–42. doi: 10.1108/JAOC-08-2020-0099
14. Andrew A, Cattan S, Costa Dias M, Farquarson C, Kraftman L, Krutikova S, et al. *How Are Mothers and Fathers Balancing Work and Family under Lockdown?* London: Institute for Fiscal Studies (2020).
15. Office for National Statistics. Parenting in Lockdown: Coronavirus and the Effects on Work-Life Balance. London: ONS (2020). American College of Obstetricians and Gynecologists [ACOG]. Committee Opinion No. 649: racial and ethnic disparities in obstetrics and gynecology. *Obstet Gynecol.* (2015) 126:130–4. doi: 10.1097/AOG.0000000000001213
16. Bureau of Labor Statistics. *American Time Use Survey Summary.* (2019). Available online at: <https://www.bls.gov/news.release/atus.nr0.htm> (accessed February 16, 2021).
17. Skopeliti C. *Older Female Workers' Twice as Likely as Men to Be Informal Carers.* London: The Guardian (2019).
18. Ahinkorah BO. Polygyny and intimate partner violence in sub-Saharan Africa: Evidence from 16 cross-sectional demographic and health surveys. *SSM Popul Health.* (2021) 13:100729. doi: 10.1016/j.ssmph.2021.100729
19. Devries KM, Mak JYT, Garcia-Moreno C, Petzold M, Child JC, Falder G, et al. The global prevalence of intimate partner violence against women. *Science.* (2013) 340:1527–8. doi: 10.1126/science.1240937
20. Yaya S, Hudani A, Buh A, Bishwajit G. Prevalence and predictors of intimate partner violence among married women in Egypt. *J Int Viol.* (2019) 1–19. doi: 10.1177/0886260519888196
21. Grierson J. *Domestic Abuse Surge in Coronavirus Lockdown Could Have Lasting Impact.* London: MPsSay, The Guardian (2020).
22. Blundell R, Costa Dias M, Joyce R, Xu X. COVID-19 and inequalities. *Fiscal Stud.* (2020) 41:291–319. doi: 10.1111/1475-5890.12232
23. Burzynska K, Contreras G. Gendered effects of school closures during the COVID-19 pandemic. *Lancet.* (2020) 395:10–16. doi: 10.1016/S0140-6736(20)31377-5
24. Hall KS, Samari G, Garbers S, Casey SE, Diallo DD, Orcutt M, et al. Centring sexual and reproductive health and justice in the global COVID-19 response. *Lancet.* (2020) 395:1175–7. doi: 10.1016/S0140-6736(20)30801-1
25. Elston JWT, Cartwright C, Ndumbi P, Wright J. The health impact of the 2015 Ebola outbreak. *Public Health.* (2017) 143:60–70. doi: 10.1016/j.puhe.2016.10.020
26. UNFPA. *Motherhood in Childhood: Facing the Challenge of Adolescent Pregnancy.* New York, NY: UNFPA (2013).
27. UNICEF. *Child Marriage, Adolescent Pregnancy and Family Formation in West and Central Africa: Patterns, Trends and Drivers of Change.* New York, NY: UNICEF (2015).
28. Blakemore K, Cooksey B. *A Sociology of Education for Africa*, Vol. 8. Routledge (2017).
29. Kachiwanda SO. Gender disparity in the acquisition of literacy in sub-Saharan Africa: the case of Malawi. *J Human.* (2010) 22:24–43.
30. Lancet T. The plight of essential workers during the COVID-19 pandemic. *Lancet.* (2020) 395:1587. doi: 10.1016/S0140-6736(20)31200-9
31. Adamu P, Kaliappan SR, Bani Y, Nor MN. *Impact of Globalization on Unemployment in Sub-Saharan African (SSA). Countries.* Serdang: Governance and Sustainability of Global Business Economics. (2017). p. 302–10.
32. Asongu S, Odhiambo N. Inequality and the economic participation of women in sub-Saharan Africa: An empirical investigation. *Afr J Eco Manag Stud.* (2020) 11, pp. 193–206. doi: 10.1108/AJEMS-01-2019-0016
33. Asongu SA, Kodila-Tedika O. Institutions and poverty: a critical comment based on evolving currents and debates. *Soc Ind Res.* (2018) 139:99–117. doi: 10.1007/s11205-017-1709-y
34. Asongu SA, le Roux S. Understanding Sub-Saharan Africa's extreme poverty tragedy. *Int J Public Administ.* (2019) 42:457–67. doi: 10.1080/01900692.2018.1466900
35. Warren MA, Bordoloi S. When COVID-19 exacerbates inequities: The path forward for generating wellbeing. *Int J Wellbeing.* (2020) 10:1–6. doi: 10.5502/ijw.v10i3.1357
36. Que J, Le Shi JD, Liu J, Zhang L, Wu S, Gong Y, et al. Psychological impact of the COVID-19 pandemic on healthcare workers: a cross-sectional study in China. *Gen Psychiatr.* (2020) 33:e100259. doi: 10.1136/gpsych-2020-100259
37. Ehrlich H, McKenney M, Elkbuli A. Protecting our healthcare workers during the COVID-19 pandemic. *Am J Emerg Med.* (2020) 38:1527–8. doi: 10.1016/j.ajem.2020.04.024
38. Bureau of Labor Statistics. *Labor Force Statistics From the Current Population Survey.* (2020). Available online at: <https://www.bls.gov/cps/cpsaat18.htm> (accessed June 15, 2021).
39. Turshen M. *Women and Health in Africa.* Africa World Press (1991).
40. World Health Organization (WHO). *Guide to Local Production: WHO Recommended Handrub Formulations.* Trenton, NJ (2010). Available online at: https://www.who.int/gpsc/5may/Guide_to_Local_Production.pdf (accessed June 15, 2021).
41. Fosu AK. Growth, inequality and poverty in Sub-Saharan Africa: recent progress in a global context. *Oxford Dev Stud.* (2015) 43:44–59. doi: 10.1080/13600818.2014.964195
42. Connor J, Madhavan S, Mokashi M, Amanuel H, Johnson NR, Pace LE, et al. Health risks and outcomes that disproportionately affect women during the Covid-19 pandemic: a review. *Soc Sci Med.* (2020) 266:113364. doi: 10.1016/j.socscimed.2020.113364
43. Germain S, Yong A. COVID-19 highlighting inequalities in access to healthcare in England: a case study of ethnic minority and migrant women. *Femin Legal Stud.* (2020) 28:301–10. doi: 10.1007/s10691-020-09437-z
44. Della Gatta AN, Rizzo R, Pilo G, Simonazzi G. Coronavirus disease 2019 during pregnancy: a systematic review of reported cases. *Am J Obstet Gynecol.* (2020) 223:36–41. doi: 10.1016/j.ajog.2020.04.013
45. Matar R, Alrahmani L, Monzer N, Debiane LG, Berbari E, Fares J, et al. Clinical presentation and outcomes of pregnant women with coronavirus disease 2019: A systematic review and meta-analysis. *Clinical Infectious Diseases: An Official Publication of the infectious Diseases Society of America,* (2021) 72, 521–33. doi: 10.1093/cid/ciaa828
46. Ahinkorah BO, Budu E, Seidu AA, Agbaglo E, Adu C, Ameyaw EK, et al. Barriers to healthcare access and healthcare seeking for childhood illnesses among childbearing women in sub-Saharan Africa: a multilevel modelling of demographic and health surveys. *PLoS ONE.* (2021) 16:e0244395. doi: 10.1371/journal.pone.0244395
47. Seidu AA. Mixed effects analysis of factors associated with barriers to accessing healthcare among women in sub-Saharan Africa: insights from demographic and health surveys. *PLoS ONE.* (2020) 15:e0241409. doi: 10.1371/journal.pone.0241409
48. Petersen EE, Davis NL, Goodman D, Cox S, Syverson C, Seed K, et al. Racial/ethnic disparities in pregnancy-related deaths —

- United States, 2007–2016. *Morb Mortal Wkly Rep.* (2019) 68:762–5. doi: 10.15585/mmwr.mm6835a3
49. Rosenthal L, Lobel M. Explaining racial disparities in adverse birth outcomes: unique sources of stress for Black American women. *Soc Sci Med.* (2011) 72:977–83. doi: 10.1016/j.socscimed.2011.01.013
 50. Moaddab A, Dildy GA, Brown HL, Bateni ZH, Belfort MA, Sangi-Haghpeykar H, et al. Health care disparity and pregnancy-related mortality in the United States, 2005–2014. *Obstet Gynecol.* (2018) 131:707–12. doi: 10.1097/AOG.0000000000002534
 51. Caul S. *Deaths Involving COVID-19 by Local Area and Socioeconomic Deprivation: Deaths Occurring Between 1 March and 30 June 2020.* Office for National Statistics. (2020). Available online at: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19bylocalareasanddeprivation/deathsoccurringbetween1marchand30june2020> (accessed July 30, 2020).
 52. Shortall C, McMorran J, Taylor K, Traianou A, Garcia de Frutos M, Jones L, et al. *Experiences of Pregnant Migrant Women Receiving ante/peri and Postnatal Care in the UK: A Longitudinal Follow-Up Study of Doctors of the World's London Drop-in Clinic Attendees.* London: Doctors of the World. (2015). p. 41–8.
 53. Chant S, McIlwaine C. *Gender Urban Development and the Politics of Space.* (2013). Available online at: <http://www.e-ir.info/2013/06/04/gender-urban-development-and-the-politics-of-space/> (accessed February 2, 2016).
 54. Chant S, McIlwaine C. *Cities, Slums and Gender in the Global South.* New York, NY: Routledge (2016).
 55. UN-Habitat. *11.1 Adequate Housing.* (2017). Available online at: https://unhabitat.org/sites/default/files/2020/06/indicator_11.1.1_training_module_adequate_housing_and_slum_upgrading.pdf (accessed March 17, 2018).
 56. OHCHR. *Women and the Right to Adequate Housing.* (2012). Available online at: https://www.ohchr.org/Documents/Publications/WomenHousing_HR.PUB.11.2.pdf (accessed May 5, 2018).
 57. Tsai J, Wilson M. COVID-19: a potential public health problem for homeless populations. *Lancet Public Health.* (2020) 5:e186–7. doi: 10.1016/S2468-2667(20)30053-0
 58. Wood L, Davies A, Khan Z. COVID-19 precautions—easier said than done when patients are homeless. *Med J Aust.* (2020) 212:384.e1. doi: 10.5694/mja2.50571
 59. UN-Habitat. *Habitat III: The New Urban Agenda.* (2017). Available online at: <http://habitat3.org/wp-content/uploads/NUA-English.pdf> (accessed February 26, 2018).
 60. UN-Habitat. *UN-Habitat Covid-19: Key Messages.* (2020). Available online at: https://unhabitat.org/sites/default/files/2020/03/covid19_key_messages_eng_1.pdf (accessed February 16, 2021).
 61. Godman B, Haque M, McKimm J, Abu Bakar M, Sneddon J, Wale J, et al. Ongoing strategies to improve the management of upper respiratory tract infections and reduce inappropriate antibiotic use particularly among lower and middle-income countries: findings and implications for the future. *Curr Med Res Opin.* (2020) 36:301–27. doi: 10.1080/03007995.2019.1700947

Conflict of Interest: EA is affiliated to L & E Research Consult.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Ahinkorah, Hagan, Ameyaw, Seidu and Schack. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Sex and Gender in COVID-19 Vaccine Research: Substantial Evidence Gaps Remain

Amy Vassallo^{1*}, Sultana Shajahan¹, Katie Harris¹, Laura Hallam¹, Carinna Hockham², Kate Womersley^{2,3}, Mark Woodward^{1,2} and Meru Sheel⁴

¹ The George Institute for Global Health, University of New South Wales, Sydney, NSW, Australia, ² The George Institute for Global Health, School of Public Health, Imperial College London, London, United Kingdom, ³ University of Edinburgh, NHS Lothian, Edinburgh, United Kingdom, ⁴ National Centre for Epidemiology and Population Health, Research School of Population Health, ANU College of Health and Medicine, Australian National University, Canberra, ACT, Australia

OPEN ACCESS

Edited by:

Sanni Yaya,
University of Ottawa, Canada

Reviewed by:

Renee Bolijn,
Academic Medical
Center, Netherlands
Julia Smith,
Simon Fraser University, Canada

*Correspondence:

Amy Vassallo
avassallo@georgeinstitute.org.au

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 19 August 2021

Accepted: 08 October 2021

Published: 01 November 2021

Citation:

Vassallo A, Shajahan S, Harris K,
Hallam L, Hockham C, Womersley K,
Woodward M and Sheel M (2021) Sex
and Gender in COVID-19 Vaccine
Research: Substantial Evidence Gaps
Remain.
Front. Glob. Womens Health
2:761511.
doi: 10.3389/fgwh.2021.761511

Since the start of the COVID-19 pandemic there has been a global call for sex/gender-disaggregated data to be made available, which has uncovered important findings about COVID-19 testing, incidence, severity, hospitalisations, and deaths. This mini review scopes the evidence base for efficacy, effectiveness, and safety of COVID-19 vaccines from both experimental and observational research, and asks whether (1) women and men were equally recruited and represented in vaccine research, (2) the outcomes of studies were presented or analysed by sex and/or gender, and (3) there is evidence of sex and/or gender differences in outcomes. Following a PubMed search, 41 articles were eligible for inclusion, including seven randomised controlled trials (RCTs), 11 cohort studies, eight cross-sectional surveys, eight routine surveillance studies, and seven case series. Overall, the RCTs contained equal representation of women and men; however, the observational studies contained a higher percentage of women. Of 10 studies with efficacy data, only three (30%) presented sex/gender-disaggregated results. Safety data was included in 35 studies and only 12 (34%) of these presented data by sex/gender. For those that did present disaggregated data, overall, the majority of participants reporting adverse events were women. There is a paucity of reporting and analysis of COVID-19 vaccine data by sex/gender. Research should be designed in a gender-sensitive way to present and, where possible analyse, data by sex/gender to ensure that there is a robust and specific evidence base of efficacy and safety data to assist in building public confidence and promote high vaccine coverage.

Keywords: COVID-19, vaccine, immunisation, evidence, gender equality, safety, gender

INTRODUCTION

The important influence of sex and gender on health has come to the forefront during the COVID-19 pandemic. Globally, shared sex-disaggregated data has led to important understanding about COVID-19 testing, incidence, severity, hospitalisations, and deaths (1–4). For example, while the proportion of COVID cases in women and men are roughly equal, men have around three times the odds of intensive care admission and a 40% higher odds of dying from COVID-19 than women (4). Known biological differences in adaptive and innate immune responses between sexes explain some of these observed differences (4). Socio-cultural gender constructs also influence

these outcomes through differing exposures to the disease (such as high occupational exposure in frontline healthcare workers, who are predominantly women), risk factors for severe disease (such as higher smoking rates in men), existence of comorbidities, and engagement with healthcare services for prevention, detection, and treatment (typically lower in men) (5–8).

Sex and gender are also important factors in understanding immunisation, including vaccine delivery, efficacy, and frequency and severity of adverse reactions (6). Sex and gender differences in immunisation outcomes have been observed across age groups for other vaccine preventable diseases, with women typically developing higher antibody responses, and reporting more local and systemic adverse reactions, compared with men (9). These differences have been observed in response to vaccines using different technologies, including the Calmette-Guerin vaccine, measles, mumps and rubella, yellow fever, and influenza vaccines (10). Several biological mechanisms have been proposed, including immunological, hormonal, genetic, and microbiota differences between females and males (10, 11).

Developing an effective vaccine against COVID-19 has been a global research priority, with several different vaccines administered on a large scale across the globe in 2020 and 2021 as part of national immunisation programs. This shift from experimental to observational (including routine surveillance) research provides valuable acceptability, effectiveness, and real world safety data (12). Effective, efficient, equitable, and publicly acceptable immunisation programs are needed for control of the COVID-19 pandemic globally. These programs need to be rooted in sex- and gender-sensitive evidence. The aim of this mini review is to scope the evidence base for efficacy, effectiveness and safety of COVID-19 vaccines, and whether (1) women and men were equally recruited and represented in each vaccine's research, (2) the outcomes of studies were presented or analysed by sex and/or gender, and (3) there is evidence of sex and/or gender differences in outcomes.

METHODS

Search Strategy and Selection Criteria

We searched PubMed for peer-reviewed literature on the efficacy, effectiveness, and/or safety of COVID-19 vaccines included in the COVID-19 Vaccines Global Access (COVAX) portfolio as of 6 May 2021: Pfizer/BioNTech (BNT162b2), Oxford/AstraZeneca (AZD1222), Novavax (NVX-CoV2373), Covovax (NVX-CoV2373), Johnson&Johnson (Ad26.COV2.S), Sanofi/GSK (VAT00002), and Moderna (mRNA-1273) (13, 14). Search terms relating to vaccine name, SARS-CoV-2, COVID-19, COVID-19 vaccines, phase 3 and 4 clinical trials, efficacy, effectiveness and mass vaccination, and relevant synonyms of these, were used (see **Appendix 1** for detailed search strategy). To identify articles containing safety data, additional search terms relating to adverse effects, safety monitoring, safety profile, and appropriate synonyms, were used. Searches were conducted using standard keywords as well as MeSH terms.

Eligible studies included phase 2/3 or 3 randomised controlled trials (RCTs) (experimental studies) and post-market observational studies including cohort studies, cross-sectional

studies, routine surveillance reports, and case series. Animal studies, phase 1 and/or 2 RCTs and case studies were excluded. All article types that presented original data were included, including research articles, editorials, responses, and letters to the editor. Immunogenicity data were excluded, however any relevant safety outcome data from these studies were included. In case of duplicate publications containing the same data, the report with the greatest amount of data or the one published first was included.

Data Extraction and Analysis

Title/abstract screening, full-text review and data extraction were conducted in duplicate by AV (all papers) and SS, KH, LH, and CH. Any disagreements between reviewers were resolved by discussion. Data were extracted for study title, author, date of publication, vaccine name(s), study design, population subgroup (e.g. healthcare workers, people with pre-existing conditions), percentage of women and men participants, vaccine efficacy and effectiveness (as defined by study authors), and the percentage of women and men who presented with adverse events (as defined by study authors). Results data for up to 12 adverse events per article were extracted. Care was taken not to report the occurrence of an adverse event as “zero” unless it was explicitly stated as such in the article (15). We were unable to distinguish between sex and gender based on the included studies, so hereafter refer to sex/gender (16, 17).

For all studies, we examined the reported sex/gender distribution of the research participants. The number of participants in a study was derived from the number of participants reported at the study end point (specifically those on whom the study was conducted); if this was not available the number at study baseline was used. If data were presented by vaccine dose in the same participant group, then the number of participants in the second dose was extracted. Participant number from national surveillance data was taken as the number of vaccine recipients within the reporting period of the study (i.e., CDC reports: 14–23 December 2020 for Pfizer, and 21 December 2020 to 10 January 2021 for Moderna).

For all studies, we examined whether efficacy or effectiveness (hereafter efficacy) and safety data were presented by sex/gender. Studies were marked “Yes” for sex/gender-disaggregated data if they presented disaggregated data for all their reported main outcomes, either in the main results or Supplementary Information. For studies other than case series that disaggregated their safety findings by sex/gender, we either extracted relative risks of adverse events in women and men, or calculated them where possible from presented sex/gender-disaggregated participant and outcome data, in order to summarise the evidence for significant sex/gender differences.

No meta-analyses were performed owing to the relatively small number of studies available, and the heterogeneity in efficacy and safety outcomes that were reported.

RESULTS

A total of 323 relevant studies were identified, and 41 were eligible for inclusion in this review (**Appendix Figure 1**). Included studies presented data on the following vaccines:

Oxford/AstraZeneca ($n = 11$), Pfizer/BioNTech ($n = 28$), Moderna ($n = 12$), Johnson&Johnson ($n = 2$), with some studies reporting data for more than one vaccine type.

Table 1 presents a summary of the content, participants, and presentation of outcomes in each of the included studies. Two adjusted for sex in their vaccine effectiveness model (30, 51), one study included sex-matched controls (43) and several articles were published as research letters and correspondence, rather than full research articles.

Across all seven RCTs, there was a 50/50 distribution in the sex/gender of participants (**Table 1**): one study included 44% women, four studies included 45–55% women, and two studies ~60% women. A total of 3/11 cohort studies included 45–55% women, with the other seven including more women (65–79%), and one not reporting. In the case of cross-sectional studies, one study included 46% women and the remainder included 64–88% women. For routine surveillance reports, 5/8 (63%) did not provide any sex/gender-disaggregated percentages of participants, and the remaining three included 61–62% women. Of the seven case studies, one did not provide disaggregated participant data, one included 100% women, and the rest included 40–89% women.

Of the 10 studies investigating vaccine efficacy, three (two RCTs and one cohort) included sex/gender-disaggregated results (**Table 1**). None of these studies reported a significant difference in their primary efficacy outcome between women and men.

A range of local and systemic adverse reactions following immunisation were reported, as indicated in **Table 1**. Of the 35 experimental and observational studies containing safety data, 12 (34%) disaggregated all their outcomes by sex/gender, none of which were RCTs and five of which were case series. An additional four studies reported sex/gender-disaggregated data for some but not all of their outcomes, and five additional studies presented summary statements by sex/gender, such as overall percentages of women and men experiencing at least one adverse event, or percentage requiring emergency department presentation. Sex/gender-specific risks of different adverse events were available from seven studies (**Figure 1**), which often indicated a higher risk reported for women. This included typical local and systemic reactions such as redness [RR = 1.97 (95% CI: 1.49–2.61)], swelling [RR = 2.24 (95% CI: 1.75–2.88)], and fever [RR = 1.41 (95% CI: 1.31–1.51)] as well as non-anaphylaxis allergic reaction [RR = 5.16 (95% CI: 2.49–10.70) for Pfizer/BioNTech vaccine and RR = 5.74 (95% CI: 2.05–16.06) for Moderna vaccine]. Risk of one reaction, arterial event, appeared lower in women [RR = 0.37 (95% CI: 0.24–0.57)].

No study justified lack of sex/gender-disaggregated data. However, two studies did acknowledge the dominance of women in their samples of healthcare workers (23, 30, 40, 43, 51).

DISCUSSION

Overall Summary of Findings

In this mini review of studies reporting efficacy and/or safety outcomes of vaccines included under COVAX, we found that women and men were equally represented in RCTs, whilst

women (and healthcare workers) comprised the majority of participants in observational studies. Despite global calls for the routine disaggregation of COVID-19 data by sex/gender (59–62), only two RCTs reported efficacy data by sex/gender, and none stratified safety data by sex/gender. Among the 34 included observational studies, 13 (38%) presented all sex/gender-disaggregated data ($n = 1$ (3%) for efficacy and $n = 12$ (35%) for safety). There was no evidence of sex/gender differences in vaccine efficacy, yet a higher risk of adverse events were reported among women compared to men. However, this evidence was limited in terms of both number and size of studies, which may not have been specifically designed to detect a difference between groups.

Our review findings demonstrate a disappointing, and potentially detrimental, lack of sex/gender-specific evidence across study types of the COVID-19 vaccine experimental research studies as well as observational reporting.

Representation by Sex/Gender in Research

We found equal representation of women and men in COVID-19 vaccine RCTs. This is despite another COVID-19 review finding that less than half of registered vaccine trials explicitly mentioned sex/gender in their recruitment strategy as part of their ClinicalTrials.gov registration (63). Therefore, our finding may be due to specific efforts by the research team to ensure equal recruitment, or because some of the usual barriers to women's participation in research, such as belief in the relevance of the health problem, concerns about risk, and trial logistical burden, may not have been as pervasive (7, 64). Women made up the majority of participants in non-RCT studies in our review. This is likely due, in part, to risk-based prioritisation of vaccine rollouts, which meant that healthcare and hospital workers, primarily women, were amongst the first to be vaccinated. For case series, it might reflect gender differences in reporting.

Reporting of Sex/Gender-Disaggregated Data

Our study identified a lack of sex/gender-disaggregated reporting or sub-group analyses in COVID-19 vaccine research. Despite roughly equal representation in RCTs, only a third of studies reported sex/gender-disaggregated efficacy data, and none reported safety data. This lack of focus on sex/gender aligns with findings of a recently published review of COVID-19 clinical trials of drug-based and biological/vaccine interventions, which found that only 18% of trials reported sex-disaggregated results or subgroup analyses (63). Another review published in early 2021 concluded that there was inadequate reporting of sex/gender in COVID-19 clinical studies, that main outcomes were rarely reported or analysed by sex/gender, and this absence was seldom justified (65). We recognise the challenges in ensuring adequate sample sizes in clinical research to conduct subgroup analyses, particularly when considering rarer adverse events. However, the presentation of sex/gender-disaggregated data, either in main results or Supplementary Appendices as recommended in the SAGER guidelines (66), will be an asset for facilitating future meta-analyses as the pandemic progresses and the volume of COVID-19 vaccine research increases.

TABLE 1 | Description of studies and their inclusion of sex/gender-disaggregated data.

Study Author (year) Journal	Population subgroup (if any)	Total n per study	%. of women participants	Efficacy/Effectiveness data		Safety data		
				Contains efficacy/ effectiveness data	Sex/gender- disaggregated outcomes	Contains safety data	Sex/gender- disaggregated outcomes	List of adverse reaction outcomes investigated
Randomised controlled trials (n = 7)		88,255	50	6	2	5	0	
Baden et al. (18) N Engl J Med	–	30,351	47	Yes	Yes	Yes	No	Local grade 1, 2, or 3 adverse reactions: Any, pain, erythema, swelling, axillary swelling/tenderness. Systemic grade 1, 2, or 3 adverse reactions: Any, fever, headache, fatigue, myalgia, arthralgia, nausea/vomiting, chills.
Emery et al. (19) Lancet	–	8,534	59	Yes	No	No	NA	NA
Frenck et al. (20) N Engl J Med	–	2,260	49	Yes	No	Yes	No	Local mild, moderate, severe, and grade 4 adverse reactions: Pain at injection site, redness, swelling. Systemic mild, moderate, severe and grade 4 adverse reactions: Fever, fatigue, headache, chills, muscle pain, vomiting, diarrhoea, joint pain.
Madhi et al. (21) N Engl J Med	–	2,021	43	Yes	No	Yes	No	General disorders, administration site conditions, infections, nervous system, respiratory, gastrointestinal, musculoskeletal, skin, reproductive system, eye, vascular, metabolism, ear, immune system, renal, blood, psychiatric disorders, and severe adverse events.
Polack et al. (22) N Engl J Med	–	37,706	49	Yes	Yes	Yes	No	Local mild, moderate, severe and grade 4 adverse reactions: Pain at injection site, redness, swelling. Systemic mild, moderate, severe and grade 4 adverse reactions: Fever, fatigue, headache, chills, vomiting, diarrhoea, muscle pain, joint pain.
Ramasamy et al. (23) Lancet	–	552	51	No	NA	Yes	No	Local mild, moderate and severe adverse reactions: Induration, itch, pain, redness, swelling, tenderness, warmth. Systemic mild, moderate and severe adverse reactions: Chills, fatigue, fever, headache, joint pain, malaise, muscle ache, nausea.
Voysey et al. (24) Lancet	–	6,831	62	Yes	No	No	NA	NA

(Continued)

TABLE 1 | Continued

Study Author (year) Journal	Population subgroup (if any)	Total n per study	% of women participants	Efficacy/Effectiveness data		Safety data		
				Contains efficacy/ effectiveness data	Sex/gender- disaggregated outcomes	Contains safety data	Sex/gender- disaggregated outcomes	List of adverse reaction outcomes investigated
Cohort study (n = 11)		1,555,243	56	2	1	9	4	
Achiron et al. (25) Mult Scler	People with multiple sclerosis	435	65	No	NA	Yes	No	Pain at injection site, fever/chills/flu-like symptoms, fatigue, headache, muscle or joint pain, new or worsening neurological symptomatology, face tingling, acute MS relapse.
Bae et al. (26) J Korean Med Sci	Healthcare workers	5,866	76	No	NA	Yes	Yes	Local pain, redness, swelling, fever, fatigue, headache, chills, vomiting, diarrhoea, muscle ache, joint pain.
Bernstine et al. (27) Clin Nucl Med	People with cancer	256	54	No	NA	Yes	Yes	Hypermetabolic axillary lymph nodes
Blumenthal et al. (28) JAMA	Hospital workers	64,900	NR	No	NA	Yes	Yes	Anaphylaxis, acute allergic reactions
Dagan et al. (29) N Engl J Med	Health service employees	1,193,236	50	Yes	Yes	No	NA	NA
Fabiani et al. (30) Euro Surveill	Healthcare workers	6,423	78	Yes	No	No	NA	NA
Jeon et al. (31) J Korean Med Sci	Healthcare workers	994	77	No	NA	Yes	Some ⁺	Fatigue, headache, malaise, arthralgia, chills, fever, nausea/vomiting, diarrhoea, local tenderness, redness, swelling, resting pain.
Kim et al. (32) J Korean Med Sci	Healthcare workers	1,511	72	No	NA	Yes	Some ⁺⁺	Pain at injection site, redness/swelling at injection site, lymphadenopathy, fever, chills, fatigue, nausea, vomiting, headache, myalgia, arthralgia, urticaria.
Krammer et al. (33) N Engl J Med	–	230	68	No	NA	Yes	No	Pain at injection site, swelling at injection site, erythema, fatigue, headache, chills, muscle pain, fever, joint pain.
Pimpinelli et al. (34) J Hematol Oncol	People with hematologic malignancies	128	48	No	NA	Yes	No	Pain, tenderness, fever, headache, malaise, myalgia, chills.
Pottegard et al. (35) BMJ	–	281,264	79	No	NA	Yes	Yes	Arterial events, venous thromboembolism./coagulation disorders, bleeding events.
Cross-sectional survey (n = 8)		7,243	77			8	0	
Boyarsky et al. (36) Transplantation	Solid organ transplant recipients	187	69	No	NA	Yes	No	Pain, redness, swelling, fever, chills, fatigue, headache, myalgia.

(Continued)

TABLE 1 | Continued

Study Author (year) Journal	Population subgroup (if any)	Total n per study	% of women participants	Efficacy/Effectiveness data		Safety data		
				Contains efficacy/ effectiveness data	Sex/gender- disaggregated outcomes	Contains safety data	Sex/gender- disaggregated outcomes	List of adverse reaction outcomes investigated
El-Shitany et al. (37) Int J Gen Med	–	455	64	No	NA	Yes	Some ⁺	Arm pain, injection site pain, injection site swelling and redness, fever, chills, fatigue, headache, nausea and vomiting, diarrhoea, muscle pain, joint pain.
Kadali et al. (38) Int J Infect Dis	Healthcare workers	803	87	No	NA	Yes	No	Generalised, weakness/fatigue, headache, chills, localised swelling at injection site, muscle pain/myalgia, arthritis/joint pain, diarrhoea, vomiting, fever, nausea, sore arm/pain, sweating.
Nittner-Marzalska et al. (39) Vaccines	Medical professionals and medical students	1,707	79	No	NA	Yes	No	Fever, arthralgia, myalgia, headache, palpitations, vomiting, local swelling, local redness, local pain, allergic reactions.
Riad et al. (40) J Clin Med	Healthcare workers	877	88	No	NA	Yes	No	General side effects: injection site pain, fatigue, headache, muscle pain, chills, joint pain, injection site swelling, injection site redness feeling unwell, lymphadenopathy, nausea. Oral side effects
Song et al. (41) J Korean Med Sci	Healthcare workers	2,478	76	No	NA	Yes	No	Injection site pain, injection site erythema, fever, headache, myalgia, arthralgia, fatigue, nausea/vomiting, rash, limitation of arm movement, facial paraesthesia, chill. Anaphylactoid reaction.
Sørvoll et al. (42) J Thromb Haemost	Healthcare workers	602	71	No	NA	Yes	No	Thrombocytopenia, anti-PF4/PVS reaction antibodies. Fever, headache, vomiting, fatigue, cutaneous bleeding, malaise, muscle/joint ache.
Waissengren et al. (43) Lancet Oncol	People with cancer	134	46	No	NA	Yes	No	Pain at injection sites, fatigue, headache, muscle pain, chills, fever, gastrointestinal complications, flu-like symptoms, local rash, local swelling.
Routine surveillance (n = 8)		41,104,426	61	2	0	6	3	
CDC COVID-19 Response Team et al. (44) Morb Mortal Wkly Rep	VAERS	1,893,360	62	No	NA	Yes	Yes	Anaphylaxis, non-anaphylaxis allergic reactions
CDC COVID-19 Response Team et al. (45) Morb Mortal Wkly Rep	VAERS	4,041,396	61	No	NA	Yes	Yes	Anaphylaxis, non-anaphylaxis allergic reactions

(Continued)

TABLE 1 | Continued

Study Author (year) Journal	Population subgroup (if any)	Total n per study	% of women participants	Efficacy/Effectiveness data		Safety data		
				Contains efficacy/ effectiveness data	Sex/gender- disaggregated outcomes	Contains safety data	Sex/gender- disaggregated outcomes	List of adverse reaction outcomes investigated
Gee et al. (46) Morb Mortal Wkly Rep	VAERS and V-safe	1,629,065	NR	No	NA	Yes	Some ⁺	Pain at injection site, fatigue, headache, myalgia, chills, fever, swelling at injection site, joint pain, nausea.
Hause et al. (47) Morb Mortal Wkly Rep	VAERS	7,988,624	NR	No	NA	Yes	Some ⁺	Anxiety related adverse events: chest pain, light-headedness or dizziness, nausea/vomiting, pallor or diaphoresis, syncope, tachycardia, seizure-like activity, hypotension.
Shay et al. (48) Morb Mortal Wkly Rep	VAERS and V-safe	7,980,000	NR	No	NA	Yes	Some [*]	Non-serious, serious events, injection site reactions, systemic reactions, health impacts, fatigue, injection site pain, headache, myalgia, fever, joint pain, nausea, diarrhoea.
Shimabukuro et al. (49) JAMA	VAERS	17,524,676	NR	No	NA	Yes	Yes	Anaphylaxis
Skowronski et al. (50) N Engl J Med	Documents submitted to Food and Drug Administration	43,355	NR	Yes	No	No	NA	NA
Thompson et al. (51) Morb Mortal Wkly Rep	Healthcare workers in HEROES- RECOVER	3,950	62	Yes	No	No	NA	NA
Case Series (n = 7)		154	71			7	5	
Farinazzo et al. (52) J Eur Acad Dermatol Venereol	–	46	89	No	NA	Yes	Yes	Cutaneous adverse reaction, any adverse event
Fernandez-Prada et al. (53) Euro Surveill	Healthcare workers	20	100	No	NA	Yes	Yes	Supraclavicular lymphadenopathy
Johnston et al. (54) JAMA Dermatol	–	16	81	No	NA	Yes	Yes	Localised cutaneous reaction (injection site reactions)
Lee et al. (55) Am J Hematol	–	20	40	No	NA	Yes	Some [*]	Thrombocytopenia, bruising, bleeding
Meylan et al. (56) Hypertension	–	9	78	No	NA	Yes	Yes	Stage 3 hypertension
Roman et al. (57) Front Immunol	–	43	47	No	NA	Yes	Some [*]	Quadriplegia, paraplegia, acute disseminated encephalomyelitis, spinal cord lesions
Shemer et al. (58) Isr Med Assoc J	–	9	NR	No	NA	Yes	Yes	Acute-onset facial nerve palsy

NR, Not reported; NA, not applicable.

^{*} Study sex/gender-disaggregated presentation of some but not all safety outcomes.⁺ Study presented sex/gender-disaggregated summary results.

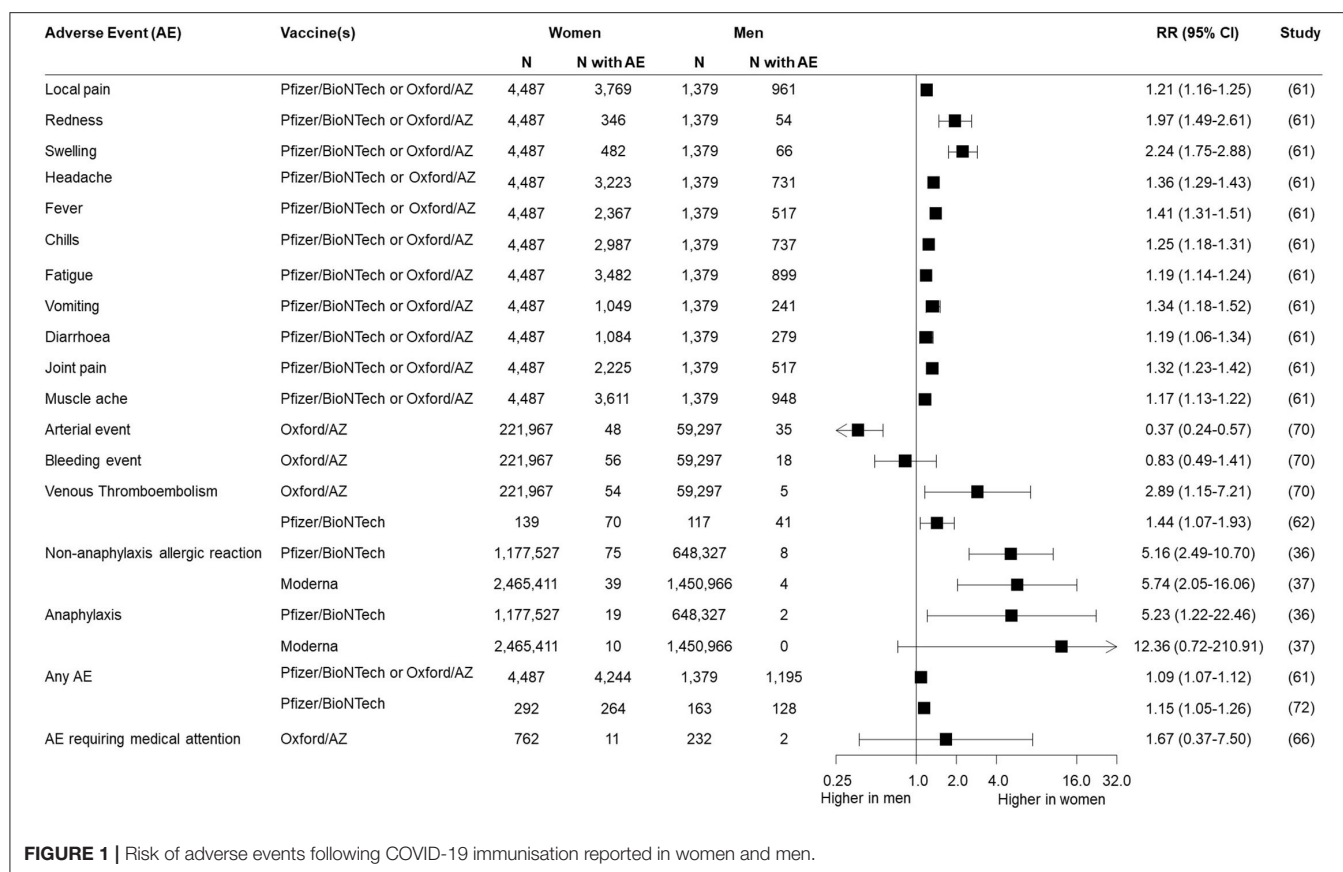


FIGURE 1 | Risk of adverse events following COVID-19 immunisation reported in women and men.

A novel element of our review is the inclusion of multiple study designs, not only RCTs. The complete absence of sex/gender-disaggregated safety data in COVID-19 vaccine trials means that post-marketing surveillance of sex/gender-specific adverse events is particularly important. Yet there was still an absence of reporting, with sex/gender-disaggregated adverse event data available in only four cohort and three national surveillance studies. While age and sex/gender data are typically collected through routine national surveillance systems (67), and shared with decision makers, the lack of data in the public domain has consequences for immunisation program delivery and uptake – further discussed below.

Evidence of Sex/Gender Differences

Of the seven studies where sex/gender-specific risk was reported, a higher risk of certain types of adverse events were observed among women. A large prospective observational study published subsequently to our searches found that local and systemic side effects were self-reported at lower frequencies than reported in RCTs, and minor events such as headache and fatigue were more common in women (68). These findings align with that of other vaccines (69), and are likely primarily due to women being more likely to report their symptoms than men (70, 71). Looking at anaphylactic and non-anaphylactic allergic reactions, although rare, 90% were reported in women (44, 45, 49). This is likely influenced by greater percentage of

women being vaccinated (45). These findings raise important questions around the gendered dimensions of immunisation, and demonstrate the value of routine collection and analysis of sex/gender-disaggregated data for further investigation of trends and mitigation strategies.

Consequences of a Lack of Sex/Gender Specific Evidence

Lack of sex/gender data in immunisation, including efficacy, safety and coverage data, has been a longstanding issue, not only one of the COVID-19 pandemic. Yet sex/gender has a critical influence on immunisation outcomes, at individual, household, community, health system, and policy levels (72). The lack of incorporation of sex/gender in COVID-19 vaccine research, as demonstrated across the spectrum of research designs in this review, results in an evidence base that does not lend itself to effective public communication around the utility and safety of vaccines. One current example is vaccine hesitancy and the slow uptake in some regions (73, 74). While a complex issue with many inter-related factors, concerns around safety (including pain) and misconceptions about effectiveness and side effects are known to be critical influences of vaccine hesitancy and delay (6, 75). Previous research has fairly consistently found that men report a higher intention to vaccinate than women (76–78), though intention does not always reflect action or access.

Therefore, an increase in sex/gender-specific information in the public domain would appear to be a prudent approach so as to help address misconceptions and mitigate vaccine hesitancy. This tailored advice is only possible if research pays more attention to sex/gender, and the particular concerns of women, men, and non-binary people.

A gendered lens should also be applied when designing research, including determining what data to collect. This includes consideration of how research design and conduct may be explicitly or implicitly sex/gender-biased, for example through exclusion of those who are pregnant or breastfeeding (79), or how research may potentially exacerbate existing sex/gender-related disparities or knowledge gaps. As an example, only one of the included studies examined adverse events related to the reproductive system, and the authors did not disaggregate these findings by sex/gender, or by age (21). Surveillance studies have also not reported data on menstrual irregularities or fertility. This may limit the ability of scientists and doctors to effectively respond to anecdotal reports and concerns within the community about such side effects post-immunisation, which have been amplified online and by the media (80–83). Greater attention to sex/gender in the design of COVID-19 vaccine research may help to address this data gap, allowing for improved public communication about adverse events with patients—particularly women.

RECOMMENDATIONS FOR FUTURE IMMUNISATION RESEARCH AND SURVEILLANCE

There are some limitations to this mini-review. In particular, the potential for missing studies, as only one database was searched and COVID-19 publications are rapidly increasing in number over time. However, this snapshot demonstrates an important evidence gap and discusses how adopting a sex/gender lens to data collection, reporting and analysis can have benefits for vaccination program outcomes. This mini-review focused only on sex/gender, without incorporating other intersectional factors, such as age and ethnicity, that may have an important impact on COVID-19 immunisation and outcomes and should be incorporated into research. Further, a quality assessment of articles was not conducted, which could be relevant for studies reporting sex/gender differences in outcomes, particularly regarding sample size and gender distribution. However, this mini review highlights substantial gaps in sex/gender-specific COVID-19 vaccine research.

Sex/gender, and other intersecting factors, impact how people are experiencing the COVID-19 pandemic (84). Therefore, research, policy and recommendations for COVID-19 vaccination must consider sex/gender in order to achieve optimally effective and equitable outcomes. Based on our findings, we present the following recommendations for future research:

- All research studies should, within reason, include a sex/gender lens in their research design and recruitment,

sex/gender-disaggregate their main outcomes and, where feasible, analyse potential sex/gender-based differences, or indeed similarities. This aligns with advice provided to the WHO on critical considerations for equitable COVID-19 vaccine research, development, and delivery (6).

- Data from research studies that collect the sex/gender of participants, but are not statistically powered to analyse results by sex/gender, should nevertheless make sex/gender results publicly available for pooling in evidence syntheses, even if only through Supplementary Data published online (66, 85).
- Medical journals and editors, as well as public health bodies, should redouble their efforts in enforcing recognition of sex/gender in reporting of COVID-19 research (65, 86) including enforcement of policies or endorsed guidelines and instructions and advice for peer reviewers
- Public health data systems, processes, and platforms should be established or adapted to collect, publicly report, and reflect on sex/gender-disaggregated outcomes from nationwide/mass immunisation programs (87).

CONCLUSION

Studies developing new vaccines or investigating their impact in populations should be designed and implemented in a sex/gender-sensitive way. Failure to recognise important sex/gender implications on efficacy, safety, and implementation will be detrimental to the global vaccine rollout, and ultimately control of the COVID-19 pandemic. Review of clinical trial data highlights missed opportunities to apply a sex/gender-sensitive lens in the development of COVID-19 vaccines. Public health data gathered through routine surveillance should be sex/gender-disaggregated and made publicly available to increase reliability of data, drive public confidence in immunisation programs, decrease vaccine hesitancy, and increase coverage.

AUTHOR CONTRIBUTIONS

AV conceived the study and wrote the initial draft. SS designed and conducted the searches in consultation with AV. AV, SS, KH, LH, and CH conducted the data screening, extraction, and analysis. SS, KH, LH, CH, MW, KW, and MS critically reviewed the study plan and manuscript and rewrote sections. All authors contributed to manuscript revisions, read, and approved the submitted version.

FUNDING

MS was funded by a Westpac Research Fellowship.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fgwh.2021.761511/full#supplementary-material>

REFERENCES

- Klein SL, Dhakal S, Ursin RL, Deshpande S, Sandberg K, Mauvais-Jarvis F. Biological sex impacts COVID-19 outcomes. *PLoS Pathog.* (2020) 16:e1008570. doi: 10.1371/journal.ppat.1008570
- Global Health 5050. *The Sex, Gender and COVID-19 Project.* (2021). Available online at: <https://globalhealth5050.org/the-sex-gender-and-covid-19-project/> (accessed June 25, 2021)
- Abate BB, Kassie AM, Kassaw MW, Aragie TG, Masresha SA. Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis. *BMJ Open.* (2020) 10:e040129. doi: 10.1136/bmjopen-2020-040129
- Peckham H, de Grujter NM, Raine C, Radziszewska A, Ciurtin C, Wedderburn LR, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ICU admission. *Nat Commun.* (2020) 11:6317. doi: 10.1038/s41467-020-19741-6
- Walter LA, McGregor AJ. Sex-and gender-specific observations and implications for COVID-19. *West J Emerg Med.* (2020) 21:507. doi: 10.5811/westjem.2020.4.47536
- Heidari S, Goodman T. *Critical Sex and Gender Considerations for Equitable Research, Development and Delivery of COVID-19 Vaccines.* World Health Organization (2021). Available online at: https://cdn.who.int/media/docs/default-source/immunization/sage/covid/gender-covid-19-vaccines-sage-background-paper.pdf?sfvrsn=899e8fca_15&download=true (accessed June 25, 2021).
- Steinberg JR, Turner BE, Weeks BT, Magnani CJ, Wong BO, Rodriguez F, et al. Analysis of female enrollment and participant sex by burden of disease in US clinical trials between 2000 and 2020. *JAMA Netw Open.* (2021) 4:e2113749. doi: 10.1001/jamanetworkopen.2021.13749
- Wolfe J, Safdar B, Madsen TE, Sethuraman KN, Becker B, Greenberg MR, et al. Sex-or gender-specific differences in the clinical presentation, outcome, and treatment of Sars-Cov-2. *Clin Ther.* (2021) 43:557–71. doi: 10.1016/j.clinthera.2021.01.015
- Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. *Semin Immunopathol.* (2019) 41:239–49. doi: 10.1007/s00281-018-0726-5
- Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Trans R Soc Trop Med Hyg.* (2015) 109:9–15. doi: 10.1093/trstmh/tru167
- Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol.* (2016) 16:626–38. doi: 10.1038/nri.2016.90
- Kim JH, Marks F, Clemens JD. Looking beyond COVID-19 vaccine phase 3 trials. *Nat Med.* (2021) 27:205–11. doi: 10.1038/s41591-021-01230-y
- World Health Organization. *Status of COVID-19 Vaccines Within WHO EUL/PQ Evaluation Process.* (2021). Available online at: https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_04May2021.pdf (accessed May 2021)
- World Health Organisation. *COVAX.* (2021). Available online at: <https://www.who.int/initiatives/act-accelerator/covax> (accessed June 2021).
- Peryer G, Golder S, Junqueira D, Vohra S, Loke YK. Chapter 19: Adverse effects. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (updated February 2021).* Cochrane (2021). Available online at: www.training.cochrane.org/handbook
- Van Anders SM. Beyond sexual orientation: integrating gender/sex and diverse sexualities via sexual configurations theory. *Arch Sex Behav.* (2015) 44:1177–213. doi: 10.1007/s10508-015-0490-8
- GenderSci Lab. *Gender/sex: An Explanation.* (2020). Available online at: <https://www.genderscilab.org/blog/covid-intro> (accessed July, 2021)
- Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* (2021) 384:403–16. doi: 10.1056/NEJMoa2035389
- Emery KRW, Golubchik T, Aley PK, Ariani CV, Angus B, Bibi S, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. *Lancet.* (2021) 397:1351–62. doi: 10.1016/S0140-6736(21)00628-0
- Frenck RW Jr, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *N Engl J Med.* (2021) 385:239–50. doi: 10.1056/NEJMoa2107456
- Madhi SA, Baillie V, Cutl, CL, Voysey M, Koen AL, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 vaccine against the B.1.351 variant. *N Engl J Med.* (2021) 384:1885–98. doi: 10.1056/NEJMoa2102214
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* (2020) 383:2603–15. doi: 10.1056/NEJMoa2034577
- Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet.* (2020) 396:1979–93. doi: 10.1016/S0140-6736(20)32466-1
- Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet.* (2020) 397:99–111. doi: 10.1016/S0140-6736(20)32661-1
- Achiron A, Dolev M, Menascu S, Zohar DN, Dreyer-Alster S, Miron S, et al. COVID-19 vaccination in patients with multiple sclerosis: what we have learnt by February 2021. *Mult Scler.* (2021) 27:864–70. doi: 10.1177/13524585211003476
- Bae S, Lee YW, Lim SY, Lee JH, Lim JS, Lee S, et al. Adverse reactions following the first dose of ChAdOx1 nCoV-19 vaccine and BNT162b2 vaccine for healthcare workers in South Korea. *J Korean Med Sci.* (2021) 36:e115. doi: 10.3346/jkms.2021.36.e115
- Bernstine H, Priss M, Anati T, Turko O, Gorenberg M, Steinmetz AP, et al. Axillary lymph nodes hypermetabolism after BNT162b2 mRNA COVID-19 Vaccination in cancer patients undergoing 18F-FDG PET/CT: a cohort study. *Clin Nucl Med.* (2021) 46:396–401. doi: 10.1097/RLU.0000000000003648
- Blumenthal KG, Robinson LB, Camargo CA Jr, Shenoy ES, Banerji A, et al. Acute allergic reactions to mRNA COVID-19 vaccines. *JAMA.* (2021) 325:1562–5. doi: 10.1001/jama.2021.3976
- Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med.* (2021) 384:1412–23. doi: 10.1056/NEJMoa2101765
- Fabiani M, Ramigni M, Gobetto V, Mateo-Urdiales A, Pezzotti P, Piovesan C. Effectiveness of the Comirnaty (BNT162b2, BioNTech/Pfizer) vaccine in preventing SARS-CoV-2 infection among healthcare workers, Treviso province, Veneto region, Italy, 27 December 2020 to 24 March 2021. *Euro Surveill.* (2021) 26:2100420. doi: 10.2807/1560-7917.ES.2021.26.17.2100420
- Jeon M, Kim J, Oh CE, Lee JY. Adverse events following immunization associated with coronavirus disease 2019 vaccination reported in the mobile vaccine adverse events reporting system. *J Korean Med Sci.* (2021) 36:e114. doi: 10.3346/jkms.2021.36.e114
- Kim SH, Wi YM, Yun SY, Ryu JS, Shin JM, Lee EH, et al. Adverse events in healthcare workers after the first dose of ChAdOx1 nCoV-19 or BNT162b2 mRNA COVID-19 vaccination: a single center experience. *J Korean Med Sci.* (2021) 36:e107. doi: 10.3346/jkms.2021.36.e107
- Krammer F, Srivastava K, Alshammery H, Amoako AA, Awawda MH, Beach KF, et al. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. *N Engl J Med.* (2021) 384:1372–4. doi: 10.1056/NEJMc2101667
- Pimpinelli F, Marchesi F, Piaggio G, Giannarelli D, Papa E, Falcucci P, et al. Fifth-week immunogenicity and safety of anti-SARS-CoV-2 BNT162b2 vaccine in patients with multiple myeloma and myeloproliferative malignancies on active treatment: preliminary data from a single institution. *J Hematol Oncol.* (2021) 14:81. doi: 10.1186/s13045-021-01090-6
- Pottg rd A, Lund LC, Karlstad  , Dahl J, Andersen M, Hallas J, et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. *BMJ.* (2021) 373:n1114. doi: 10.1136/bmj.n1114
- Boyersky BJ, Ou MT, Greenberg RS, Teles AT, Werbel WA, Avery RK, et al. Safety of the first dose of SARS-CoV-2 vaccination in solid organ transplant recipients. *Transplantation.* (2021) 105:e56–7. doi: 10.1097/TP.0000000000003654

37. El-Shitany NA, Harakeh S, Badr-Eldin SM, Bagher AM, Eid B, Almkadi H, et al. Minor to moderate side effects of Pfizer-BioNTech COVID-19 vaccine among Saudi residents: a retrospective cross-sectional study. *Int J Gen Med.* (2021) 14:1389–401. doi: 10.2147/IJGM.S310497
38. Kadali RAK, Janagama R, Peruru S, Malayala SV. Side effects of BNT162b2 mRNA COVID-19 vaccine: a randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. *Int J Infect Dis.* (2021) 106:376–81. doi: 10.1016/j.ijid.2021.04.047
39. Nittner-Marszalska M, Rosiek-Biegus M, Kopeć A, Pawłowicz R, Kosińska M, Łata A, et al. Pfizer-BioNTech COVID-19 vaccine tolerance in allergic versus non-allergic individuals. *Vaccines.* (2021) 9:553. doi: 10.3390/vaccines9060553
40. Riad A, Pokorná A, Attia S, Klugarová J, Koščik M, Klugar M. Prevalence of COVID-19 vaccine side effects among healthcare workers in the Czech Republic. *J Clin Med.* (2021) 10:1428. doi: 10.3390/jcm10071428
41. Song JY, Cheong HJ, Kim SR, Lee SE, Kim SH, Noh JY, et al. Early safety monitoring of COVID-19 vaccines in healthcare workers. *J Korean Med Sci.* (2021) 36:e110. doi: 10.3346/jkms.2021.36.e110
42. Sørvoll IH, Horvei KD, Ernsten SL, Laegreid IJ, Lund S, Grønli RH, et al. An observational study to identify the prevalence of thrombocytopenia and anti-PF4/polyanion antibodies in Norwegian health care workers after COVID-19 vaccination. *J Thromb Haemost.* (2021) 19:1813–8. doi: 10.1111/jth.15352
43. Waissengrin B, Agbarya A, Safadi E, Padova H, Wolf I. Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors. *Lancet Oncol.* (2021) 22:581–3. doi: 10.1016/S1470-2045(21)00155-8
44. CDC COVID-19 Response Team and Food and Drug Administration. Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine - United States, December 14–23, 2020. *Morb Mortal Wkly Rep.* (2021) 70:46–51. doi: 10.15585/mmwr.mm7002e1
45. CDC COVID-19 Response Team and Food and Drug Administration. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine - United States, December 21, 2020–January 10, 2021. *Morb Mortal Wkly Rep.* (2021) 70:125–9. doi: 10.15585/mmwr.mm7004e1
46. Gee J, Marquez P, Su J, Calvert GM, Liu R, Myers T, et al. First Month of COVID-19 vaccine safety monitoring - United States, December 14, 2020–January 13, 2021. *Morb Mortal Wkly Rep.* (2021) 70:283–8. doi: 10.15585/mmwr.mm7008e3
47. Hause AM, Gee J, Johnson T, Jazwa A, Marquez P, Miller E, et al. Anxiety-related adverse event clusters after Janssen COVID-19 vaccination - Five U.S. Mass Vaccination Sites, April 2021. *Morb Mortal Wkly Rep.* (2021) 70:685–8. doi: 10.15585/mmwr.mm7018e3
48. Shay DK, Gee J, Su JR, Myers TR, Marquez P, Liu R, et al. Safety monitoring of the Janssen (Johnson & Johnson) COVID-19 vaccine - United States, March–April 2021. *Morb Mortal Wkly Rep.* (2021) 70:680–4. doi: 10.15585/mmwr.mm7018e2
49. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US–December 14, 2020–January 18, 2021. *JAMA.* (2021) 325:1101–2. doi: 10.1001/jama.2021.1967
50. Skowronski DM, De Serres G. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* (2021) 384:1576–7. doi: 10.1056/NEJMc2036242
51. Thompson MG, Burgess JL, Naleway AL, Tyner HL, Yoon SK, Meece J, et al. Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among health care personnel, first responders, and other essential and frontline workers - eight U.S. Locations, December 2020–March 2021. *Morb Mortal Wkly Rep.* (2021) 70:495–500. doi: 10.15585/mmwr.mm7013e3
52. Farinazzo E, Ponis G, Zelin E, Errichetti E, Stinco G, Pinzani C, et al. Cutaneous adverse reactions after mRNA COVID-19 vaccine: early reports from North-East Italy. *J Eur Acad Dermatol Venereol.* (2021) 35:e548–51. doi: 10.1111/jdv.17343
53. Fernández-Prada M, Rivero-Calle I, Calvache-González A, Martínón-Torres F. Acute onset supraclavicular lymphadenopathy coinciding with intramuscular mRNA vaccination against COVID-19 may be related to vaccine injection technique, Spain, January and February 2021. *Euro Surveill.* (2021) 26:2100193. doi: 10.2807/1560-7917.ES.2021.26.10.2100193
54. Johnston MS, Galan A, Watsky KL, Little AJ. Delayed localized hypersensitivity reactions to the Moderna COVID-19 vaccine: a case series. *JAMA Dermatol.* (2021) 157:716–20. doi: 10.1001/jamadermatol.2021.1214
55. Lee EJ, Cines DB, Gernsheimer T, Kessler C, Michel M, Tarantino MD, et al. Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol.* (2021) 96:534–7. doi: 10.1002/ajh.26132
56. Meylan S, Livio F, Foerster M, Genoud PJ, Marguet F, Wuerzner G. Stage III hypertension in patients after mRNA-based SARS-CoV-2 vaccination. *Hypertension.* (2021) 77:e56–7. doi: 10.1161/HYPERTENSIONAHA.121.17316
57. Román GC, Gracia F, Torres A, Palacios A, Gracia K, Harris D. Acute Transverse Myelitis (ATM): clinical review of 43 patients with COVID-19-associated ATM and 3 post-vaccination ATM serious adverse events with the ChAdOx1 nCoV-19 vaccine (AZD1222). *Front Immunol.* (2021) 12:653786. doi: 10.3389/fimmu.2021.653786
58. Shemer A, Pras E, Hecht I. Peripheral facial nerve palsy following BNT162b2 (COVID-19) vaccination. *Isr Med Assoc J.* (2021) 23:143–4.
59. Global Health 5050. *Gender and Sex-Disaggregated Data: Vital to Inform an Effective Response to COVID-19.* (2020). Available online at: <https://globalhealth5050.org/wp-content/themes/global-health/covid/media/ISSUE%20BRIEF%20-%20Sex-Disaggregated%20Data%20&%20COVID-19%20-%20Sept%202020.pdf> (accessed June 25, 2021).
60. Vijayasingham L, Bischof E, Wolfe J. Sex-disaggregated data in COVID-19 vaccine trials. *Lancet.* (2021) 397:966–7. doi: 10.1016/S0140-6736(21)00384-6
61. Bischof E, Wolfe J, Klein SL. Clinical trials for COVID-19 should include sex as a variable. *J Clin Invest.* (2020) 130:3350–2. doi: 10.1172/JCI139306
62. Evagora-Campbell M, Borkotoky K, Sharma S, Mbuthia M. From routine data collection to policy design: sex and gender both matter in COVID-19. *Lancet.* (2021) 397:2447–9. doi: 10.1016/S0140-6736(21)01326-X
63. Brady E, Nielsen MW, Andersen JB, Oertelt-Prigione S. Lack of consideration of sex and gender in COVID-19 clinical studies. *Nat Commun.* (2021) 12:4015. doi: 10.1038/s41467-021-24265-8
64. Carcel C, Reeves M. Under-enrollment of women in stroke clinical trials: what are the causes and what should be done about it? *Stroke.* (2021) 52:452–7. doi: 10.1161/STROKEAHA.120.033227
65. Palmer-Ross A, Ovseiko PV, Heidari S. Inadequate reporting of COVID-19 clinical studies: a renewed rationale for the Sex and Gender Equity in Research (SAGER) guidelines. *BMJ Glob Health.* (2021) 6:e004997. doi: 10.1136/bmjgh-2021-004997
66. Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. *Res Integr Peer Rev.* (2016) 1:1–9. doi: 10.1186/s41073-016-0016-5
67. AusVaxSafety. *COVID-19 Vaccine Safety Surveillance.* (2021). Available online at: <https://www.ausvaxsafety.org.au/our-work/covid-19-vaccine-safety-surveillance>
68. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infect Dis.* (2021) 21:939–49. doi: 10.1016/S1473-3099(21)00224-3
69. McCartney PR. Sex-based vaccine response in the context of COVID-19. *J Obstet Gynecol Neonatal Nurs J.* (2020) 49:405–8. doi: 10.1016/j.jogn.2020.08.001
70. Himmelstein MS, Sanchez DT. Masculinity impediments: Internalized masculinity contributes to healthcare avoidance in men and women. *J Health Psychol.* (2016) 21:1283–92. doi: 10.1177/1359105314551623
71. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. *BMC Fam Pract.* (2016) 17:38. doi: 10.1186/s12875-016-0440-0
72. Fletto M, Sharkey A. The influence of gender on immunisation: using an ecological framework to examine intersecting inequities and pathways to change. *BMJ Glob Health.* (2019) 4:e001711. doi: 10.1136/bmjgh-2019-001711
73. Sherman SM, Smith LE, Sim J, Amlót R, Cutts M, Dasch H, et al. COVID-19 vaccination intention in the UK: results from the COVID-19 vaccination acceptability study (CoVAccS), a nationally representative cross-sectional survey. *Hum Vaccin Immunother.* (2021) 17:1612–21. doi: 10.1080/21645515.2020.1846397

74. Loomba S, de Figueiredo A, Piatek SJ, de Graaf K, Larson HJ. Measuring the impact of COVID-19 vaccine misinformation on vaccination intent in the UK and USA. *Nat Hum Behav.* (2021) 5:337–48. doi: 10.1038/s41562-021-01056-1
75. Brewer NT, Chapman GB, Rothman AJ, Leask J, Kempe A. Increasing vaccination: putting psychological science into action. *Psychol Sci Public Interest.* (2017) 18:149–207. doi: 10.1177/1529100618760521
76. Bish A, Yardley L, Nicoll A, Michie S. Factors associated with uptake of vaccination against pandemic influenza: a systematic review. *Vaccine.* (2011) 29:6472–84. doi: 10.1016/j.vaccine.2011.06.107
77. Solis Arce J, Warren S, Meriggi N, Scacco A, McMurry N, Voors M, et al. COVID-19 vaccine acceptance and hesitancy in low and middle income countries, and implications for messaging. *Nat Med.* (2021) 27:1385–94. doi: 10.1101/2021.03.11.21253419
78. Zintel S, Flock C, Arbogast AL, Forster A, von Wagner C, Sieverding M. *Gender Differences in the Intention to Get Vaccinated against COVID-19 - A Systematic Review and Meta-Analysis* (March 12, 2021). Available online at: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3803323 (accessed June 25, 2021)
79. Vassallo A, Womersley K, Norton R, Sheel M. Pregnant women's appetite for risk. *Lancet Global Health.* (2021) 9:e593. doi: 10.1016/S2214-109X(21)00044-9
80. Villarreal A. 'No data' linking Covid vaccines to menstrual changes, US Experts Say. *The Guardian* (2021). Available online at: <https://www.theguardian.com/world/2021/apr/23/covid-vaccines-periods-menstruation-changes-data-experts> (accessed June 2021).
81. Robinson OSR. *Covid Vaccine: Period Changes Could be a Short-Term Side Effect.* BBC (2021). Available online at: <https://www.bbc.com/news/health-56901353> (accessed June 2021).
82. Schraer R. *Covid: Claims Vaccinations Harm Fertility Unfounded.* BBC (2021). Available online at: <https://www.bbc.com/news/health-56012529> (accessed June 2021).
83. Wise M. *Could the COVID Vaccines Affect Your Period? We don't Know Yet — but There's no Cause for Concern.* The Conversation. (2021). Available online at: <https://theconversation.com/could-the-covid-vaccines-affect-your-period-we-dont-know-yet-but-theres-no-cause-for-concern-159912> (accessed June 2021).
84. Ahmed SB, Dumanski SM. Sex, gender and COVID-19: a call to action. *Can J Public Health.* (2020) 111:980–3. doi: 10.17269/s41997-020-00417-z
85. Woodward M. Rationale and tutorial for analysing and reporting sex differences in cardiovascular associations. *Heart.* (2019) 105:1701–8. doi: 10.1136/heartjnl-2019-315299
86. World Health Organization. *Strategy for Integrating Gender Analysis and Actions Into the Work of WHO.* Geneva: WHO Department of Gender, Women and Health (2008).
87. Heidari S, Ahumada C, Kurbanova Z. Towards the real-time inclusion of sex- and age-disaggregated data in pandemic responses. *BMJ Glob Health.* (2020) 5:e003848. doi: 10.1136/bmjgh-2020-003848

Conflict of Interest: MW is a consultant to Amgen, Kyowa Kirin, and Freeline.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Vassallo, Shajahan, Harris, Hallam, Hockham, Womersley, Woodward and Sheel. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Sex and Gender Bias in Covid-19 Clinical Case Reports

Aysha E. Salter-Volz^{1†}, Abigail Oyasu^{1,2†}, Chen Yeh³, Lutfiyya N. Muhammad³ and Nicole C. Waitowich^{1*}

¹ Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States,

² University of Illinois at Urbana-Champaign, Champaign, IL, United States, ³ Division of Biostatistics, Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

OPEN ACCESS

Edited by:

Kelly Jane Thompson,
University of New South
Wales, Australia

Reviewed by:

Amy Vassallo,
University of New South
Wales, Australia
Kate Womersley,
The George Institute for Global Health,
United Kingdom

*Correspondence:

Nicole C. Waitowich
nicole.waitowich@northwestern.edu

[†]These authors have contributed
equally to this work

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 10 September 2021

Accepted: 29 October 2021

Published: 22 November 2021

Citation:

Salter-Volz AE, Oyasu A, Yeh C,
Muhammad LN and Waitowich NC
(2021) Sex and Gender Bias in
Covid-19 Clinical Case Reports.
Front. Glob. Womens Health
2:774033.
doi: 10.3389/fgwh.2021.774033

Clinical case reports circulate relevant information regarding disease presentation and describe treatment protocols, particularly for novel conditions. In the early months of the Covid-19 pandemic, case reports provided key insights into the pathophysiology and sequelae associated with Covid-19 infection and described treatment mechanisms and outcomes. However, case reports are often subject to selection bias due to their singular nature. To better understand how selection biases may have influenced Covid-19-related case reports, we conducted a bibliometric analysis of Covid-19-related case reports published in high impact journals from January 1 to June 1, 2020. Case reports were coded for patient sex, country of institutional affiliation, physiological system, and first and last author gender. Of 494 total case reports, 45% ($n = 221$) of patients were male, 30% ($n = 146$) were female, and 25% ($n = 124$) included both sexes. Ratios of male-only to female-only case reports varied by physiological system. The majority of case reports had male first (61%, $n = 302$) and last (70%, $n = 340$) authors. Case reports with male last authors were more likely to describe male patients [χ^2 (2, $n = 465$) = 6.6, $p = 0.037$], while case reports with female last authors were more likely to include patients of both sexes [OR = 1.918 (95% CI = 1.163–3.16)]. Despite a limited sample size, these data reflect emerging research on sex-differences in the physiological presentation and impact of Covid-19 and parallel large-scale trends in authorship patterns. Ultimately, this work highlights potential biases in the dissemination of clinical information via case reports and underscores the inextricable influences of sex and gender biases within biomedicine.

Keywords: COVID-19, sex bias, gender bias, case reports (publication type), bibliometrics

INTRODUCTION

Longstanding sex and gender biases impact many facets of the biomedical research enterprise including research practices (1, 2), clinical care (3, 4), and workforce development (5–7). The persistent overrepresentation of males as research subjects, scientists, and physicians has informed our understanding of health and disease, oftentimes to the detriment of women, transgender, and gender non-binary, or non-conforming individuals.

Clinical case reports serve as an important educational tool to disseminate pertinent information regarding disease or disorder presentation, diagnosis, treatment, and prognosis (8). During the initial months of the Covid-19 pandemic, case reports provided key insights into

Covid-19 pathophysiology, sequelae, and treatment and in certain circumstances, served as primary evidence for clinical decision-making.

Case report subjects are often selected semi-retrospectively for their novelty or educational benefit. As a result, singular case reports are inherently prone to selection bias. In contrast to clinical research studies which have predefined study populations and stringent inclusion or exclusion criteria, the decision to select a case report subject may lie solely with a member of the patient's care team. However, it is reasonable to expect that if case studies were compiled for a particular disease or disorder, they would closely mirror the respective patient population. In 2017, Allotey and colleagues (9) identified a significant male bias in case reports published in high-impact medical journals, which suggests that inherent biases may play a larger role than anticipated in case report selection and publication. We hypothesized that female patients may be underrepresented in Covid-19 research and clinical care due to sex differences in Covid-19 disease or due to gender biases. To determine whether Covid-19-related case reports were, in fact, subject to sex or gender biases, we characterized 494 Covid-19-related case reports published between January 1, 2020, and July 1, 2020, from 103 journals by patient sex, physiological system, country of institutional affiliation and first and last author gender.

METHODS

Citation data for 1,817 articles classified as case reports were downloaded on July 1, 2020, from LitCovid, a categorical database of Covid-19 literature from PubMed (10, 11). The LitCovid database identifies relevant articles using the National Center for Biotechnology Information's E-Utilities tool which is then further refined and categorized by machine learning and manual creation (11). Case reports were further refined by additional inclusion and exclusion criteria (Figure 1). Journal impact factors [(IF), 2019 Journal Citation Reports Science Edition, Clarivate Analytics] were available for 1,466 (81%) case reports, and only those with an IF of 5 or above ($n = 498$, 27%) were considered medium-to-high visibility and selected for inclusion in the study and further review. Four articles were excluded because they did not reference patients, resulting in a final sample of 494 articles. Two of the authors (ASV, AO) manually and independently screened and coded case reports for patient sex, physiological system, author first names, and country of institutional affiliation. Patient sex was determined by the use of descriptive terms such as male/female, man/woman, or inferred by the use of he/she pronouns. Only one article (0.2%) included transgender patients and did not report biological sex or gender identity. The country of institutional affiliation was determined by the institutional location of the corresponding author if the article was authored by a multinational cohort. These data were cross-checked, and the coding agreement was almost perfect for a representative subset of 55 articles (Cohen's kappa = 0.97, $p < 0.001$). The first and last author's gender were inferred using the name-to-gender assignment algorithm Gender API (<https://gender-api.com/>). Gender API was selected due to

its low rate of inaccuracies (7.9%) or non-classifications (3%) (12). Articles authored by an unspecified group or without full first names listed were coded as unknown.

Chi-Square tests and multinomial logistic regression models were used to examine the association between author gender and patient sex. Chi-Square tests were also used to compare patient sex by physiological system and country of institutional affiliation. Results from the multinomial logistic regression models are summarized by odds ratios (OR) and 95% confidence intervals (CI). P -values < 0.05 were considered significant.

Descriptions of patient sex or author gender follow American Psychological Association reporting standards where male/female terminology is used as descriptive adjectives when appropriate or when specifically referring to biological sex. The terms men and women are commonly used as nouns to describe groups of people.

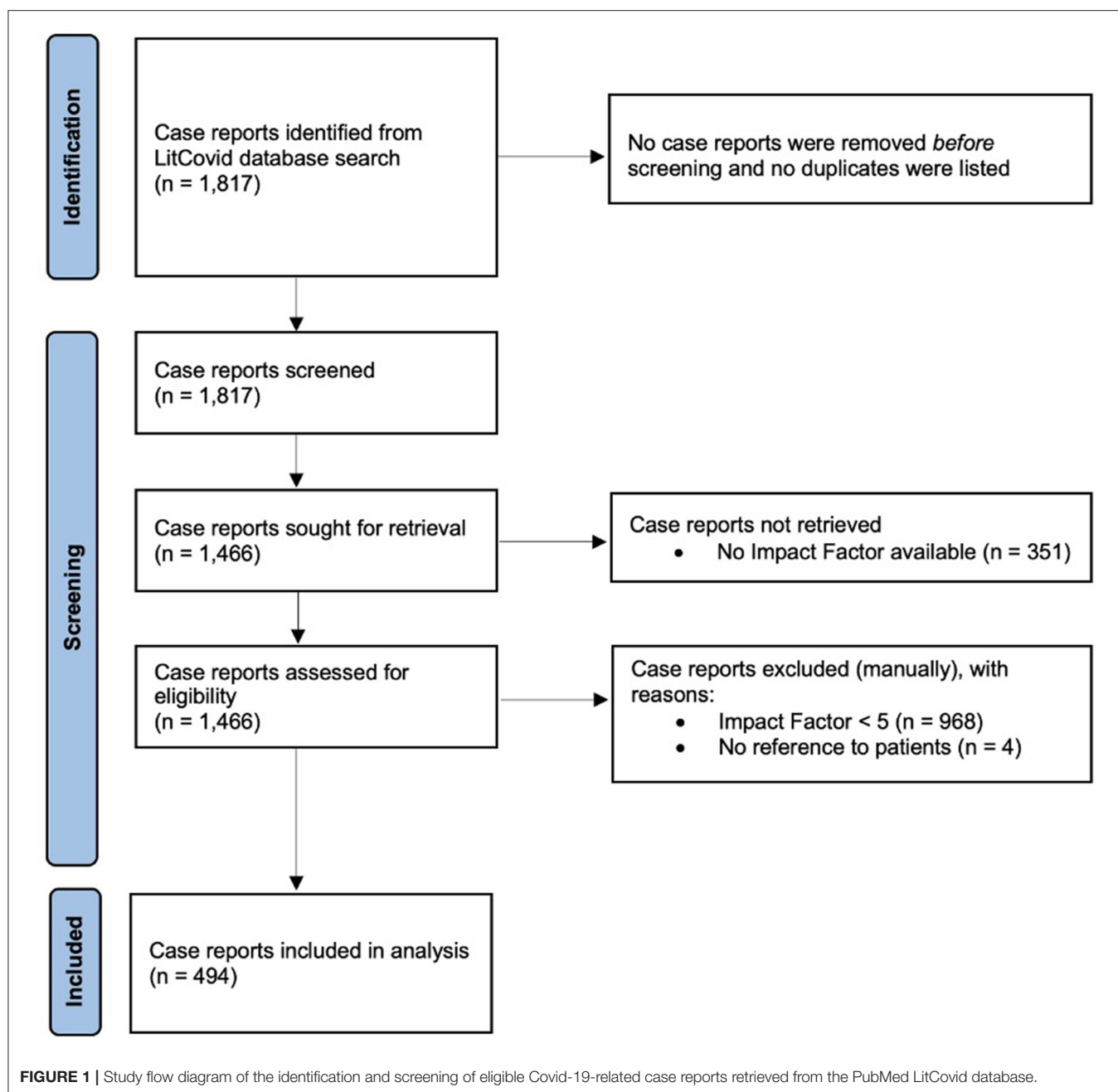
RESULTS

Of the 494 case reports analyzed, the majority were related to respiratory, multi-systemic, dermatologic, hematologic, or neurologic systems (Table 1). Of the patients described in the 494 case reports, forty-five % ($n = 221$) were male and 30% ($n = 146$) were female (Figure 2). Patients of both sexes were included in 25% ($n = 124$) of case reports and 0.6% ($n = 3$) failed to report patient sex (Figure 1). The ratio of articles reporting on male-only vs. female-only patients was highest in renal (11:1), hepatic (3.5:1), respiratory (2.3:1), multi-systemic (2.2:1), and cardiovascular (2.2:1) systems. Reproductive reports were almost exclusively female (95%, $n = 20$).

Case reports were primarily authored by groups with institutional affiliations in the United States (20%, $n = 97$), China (18%, $n = 89$), Italy (13%, $n = 65$), France (12%, $n = 60$), and Spain (7%, $n = 34$). The majority of case reports had male first (61%, $n = 302$) and last (70%, $n = 340$) authors, with 43% ($n = 214$) of all reports having male first and last author dyads. The last author's gender is associated with the sex of the case report patient (Table 1). Case reports with male last authors are more likely to include male-only patients ($p = 0.037$) compared to female last authors. Female last authors are more likely to include patients of both sexes [OR = 1.918 (95% CI = 1.163–3.16)] in unadjusted and adjusted models [OR = 1.774 (95% CI = 1.055–2.984)] which control for impact factor, country, and physiological system.

DISCUSSION

While male bias in case reports has been previously reported (9), this is the first study to examine this in Covid-19-related case studies. The overrepresentation of male patients in Covid-19 case reports may be reflective of sex differences in disease prevalence, severity, and immune response (13, 14). Likewise, sex and gender differences in the presence of contributing comorbidities may also influence Covid-19 disease severity and treatment outcomes (15). The high ratio of male-to-female case reports in the renal category parallels clinical data which suggests that



male sex risk factor for Covid-19-related acute kidney injury (15, 16). In comparison, the high female-to-male ratio observed in the reproductive category can be attributed to pregnancy-related case reports. Overall, the differences in patient sex ratios across physiological categories may provide insight into Covid-19 disease mechanisms. Yet, it is important to note that these data fail to fully capture the sociocultural influences on Covid-19 testing, case identification, and access to care which may differ based on gender, race, ethnicity, socioeconomic status, and geographic location as case reports typically originate from a hospital-based setting.

Gender disparities in authorship are common within the biomedical sciences (17, 18) and have been documented for case reports (19). In a large-scale bibliometric analysis of over 20,000 case reports, Hsiehchen and colleagues (19) found that 36% of first authors and 25% of last authors are women. The data presented here are similar with female authors comprising 39% and 26% of first and last authors, respectively. Of interest, is the unique influence of the Covid-19 pandemic on gender authorship patterns. Early in the pandemic, several groups reported that women were publishing less to biomedical preprint servers compared to the same

TABLE 1 | Case study characteristics and article metadata.

	Total		Male only		Female only		Both sexes		Chi-square test <i>p</i> -value
	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	
Body system	494	(100)	221	(100)	146	(100)	124	(100)	<0.001
Respiratory*	74	(15)	39	(18)	17	(12)	17	(14)	
Multi-system	70	(14)	29	(13)	13	(9)	28	(23)	
Integumentary*	61	(12)	22	(10)	22	(15)	16	(12)	
Hematological	47	(10)	21	(10)	15	(10)	11	(9)	
Neurological	48	(10)	17	(8)	14	(10)	17	(14)	
Cardiovascular*	42	(9)	24	(11)	11	(7)	6	(5)	
Immunological	33	(7)	14	(6)	10	(7)	9	(7)	
Renal	32	(6)	23	(10)	2	(1)	8	(6)	
Gastrointestinal	22	(4)	10	(5)	7	(5)	5	(4)	
Reproductive	21	(4)	1	(0)	20	(14)	0	(0)	
Hepatic	10	(2)	7	(3)	2	(1)	1	(1)	
Other	34	(7)	14	(6)	14	(10)	6	(5)	
Country of institutional affiliation									0.294
USA	97	(20)	37	(17)	32	(22)	28	(23)	
China	89	(18)	38	(17)	20	(14)	31	(25)	
Italy	65	(13)	32	(14)	21	(14)	12	(10)	
France	60	(12)	25	(11)	17	(11)	15	(12)	
Spain	34	(7)	14	(6)	12	(8)	8	(6)	
Other	149	(30)	75	(34)	45	(31)	30	(24)	
First author gender									0.639
Male	302	(61)	137	(62)	92	(63)	72	(58)	
Female	182	(39)	77	(35)	53	(36)	50	(40)	
Unknown	10	(2)	7	(3)	1	(1)	2	(2)	0.037
Last author gender									
Male	340	(69)	155	(70)	104	(71)	79	(58)	
Female	128	(26)	44	(20)	40	(27)	43	(40)	
Unknown	26	(5)	22	(10)	2	(1)	2	(2)	0.135
Author dyads	457	(100)	194	(100)	143	(100)	120	(100)	
Male first / male last	214	(43)	96	(50)	71	(33)	47	(39)	
Male first / female last	72	(15)	28	(14)	19	(26)	25	(21)	
Female first / male last	116	(24)	54	(28)	32	(28)	30	(25)	
Female first / female last	55	(11)	16	(8)	21	(38)	18	(15)	

*Sex unspecified for one article in each of the following categories: respiratory, integumentary, and cardiovascular.

period in 2019 (20, 21). Meanwhile, others found that women were underrepresented as first authors on Covid-19-related research studies (22, 23). The case reports analyzed here were authored during the first 6 months of the pandemic yet reflect pre-pandemic authorship trends. This suggests that authorship trends should not solely be used as a metric for assessing the impact of Covid-19 on research productivity and more long-term, holistic evaluations of the biomedical enterprise are warranted. In depth analyses which evaluate other metrics of productivity such as grant submission and award patterns and hiring, retention, and promotion rates, at discipline- or specialty-specific levels and the availability and/or accessibility of institutional support structures would provide added insight into the impact of Covid-19 on the biomedical workforce.

Lastly, emerging evidence suggests that author gender may also influence how data are analyzed and presented (24, 25). Prior work by Sugimoto and colleagues found that women are more likely to report and analyze data by sex (25). Here, we find that female authors are more likely to include patients of both sexes within case reports. These data suggest that female authors may be more likely to find inherent value in including clinical data derived from both sexes in case reports. Alternatively, they may be more keenly aware of, and actively seek to address sex- and gender biases in biomedicine through inclusivity. On the contrary, case reports with male last authors were more likely to include male-only patients. As last authorship generally confers seniority and intellectual leadership, these data suggest that sex or gender biases held by the senior author, whether implicit or explicit, may influence the selection of case report patients

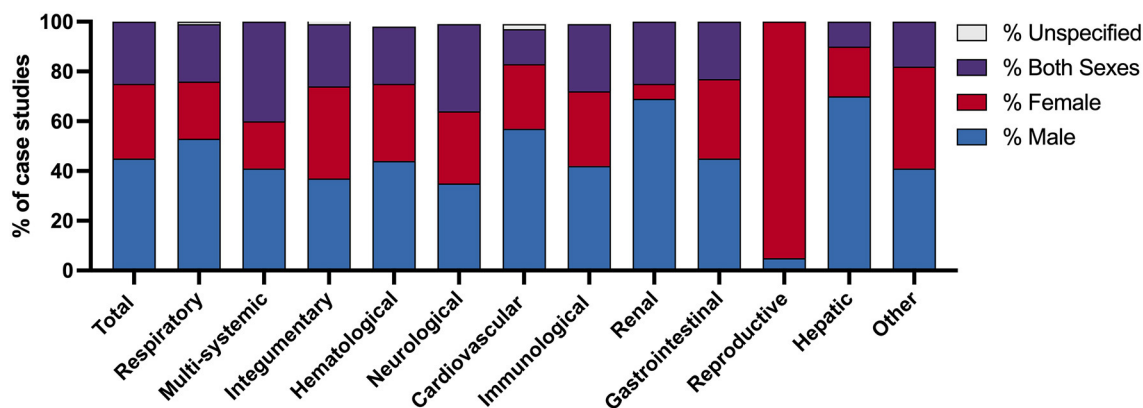


FIGURE 2 | Comparison of Covid-19 case studies by patient sex and physiologic body system. The percentage of Covid-19 case studies which describe patient sex as male, female, both sexes, and unspecified. Data are presented by the category of case study, coded by physiologic body system, as well as the sum of all case studies evaluated.

and reporting outcomes. The male-bias observed in Covid-19 case reports may be reflective of the patient population, as men who are diagnosed with Covid-19 are more likely to require hospitalization and critical care (26), however it does not fully explain the authorial differences in case report selection. The fact that female authors are more likely to include patients of both sexes is of interest and warrants further examination particularly in disease areas which are predominantly sex-specific.

This study is not without limitations. First, the sample size of case reports analyzed was limited due to stringent inclusion criteria related to journal impact factor and date of publication; although it is important to note that this sample size remains a significant and representative subset of the original sample of case reports. Journal impact factors of 5 and above were selected to represent case reports likely to be of medium-to-high visibility within the biomedical community. However, we recognize that journal impact factors are variable across biomedical disciplines and medical specialties and serve only as one metric to assess the quality, impact, and visibility of an article. As a result, case reports published in journals related to obstetrics and gynecology and reproductive health were likely omitted due to traditionally lower impact factors. The inclusion of case reports from women's health-related journals may have made the data appear more balanced and less suggestive of a sex-bias. Yet, by excluding these articles the data more broadly reflects sex and gender biases that exist outside of sex-specific fields of medicine, although we recognize that obstetric, gynecologic, and reproductive care is provided to those who identify across the gender spectrum.

In addition, these data were collected from the first 6 months of the Covid-19 pandemic, during which time the diagnosis, treatment, and understanding of the disease were rapidly evolving. We therefore cannot quantify the potential biases associated with clinical care that occurred later in the pandemic. The *in silico* tools to assign author gender also present another limitation as these are currently limited to gender binary options (male, female, or unknown) and therefore exclude or

misrepresent the identity of those who are gender non-binary, non-conforming, two-spirit, or third gender. Moreover, some case reports did not explicitly define patient's sex or gender. For coding purposes, patient sex for these was inferred through the use of terms such as man/woman, male/female, or descriptive he/she pronouns, and there may be instances where patient sex and gender identity do not correspond. Often the terms "sex" and "gender" were used interchangeably within case reports, making it difficult to separate patient's biological sex from their gender identity. The distinctions of both biological sex and gender should be noted in case reports, as gender is a contributing social determinant of health.

CONCLUSION

The associations between author gender and patient sex suggests that sex or gender biases are contributing factors which impact patient reporting. The coordinated efforts of clinicians, reviewers, editors, and publishers are required to ensure a balanced representation of the relevant patient population. Gender has been widely recognized as a social determinant of health and as such gender biases can contribute to gender-based health disparities. Diversification of the biomedical workforce appears to be critical, but rate-limiting factor, in reducing sex- and gender biases that permeate biomedicine. As more gender-diverse perspectives are included in the selection, writing, reviewing, and publishing of case reports, their subsequent quality, and educational value are likely to improve. Acknowledging and actively addressing biases may further a better understanding of the influences of sex and gender on health and disease, ultimately minimizing health disparities.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

NW: full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, obtained funding, administrative, technical, or material support, supervision, concept, and design. AS-V, AO, and NW: drafting of the manuscript. CY, LM, and NW: statistical analysis. All authors: acquisition, analysis, or interpretation of data and critical revision of the manuscript for important intellectual content.

REFERENCES

1. Woitowich NC, Beery A, Woodruff T. A 10-year follow-up study of sex inclusion in the biological sciences. *eLife*. (2020) 9:e56344. Available online at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7282816/> (accessed May 18, 2021). doi: 10.7554/eLife.56344
2. Shansky RM, Murphy AZ. Considering sex as a biological variable will require a global shift in science culture. *Nat Neurosci*. (2021) 24:457–64. doi: 10.1038/s41593-021-00806-8
3. Alcalde-Rubio L, Hernández-Aguado I, Parker LA, Bueno-Vergara E, Chilet-Rosell E. Gender disparities in clinical practice: are there any solutions? Scoping review of interventions to overcome or reduce gender bias in clinical practice. *Int J Equity Health*. (2020) 19:166. doi: 10.1186/s12939-020-01283-4
4. Hay K, McDougal L, Percival V, Henry S, Klugman J, Wurie H, et al. Disrupting gender norms in health systems: making the case for change. *Lancet Lond Engl*. (2019) 393:2535–49. doi: 10.1016/S0140-6736(19)30648-8
5. Huang J, Gates AJ, Sinatra R, Barabási A-L. Historical comparison of gender inequality in scientific careers across countries and disciplines. *Proc Natl Acad Sci*. (2020) 117:4609–16. doi: 10.1073/pnas.1914221117
6. Butkus R, Serchen J, Moyer DV, Bornstein SS, Hingle ST. Achieving gender equity in physician compensation and career advancement: a position paper of the american college of physicians. *Ann Intern Med*. (2018) 168:721–3. doi: 10.7326/M17-3438
7. Silver JK, Bean AC, Slocum C, Poorman JA, Tenforde A, Blauwet CA. Physician workforce disparities and patient care: a narrative review. *Health Equity*. (2019) 3:360–77. doi: 10.1089/health.2019.0040
8. Nissen T, Wynn R. The clinical case report: a review of its merits and limitations. *BMC Res Notes*. (2014) 7:264. doi: 10.1186/1756-0500-7-264
9. Allotey P, Allotey-Reidpath C, Reidpath DD. Gender bias in clinical case reports: a cross-sectional study of the “big five” medical journals. *PLoS ONE*. (2017) 12:e0177386. doi: 10.1371/journal.pone.0177386
10. Chen Q, Allot A, Lu Z. Keep up with the latest coronavirus research. *Nature*. (2020) 579:193. doi: 10.1038/d41586-020-00694-1
11. Chen Q, Allot A, Lu Z. LitCovid: an open database of COVID-19 literature. *Nucleic Acids Res*. (2021) 49:D1534–40. doi: 10.1093/nar/gkaa952
12. Santamaria L, Mihaljević H. Comparison and benchmark of name-to-gender inference services. *PeerJ Comput Sci*. (2018) 4:e156. doi: 10.7717/peerj-cs.156
13. Scully EP, Haverfield J, Ursin RL, Tannenbaum C, Klein SL. Considering how biological sex impacts immune responses and COVID-19 outcomes. *Nat Rev Immunol*. (2020) 20:442–7. doi: 10.1038/s41577-020-0348-8
14. Takahashi T, Iwasaki A. Sex differences in immune responses. *Science*. (2021) 371:347–8. doi: 10.1126/science.abe7199
15. Vahidy FS, Pan AP, Ahnstedt H, Munshi Y, Choi HA, Tiruneh Y. Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area. *PLoS ONE*. (2021) 16:e0245556. doi: 10.1371/journal.pone.0245556
16. Zahid U, Ramachandran P, Spitalewitz S, Alasadi L, Chakraborti A, Azhar M. Acute Kidney Injury in COVID-19 Patients: an inner city hospital experience and policy implications. *Am J Nephrol*. (2020) 51:786–96. doi: 10.1159/000511160
17. Filardo G, da Graca B, Sass DM, Pollock BD, Smith EB, et al. Trends and comparison of female first authorship in high impact medical journals: observational study (1994–2014). *BMJ*. (2016) 352:i847. doi: 10.1136/bmj.i847

FUNDING

This work was supported by a Women’s Health Access Matters Grant to NW. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

18. Kleijn de, Jayabalasingham M, Falk-Krzesinski B, Collins H, Kupier-Hoyng T, Cingolani LI, et al. *The Researcher Journey Through a Gender Lens: An Examination of Research Participation, Career Progression and Perceptions Across the Globe*. Elsevier (2020). Available online at: <http://www.elsevier.com/gender-report> (accessed May 19, 2021).
19. Hsiehchen D, Hsieh A, Espinoza M. Prevalence of female authors in case reports published in the medical literature. *JAMA Netw Open*. (2019) 2:e195000. doi: 10.1001/jamanetworkopen.2019.5000
20. Vincent-Lamarre P, Sugimoto C, Larivière V. *The Decline Of Women’s Research Production During The Coronavirus Pandemic*. Nature Index (2020). Available online at: <https://www.natureindex.com/news-blog/decline-women-scientist-research-publishing-production-coronavirus-pandemic> (accessed May 19, 2021).
21. Wehner MR, Li Y, Nead KT. Comparison of the proportions of female and male corresponding authors in preprint research repositories before and during the COVID-19 pandemic. *JAMA Netw Open*. (2020) 3:1–4. doi: 10.1001/jamanetworkopen.2020.20335
22. Andersen JP, Nielsen MW, Simone NL, Lewiss RE, Jaggi R. COVID-19 medical papers have fewer women first authors than expected. *eLife*. (2020) 9:e58807. doi: 10.7554/eLife.58807
23. Lerchenmüller C, Schmallenbach L, Jena AB, Lerchenmueller MJ. Longitudinal analyses of gender differences in first authorship publications related to COVID-19. *BMJ Open*. (2021) 11:e045176. doi: 10.1136/bmjopen-2020-045176
24. Nielsen MW, Andersen JP, Schiebinger L, Schneider JW. One and a half million medical papers reveal a link between author gender and attention to gender and sex analysis. *Nat Hum Behav*. (2017) 1:791–6. doi: 10.1038/s41562-017-0235-x
25. Sugimoto CR, Ahn Y-Y, Smith E, Macaluso B, Larivière V. Factors affecting sex-related reporting in medical research: a cross-disciplinary bibliometric analysis. *Lancet*. (2019) 393:550–9. doi: 10.1016/S0140-6736(18)32995-7
26. Gomez JMD, Du-Fay-de-Lavallaz JM, Fugar S, Sarau A, Simmons JA, Sanghani RM, et al. Sex Differences in COVID-19 Hospitalization and Mortality. *J Womens Health (Larchmt)*. (2021) 30:646–53. doi: 10.1089/jwh.2020.8948

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher’s Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Salter-Volz, Oyasu, Yeh, Muhammad and Woitowich. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



A Perspective on Intimate Partner Violence Since COVID-19

Raveed Khan* and Syriah David

Department of Paraclinical Sciences, University of the West Indies, St. Augustine, Trinidad and Tobago

Keywords: partner abuse, COVID-19 pandemic, intimate abuse, Trinidad and Tobago, primary care (MeSH)

OPEN ACCESS

Edited by:

Hamid Allahverdipour,
Tabriz University of Medical
Sciences, Iran

Reviewed by:

Shuchita Ramesh Mundle,
All India Institute of Medical Sciences
Nagpur, India
Mallory Williams,
Howard University, United States

*Correspondence:

Raveed Khan
raveed.khan@sta.uwi.edu

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 01 October 2021

Accepted: 18 November 2021

Published: 08 December 2021

Citation:

Khan R and David S (2021) A
Perspective on Intimate Partner
Violence Since COVID-19.
Front. Glob. Womens Health
2:788061.
doi: 10.3389/fgwh.2021.788061

The advent of the COVID-19 pandemic saw the introduction of many unprecedented actions occurring within our communities and by extension our country. Whilst many of us may have heard the term pandemic before, few would have had the knowledge or experience of the measures that were taken to contain coronavirus in our country. The introduction of lockdown measures such as the closure of public places like bars restaurants, malls, places of worship, gyms, spas and beauty services, casinos, cinemas (1); as well as, stay-at-home orders like working from home for non-essential persons and closure of all schools were just a few of the measures that were put into place to help curb the spread of COVID-19. The ramifications of these measures would pan out over time with some becoming apparent earlier than others and with grave consequences, particularly, an increase in acts of intimate partner violence.

Intimate partner violence is sometimes referred to as domestic violence since a large number of acts committed by perpetrators occur in the home. Locally, in Trinidad and Tobago prevalence rates as high as 41% have been reported with alcohol and drug abuse being cited as the leading cause (2). In 2017 alone the Trinidad and Tobago Police Service (TTPS) reported that there were 1,100 reports of domestic violence with 43 murders linked to domestic violence. According to the August 2020 report from the Trinidad and Tobago Central Registry on Domestic Violence, there were 7,594 reports related to domestic violence between the period 2014 to 2019. Approximately 75% of these reports were related to female victims. In 2019, there were 232 reports of domestic violence with 81% of reports being made by women, where 48.5% were between 30 to 49 years of age and 22.5% of women were between 18 to 29 years of age. In 2020, there were 556 cases of domestic violence that were reported. During the period of January to March 2021, there were 826 reports of domestic violence (3).

Based on these findings it would appear that COVID-19 created a milieu conducive for a domestic violence surge with the background of an existing high prevalence rate compounded by confinement and possibly increased consumption of alcohol and drugs at home. The Centres for Disease Control and Prevention (CDC) highlights individual, relational, community and societal risk factors for domestic violence. These risk factors include common themes such as heavy alcohol and drug use, economic stress (for example, unemployment), having few friends, being isolated from other people and a desire for power and control in relationships (4). Alcohol use/abuse in particular has been associated with male-to-female partner violence (5). Alcohol plays a key role in the power and control wheel concept by increasing the user's sense of personal power and domination over others. An increased sense of power and control can, in turn, make it more likely that an abuser will attempt to exercise that power and control over another (6).

The power and control wheel can also be turned through isolation and economic abuse. Isolation of the victim is further enhanced by stay-at-home measures aimed at preventing the spread of COVID-19, but also trapping victims of domestic violence with their abusers. Notwithstanding communication technologies, there are also physical constraints on the victim preventing them from accessing direct in person support and retreat to the safety of family, friends and shelters. Behaviours such as constant surveillance and enforcement of rigid rules by perpetrators serve to fuel the isolation and propagate acts of violence in the home. The potential for economic abuse has

also increased since the pandemic due to the effects of job-losses, furloughs, reduced working hours and general declines in economic activity. Consequently perpetrators' financial stresses coupled with the propensity to consume alcohol as an escape, create a highly charged home environment with acts of violence becoming likely possibilities. In addition, some victims of domestic violence are financially dependent on their abusers, therefore making it difficult for them to leave these home environments. Local data reported by UN Women suggests that as of December 2020, only 39.3% of indicators needed to monitor the sustainable developmental goals (SDGs) from a gender perspective were available. There were gaps in key areas such as unpaid care and domestic work, and information on the gender pay gap. However, it can be noted that the unemployment rate among women over 15 years of age was found to be 6.3% compared to 4.6% of men in the same age range (7).

The concept of male privilege may have also been strengthened during the COVID-19 pandemic as men occupying supervisory and managerial roles at their workplaces have become day to day bosses at home thereby increasing their tendency to act like masters of the castle and relegating the woman's role to that of a servant. Indeed, this domination and control through the use of male privilege plays a significant role in male abusers who often consider abusive behaviour as a right and a privilege. A Trinidadian qualitative report revealed that male dominance in the family is a key factor creating a risk of violence. Controlling behaviours such as isolation tactics, accusations, threats and stalking also highlight the relationship between male dominance in the family and multiple, intersecting forms of violence. Accusation by partners is common, repetitive and used to precipitate threatening, hitting, slapping, cursing and choking (8).

Tactics used to maintain power and control through the use of male privilege in the context of COVID-19 were highlighted by the Battered Women's Justice Project. These tactics include violation of others' personal space, using all the work and study areas in the home, disrupting routines and refusing to share the computer (10).

The COVID-19 pandemic in itself can be leveraged by perpetrators. Indeed those suffering from domestic violence may be less inclined to go to the hospital on account of fear of infection. Ultimately, the social distancing, albeit essential to

contain COVID-19, may exacerbate the violence and maintain it less visible (9). Usher et al. also reported that COVID-19 is used as a coercive control mechanism whereby perpetrators exert further control in an abusive relationship, specifically in the use of containment, fear, and threat of contagion as a mechanism of abuse (11).

Increased acts of sexual violence have also been documented during this pandemic. A UK and Kenyan based study reported that Sexual and gender-based violence (SGBV), and particularly intimate partner violence (IPV), had spiked dramatically during the COVID-19 pandemic (12). India noted a surge of porn usage and sale of condoms and sex toys, reflecting increase in sexual activity thereby indirectly indicating increase in chances of sexual rights violation (13).

As a family physician, it is my view that we make the best use of the limited resources available to us to protect our population from the scourge of domestic violence that is accompanying the COVID-19 pandemic. Now more than ever comes the time for innovation and tact in the implementation of measures to screen, guide and act definitively to protect the victims of domestic violence. Toward this end, the WHO's ALIVES framework for inquiring and responding to a disclosure of domestic violence serves as a primer for facilitating disclosure, validating concerns and enhancing safety and support (14).

This framework can perhaps best be implemented through the use of telehealth which has now become a standard of care in order to mitigate against COVID-19. It is well-documented that women and children are the main seekers of health care. As health care providers, we must capitalise on that by tactfully screening for domestic violence during virtual encounters through the use of safe words or even advice on the wearing of certain colours of clothing as a signal that a survivor is concerned about their risk (15).

As a society we must never condone acts of domestic violence. Rather, we should seek to educate the victims about avenues for relief and try our best to dissuade perpetrators by creating a supportive environment especially in the era of COVID-19.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

REFERENCES

- Office of the Prime Minister–Republic of Trinidad and Tobago. *Prime Minister's Media Conference–Thursday 29th April, 2021*. Office of the Prime Minister–Republic of Trinidad and Tobago. Available online at: <https://www.opm.gov.tt/prime-ministers-media-conference-thursday-29th-april-2021/>
- Nagassar RP, Rawlins JM, Sampson NR, Zackerali J, Chankadyal K, Ramasir C, et al. The prevalence of domestic violence within different socio-economic classes in Central Trinidad. *West Indian Med J*. (2010) 59:20–5.
- Cox D. *Statement by Senator the Honourable Donna Cox, Minister of Social Development and Family Services on Incidence of Violent Crimes Against Women and Girls*. (2021). Available online at: <http://www.social.gov.tt/wp-content/uploads/2021/04/Statement-on-Violent-Crimes-Against-Women-and-Girls-April-27th-2021.pdf>
- Centers for Disease Control and Prevention. *Risk and Protective Factors for Perpetration*. (2021). Available online at: <https://www.cdc.gov/violenceprevention/intimatepartnerviolence/riskprotectivefactors.html>
- Foran HM, O'Leary KD. Alcohol and intimate partner violence: a meta-analytic review. *Clin Psychol Rev*. (2008) 28:1222–34. doi: 10.1016/j.cpr.2008.05.001
- Boodram A. *Alcohol is not a Root Cause for Abuse" It's a Trigger*. The Caribbean Voice (2019). Available online at: <https://www.caribbeannewsglobal.com/alcohol-is-not-a-root-cause-for-abuse-its-a-trigger/>

7. UN Women. *Americas-Trinidad and Tobago*. (2021). Available online at: <https://data.unwomen.org/country/trinidad-and-tobago> (accessed November 15, 2021).
8. UN Women. *Gender-Based Violence in Trinidad and Tobago. A Qualitative Study*. (2018). Available online at: <https://www.undp.org/content/dam/unct/caribbean/docs/20181011%20AF%20Trinidad%20and%20Tobago%20Health%20for%20digital.pdf>
9. Battered Women's Justice Project. *Covid-19 Tactics*. Available online at: <https://www.bwjp.org/news/covid-coercive-control-wheel-combined.pdf>
10. Pedrosa AL, Bitencourt L, Fróes ACF, Cazumbá MLB, Campos RGB, de Brito BCS, et al. Emotional, behavioral and psychological impact of the Covid-19 pandemic. *Front Psychol.* (2020) 11:566212. doi: 10.3389/fpsyg.2020.566212
11. Usher K, Bhullar N, Durkin J, Gyamfi N, Jackson D. Family violence and COVID-19: increased vulnerability and reduced options for support. *Int J Mental Health Nurs.* (2020) 29:549–52. doi: 10.1111/inm.12735
12. Johnson K, Green L, Volpellier M, Kidenda S, McHale T, Naimer K, et al. The impact of COVID-19 on services for people affected by sexual and gender-based violence. *Int J Gynecol Obstetr.* (2020) 150:285–7. doi: 10.1002/ijgo.13285
13. Malathesh BC, Das S, Chatterjee SS. COVID-19 and domestic violence against women. *Asian J Psychiatr.* (2020) 53:102227. doi: 10.1016/j.ajp.2020.102227
14. World Health Organization. *Caring for Women Subjected to Violence: A WHO Curriculum for Training Health-Care Providers*. Geneva: WHO (2019).
15. Neil J. Domestic violence and COVID-19: our hidden epidemic. *Aust J Gen Pract.* (2020) 49 (Suppl. 25). doi: 10.31128/AJGP-COVID-25

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Khan and David. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Isolation in COVID, and COVID in Isolation—Exacerbated Shortfalls in Provision for Women's Health and Well-Being Among Marginalized Urban Communities in India

Lakshmi K. Josyula^{1,2,3*}, Shrutika Murthy⁴, Himabindu Karampudi⁵ and Surekha Garimella^{2,4,6}

¹ The George Institute for Global Health, Hyderabad, India, ² Prasanna School of Public Health, Manipal Academy of Higher Education, Manipal, India, ³ University of New South Wales, Sydney, NSW, Australia, ⁴ The George Institute for Global Health, New Delhi, India, ⁵ Dalit Bahujan Resource Centre, Guntur, India, ⁶ Institute of Public Health, Bengaluru, India

OPEN ACCESS

Edited by:

Vijay Kumar Chattu,
University of Toronto, Canada

Reviewed by:

Paula Munoz Venturelli,
Universidad del Desarrollo, Chile
John Koku Awoonor-Williams,
Ghana Health Service, Ghana

*Correspondence:

Lakshmi K. Josyula
ljakshmi@georgeinstitute.org.in

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 01 September 2021

Accepted: 29 November 2021

Published: 04 January 2022

Citation:

Josyula LK, Murthy S, Karampudi H and Garimella S (2022) Isolation in COVID, and COVID in Isolation—Exacerbated Shortfalls in Provision for Women's Health and Well-Being Among Marginalized Urban Communities in India. *Front. Glob. Womens Health* 2:769292. doi: 10.3389/fgwh.2021.769292

This paper describes the lived experiences of health seeking, health care recourse, and well-being of women waste pickers, a highly marginalized sub-population in urban areas in India, highlighting the intersectionality of gender, socioeconomic and cultural contexts, and occupational hazards that they face, as studied by a research team engaged in participatory action research with waste workers in urban India. We note the impact of the superimposition of the COVID-19 pandemic, with the restrictions on movement and access to livelihoods, social support, and health care, and policies made and enforced in a fragmented manner, on the already deprived conditions of the waste pickers. We reflect on the women waste pickers' practices of health seeking, their access to health care, the provisions made for them and made use of by them, and the support they could tap in protecting and restoring their health. A range of these experiences is illustrated through three case studies. Finally, recommendations are made for better provision for women's health and well-being, and improved preparedness for emergency situations.

Keywords: lived experiences, women waste pickers, COVID-19, health and well-being, marginalized urban communities, India

INTRODUCTION

Working with waste in urban areas in India comprises a wide range of occupations, from street cleaning, to door-to-door garbage collection, to picking, sorting, sale, and processing of reusable and recyclable waste from streets and dumps (1); and various degrees of formality of employment, from regular government jobs, to fixed-term contracts with the government or private organizations, to informal self-employment. Waste workers generally belong to marginalized urban communities facing multiple social, economic, and occupational disadvantages (2, 3).

Waste workers' experiences of seeking and practising livelihoods, protecting and restoring health, and interacting with community members evince intersectionality of gender, caste, religion, region of origin and migration status, language, and nature of employment (regular, contractual, informal, or self-employed) (3). The challenges posed by the COVID-19 pandemic have been superimposed on the pre-existing privations faced by waste picker communities. In

particular, the experiences of, and challenges faced by, women in the waste picking communities, which demonstrate the concurrent and compounded impacts of gender, socioeconomic status, cultural identity, and occupation, have tended to be grouped without adequate disaggregation with the experiences of all waste workers, or worse, all socioeconomically disadvantaged urban communities.

WHAT WE DID

Accountability for Informal Urban Equity (ARISE) (4) is a consortium of interdisciplinary research hubs across Africa, South Asia, and the United Kingdom, working on addressing the challenges of ill-health, inequity, and insecurity in informal urban settlements in low- and middle-income countries (LMICs), through participatory research and community action to build government accountability, and inform policy change. At the George Institute for Global Health, India, one of the ARISE hubs, we focus our work on waste workers across three states in India, through partnerships with civil society organizations working with the communities in these action sites.

Over the course of our work on the ARISE project, we conducted a review of the literature on waste workers, with an emphasis on waste pickers in the informal sector. We engaged in participant and non-participant observation, interviews, focus group discussions, community meetings, and workshops with waste picker communities, and civil society organizations, to understand the lived experiences of waste pickers, and the physical, social, and policy environments that they live and work in. We undertook a detailed policy landscaping exercise, including key informant interviews, to review policies related to the health, health care recourse, occupational health and safety, and social security of waste workers. Further, we examined 97 COVID-19 specific policies made by the Indian central and state governments, and analyzed policies that pertained to the health, security, livelihood, and well-being of disadvantaged urban communities.

WHAT WE FOUND

Preliminary learnings from our review of the literature highlight waste workers' position among the most disenfranchised, marginalized, and oppressed communities in India (5). Women waste workers, in particular, experience excessive discrimination and precarity, shouldering multiple burdens arising from gendered division of labor and informal work arrangements, having inadequate access to sexual and reproductive health opportunities and care, and being invisible in existing leadership spaces (6–9).

While there are no clear estimates on how many women are involved in waste work, the information that is available from some cities indicates that women constitute up to 70–90% of this workforce (10). Low literacy levels and pre-existing gender differentials make occupational mobility for women waste workers more difficult than for men (11, 12). Even

within the waste-to-recovery chain, positions of authority are predominantly occupied by men (13–15). Women waste workers in India tend to perform the most physically arduous tasks, are predominantly engaged in informal work contracts or are own account workers, and get trapped in exploitative arrangements (11). Consequently, they are often not recognized as “workers,” and are thereby excluded from attaining and accessing social security and welfare schemes. These vulnerabilities of women waste workers are insufficiently examined in scholarship on gender, labor, informal work, the waste economy, and health systems. Research on the health and well-being of women waste workers is mostly limited to a few discrete studies on occupational health and safety (16–18). There is a dearth of relational, intersectional, and contextual research that explores and understands the health and well-being concerns and embodied experiences of women waste workers.

In the advent of the COVID-19 pandemic, the federal and state governments in India developed a slew of orders, guidelines, and rules to deal with the disease and its impact (19). Issues specific to COVID-19 that found mention in policies were containment, including lockdowns; testing; stranded persons, particularly migrants, students, and pilgrims; waste management, especially disposal; discrimination, and inhumane treatment of persons in the pandemic; and specific groups of persons, e.g., senior citizens, vulnerable to COVID-19 infection and complications. However, most of the social assistance schemes were directed at population groups that were broadly categorized as “poor” and “vulnerable.” The majority of the policies did not apply to the specific precarities and vulnerabilities faced by waste workers in the informal sector, but were aimed at assuring food and shelter to those who had lost their livelihoods in the pandemic. This included schemes for the provision of relief kits and meals, but these too were limited to a 3-month period at the beginning of the lockdown in 2020. Most of the policy announcements were built on to pre-existing schemes (see **Supplementary Material 1** for a list of policies pertaining to waste workers) and did not adequately address the impact of loss of work, hunger, and inability to access health care.

Some state governments in India provided financial assistance to all frontline workers, including sanitation workers, who were involved in the efforts against COVID-19, and thereby had disproportionate exposure to the disease. Among waste workers, only tenured or regular sanitation workers engaged in the cleanliness and upkeep of cities had policies specifically addressing their health insurance, financial incentives, and personal protective equipment (PPE) requirements. We noted no reference or provision for waste workers in informal employment, particularly migrant workers who lacked government-issued documentation. While many of the policies developed and enforced to address the transmission of COVID-19 were sound in biological and epidemiological terms, they failed to take into account the lives, and especially the constraints, faced by disadvantaged communities, leading to situations in which people found themselves protected to some extent from COVID-19, but vulnerable to loss of livelihoods, precarious nutritional intake, disrupted social interaction and support, and violence.

"If the NGO had not helped us with relief packages, we would have died of starvation, not corona."—informal waste picker, Andhra Pradesh.

Pre- and Intra-Pandemic Experiences of Health Recourse

The pre-COVID-19 scenario of women waste pickers' health seeking, provision, and access was one of lack of awareness of services, such as antenatal check-ups, nutrition supplementation, vaccination, maternity/sick leave; hesitation to access health protection, screening, and curative services; difficulty in accessing health care owing to conflicting occupational and family priorities, administrative requirements, and pragmatic needs, such as of transport; and adverse experiences of poor quality care and hostility in interactions with the health system. Support from civil society organization champions as well as community health volunteers was acknowledged as essential to shepherd women through the health system. Some families had availed themselves of the provisions offered by governments for the care of children in government hostels, and for education and nutritional supplementation for community-dwelling children, while many families were unable to access these provisions owing to administrative hurdles that they could not overcome.

In the course of the pandemic, restrictions applied to prevent and contain COVID-19 impeded women's lives, livelihoods, and their families' health and well-being. With the lockdowns imposed early in the pandemic, children from disadvantaged communities had to return home from government hostels which supported their boarding, lodging, and educational expenses. The switch of residence from hostels to parents' homes meant that all expenses on the children switched abruptly to the unprepared parents, whose livelihoods had been stalled at the same time. Relief measures proposed and implemented by government, civil society organizations, and individual philanthropists were helpful, but piecemeal, and did not reach all in need. Households were compelled to incur loans, and experienced further compromised nutrition, and further impaired access to information. COVID-19 screening and treatment were associated with fear, misinformation, stigma, and adverse impact on the care of family members. Routine or emergent non-COVID-19 healthcare were affected in these communities, with health care facilities out of bounds, health care providers under pressure, and transport exorbitantly priced. The burden of care as well as the brunt of the distress and vulnerability to violence within the home fell to women.

Health Problems Frequently Encountered by Women Waste Pickers

Most waste pickers in the informal sector cannot afford protective gear, making them vulnerable to mechanical, chemical, and biological injuries. Considering that activities that involve direct contact with mixed waste are predominantly carried out by women and that too by informal workers, they are the persons who need PPE the most but are least likely

to have and use them. The few waste workers who do use some protective equipment are generally provided them by their employers.

Most women report acute or chronic pain in one or more parts of their body, including the head, eyes, arms, stomach, pelvic region, knees, and legs. Women often neglect such pain and sickness until they cannot function without treatment, at which point they take recourse to local pharmacies, private or government clinics, or local health traditions and home remedies. Some women, despite having health cards issued by the state government, are disinclined toward seeking care at government health care facilities on account of the waiting periods and adverse interactions involved at these institutions.

Women waste pickers have practically no access to civic amenities such as toilets while they are working. They are forced to constrain their toilet use to before and after work timings, a situation that is especially inconvenient during menstruation. Menstrual hygiene management is a highly neglected aspect of waste pickers' health, with shortfalls in awareness, affordability, safe storage, and amenities for use, changing, post-use treatment of reusable menstrual absorbents, and disposal of one-time use products.

Gynecological morbidities leading to repeated sickness, chronic anemia, and impaired functioning, and paving the way to surgeries such as hysterectomy, are common. Antenatal check-ups and institutional deliveries are not the norm among waste picker women. Pregnant women work until a few days before childbirth, and return to work within about a month after childbirth, taking the infant with them or leaving the infant at home with a caretaker, if any. Longer periods of post-partum rest at home represent lost income, and are not sought.

Waste pickers experience constant insecurity during work, as they perceive that residents suspect them of thieving. Many waste pickers report having to check in at the local police station every week in the course of police cases lodged against them by residents. During the pandemic, waste pickers observe that they are shunned as potential disease-transmitters by residents of the areas that they work in, making it additionally difficult for them to obtain work. Women in waste picker communities, besides experiencing several forms of social and structural violence and neglect, are also exposed to domestic violence perpetrated by drunk men.

Case Studies

We illustrate some of these findings through case studies of women waste pickers' experiences in health management and healthcare recourse, from two states in India. Topics explored in our discussions and observations included: the current intra-COVID-19 situation of family and social support, engagement with civil society organizations, and awareness of government health services; how the intra-COVID-19 situation differed from the pre-COVID-19 one in terms of policy, implementation, provision, and financial and social support; the impact on work and income; and needs—met and unmet—related to services, amenities, security, and equity.

Case study 1: Shivani*, 44, Andhra Pradesh

Shivani was married at the age of 15, and had three children in quick succession. She has always been the primary breadwinner of the family. Her alcoholic husband not only did not contribute to the household, but spent a large proportion of her earnings on alcohol besides. In her mid-twenties, she suffered painful and heavy menstruation, which she tried to keep at bay with over-the-counter painkillers as she continued to work despite her pain and discomfort. She put off check-ups and hospital visits to save time and money, until her condition became too serious to ignore. Finally, she visited a hospital where a severe uterine infection was diagnosed, and the doctor expressed the potential risk of cancer if the problem continued unchecked. She underwent hysterectomy in a private hospital at the age of 26. She received moral and financial support from her parents through this crisis. Post-hysterectomy, Shivani is relieved that she is enabled to work all month without any constraints posed by menstruation.

Three years ago, she had typhoid and fell unconscious while working. She got admitted to a government hospital where she underwent multiple tests, and was diagnosed with diabetes. While the consultation was of free of cost, she had to bear the medication expenses, although medications are notionally to be made available free of cost too (20). Shivani found herself in the quandary of taking medication to control blood sugar levels, but not having enough food to eat commensurate with the medication. Over time, she developed low blood pressure and had seizures at times while at work. She cultivated a routine of regular check-ups at the government clinic, and replenishing her medications at a private pharmacy (21). Her deteriorating health left her capable of work only about half the month.

The lockdowns occasioned by the COVID-19 pandemic placed critical constraints on Shivani's livelihood and slashed her income drastically as access to waste picking was not allowed in many parts of the city. In parallel, as a measure to tackle the pandemic, (formally employed) municipal workers were instructed to step up their waste collection activities, leaving practically no scope for informal waste pickers to work. An additional obstacle that waste pickers faced was the hostility that residents expressed, viewing waste pickers as potential disease-transmitters.

With the reduction in income, the entire family's nutrition worsened. Even the infrequent relief packages from the government, NGOs, and individual philanthropists could not fulfill all the household's needs. The lockdowns affected Shivani's healthcare routine adversely as well: the government hospital did not allow patients inside the facility, and the patients did not feel as well-treated by the doctors as they had in pre-COVID-19 consultations. The regularity of Shivani's tests for diabetes was affected, with the interval between tests prolonged to 2–3 months.

In the past 2 months, Shivani has had a further health setback: An inch-long nail from the waste she was picking through, pierced her foot and led to a non-healing wound, which comes in the way of her walking, and therefore working. Besides the impact of this on the fulfillment of her immediate needs, Shivani is apprehensive about its implications for her ability to repay the debts that she incurred in the past few years for the celebration of her daughters' weddings. She reports that her sleep is disturbed nightly with these worries, and that her peace of mind is lost. She seeks support for an alternative livelihood, such as vegetable vending, which would not require her to walk a lot, to help her get back on track with earning, and ideally, saving.

Case study 2: Saroj*, 24, Himachal Pradesh

Saroj was born in Shimla, into a migrant family of manual laborers from Nepal. In childhood, her family kept traveling between Nepal and Shimla, as her parents' work assignments dictated. The continual shifting affected the continuity of her education, which she, although a good student, had to give up when she was around 12 years of age to take up manual labor to contribute to the household income.

Saroj got married at the age of 14 years, and was pregnant with her first child at 16, although she lied about her age for fear of admonishment from health care providers for marrying and getting pregnant so young. Based on this encounter with the health system, her Aadhar card (an identity card issued by the government of India) reflects an older age.

All three of her children were delivered in government hospitals, however, her experiences of care were not uniform. Despite undergoing routine ante-natal check-ups at the government hospital, Saroj was not aware of the requirement of an HIV test prior to admission for labor. She was denied admission to a government hospital for women and children on grounds of not having been tested for HIV. She was rushed by her family to another government hospital for delivery as she was already in labor and needed care urgently. The requirements for admission differed between these government hospitals.

After her third delivery, Saroj suffered a degree of uterine prolapse, for which she sought the help of a local masseuse, who administered a brief massage to adjust the position of her uterus. Saroj, who was engaged in manual labor, found that lifting and carrying loads aggravated her uterine prolapse. She switched to office cleaning, a job that did not involve lifting and carrying loads. However, the long working hours came in the way of childcare, especially since she was the only adult in the household on a regular basis, as her husband lives and works at an orchard around 2 hours away. Saroj then switched to door-to-door garbage collection, which has more convenient work timings. However, this job involves lifting and carrying loads across hilly terrain, aggravating her uterine prolapse, and necessitating frequent visits to the masseuse.

Both Saroj and her husband contracted COVID-19 in the second wave of the pandemic. Saroj had had a fever and cough for about a week, through which she continued to work to ensure uninterrupted income, before the death of one of her neighbors prompted the local health workers to set up a testing camp in their locality. On testing, Saroj and her husband were found to be COVID-positive. The local Primary Health Centre as well as the community health volunteer coordinated their care at this time, delivering medication and facilitating tests. The local government doctor and community health volunteer also coordinated continued support of the COVID-positive community members through a WhatsApp group for follow-up and query resolution. Saroj had certain incorrect beliefs about the course of COVID-19, such as that perspiration caused by ambient heat would eliminate the disease. Saroj's family of five had to undertake isolation as a unit, although the children were not infected, as they did not have the resources to quarantine the children elsewhere. Their living arrangements are such that although each household has access to a separate toilet and bathroom, the access is through a common corridor. So, the family had to exert constant caution to isolate from neighbors. Saroj and her husband had a harrowing time dealing with their own sickness, and their worries about the children's susceptibility to COVID-19 as well as their future vulnerability in the event of the loss of their parents from COVID-19.

Saroj's children were going to school before the pandemic. Online classes were not a feasible and sustainable option for Saroj. She enrolled her children for private tutoring with a local teacher, but is distressed to note that the teacher is very harsh about punishment for schoolwork not done as specified. However, Saroj has no other affordable option for her children's education at this time.

Besides her gynecological troubles, Saroj suffers frequent headaches, for which she uses over-the-counter painkillers or home remedies of spiced oil. She also experiences distress in encounters with some residents in her work zones, who sometimes make discriminatory remarks about her occupation of garbage collection, which stings her. Saroj derives a sense of belonging and social support in her community that has a shared history of migration from Nepal, and tends to be isolated from other communities.

Case study 3: Srilatha*, 30, Andhra Pradesh

Srilatha lives in a makeshift settlement a few meters from a dump yard. After an early marriage in her teens, she had two daughters, whom she gave birth to at home. She reports that her pregnancies and childbirth were uneventful, and that her children were healthy. Three years ago, her husband took their daughters away and deserted her. She migrated to the settlement next to the dump yard then, and has had no contact with her husband or her children since. Srilatha heard recently that her younger daughter is dead, however, she does not know the circumstances of her death.

Two years ago, Srilatha began living with a 42-year old man who had been abandoned by his wife. She became pregnant during the COVID-19 pandemic. She did not have any routine antenatal check-up, and was not eligible for any government-sponsored benefits at the Anganwadi center (for supplemental nutrition) for want of documentation. Srilatha had made no plans for an institutional delivery. However, she unexpectedly went into labor in the 7th month of pregnancy, and got admitted to a government hospital with the assistance of NGO volunteers. Although she underwent normal labor and delivery, the baby was stillborn. The doctors explained that the baby had died in the womb from an infection. Srilatha attributes the death of her unborn child to her "negligence," which is how she describes her regimen of low priority for cleanliness, nutrition, and rest, and steady routine of waste picking throughout her pregnancy. She rues the low level of personal and environmental hygiene that she can reasonably maintain in waste picking and living next to a dump yard, with no access to civic amenities.

To compound Srilatha's distress, the nurses at the hospital refused to hand over the body of her stillborn child to her without receiving some payment, as bribe. The intervention of the NGO volunteer, who was not unused to the demand for bribe for the handover of babies to mothers at the hospital, ensured that Srilatha got her baby's body without having to expend money for it.

Srilatha declares that she is not bothered about contracting COVID-19 or any other disease. She is completely against the formal healthcare system itself, and believes that hospitals are unsafe and unaffordable. She prefers local health traditions to address any sickness she suffers, and to give birth at home rather than in hospital. Had the NGO volunteers not been available to assist her, she would have given birth at home again rather than undergo the difficult process of hospital admission without government-issued documents, and have to incur transport and other expenses as well.

Srilatha considers herself tough and resilient, mentally and physically. She believes that this hardiness is critical to her daily toil to support herself and her family. She recounted her return to waste picking in a week after her delivery and child's death in the womb, as "nothing should stop [her] from working."

*Names changed to preserve anonymity.

DISCUSSION

Women waste pickers demonstrate intersectionality of multiple disadvantages in their personal, social, and occupational lives. Their deprived educational and sociocultural backgrounds predispose them to low health awareness, and their low autonomy leaves them with very little agency and behavioral control in the face of high vulnerability and varied responsibilities.

The health and well-being needs of women waste pickers are not understood and addressed adequately. They are often clubbed with the occupational pitfalls common to men and women, without regard to the differential experiences based on sex and gender. This is particularly problematic considering that the genders are non-uniformly divided among the range of activities in waste work. Certain activities, such as picking recyclable waste on the streets and in dump yards, are disproportionately performed by women, and their execution needs to take into account the other health and civic conditions of women, rather than be considered as a neutral human response to exposure to particular physical, chemical, or biological hazards.

Health and well-being are an early casualty in emergency situations affecting entire populations, such as the COVID-19 pandemic, but also in the frequent and varied crises endured by communities and individuals experiencing multiple disadvantages and living and working in precarious conditions. Economic challenges clearly move the health and well-being of all household members down the list of priorities. Further, the lowest priority is accorded to the health and well-being of girls and women, often by themselves too. The pervasive sociocultural norms prioritizing men, particularly those engaged in earning for the household, persist in the communities of waste workers notwithstanding the frequent occurrence of

unemployment in males, and the disproportionate burden of economic, social, and nurturing support falling on the female household members.

Recommendations

Our pre- and intra-pandemic studies highlight the imperative to assure the following basic facilities for the health and well-being of waste picker (and other) women:

- civic amenities, including secure housing, electricity, water, and sanitation facilities;
- livelihood security, through registration, recognition of waste work, and assurance of wages;
- access to reproductive and child health, including menstrual hygiene management, antenatal care, institutional delivery, immunization, and nutrition;
- education;
- health care, encompassing health protection, disease and injury prevention, health promotion, and therapeutic options;
- occupational safety, including the provision and enforcement of PPE use, and regular check-ups for secondary prevention of occupational disorders;
- security from crime, and intentional injuries; and
- opportunities for social participation.

In addition, societies need to recognize the vital contributions of waste workers in ensuring the cleanliness of urban areas and environmental sustainability. In a context of such institutionalized provision and societal sensitization, responding effectively and equitably to a crisis such as a disease outbreak or natural disaster would not deprive disadvantaged girls and women of essential health access as the response to the COVID-19 pandemic has.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethics clearance for this work was obtained from the Liverpool School of Tropical Medicine Research Governance and Ethics Office, and the Institutional Ethics Committee, The George Institute for Global Health, India. Participants provided written informed consent for participation in this study.

AUTHOR CONTRIBUTIONS

LJ drafted and revised the manuscript. SM contributed to a case study and to manuscript revision. HK contributed to two case studies. SG guided the development of the manuscript. All authors engaged in data-collection, analysis, and interpretation of findings.

REFERENCES

- Government of India, Ministry of Environment and Forests. *Solid Waste Management Rules*. (2016). New Delhi: Government of India, Ministry of Environment and Forests.
- Bose R, Bhattacharya A. *Why Ragpickers, Unrecognized and Unpaid, Are Critical for Waste Management in India*. (2017). Available online at: www.indiaspend.com/why-ragpickers-unrecognised-and-unpaid-are-critical-for-waste-management-in-india-43164 (accessed July 5, 2021).
- Josyula, KL, Nakkeeran, B, Murthy, S, Whittaker, L, Botlagunta, R, Sai, V, et al. *Health and Well-Being of Waste Workers in India. Policy Brief*. Available online at: <https://www.georgeinstitute.org.in/health-and-well-being-of-waste-workers-in-india> (accessed September 1, 2021).
- Accountability for Informal Urban Equity (ARISE). *The George Institute for Global Health*. Available online at: www.georgeinstitute.org.in/projects/accountability-for-informal-urban-equity-arise (accessed July 6, 2021).
- Harriss-White B. Waste, social order, and physical disorder in small-town India. *J Dev Stud.* (2020) 56:239–58. doi: 10.1080/00220388.2019.1577386
- Hunt C. Child waste pickers in India: the occupation and its health risks. *Environ Urban.* (1996) 8:111–8. doi: 10.1177/095624789600800209
- Marques CP, Zolnikov TR, Noronha JM, Angulo-Tuesta A, Bashashi M, Cruvinel VR. Social vulnerabilities of female waste pickers in Brasília, Brazil. *Arch Environ Occup Health.* (2021) 76:173–80. doi: 10.1080/19338244.2020.1787315
- Martínez L, Zuluaga B, Prada SI. Analyzing factors associated with trash pickers' health status: Census data in a major city in Colombia. *J Community Health.* (2020) 45:133–40. doi: 10.1007/s10900-019-00725-7
- Coelho, AP, Beck, CL, Fernandes, MN, Freitas, NQ, Prestes, FC, Tonel, JZ. Women waste pickers: living conditions, work, and health. *Revista Gaucha de Enfermagem.* (2016) 37:57321. doi: 10.1590/1983-1447.2016.03.57321
- Chikarmane P. *Informal Economy Monitoring Study: Waste Pickers in Pune, India*. (2014). Available online at: <https://www.wiego.org/sites/default/files/publications/files/IEMS-Pune-Waste-Pickers-City-Report.pdf> (accessed March 31, 2021).
- OECD. *Issues Note. Session 5: Gender-Specific Consumption Patterns, Behavioural Insights, and Circular Economy*. 2020 Global Forum on Environment. Mainstreaming Gender and

FUNDING

The GCRF Accountability for Informal Urban Equity Hub (ARISE) is a UKRI Collective Fund award with award reference ES/S00811X/1.

ACKNOWLEDGMENTS

The authors are grateful to Prasanna S. Saligram, Varun Sai, Botlagunta Ramanamurthi, Barathi Nakkeeran, and the ARISE consortium for their contributions to the project; to the civil society partners at the ARISE action sites for their partnership; and to the participants for sharing their experiences and insights. They also thank the reviewers for their questions and suggestions that helped make this article clearer and more informative.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fgwh.2021.769292/full#supplementary-material>

- Empowering Women for Environmental Sustainability*. Paris, 5–6 March. (2020). Available online at: <http://www.oecd.org/env/GFE-Gender-Issues-Note-Session-5.pdf> (accessed November 16, 2021).
- Heise L, Greene ME, Oppen N, Stavropoulou M, Harper C, Nascimento M, et al. Gender inequality and restrictive gender norms: framing the challenges to health. *Lancet.* (2019) 393:2440–54. doi: 10.1016/S0140-6736(19)30652-X
- ARISE. *Shades of Informality: Working With Waste Pickers in ARISE*. (2019). Available online at: <http://www.ariseconsortium.org/learn-more-archive/shades-of-informality-working-with-waste-pickers-in-arise> (accessed November 16, 2021).
- Salve PS, Jungari S. Sanitation workers at the frontline: work and vulnerability in response to COVID-19. *Local Environ.* (2020) 25:627–30. doi: 10.1080/13549839.2020.1792430
- Gupta SK. Integrating the informal sector for improved waste management. *Private Sect Dev.* (2020) 15:12–7. Available online at: <https://blog.private-sector-and-development.com/2012/11/12/integrating-informal-sector-for-improved-waste-management/> (accessed December 5, 2021).
- Bonini-Rocha AC, de Oliveira RA, Bashash M, do Couto Machado G, Cruvinel VR. Prevalence of musculoskeletal disorders and risk factors in recyclable material waste pickers from the dump of the structural city in Brasília, Brazil. *Waste Manag.* (2021) 125:98–102. doi: 10.1016/j.wasman.2021.02.018
- Mondal NK, Siddique S, Banerjee M, Roychoudhury S, Mukherjee S, Slaughter MS, et al. Alteration in leukocyte subsets and expressions of FcγR and complement receptors among female ragpickers in Eastern India. *Saf Health Work.* (2017) 8:198–205. doi: 10.1016/j.shaw.2016.10.004
- Ravindra K, Kaur K, Mor S. Occupational exposure to the municipal solid waste workers in Chandigarh, India. *Waste Manag Res.* (2016) 34:1192–5. doi: 10.1177/0734242X16665913
- Manderson L, Burke NJ, Wahlberg A. *Viral Loads: Anthropologies of Urgency in the Time of COVID-19*. London: UCL Press (2021). doi: 10.2307/j.ctv1j13zb3
- Government of India, Ministry of Health and Family Welfare. *National Health Policy*. (2017). New Delhi: Government of India, Ministry of Health and Family Welfare.
- Alfers L. *Informal Workers' Access to Health Services*. (2015). Available online at: www.wiego.org/blog/informal-workers-access-health-services (accessed July 6, 2021).

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may

be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Josyula, Murthy, Karampudi and Garimella. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



“Worn-out but happy”: Postpartum Women’s Mental Health and Well-Being During COVID-19 Restrictions in Australia

Hannah E. Christie^{1,2}, Kassia Beetham³, Elizabeth Stratton⁴ and Monique E. Francois^{1,2*}

¹ School of Medicine, University of Wollongong, Wollongong, NSW, Australia, ² Illawarra Health and Medical Research Institute, University of Wollongong, Wollongong, NSW, Australia, ³ School of Behavioural and Health Sciences, Australian Catholic University, Banyo, QLD, Australia, ⁴ Faculty of Medicine and Health, Central Clinical School, University of Sydney, Sydney, NSW, Australia

OPEN ACCESS

Edited by:

Emma Motrico,
Loyola Andalusia University, Spain

Reviewed by:

Sandra Nakić Radoš,
Catholic University of Croatia, Croatia
Miguel Landa-Blanco,
National Autonomous University of
Honduras, Honduras

*Correspondence:

Monique E. Francois
francois@uow.edu.au

Specialty section:

This article was submitted to
Women’s Mental Health,
a section of the journal
Frontiers in Global Women’s Health

Received: 12 October 2021

Accepted: 13 December 2021

Published: 07 January 2022

Citation:

Christie HE, Beetham K, Stratton E
and Francois ME (2022) “Worn-out
but happy”: Postpartum Women’s
Mental Health and Well-Being During
COVID-19 Restrictions in Australia.
Front. Glob. Womens Health
2:793602.
doi: 10.3389/fgwh.2021.793602

Background: From late 2019, COVID-19 disease has infiltrated the global population causing widespread challenges to public health. One cohort that has received less attention, but who may be more vulnerable to the mental and physical health related impacts of COVID-19 restrictions are postpartum mothers. The aim of this study was to explore the mental health, well-being, and health behaviours of mothers up to 12 months postpartum whilst living in Australia under COVID-19 level 3 and 4 restrictions.

Methods: 351 women in their first year postpartum residing in Australia whilst under level 3/4 social distancing restrictions (during April 13 and June 11, 2020) were recruited to participate in an online questionnaire. The survey measured symptoms of depression, anxiety, and stress (DASS), wellness (SF-36), physical activity (Godin-Shephard score), perceived value of health outcomes, diet, and sleep. Descriptive statistics and linear regressions were performed.

Results: Data was analysed for 139 eligible women. Of these women, 74% scored “normal” for depression, 84% for anxiety, and 72% for stress. Over half (58%) of women reported being worn out all, most, or a good bit of the time and 77% reported being a happy person all, most, or a good bit of the time. Analysis of the perceived values of health outcome revealed women had high value for “getting out of the house,” “achieving a better overall mood,” and “to feel better physically.” Women were considered physically active according to the Godin Leisure score, however only 41% of women met the current Australian national physical activity guidelines of 150 min.week⁻¹.

Conclusions: Overall the majority of postpartum mums that were surveyed, have normal mental health symptoms, and despite being worn out most are happy at least a good bit of the time. This study highlights the importance of health values in maintaining leisure physical activity and mental health. In addition it appears women may benefit from virtual group exercise and community programs to encourage being physically active and socialising with friends simultaneously.

Keywords: physical activity, post-pregnancy, pandemic, maternal, mood, exercise, depression, isolation

INTRODUCTION

From late 2019, novel coronavirus disease (COVID-19) has infiltrated the global population causing widespread challenges to public health. The economic and social disruption has caused unprecedented stress and anxiety for many families. To minimise the spread of COVID-19 governments across the world, including Australia, have enforced various restrictions such as lockdown stay-at-home orders and the closure of many businesses, schools, and public spaces. Furthermore, restrictions in Australia included strict international and state border closures and limits on house and family visitation (1). The two highest levels of COVID-19 restrictions in Australia are the Level 3 and 4. These restrictions closed all services considered non-essential such as gym and fitness centres, dining, arts and entertainment, retail, and online home-schooling for most students. Reasons to leave the house were minimised to exercise (often time-restricted), essential shopping, and essential medical appointments. There has been much speculation on the impact of COVID-19 on mental health in the general population, with predictions of a 25% increase in suicides (2). One cohort that has received less attention, but who may be more vulnerable to the mental and physical health related impacts of disasters, such as, COVID-19 restrictions are postpartum mothers (3).

Notwithstanding the COVID-19 pandemic, the postpartum period poses many physical and emotional challenges and triumphs. In a cohort of ~10,000 Australian-born and migrant postpartum women, ~95% reported one or more emotional health issues within 6 months after birth; ~70% experienced extreme exhaustion (4), and 43% and 25% experienced heightened symptoms of depression and anxiety (5). These findings are of particular importance as links have been established between increased mental health symptoms and the impact on mother-infant bond as well as the psychological development of the infant (6). Achieving physical activity and diet guidelines are important during the postpartum period to improve cardiovascular fitness (7), facilitate weight loss (8), increase positive mood, decrease anxiety and depression, and promote greater alertness following exercise (9). Hence, it is important to explore the mental health and health behaviours of women during this pandemic in order to develop and strengthen support systems for postpartum mothers (10).

Recent studies across the world have reported mixed findings on the mental health and well-being of perinatal women during COVID-19 (11–18). Six studies in postpartum mothers across the world, North-eastern Italy, Belgium, China, and America have found increased depressive and anxiety symptoms (11, 12, 14–17), whilst another study in postpartum women in Japan reported normal levels of mental health and well-being (13). In addition, emerging evidence suggests the amount of physical activity women across the world partake in is also an important factor when considering maternal mental health during the pandemic (11). It is well-known that higher levels of physical activity can

prevent (19) and reduce (20) mental health symptoms in the postpartum mother (21). However, due to COVID-19 restrictions there may be fewer opportunities for physical activity, potentially contributing to poorer mental health. One survey reported 64% of pregnant and postpartum women across the world decreased their physical activity levels during the COVID-19 pandemic, those who met the physical activity recommendations had lower levels of depression symptoms and anxiety compared to women who did not (11). Similarly, it is important to explore the impact of diet and nutrition. For example, recent research reports 54% of Australians were bothered by overeating during the pandemic (22). In addition, 43% of Danes have reported eating more, 42% have been snacking more, 48% are exercising less, and 30% have gained weight (23). To our knowledge, no studies have explored the impacts of COVID-19 restrictions on mental health and physical activity in postpartum women in Australia.

The aim of this study was to provide data on the mental health, well-being, and health behaviours of mothers up to 12 months postpartum whilst living in Australia under COVID-19 level 3 and 4 restrictions. It was hypothesised maternal mental health symptoms (depression, anxiety, and stress), and well-being would be lower than previously reported national averages. Physical activity levels were also expected to be low. The possible influence of important predictors of mental health such as physical activity, values and nutrition were also included as exploratory outcomes.

MATERIALS AND METHODS

Sample and Procedure

Women >18 years, within their first year postpartum, and currently under Australian Government enforced Level 3 or 4 restrictions (24) were invited to complete an online questionnaire between April 13 and June 11 (all Australian states) and additionally, from September 10 to 22 (Victoria only) 2020. Women were recruited via advertisement on social media (Twitter, Facebook, and Instagram). This study was approved by the joint University of Wollongong and the Illawarra Shoalhaven Local Health District (ISLHD) Ethics Committee (HREC: 2019/ETH13571). Informed consent was provided by all women.

Instruments

The questionnaire and consent were completed by women via the online platform CoreXM (Qualtrics, Sydney, Australia). Demographics including such as age, months since delivery, education, and postcode were collected, followed by questions on well-being, mental health, and health related behaviours.

Mental Health

Mental health symptoms were collected via the *Depression, Anxiety, and Stress Scale—21 items* [DASS-21 (25)]; a set of three self-report scales assessing seven-items across anxiety, depression, and stress symptoms. Mental health is analysed and reported categorically using the classifications provided in the DASS: normal, mild, moderate, severe, and extremely severe. The short version has good reliability and validity (Cronbach's

Abbreviations: DASS, Depression, anxiety, stress scale; EPDS, Edinburgh postnatal depression scale; BMI, Body mass index; SF-36, 36-item short form survey.

alpha 0.94, 0.87, and 0.91 for the depression, anxiety, and stress subscales, respectively), along with good construct validity.

Well-Being

Well-being was assessed using the 36-item *Short Form Health Survey questionnaire* (SF-36). The SF-36 is a validated instrument for evaluating Health-Related Quality of Life. The SF-36 measures eight domains of health status: physical functioning (10 items), physical role limitations (four items), bodily pain (two items), general health perceptions (five items), energy/vitality (five items), social functioning (two items), emotional role limitations (three items), and mental health (five items). This version has good reliability and validity (Cronbach's alpha for physical functioning: 0.93; social functioning: 0.73; physical role limitations: 0.96; emotional role limitations: 0.96; bodily pain: 0.85; mental health: 0.95; energy/vitality: 0.96; and general health perceptions: 0.95) (26). The scores were transformed to score from zero (worst possible health) to 100 (best possible health) using RAND (Research and Development) Corporation's scoring guidelines (27).

Perceived Value of Outcomes

Perceived value of outcomes for general health was assessed using a 12-item outcome expectations measure designed to be relevant to the study population. Participants were asked to rate items by "How much value do you place on attaining each of the following" followed by items such as "get out of the house," "weight control," and "lower risk of type 2 diabetes" (Table 5). Each item was scored on a 9-point Likert scale ranging from 1 (no value) to 9 (the highest of value) (28). The questionnaire has good validity and reliability (Cronbach's alpha for this study: 0.82).

Sleep

Sleep was assessed using a 4-item questionnaire evaluating the length of sleep, the length of uninterrupted sleep, and awake hours during night (all measured in hours) as well as the number of interruptions. Interruptions were assessed on a categorical scale of 0–1, 2–3, 4–5, 6–7, and 7 or more-times sleep was interrupted per night. The questionnaire has good validity and reliability (Cronbach's alpha for this study: 0.73).

Physical Activity

Physical activity was assessed using the validated *Godin-Shephard Leisure-Time Physical Activity Questionnaire* [Godin Score, (29); kappa index 0.74 (30)]. The questionnaire asked participants to report how often they completed 15 min bouts of strenuous, moderate, and light/mild exercise over a typical 7-day period before, and during their pregnancy, as well-currently (postpartum). These values were then placed into the following equation to provide their leisure score separately during each time period:

$$\text{Weekly leisure activity score} = (9 \times \text{Strenuous}) + (5 \times \text{Moderate}) + (3 \times \text{Light})$$

Godin scores are categorised into active (score: ≥ 24), moderately active (score: 14–23), or insufficiently active (score: ≤ 13).

Physical activity minutes per week were then calculated from the reported Godin scores.

Dietary Intake

Dietary intake of the core food groups [including vegetables (fresh), vegetables (frozen), fruit (fresh), fruit (frozen), grains, legumes, meat, dairy, and snacks] were assessed using a questionnaire developed in line with Australian Dietary Guidelines (31). Each item was scored on a 4-point scale including 1 (daily), 2 (3–4 days.week⁻¹), 3 (weekly), and 4 (rarely). Food groups were separately analysed. Dietary intake was compared with the Australian Dietary Guidelines (31).

Data Analysis and Statistics

SPSS Version 26.0 (Armonk, NY, USA) was used for quantitative analysis. Univariate data for baseline demographics, mental health, physical activity, sleep, dietary intake, and wellness outcomes are shown as a proportion (percentage) or mean (SD). Correlations of all variables were carried prior to regression analysis (Supplementary Tables 1–7). Multiple linear regression analysis was used to explore the relationship between mental health score (dependent variable) and predictor variables—education, postpartum BMI, physical activity, and food intake (fresh vegetables, fresh fruits). Multiple linear regression was also used to establish the relationship between postpartum physical activity (dependent variable) and the above predictors with the addition of pregnancy physical activity levels. Linear regression was also used to determine the relationship between postpartum physical activity (dependent variable) and values for general health. Variables used in the regression analysis (education, BMI, maternal age, fruit and vegetables and physical activity) were based on known relationships of between variables and mental health/physical activity. Regression tables are presented with standardised coefficients β , t-statistic (t), significance (p), and 95% confidence intervals for β (upper and lower bounds). Statistical significance was noted as $p \leq 0.05$. Participant data was only used for those participants that completed each section (ie mental health, well-being etc) in full, incomplete sections were excluded from analysis. *Post-hoc* power analysis for mental health (depression, anxiety, and stress) revealed a sample size of 118 was required.

RESULTS

A total of 351 participants expressed interest in the study. Of the 351, 212 met inclusion criteria but did not complete the survey for unknown reasons. Data for 139 eligible participants were available for most analyses. However, where fewer women completed a survey section (i.e., DASS $n = 114$) the sample size is reported. Women had a mean age of 32.5 ± 4.2 years, were 6.2 ± 3.6 months post-delivery, and had a mean postpartum BMI of $25.8 \pm 4.2 \text{ kg.m}^{-2}$ (Table 1). Of these women, 40% were primiparous, 44% had two children, 3% had 3 children, and 2% had 4 children. Further, 85% were married, and 80.3% had at least a bachelor degree.

TABLE 1 | Physical activity, body mass index (BMI), sleep, dietary intake, and perceived value of achieving outcomes of women reported pre-, during, and post-pregnancy (during COVID-19 social distancing restrictions).

	Pre-pregnancy mean ± SD		Pregnancy mean ± SD		Post-partum mean ± SD
Physical activity (min/wk)	149.1 ± 58.9		124.7 ± 52.9		133.5 ± 58.8
Godin score	52.6 ± 22.9		40.3 ± 18.5		43.6 ± 20.4
Strenuous	2.7 ± 1.9		1.6 ± 1.3		1.9 ± 1.5
Moderate	3.4 ± 2.0		2.8 ± 2.0		3.0 ± 2.3
Light	3.9 ± 2.2		3.9 ± 2.2		4.1 ± 2.4
BMI (kg.m ⁻²)	24.4 ± 4.1		13.2 ± 6.0*		25.8 ± 4.2
*pregnancy weight gain (kg)					
Postpartum sleep	0–1%	2–3%	4–5%	6–7%	7+%
Hours of sleep total	0	0.8	24.4	53.5	21.3
Uninterrupted sleep (hours)	7.9	49.6	28.3	9.4	4.7
How many times sleep interrupted? (n)	16.5	45.7	22.0	4.7	11.0
Awake time during night (hours)	15.7	61.4	20.5	1.6	0.8
Food	Daily %	3–4 times weekly %		Weekly %	Rarely %
Vegetables (Fresh)	66.7	28.1		3.7	1.5
Vegetables (Frozen, dried, or canned)	14.4	23.2		30.4	32.0
Fruit (Fresh)	51.2	24.4		18.1	6.3
Fruit (Frozen, dried, or canned)	9.6	6.4		24.0	60
Grains	70.6	21.4		4.8	3.2
Meat	71.7	25.2		1.6	1.6
Legumes	19.0	24.6		37.3	19.0
Dairy	71.7	14.2		7.9	6.3
Snacks	32.3	26.8		33.1	7.9
Mean ± SD					
Get myself out of the house	7.8 ± 1.6				
Feel better physically	7.7 ± 1.5				
Better overall mood	7.5 ± 1.7				
Sense of accomplishment	7.3 ± 1.7				
Reduce stress	7.1 ± 2.0				
Socialise with friends	7.1 ± 1.8				
Have more energy	7.0 ± 1.9				
Increase fitness	6.8 ± 2.0				
Weight control	6.4 ± 2.2				
Lower risk of type 2 diabetes	4.8 ± 2.8				
Meet new people	4.4 ± 2.0				
Praise from friends and family	4.1 ± 2.5				

Mental Health and Well-Being

A majority of women reported normal scores in depression, anxiety, and stress symptoms during Australian level 3 and 4 social distancing restrictions. Women had a mean depression score of 3.16 ± 3.08 . Of these, 74% ($n = 84/114$) scored as normal, 11% ($n = 12/114$) mild, 12% ($n = 14/114$) moderate, and 4% ($n = 4/114$) severe depression. No participants scored extremely severe range.

Women in the study had a mean anxiety score of 2.09 ± 2.80 . Of these, 84% ($n = 94/112$) scored normal, 7% ($n = 8/112$) mild, 6% ($n = 6/112$) moderate, 4% ($n = 4/112$) severe, and 4% ($n = 4/112$) extremely severe anxiety.

Women in the study had a mean stress score of 6.14 ± 3.95 . Of these, 72% ($n = 82/114$) scored normal, 11% ($n = 12/114$) mild, 9% ($n = 10/114$) moderate, 8% ($n = 9/114$) severe, and 1% ($n = 1/114$) extremely severe stress.

TABLE 2 | Postpartum well-being of women as measured through an SF-36 ($n = 121$), compared with Australian female norms aged 25–34 years ($n = 2,182$).

SF-36	Mean \pm SD (a.u.)	Australian norms, females 25–34 years (32)	P-value
Physical functioning	94.8 \pm 6.9	89.3 \pm 23.4	0.010*
Physical role limitations	78.6 \pm 28.2	83.5 \pm 46.7	0.253
Bodily pain	74.2 \pm 22.0	79.8 \pm 32.7	0.063
General health	65.3 \pm 18.6	75.9 \pm 28.0	<0.001*
Vitality	45.4 \pm 19.0	62.3 \pm 28.0	<0.001*
Social functioning	78.5 \pm 23.5	84.0 \pm 32.7	0.068
Emotional role limitations	60.9 \pm 38.9	83.7 \pm 46.7	<0.001*
Mental health	70.0 \pm 16.6	74.2 \pm 23.4	0.052

Missing values due to incomplete datasets. *Significance < 0.05.

SF-36 scores, separated into the eight core wellness concepts (physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health), are provided in **Table 2**. Compared to Australian norms, our population had significantly higher levels of physical functioning (94.8 \pm 6.9 vs. 89.3 \pm 23.4 u.a.; $p = 0.010$) and lower levels of general health (65.3 \pm 18.6 vs 75.9 \pm 28.0 u.a.; $p < 0.001$), vitality (45.4 \pm 19.0 vs. 62.3 \pm 28.0 u.a.; $p < 0.001$), and emotional role (60.9 \pm 38.9 vs. 83.7 \pm 46.7 u.a.; $p < 0.001$). Within these concepts, 58.1% of women reported being worn out all, most, or a good bit of the time and 76.9% of women reported being a happy person all, most, or a good bit of the time.

Sleep

Half of the women (53.5%) reported getting 6–7 h of sleep per night total. Many women (49.6%) reported getting 2–3 h of uninterrupted sleep each night and 45.7% reporting being interrupted 2–3 times a night. 61.4% of women reported spending 2–3 h awake during the night. Sleep frequencies are provided in **Table 1**.

Perceived Value of Outcomes

The average perceived value (1–low value to 9–highest value) placed on achieving outcomes of general health are shown in **Table 1**. In regard to value toward various health components, postpartum women reported high value for “getting out of the house,” achieving a “better overall mood,” and “to feel better physically.” Lowest value was reported for “receiving praise from family and friends,” “meeting new people,” and “lowering the risk of type 2 diabetes.”

Physical Activity

On average, women in the present study were classified as being physically active pre-, during and postpartum according to the Godin classification (average min.wk⁻¹ **Table 1**). Pre-pregnancy, women had a Godin score of 53 \pm 23 a.u. Of these, 0% were classed as sedentary or physically inactive, 7% ($n = 9/125$) moderately active, and 93% ($n = 116/125$) physically active according to the Godin score.

During pregnancy, women had a mean Godin score of 40 \pm 19 a.u. 0% ($n = 0/121$) were classed as sedentary or physically inactive, 18% ($n = 22/121$) were considered moderately active, and 82% ($n = 99/121$) were considered physically active according to the Godin score.

Postpartum, during Australian level 3 and 4 COVID-19 restrictions, women had a Godin score of 44 \pm 20 a.u. Of these, 0% ($n = 0/121$) were classed as sedentary or physically inactive, 16% ($n = 19/121$) moderately active, and 84% ($n = 102/121$) physically active according to the Godin score. Despite the positive scores derived from the Godin scores, only 41% of women met the current physical activity guidelines of 150 min.week⁻¹ according to Australian national guidelines (33). Godin scores for vigorous, moderate, and light physical activity is presented in **Table 1**.

Nutrition

Women in the study reported eating fresh vegetables (66.7%), fresh fruit (51.2%), grains (70.6%), meat (71.6%), and dairy (71.7%) daily. Frozen fruit and vegetables were reported as being eaten rarely (60.0 and 32.0%, respectively). Legumes were most commonly (37.3%) reported as being eaten weekly, whilst snacks were reported as being eaten both daily and weekly (32.3 and 33.1%, respectively). Based on this survey, the proportion of women in this study that do not meet healthy eating guidelines is 33.3% for vegetables, 48.8% for fruits, 29.4% for grains, 28.8% for meats, 81% for legumes, and 28.3% for dairy. The proportion of women who answered daily, 3–4x per week, weekly or rarely to each food group is shown in **Table 1**.

Relationship Between Physical Activity and Maternal Mental Health, Values, and Well-Being

Correlation analysis was performed on all variables, and significant outcome variables were entered into regression analysis (**Supplementary Tables 1–7**). Several regression analyses were conducted with depression, anxiety, and stress scores with education, postpartum BMI, vegetable intake, fruit intake, pre-pregnancy physical activity, and postpartum physical activity as potential predictors. Fruit intake ($p = 0.039$) was a significant predictor for depression symptoms and accounted for 12.6% of depression score variance (**Table 3**). Fruit intake ($p < 0.001$) was a significant predictor for anxiety symptoms and accounted for 26.8% of anxiety score variance (**Table 3**). Fruit intake ($p = 0.007$) was a significant predictor for stress symptoms and accounted for 17.1% of stress score variance (**Table 3**). Physical activity carried out pre-pregnancy ($p = 0.050$) and during pregnancy ($p = 0.001$) were both significant predictors for postpartum physical activity and together accounted for 40.4% of postpartum physical activity time (**Table 4**). Value in feeling better physically ($p = 0.006$), getting out of the house ($p = 0.034$) and socialising with friends ($p = 0.033$) were all significant predictors for postpartum physical activity and together accounted for 16.9% of post-pregnancy physical activity time variance (**Table 5**).

TABLE 3 | Linear regression analysis for mental health scores against education level, post-partum BMI, fresh vegetable and fruit intake, pre-pregnancy physical activity, postpartum physical activity.

	Standardised coefficients beta	T	Sig	95% confidence interval lower bound	95% confidence interval upper bound
Depression					
Constant		0.35	0.729	−3.52	−5.01
Education	0.01	0.05	0.957	−0.64	0.68
Postpartum BMI	−0.06	−0.60	0.548	−0.18	−0.09
Vegetables: fresh	0.21	1.92	0.058	−0.04	2.13
Fruit: fresh	0.23	2.10	0.039*	0.04	1.53
Pre-pregnancy PA min	0.01	0.08	0.936	−0.01	0.015
Postpartum PA min	0.10	0.83	0.411	−0.01	0.02
$F_{(6,89)} = 2.147; p = 0.056; R^2 = 0.126$					
Anxiety					
Constant		0.55	0.586	−2.48	4.36
Education	−0.18	−1.89	0.063	−1.03	0.03
Postpartum BMI	−0.02	−0.21	0.835	−0.12	0.10
Vegetables: fresh	0.14	1.35	0.180	−0.28	1.46
Fruit: fresh	0.39	3.82	< 0.001*	0.55	1.74
Pre-pregnancy PA min	0.06	0.54	0.590	−0.01	0.02
Postpartum PA min	−0.09	−0.84	0.403	−0.02	0.01
$F_{(6,89)} = 5.423; p < 0.001; R^2 = 0.268$					
Stress					
Constant		1.03	0.307	−2.53	7.97
Education	0.04	0.39	0.695	−0.65	0.98
Postpartum BMI	−0.10	−0.96	0.340	−0.25	0.09
Vegetables: fresh	0.21	1.96	0.053	−0.02	2.66
Fruit: fresh	0.30	2.76	0.007*	0.36	2.19
Pre-pregnancy PA min	0.01	0.05	0.957	−0.02	0.02
Postpartum PA min	0.14	1.19	0.239	−0.01	0.03
$F_{(6,89)} = 3.055; p = 0.009; R^2 = 0.171$					

* $p < 0.05$.**TABLE 4 |** Linear regression analysis for postpartum physical activity against education level, post-partum BMI, Fresh vegetable and fruit intake, pre-pregnancy physical activity, pregnancy physical activity.

	Standardised coefficients beta	T	Sig	95% confidence interval lower bound	95% confidence interval upper bound
Postpartum physical activity (minutes)					
Constant		1.59	0.116	−11.71	104.63
Education	0.00	0.01	0.992	−9.20	9.29
Postpartum BMI	−0.02	−0.19	0.847	−2.06	1.69
Vegetables: fresh	−0.08	−0.89	0.378	−22.69	8.69
Fruit: fresh	−0.01	−0.13	0.894	−11.61	10.15
Pre-pregnancy PA min	0.24	1.99	0.050*	0.00	0.49
Pregnancy PA min	0.40	3.27	0.001*	0.18	0.72
$F_{(6,99)} = 11.178; p < 0.001; R^2 = 0.404$					

* $p < 0.05$.

DISCUSSION

This study is the first to explore the mental health, well-being, and physical activity levels of postpartum (<1 year) mothers

living in Australia during COVID-19 level 3 and 4 restrictions. The present study found that despite feeling worn out, and being sleep-deprived, postpartum women during COVID-19 reported (i) normal symptoms of mental health (depression,

TABLE 5 | Linear regression analysis for postpartum physical activity against reported values for general health.

	Standardised coefficients beta	T	Sig	95% confidence interval lower bound	95% confidence interval upper bound
Postpartum physical activity (minutes)					
Constant		0.84	0.401	−43.88	108.77
Get out of the House	0.22	2.15	0.034*	0.61	15.25
Feel better physically	0.41	2.79	0.006*	4.50	26.85
Better overall mood	−0.12	−0.079	0.434	−16.57	7.17
Reduce stress	0.20	1.38	0.172	−2.66	14.71
Sense of accomplishment	−0.21	−1.66	0.100	−17.02	1.52
Gain more energy	−0.20	−1.40	0.164	−15.35	2.64
Lower the risk of type 2 diabetes	0.15	1.37	0.174	−1.34	7.27
Praise from family and friends	0.05	0.51	0.613	−3.40	5.74
Socialise with friends	−0.22	−2.16	0.033*	−13.79	−0.58
$F_{(9,97)} = 2.184; p = 0.029; R^2 = 0.169$					

* $p < 0.05$.

anxiety, and stress) and well-being, and (ii) were classed as being physically active postpartum (that being during COVID restrictions) according to the Godin Leisure questionnaire. Of interest, the women held high value for achieving a “better overall mood” and “feeling better physically,” even though they reported having normal mental health symptoms and well-being. The value placed upon feeling better physically was positively correlated to the minutes of postpartum physical activity women achieved during COVID-19 restrictions. Fruit and vegetable intake were also positive predictors of better mental health. Taken together, our findings highlight the benefits of maintaining physical activity and healthy eating, and the importance of women’s value toward achieving a better mood and feeling better physically, during a global pandemic such as COVID-19; at a time when barriers to maintaining emotional and physical behaviours are high. This is in line with other COVID-19 research that has found physical activity participation correlates with lower depression and anxiety scores (11) and that perceived stress is related to how women perceive the rewards over challenges, during COVID-19 restrictions (34).

Women in the present study had higher proportions of normal mental health symptoms compared to a recent international survey also conducted during COVID-19 (comprising of pregnant and postpartum participants mostly from North America) (11). In contrast with that study, we did not find strong relationships between physical activity (whether pre-pregnancy, or postpartum) and mental health. Based on prior research in pregnant and postpartum mums internationally (11, 35, 36), it was anticipated that social distancing and isolation measures during COVID-19 restrictions would negatively impact the mental health of Australian postpartum mothers. Previous international research during COVID-19 has been mixed reporting depressive symptoms in the general population were worse (11, 35), better (37) or the same (13). Worsening mental health symptoms were reported by countries such as Southern Italy and North America, where the number of cases

and fatalities were much higher than Australia and stricter levels of stay-at-home restrictions (i.e., only one household member able to shop for food) (11, 12). However, our study found Australian women’s depression scores (DASS; 26% with values categorised not “normal”) were similar to a survey in North-Eastern Italy [Edinburgh Postnatal Depression Score (EPDS): 28.6% above 12], despite Italy having more cases of COVID-19 and having stricter isolation restrictions than Australia (12). Further investigation into the sociocultural differences is warranted as a potential explanation rates of depression in Italy despite worse COVID-19 conditions. Furthermore, relationships were found between improved mental health and daily fruit and vegetable intake though future research may begin to further investigate the intricacies of this relationship.

The health values’ women hold is important as they drive health behaviours which may be compromised during the COVID-19 pandemic. During the COVID-19 pandemic postpartum women held the highest value for *getting out of the house, feeling better physically, and improving overall mood*. Correlations have previously been established between moderate physical activity and improved mood in healthy populations (38, 39). The value women in this study placed on feeling better physically was associated with more minutes per week of physical activity, which, based on the above relationship, will likely lead to improved mental health. Indeed, prior research has already shown that higher levels of physical activity are associated with better mental health during the COVID-19 pandemic (12). A small, but significant relationship was identified between having a high value toward socialising with friends and lower levels of physical activity during COVID-19 restrictions. This suggests women were not participating in physical activity whilst socialising with friends during COVID restrictions. Here, women were likely socialising over social media or video conferencing, which in turn may encourage sustained sedentary behaviours. Strategies to reach physical activity guidelines whilst socialising with others may be of importance to women during the (or a

future) pandemic. For example, future research should explore whether women would benefit from virtual group exercise and community programs to encourage being physically active and socialising with friends simultaneously.

It is well-known that regular participation in physical activity can improve and maintain mental health and well-being (19–21), however, many women fail to maintain sufficient physical activity during and following pregnancy (40). Based on previous research (11, 36) and given the closure of gyms and fitness facilities in Australia, it was widely anticipated that physical activity would be low during COVID-19 social distancing measures. Despite women reporting being physically active on the Godin Leisure questionnaire, on average, only 41% of the postpartum women we sampled were meeting Australian physical activity guidelines of 150 min.week⁻¹ during COVID-19 social distancing restrictions. This is lower than previously reported in Australia prior to the pandemic (2008–2010) which reported 63% of postpartum women in Australia meet the physical activity guidelines (40). Interestingly, one study reported 76% of pregnant women in the United States had no change in physical activity throughout lockdown protocols (41), though this may be due to the stringency of the lockdown enforcements at the time of data collection. Mothers in this study, whilst not meeting traditional structured exercise guidelines, may actually still be active and regularly move (a common occurrence when looking after small children), thereby meeting the physical activity leisure guidelines, which still likely have health enhancing benefits. The findings from this study provide important impetus for future research investigating the benefits of regular active movement objectively (i.e., measured by steps/day) versus structured physical activity for mental health and well-being.

Strengths, Limitations, and Future Directions

This is the first study to explore health behaviours in mothers in Australia (<1 year postpartum) during COVID-19 social distancing restrictions. Whilst this was one of the first studies internationally to investigate the wellness, physical activity and dietary patterns of postpartum women during COVID-19, the diet questionnaire used has not been validated. Future research which collects food records may provide more specific and accurate data regarding nutrition in a pandemic. Our study did not account for a control (pre-pandemic group), however given this was not possible (without asking women to recall retrospectively) we have compared our findings to large-scale data, validated, Australian population norms. Future research may benefit in examining the health behaviours of women during and post the COVID-19 restrictions (42, 43). The exploratory regression relationships between outcomes require further research given our small sample size. In addition to differing quarantine levels and number of cases, discretions in mental health might also be due to the level of support, physical activity and health habits, values and outcome expectations, and the type and timing of postpartum data collection. Regardless, this study shows that even in times of additional barriers, such as with the COVID-19 lockdown and restrictions, women can still maintain physical activity, health, and well-being, if they place

value on these parameters and therefore future research should be placed on increasing these values through strategies such as community programs.

CONCLUSIONS

In general, postpartum mums in Australia had normal mental health symptoms during COVID-19 restrictions. This study provides evidence for the importance of health values in maintaining mental health and physical activity during times of additional barriers, such as the COVID-19 pandemic. Results provided suggest if postpartum women in the Australian population can be educated on the benefits of physical activity and well-being and thus find value in improving mood and feeling better physically, they may also be able to reach physical activity guidelines and overcome any barriers faced during the COVID-19 pandemic. Future research should explore the potential for a virtual community group exercise program to encourage women to combine socialising and physical activity for improved mental health. The provision of specialists in exercise physiology and nutrition may encourage women to place a value on attaining greater fitness, and subsequently improve physical and mental health.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Wollongong Human Ethics Research Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HC and MF designed the trial and wrote the original manuscript. HC carried out recruitment and data collection. HC, MF, ES, and KB carried out data analysis. All authors edited and approved the final manuscript.

FUNDING

MF was supported by an Australian National Health and Medical Research Council (NHMRC) Investigator grant.

ACKNOWLEDGMENTS

We would like to thank all the women who participated in the study.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fghw.2021.793602/full#supplementary-material>

REFERENCES

- NSW Government. *New COVID-19 Restrictions Begin as Schools Move Towards Online Learning*. NSW Government (2020). Available online at: <https://www.nsw.gov.au/media-releases/new-covid-19-restrictions-begin-as-schools-move-towards-online-learning> (accessed May 9, 2020).
- Bartone T, Hickie I, McGorry P. *COVID-19 Impact Likely to Lead to Increased Rates of Suicide and Mental Illness*. Australian Medical Association Limited (2020). Available online at: <https://ama.com.au/media/joint-statement-covid-19-impact-likely-lead-increased-rates-suicide-and-mental-illness> (accessed May 12, 2021).
- Harville E, Xiong X, Buckens P. Disasters and perinatal health: a systematic review. *Obstet Gynecol Surv.* (2010) 65:713–28. doi: 10.1097/OGX.0b013e31820eddb6
- Navodani T, Gartland D, Brown SJ, Riggs E, Yelland J. Common maternal health problems among Australian-born and migrant women: a prospective cohort study. *PLoS ONE.* (2019) 14:e0211685. doi: 10.1371/journal.pone.0211685
- Bandyopadhyay M, Small R, Watson LF, Brown S. Life with a new baby: How do immigrant and Australian-born women's experiences compare? *Aust N Z J Public Health.* (2010) 34:412–21. doi: 10.1111/j.1753-6405.2010.00575.x
- Bauer A, Pawlby S, Plant DT, King D, Pariante CM, Knapp M. Perinatal depression and child development: exploring the economic consequences from a South London cohort. *Psychol Med.* (2015) 45:51–61. doi: 10.1017/S0033291714001044
- Nystoriak MA, Bhatnagar A. Cardiovascular effects and benefits of exercise. *Front Cardiovasc Med.* (2018) 5:135. doi: 10.3389/fcvm.2018.00135
- Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis.* (2014) 56:441–7. doi: 10.1016/j.pcad.2013.09.012
- Koltyn KF, Schultes SS. Psychological effects of an aerobic exercise session and a rest session following pregnancy. *J Sports Med Phys Fitness.* (1997) 37:287–91.
- Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry.* (2020) 7:547–60. doi: 10.1016/S2215-0366(20)30168-1
- Davenport MH, Meyer S, Meah VL, Strynadka MC, Khurana R. Moms are not OK: COVID-19 and maternal mental health. *Front Glob Womens Health.* (2020) 1:1. doi: 10.3389/fgwh.2020.00001
- Zanardo V, Manghina V, Giliberti L, Vettore M, Severino L, Straface G. Psychological impact of COVID-19 quarantine measures in northeastern Italy on mothers in the immediate postpartum period. *Int J Gynecol Obstetr.* (2020) 150:184–8. doi: 10.1002/ijgo.13249
- Suzuki S. Psychological status of postpartum women under the COVID-19 pandemic in Japan. *J Mater Fetal Neonatal Med.* (2020) 18:1–3. doi: 10.1080/14767058.2020.1763949
- Peng S, Zhang Y, Liu H, Huang X, Noble DJ, Yang L, et al. A multi-center survey on the postpartum mental health of mothers and attachment to their neonates during COVID-19 in Hubei Province of China. *Ann Transl Med.* (2021) 9:382. doi: 10.21037/atm-20-6115
- Perzow SED, Hennessey E-MP, Hoffman MC, Grote NK, Davis EP, Hankin BL. Mental health of pregnant and postpartum women in response to the COVID-19 pandemic. *J Affect Disord Rep.* (2021) 4:100123. doi: 10.1016/j.jadr.2021.100123
- Ceulemans M, Hompes T, Foulon V. Mental health status of pregnant and breastfeeding women during the COVID-19 pandemic: a call for action. *Int J Gynecol Obstetr.* (2020) 151:146–7. doi: 10.1002/ijgo.13295
- Farewell CV, Jewell J, Walls J, Leiferman JA. A mixed-methods pilot study of perinatal risk and resilience during COVID-19. *J Prim Care Community Health.* (2020) 11:2150132720944074. doi: 10.1177/2150132720944074
- Yan H, Ding Y, Guo W. Mental health of pregnant and postpartum women during the coronavirus disease 2019 pandemic: a systematic review and meta-analysis. *Front Psychol.* (2020) 11:617001. doi: 10.3389/fpsyg.2020.617001
- Schuch FB, Vancampfort D, Firth J, Rosenbaum S, Ward PB, Silva ES, et al. Physical activity and incident depression: a meta-analysis of prospective cohort studies. *Am J Psychiatry.* (2018) 175:631–48. doi: 10.1176/appi.ajp.2018.17111194
- Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B. Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. *J Psychiatr Res.* (2016) 77:42–51. doi: 10.1016/j.jpsychires.2016.02.023
- Pritchett RV, Daley AJ, Jolly K. Does aerobic exercise reduce postpartum depressive symptoms? A systematic review and meta-analysis. *Br J Gen Pract.* (2017) 67:e684–91. doi: 10.3399/bjgp17X692525
- Owen AJ, Tran T, Hammarberg K, Kirkman M, Fisher J, COVID-19 Restrictions Impact Research Group. Poor appetite and overeating reported by adults in Australia during the coronavirus-19 disease pandemic: a population-based study. *Public Health Nutr.* (2021). 24:275–81. doi: 10.1017/S1368980020003833
- Giacalone D, Frøst MB, Rodríguez-Pérez C. Reported changes in dietary habits during the COVID-19 lockdown in the Danish population: the Danish COVIDiet Study. *Front Nutr.* (2020) 7:592112. doi: 10.3389/fnut.2020.592112
- Department of Health. Victoria A. *Directions Issued by Victoria's Chief Health Officer*. State Government of Victoria, Australia. Available online at: <http://www.health.vic.gov.au/covid-19/directions-issued-by-victorias-chief-health-officer> (accessed December 20, 2020).
- Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the depression anxiety stress scales (DASS) with the beck depression and anxiety inventories. *Behav Res Ther.* (1995) 33:335–43. doi: 10.1016/0005-7967(94)00075-U
- Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ.* (1992) 305:160–4. doi: 10.1136/bmj.305.6846.160
- RAND Corporation. *36-Item Short Form Survey (SF-36) Scoring Instructions. Scoring Instructions for the SF-36 Survey Instrument*. Available online at: https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form/scoring.html (accessed November 4, 2020).
- Locke SR, Bourne JE, Beauchamp MR, Little JP, Barry J, Singer J, et al. High-Intensity interval or continuous moderate exercise: a 24-week pilot trial. *Med Sci Sports Exerc.* (2018) 50:2067–75. doi: 10.1249/MSS.0000000000001668
- Godin G. The godin-shephard leisure-time physical activity questionnaire. *Health Fitn J Canada.* (2011) 4:18–22. Available online at: <https://doi.org/10.14288/hfjc.v4i1.82>
- Godin G, Shepherd RJ. A simple method to assess exercise behaviour in the community. *Can J Appl Sport Sci.* (1985) 10:141–6.
- National Health and Medical Research Council. *Australian Dietary Guidelines*. (2013). Available online at: https://www.eatforhealth.gov.au/sites/default/files/content/n55_australian_dietary_guidelines.pdf
- Australia Bureau of Statistics. *National Health Survey: SF-36 Population Norms 1995*. (1997). Available online at: https://www.ausstats.abs.gov.au/ausstats/free.nsf/0/AF34940625286915CA257225000495F3/\protect\T1\textdollarFile/43990_1995.pdf
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists Women's Health Committee. *Exercise During Pregnancy*. (2020). Available online at: [https://ranzcof.org.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Exercise-during-pregnancy-\(C-Obs-62\).pdf?ext=.pdf](https://ranzcof.org.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Exercise-during-pregnancy-(C-Obs-62).pdf?ext=.pdf)
- Herbert JS, Mitchell A, Brentnall SJ, Bird AL. Identifying rewards over difficulties buffers the impact of time in COVID-19 lockdown for parents in Australia. *Front Psychol.* (2020) 11:606507. doi: 10.3389/fpsyg.2020.606507
- Saccone G, Florio A, Aiello F, Venturella R, De Angelis MC, Locci M, et al. Psychological impact of coronavirus disease 2019 in pregnant women. *Am J Obstet Gynecol.* (2020) 223:293–5. doi: 10.1016/j.ajog.2020.05.003
- Stampini V, Monzani A, Caristia S, Ferrante G, Gerbino M, De Pedrini A, et al. The perception of Italian pregnant women and new mothers about their psychological wellbeing, lifestyle, delivery, and neonatal management experience during the COVID-19 pandemic lockdown: a web-based survey. *BMC Preg Childbirth.* (2021) 21:473. doi: 10.1186/s12884-021-03904-4

37. Oskovi-Kaplan ZA, Buyuk GN, Ozgu-Erdinc AS, Keskin HL, Ozbas A, Moraloglu Tekin O. The effect of COVID-19 pandemic and social restrictions on depression rates and maternal attachment in immediate postpartum women: a preliminary study. *Psychiatr Q.* (2020) 92:675–82. doi: 10.1007/s11126-020-09843-1
38. Peluso MAM, Andrade LHSG. Physical activity and mental health: the association between exercise and mood. *Clinics.* (2005) 60:61–70. doi: 10.1590/S1807-59322005000100012
39. Sexton H, Søgaard AJ, Olstad R. How are mood and exercise related? Results from the finnmark study. *Soc Psychiatry Psychiatr Epidemiol.* (2001) 36:348–53. doi: 10.1007/s001270170040
40. van der Pligt P, Olander EK, Ball K, Crawford D, Hesketh KD, Teychenne M, et al. Maternal dietary intake and physical activity habits during the postpartum period: associations with clinician advice in a sample of Australian first time mothers. *BMC Preg Childbirth.* (2016) 16:27. doi: 10.1186/s12884-016-0812-4
41. Whitaker KM, Hung P, Alberg AJ, Hair NL, Liu J. Variations in health behaviors among pregnant women during the COVID-19 pandemic. *Midwifery.* (2021) 95:102929. doi: 10.1016/j.midw.2021.102929
42. Benewick RJ, Birch AH, Blumler JG, Ewbank A. The floating voter and the liberal view of representation. *Polit Stud.* (1969) 17:177–95. doi: 10.1111/j.1467-9248.1969.tb00634.x
43. Himmelweit HT, Biberian MJ, Stockdale J. Memory for past vote: implications of a study of bias in recall. *Br J Polit Sci.* (1978) 8:365–75. doi: 10.1017/S0007123400001411

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Christie, Beetham, Stratton and Francois. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Molecular and Physiological Aspects of SARS-CoV-2 Infection in Women and Pregnancy

Anna Liu¹, Janet Raja xavier¹, Yogesh Singh^{1,2}, Sara Y. Brucker¹ and Madhuri S. Salker^{1*}

¹ Research Institute of Women's Health, Eberhard Karls University, Tübingen, Germany, ² Institute of Medical Genetics and Applied Genomics, Eberhard Karls University, Tübingen, Germany

OPEN ACCESS

Edited by:

Lakshmi Surya Prabha Manem,
Dr. NTR University of Health
Sciences, India

Reviewed by:

Daisy Motta-Santos,
Federal University of Minas
Gerais, Brazil
Katie Harris,
University of New South
Wales, Australia

*Correspondence:

Madhuri S. Salker
madhuri.salker@med.uni-tuebingen.de

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 10 August 2021

Accepted: 01 February 2022

Published: 24 February 2022

Citation:

Liu A, Raja xavier J, Singh Y,
Brucker SY and Salker MS (2022)
Molecular and Physiological Aspects
of SARS-CoV-2 Infection in Women
and Pregnancy.
Front. Glob. Womens Health
3:756362.
doi: 10.3389/fgwh.2022.756362

Whilst scientific knowledge about SARS-CoV-2 and COVID-19 is rapidly increasing, much of the effects on pregnant women is still unknown. To accommodate pregnancy, the human endometrium must undergo a physiological transformation called decidualization. These changes encompass the remodeling of endometrial immune cells leading to immunotolerance of the semi-allogenic conceptus as well as defense against pathogens. The angiotensin converting enzyme 2 (ACE2) plays an important regulatory role in the renin-angiotensin-system (RAS) and has been shown to be protective against comorbidities known to worsen COVID-19 outcomes. Furthermore, ACE2 is also crucial for decidualization and thus for early gestation. An astounding gender difference has been found in COVID-19 with male patients presenting with more severe cases and higher mortality rates. This could be attributed to differences in sex chromosomes, hormone levels and behavior patterns. Despite profound changes in the female body during pregnancy, expectant mothers do not face worse outcomes compared with non-pregnant women. Whereas mother-to-child transmission through respiratory droplets during labor or in the postnatal period is known, another question of *in utero* transmission remains unanswered. Evidence of placental SARS-CoV-2 infection and expression of viral entry receptors at the maternal-fetal interface suggests the possibility of *in utero* transmission. SARS-CoV-2 can cause further harm through placental damage, maternal systemic inflammation, and hindered access to health care during the pandemic. More research on the effects of COVID-19 during early pregnancy as well as vaccination and treatment options for gravid patients is urgently needed.

Keywords: COVID-19, SARS-CoV-2, pregnancy, vertical transmission, decidualization, ACE2, women

INTRODUCTION

Since its emergence in December 2019 in Wuhan, China, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has infected over 250 million people and caused more than 4.9 million deaths worldwide (as of October 2021) (1, 2). The disease caused by SARS-CoV-2 is termed Coronavirus Disease 2019 (COVID-19) and was declared a global pandemic in March 2020 (3). Whilst scientific knowledge about this disease is rapidly increasing, much of its effects on pregnant women is still unknown.

Pregnancy is a unique physiological state during which the female body undergoes profound transformations. The immune system is altered during pregnancy, resulting in immunotolerance

of the semi-allogenic conceptus as well as protection of both mother and fetus against pathogens (4). Research indicates that during pregnancy, expectant mothers are more susceptible to some infectious diseases, such as influenza or Ebola (5, 6).

The aim of this review is to illustrate what is known about COVID-19 and how it affects pregnancy. First, changes in the human endometrium enabling embryo implantation and pregnancy will be discussed – a process coined decidualization. Special emphasis will be put on the endometrial immune microenvironment, angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2). What follows is a brief overview of SARS-CoV-2 and of COVID-19. The review will further describe the gender differences found in COVID-19 and offer possible explanations. Lastly, what is known about implications of COVID-19 infection during pregnancy will be reviewed, with particular focus on the possibility of vertical transmission of SARS-CoV-2.

THE HUMAN ENDOMETRIUM AND DECIDUALIZATION

The human menstrual cycle is approximately 28 days long and can be divided into two phases: the follicular (proliferative) phase and the luteal (secretory) phase (7, 8). The start of each cycle is marked by the onset of menstruation (9). During the first phase, estrogen is produced by granulosa cells in the ovaries, which leads to thickening of the endometrium (7). This thickening is the result of proliferating epithelial and stromal cells, as well as angiogenesis (7, 10). Ovulation marks the start of the second phase, when the corpus luteum produces progesterone, further preparing the endometrium for the possibility of embryo implantation and pregnancy; a process known as decidualization (11, 12). In the case of no pregnancy, the corpus luteum deteriorates leading to a drop in progesterone levels, vasoconstriction in the endometrium with hypoxia and desquamation of the stratum functionalis (11–13).

The process of decidualization involves the differentiation of endometrial stromal cells, which are of mesenchymal origin and resemble fibroblasts, into decidual cells, similar to epithelial cells (Figure 1) (14–16). During this mesenchymal-epithelial transition, the cells become larger and rounder with an expansion of the rough endoplasmic reticulum and the Golgi apparatus (11, 14). There is an increase in the number of nucleoli and an accumulation of lipid and glycogen droplets within the cytoplasm (11, 16). It was also shown that polyploidy is common among decidual cells, which might limit their lifespan but could benefit the growth of the embryo due to increased protein synthesis (17, 18). Decidual cells produce large quantities of prolactin and insulin-like growth factor binding protein-1, among others, which can also be used as *bona fide* markers for decidualization (11, 14).

The human endometrium is subject to cyclic transformations to provide an optimal environment for embryo implantation, however, the window of implantation is brief (19). The uterus is only receptive to a blastocyst during the limited duration of about 4 days, approximately 6 to 10 days after ovulation

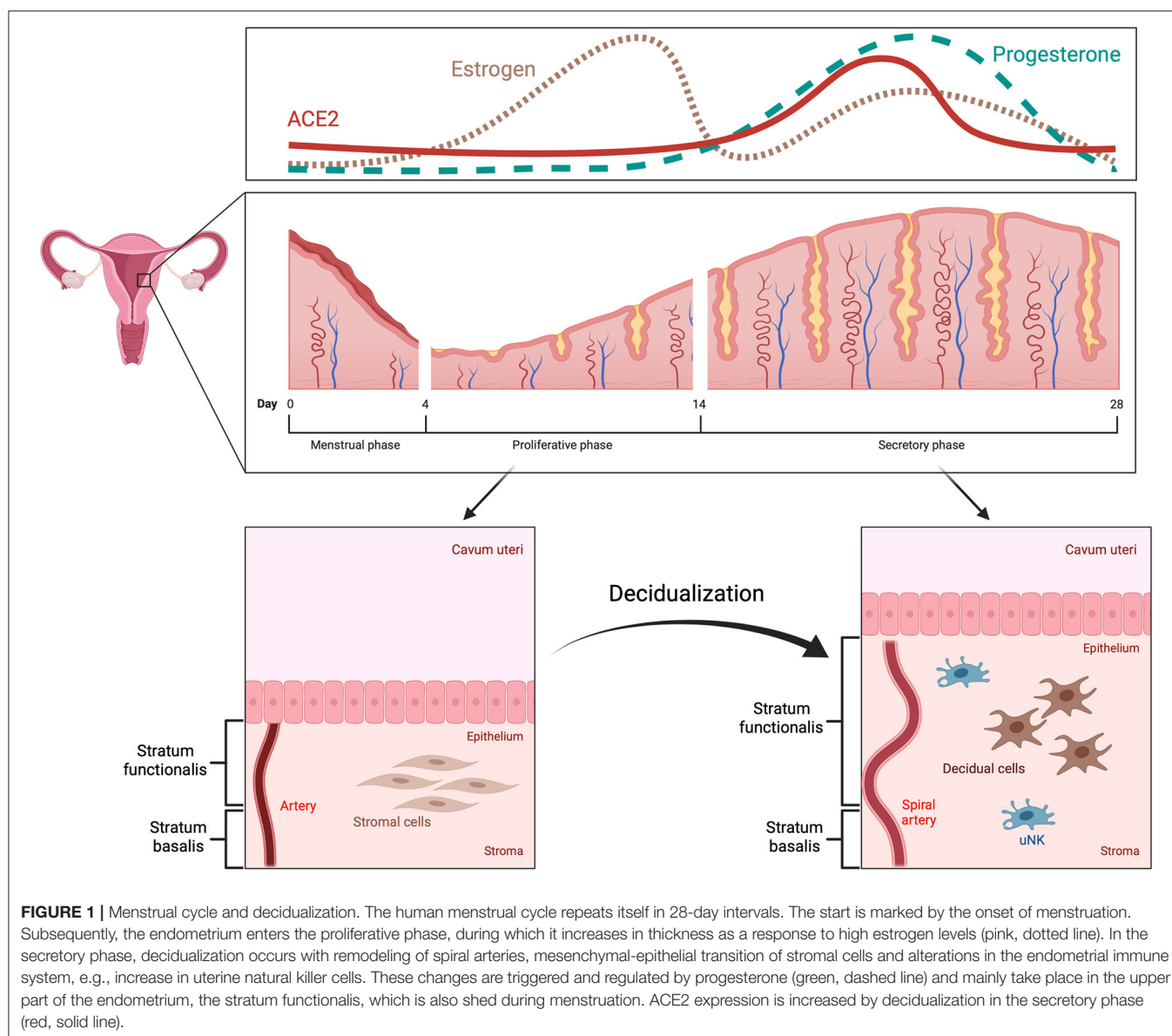
(20, 21). Not only does decidualization influence the timing of implantation but it also controls the extent of invasion by the embryo (22). Some studies even suggest that decidual cells are not passively invaded by the trophoblast but actively encapsulate the embryo (23–25). Moreover, the endometrium has the capability to sense the quality of the conceptus and makes a distinction between healthy and impaired embryos (26, 27). Therefore, the decidua promotes implantation of high-quality embryos while rejecting developmentally impaired ones through modulation of gene expression (26–28). Defective decidualization can lead to a plethora of pregnancy complications such as preeclampsia, preterm birth or even recurrent pregnancy loss, highlighting the importance of adequate decidualization in early pregnancy (15, 29).

THE ENDOMETRIAL IMMUNE MICROENVIRONMENT

Changes in morphology and function are not solely limited to stromal cells. Remodeling of the extracellular matrix as well as cell-cell interactions play a crucial role in decidualization (30, 31). Since pregnancy requires a well-calibrated balance between immunological responsiveness and tolerance, immune cells are another relevant component of the decidua (32, 33). During early pregnancy, up to 40% of all cells within the decidual tissue are leukocytes, such as macrophages, T and B cells and, most prominently, uterine natural killer cells (uNK) (34). The latter sees an increase in number during decidualization and is most abundant in the vicinity of spiral arteries, endometrial glands and at the maternal-fetal interface (7, 35). Although their function is not completely clear, studies suggest that uNK are involved in remodeling of spiral arteries, clearance of senescent decidual cells, regulating maternal immune tolerance and defense against pathogens (15, 35, 36).

The maternal immune system is modulated during pregnancy, which is particularly meaningful when trying to understand the effects of COVID-19 on pregnancy and vice versa. The decidualized cells play an important role in providing immunotolerance toward the allogenic embryo by modulating the spectrum of immune cells at the maternal-fetal interface (32, 37). While there are plenty uNK cells (70% of total leukocytes) and macrophages (20–25%) in the decidual tissue, dendritic cells and B and T lymphocytes are rare (11, 32, 38). It has been shown that dendritic cells, which regularly trigger T cell reaction, are entrapped in the tissue through decidualization and that their density throughout the decidua is reduced (39). Due to this entrapment, the dendritic cells are ineffective in facilitating T cell activation, thus, lowering the chance of immunological attack on the fetus. Furthermore, decidual cells inhibit T cell proliferation, suppress inflammation and prompt apoptosis of activated T cells *via* the expression of Galectin-1, indoleamine-2,3-dioxygenase and FAS-ligand (40–42).

In summary, decidualization is part of the cyclic morphological alterations in the endometrium. This process is of utmost importance for embryo implantation and early pregnancy. Decidualization mainly encompasses modifications



in endometrial stromal cells and is regulated predominantly by progesterone. Further, changes also occur in endometrial immune cells, and uNK cells are of particular interest, as they play an important role in endometrial remodeling during decidualization as well as immune tolerance and defense.

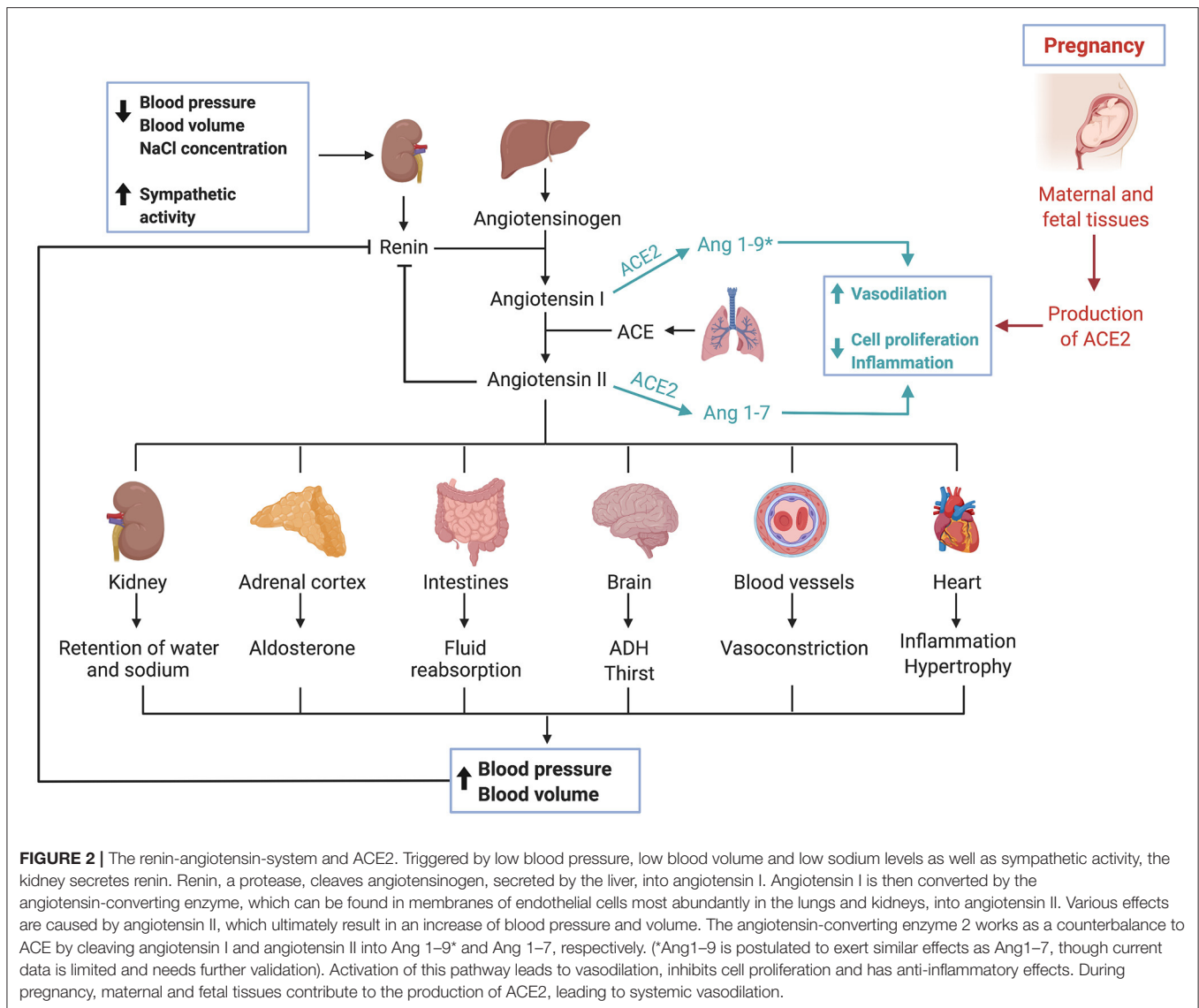
ACE2 – PHYSIOLOGY AND ROLE IN DECIDUALIZATION

The angiotensin-converting enzyme 2 (ACE2) is a typical zinc metallopeptidase that plays an important role in the renin-angiotensin system (RAS) (43). It is an integral membrane glycoprotein, consisting of 805 amino acids and containing a single catalytic domain (44). Major functions of ACE2 include converting angiotensin (Ang) I into Ang 1-9 and Ang II into

Ang 1-7 (45, 46). ACE typically converts Ang I into Ang II, causing vasoconstriction, leading to inflammation and fibrosis, ACE2 can be seen as a counterbalance to ACE (44). Thus, ACE2 is a negative regulator of RAS and therefore crucial in regulating blood pressure, fluid and electrolyte balance (**Figure 2**) (47).

Despite being expressed ubiquitously in the human body, some tissues contain remarkably high amounts of ACE2 including the kidneys, heart, lungs, testes and intestines as well as endothelial and vascular smooth muscle cells (43, 48, 49). ACE2-expressing tissues are potential targets for SARS-CoV-2 (50).

Notably, ACE2 has been shown to be protective against heart failure, hypertension, diabetes, renal dysfunction and pulmonary diseases (51–55). These are also comorbidities that have been identified to worsen the outcome of COVID-19 patients, which might be linked to a dysregulation of RAS (43, 56, 57). After facilitating the entry of SARS-CoV-2 into the host cell, ACE2



expression is downregulated (58). Loss of ACE2 is initiated during virus infection since the SARS-CoV-2-ACE2-complex is internalized through endocytosis (59, 60). This depletion of ACE2 leads to a dysregulation of RAS, further aggravating harmful effects of COVID-19, such as acute respiratory distress syndrome (ARDS) and endothelial dysfunction (61–63).

A controversial debate over the continued usage of angiotensin II receptor blockers and ACE inhibitors among COVID-19 patients with preexisting hypertension arose after the ACE2 receptor became known as the entry factor for SARS-CoV-2 (64). Since these drugs were thought to increase the expression of ACE2, it was hypothesized that their application would lead to higher infection rates and more severe COVID-19 cases (65, 66). However, several studies found no significant difference between patients treated with or without ACE inhibitors and/or angiotensin II receptor blockers regarding the infection rate and COVID-19 outcome (67–70). Controversially, others even

reported a lowered risk of SARS-CoV-2 infection or critical illness and death, respectively (71, 72). Notably, it was speculated that geographic and ethnic factors may influence the interaction between these drugs and COVID-19 (69, 71). Further studies are required to substantiate these findings.

The influence of gender and age on ACE2 expression is not fully understood yet. While several studies did not prove significant differences of ACE2 expression between young males and females (<55 years), it has been shown that the correlation between ACE2 and immune signatures in the lungs differ between the two sexes (49, 73–75). There have been contrasting results regarding the relation of ACE2 content to increasing age, with some finding an increase, a decrease, or no change at all (49, 73, 74). However, it has been suggested that steroid hormones may affect ACE2 activity with withdrawal of estrogen or testosterone causing an increase or a decrease, respectively (75).

Another important albeit overlooked function of ACE2 was illustrated in a recent study. Chadchan et al. found that the ACE2 protein is not only highly expressed in human endometrial stromal cells (HESCs), in particular during the secretory phase of the menstrual cycle, but it also increases significantly in stromal cells undergoing decidualization *in vitro* (76). They further observed that loss of ACE2 impeded decidualization (76). Additionally, Chadchan et al. described that ACE2 expression in the endometrium is induced by progesterone. Considering these results, it is plausible that ACE2 plays a vital role in decidualization of the human endometrium.

Furthermore, other studies have found that ACE2 and other components of RAS are expressed both in maternal and fetal tissues during pregnancy, suggesting their crucial role during implantation, vascular remodeling and labor (77–81). During pregnancy, the uterus and placenta contribute substantially to ACE2 production, thus causing a twofold increase in ACE2 activity with subsequent systemic vasodilation (82). The upregulation of RAS in the maternal decidua as well as in the endothelial and perivascular stromal cells during the first trimester of pregnancy coincides with spiral artery remodeling and angiogenesis (83). Dysregulation of uteroplacental RAS is reported to alter the tightly regulated maternal homeostasis causing pregnancy complications such as miscarriage, still birth and preeclampsia (84–86). It was also shown that plasma Ang 1-7, a product of ACE2, is elevated during healthy pregnancies and that preeclamptic mothers had lower levels of Ang 1-7 (87).

Remarkably, ACE2 is most abundant in the decidua in comparison with chorionic or amniotic tissues (77). Another compelling finding is that ACE2 expression is highest during early pregnancy and is negatively correlated with gestational age (88, 89). Moreover, fetal sex might affect maternal RAS and for instance, ACE2 mRNA levels were higher in decidual explants after 24h from women carrying a female fetus compared with those carrying a male fetus (90).

Briefly, ACE2 has essential functions for the RAS and contributes to the control of blood pressure as well as fluid and electrolyte homeostasis. ACE2 is expressed in various tissues throughout the human body and is protective against cardiovascular and respiratory diseases, among others. ACE2 is essential for decidualization and its production increases during pregnancy. Since ACE2 is also the entry receptor for SARS-CoV-2, its high expression in placental tissues has implications for pregnancies during COVID-19 infection, which will be covered in detail below.

SARS-COV-2 AND COVID-19

SARS-CoV-2 belongs to the same genus betacoronavirus as SARS-CoV and MERS-CoV, which are all enveloped viruses with a single-stranded positive-sense RNA (91, 92). Although the origin of SARS-CoV-2 has not been fully clarified yet, it is most likely that it originated from bats, which are a natural reservoir for coronaviruses, and was passed on to humans *via* an intermediate host such as pangolins (93, 94).

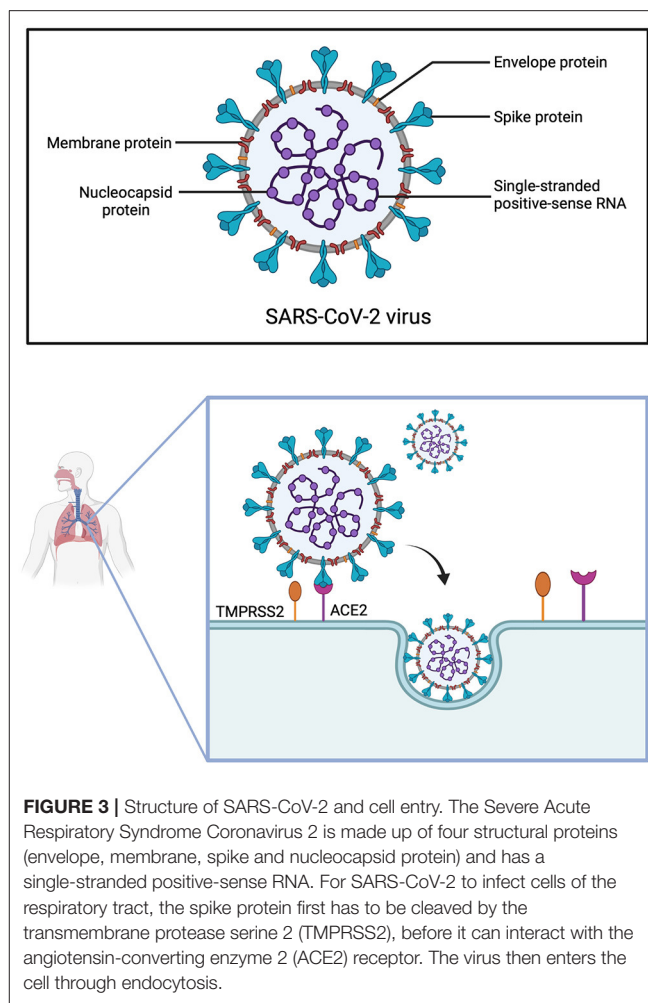


FIGURE 3 | Structure of SARS-CoV-2 and cell entry. The Severe Acute Respiratory Syndrome Coronavirus 2 is made up of four structural proteins (envelope, membrane, spike and nucleocapsid protein) and has a single-stranded positive-sense RNA. For SARS-CoV-2 to infect cells of the respiratory tract, the spike protein first has to be cleaved by the transmembrane protease serine 2 (TMPRSS2), before it can interact with the angiotensin-converting enzyme 2 (ACE2) receptor. The virus then enters the cell through endocytosis.

SARS-CoV-2 consists of four structural proteins: spike (S), nucleocapsid (N), membrane (M) and envelope (E) protein (95). The S-protein is of utmost interest, as it facilitates virus entry into host cells (96, 97). Due to the similarity of their S-proteins, SARS-CoV and SARS-CoV-2 both utilize the cell surface receptor ACE2 for attachment and penetration of host cells (97). However, the receptor-binding domain (RBD) of the S-protein differs among SARS-CoV and SARS-CoV-2, resulting in higher binding affinity to ACE2 of the latter (98). A precondition for the interaction of SARS-CoV-2 with ACE2 is S-protein priming by host proteases, among which the most relevant seems to be transmembrane protease serine 2 (TMPRSS2) (Figure 3) (99).

The main route of transmission is through respiratory droplets, nevertheless, SARS-CoV-2 can be further spread *via* aerosols, direct and indirect contact, and feces (100–103). While it has been suggested that SARS-CoV-2 could be passed on *via* sexual contact and breastfeeding, more evidence is necessary (104, 105).

For COVID-19, the incubation period, defined as the time between infection and onset of symptoms, is approximately 5 days (106, 107). The basic reproduction number R_0 of SARS-CoV-2 is estimated to lie between 2 and 3 with a peak viral load

in the upper respiratory tract around symptom onset or shortly after (108–110). Not only can patients be infectious 1 to 3 days before any symptoms occur, but there have also been reports of asymptomatic transmission (110, 111).

The clinical presentation of COVID-19 varies greatly from asymptomatic and mild to critical and even fatal cases (112). Diagnosis is further impeded by unspecific symptoms, which resemble the clinical picture of the common cold, influenza or other respiratory diseases (113). The most common manifestations are fever and cough, which are present in the majority of the patients, followed by fatigue and shortness of breath (50, 92, 114). Anosmia, ageusia, myalgia and diarrhea are less frequent among COVID-19 patients (115, 116). Some symptoms, for instance fatigue or dyspnea, can persist despite microbiological recovery – a condition termed Long COVID (117, 118).

COVID-19 originally revealed itself through an outbreak of pneumonia (97). In severe cases, patients develop ARDS with hypoxia or even respiratory failure (119). Histopathological findings are diffuse alveolar damage with desquamation of pneumocytes, formation of hyaline membranes, edema and inflammatory infiltration by lymphocytes, as well as microvascular injury (120, 121). Correspondingly, chest computed tomography (CT) scans of COVID-19 patients commonly show bilateral distribution of ground-glass opacities with or without consolidations, “crazy paving” patterns and air bronchogram signs (122, 123).

COVID-19 not only involves the lungs and the respiratory tract, but also multiple organ systems (124). This includes cardiovascular (e.g. acute cardiac injury, myocarditis), gastrointestinal (e.g. nausea and vomiting, diarrhea), neurological (e.g. dizziness, stroke) and hematological manifestations (e.g. lymphocytopenia, thrombotic events, disseminated intravascular coagulation (DIC)) (124–128). A case point feature of COVID-19 is, that it triggers an extensive inflammatory response, the “cytokine storm”, which further aggravates damage done by the virus (129). A delay in immune response due to immune evasion of SARS-CoV-2 with consequentially unhindered virus replication is found in severe cases of COVID-19 (130–132). Virus-induced cell death prompts the recruitment of macrophages and neutrophils, followed by hyperinflammation (130). Subsequent tissue damage and multi-organ failure are the main cause of death in COVID-19 (133, 134).

The vast majority (80–90%) of COVID-19 cases are asymptomatic or mildly symptomatic, whereas among the critically ill the mortality rate is as high as 49% (112, 119, 135). The most important prognostic factor is age, with children mainly being asymptomatic or only exhibiting mild symptoms whereas elderly patients are at high risk for mortality (136–138). Other factors contributing to poor outcome are comorbidities such as hypertension, heart disease, diabetes mellitus, Chronic Obstructive Pulmonary Disease (COPD) and chronic renal disease (139–141). Furthermore, obesity and the male sex have been linked to increased severity of COVID-19 (141–143). Genetic factors also have an impact on COVID-19 infection and outcome with some studies

suggesting links to HLA or ABO blood type (**Table 1**) (164–167).

COVID-19 AND WOMEN

Historically, women were overlooked in biomedical research and the male model was seen as the “norm”. Women were and are still underrepresented in clinical trials due to the notion that studies could be complicated by the menstrual cycle and that a potential fetus could be harmed (173). This practice of exclusion from clinical trials is even more common for pregnant women (174). Indeed, sex discrepancy also applies to animal models with a male bias in the majority of research fields (175). The belief that male data can be simply extrapolated to women leads to inadequate treatment of female patients, such as wrong dosage of drugs or more severe side effects (173, 176).

An astounding gender difference has been found in COVID-19; in that whilst infection rates are similar in both sexes, men are prone to having more severe infection and higher mortality (two- to threefold) (138, 144, 145, 177). Likewise, this bias toward males was also present in the MERS outbreak in 2014 (178). However, this pattern was not as consistent in the previous SARS epidemic in 2002, with only one study showing a significant difference in case fatality ratio between men and women (179, 180). Controversially, another review even reported that mainly females were affected by SARS (181).

One possible rationale for the female advantage lies in the sex chromosomes (182, 183). Since women possess two X-chromosomes, one of the X-chromosomes is silenced to compensate gene dosage (184). Some genes escape inactivation resulting in differential expression between sexes (185). The gene of the SARS-CoV-2 receptor ACE2 is located on the X-chromosome and is further recognized as an escape gene (185, 186). This implies that women might be in a more favorable position of elevated ACE2 expression which counterbalances the downregulation of ACE2 upon SARS-CoV-2 infection and therefore protects from an overactive RAS. However, expression does not equal enzyme activity and as described above, sex differential expression of ACE2 is still controversial (187, 188). Notably, soluble ACE2 (sACE2), which is generated through shedding of membrane-bound ACE2, was found to be higher in men compared with women as well as postmenopausal compared with premenopausal women (189–191). As higher levels of sACE2 are correlated with cardiovascular disease and diabetes, known risk factors for more severe cases of COVID-19, this may contribute to the male disadvantage (192).

Another potential link between genetics and the purported reduced risk in females is the fact that the X-chromosome contains a great repertoire of immune-related genes (193). It is noteworthy that women generally mount a faster and stronger innate and adaptive immune response whereas men are subject to reduced immune response and higher pathogen load (194). X-linked genes are suggested to play a pivotal role in autoimmune diseases, which are characterized by a heightened immune response against the patient's own cells and primarily affect women (195, 196). Genes encoding for pattern recognition

TABLE 1 | Risk factors for poor outcome in COVID-19.

Risk factors	Association with COVID-19
Demographic characteristics	
Age	Children and younger people generally exhibit more asymptomatic or mild cases, whereas older patients are at higher risk for severe cases and death (136–138).
Sex	The male sex is associated with higher infection rates and worse outcomes compared with the female sex (138, 143–145).
Socioeconomic status	People with lower income are at increased risk of COVID-19 infection and higher mortality compared to those with higher income (146, 147).
Comorbidities	
Hypertension	Most common comorbidity among COVID-19 patients, increases risk for poor outcome (138–140, 143)
Heart disease	Increases risk for poor outcome (138–141, 143)
Diabetes mellitus	Type 1 and type 2 diabetes as well as uncontrolled hyperglycemia increase the risk for poor COVID-19 outcome (139, 140, 143, 148–150). The association between high HbA _{1c} and increased mortality remains controversial (151–154). Especially for type 2 diabetes, use of insulin is linked to higher mortality (153, 155).
COPD	Increases risk for poor outcome (139, 140, 143, 156)
Chronic kidney disease	Increases risk for poor outcome (141, 157)
Obesity	Increases risk for poor outcome (140–143)
Cancer	Increases risk for poor outcome (139, 141, 158)
Chronic liver disease	Increases risk for poor outcome (159, 160)
Genetic factors	
ACE2 (Angiotensin-converting enzyme 2)	Some polymorphisms increase susceptibility to SARS-CoV-2 (e.g., S19P, K26R, E23K), others hinder interactions between the spike protein and ACE2 (e.g., K31R, N33I, E329G) (161, 162).
TMPRSS2 (Transmembrane serine protease 2)	Some variants are linked to increased TMPRSS2 expression and higher susceptibility to SARS-CoV-2 (e.g., rs12329760) (163).
HLA (Human leukocyte antigen)	Variants encoding proteins with low binding affinity to SARS-CoV-2 (e.g., B*46:01, C*14:02) increase vulnerability, whereas variants encoding proteins with high binding affinity to SARS-CoV-2 (e.g., B*15:03, A*02:02) encourage immunity (164, 165).
ABO (blood groups)	Higher risk of infection for blood type A, lower risk for blood type O (166, 167).
Lifestyle	
Smoking	Increases risk for poor outcome (156, 168)
Alcohol abuse	Uncertain, likely increases risk for poor outcome (169, 170)
Physical activity	Decreases risk for poor outcome (171, 172)

* indicates Nomenclature of HLA alleles.

receptors (PRRs) have a vital function in the innate immune system and consequently are of special interest regarding the delayed immune response in COVID-19 (197). Among them, Toll-like receptor 7 (TLR7) is not only responsible for the recognition of single-stranded viral RNA in endosomes, but its gene is also located on the X-chromosome and known to escape silencing in immune cells (198–200). Furthermore, reaction to TLR7 stimulation also differs depending on sex as peripheral blood mononuclear cells from females produce more Interferon- α (IFN- α), eliciting an anti-viral response, whereas in males higher production of Interleukin-10 (IL-10), an immunosuppressive cytokine, is induced (201, 202). Considering that differences in the immune response between the sexes occurs across all age groups, it is perhaps plausible that sex chromosomes are part of the reason why females seem to clear pathogens faster and have less severe COVID-19 cases (203).

Endocrine factors are another conceivable explanation for sex disparities in COVID-19 outcomes as the mortality rate in postmenopausal women is higher than in premenopausal women (204, 205). Estrogen has potent immunomodulatory

effects and estrogen receptors are expressed by several immune cells (206). At high concentrations, as found periovulatory or during pregnancy, estrogen has mainly anti-inflammatory effects, for instance decreasing levels of C-reactive protein (CRP), IL-6 and TNF- α (207–210). In contrast, estrogen triggers pro-inflammatory pathways at lower doses (211). Furthermore, estrogen has proven to reduce morbidity of influenza infection through modifying immune cell recruitment and cytokine production, as well as scaling down virus replication in females (212, 213). Despite less elderly women succumbing to COVID-19 in comparison to elderly men, climacteric women are still at higher risk of worse outcomes than their premenopausal counterparts, and further, estradiol treatment was shown to improve survival (214, 215).

Certain comorbidities are known to negatively impact COVID-19 outcomes; it is noteworthy that the prevalence of hypertension, diabetes and COPD is lower in the female population (216–218). This can be attributed to women leading healthier lifestyles, such as less smoking, lower alcohol consumption and more physical activity (219–221). Nonetheless,

biological factors might also have an impact on the development of the said comorbidities. Aside from ACE2 activity positively correlating with estrogen levels, protective effects of estrogen on atrial tissue through modulation of RAS and upregulation of ACE2 were observed (222, 223). Moreover, in a study on mice, obese females had higher adipose ACE2 activity and, unlike obese males, did not develop hypertension (224). When ovariectomized, female mice also showed reduced ACE2 activity and obesity-hypertension, which could be reversed through treatment with estrogen (224, 225). Akin to estrogen's shielding properties in hypertension, estrogen also guards premenopausal women from diabetes mellitus and estrogen replacement therapy in postmenopausal patients is beneficial for metabolic health (226, 227). In respect to COVID-19, it is noteworthy to point out that estrogen was shown to decrease ACE2 expression of differentiated airway epithelial cells, providing another clue for sex-difference in infection (228).

In summary, COVID-19 affects men with disproportionately higher infection rates, more severe cases, and higher mortality than women. This can be attributed to sex chromosomes, as the ACE2 gene lies on the X-chromosome and is known to escape silencing. Several genes related to immune response are also located on the X-chromosome, resulting in a faster and stronger immune defense in females. Additionally, hormones might cause sex differences in COVID-19 outcomes. High concentrations of estrogen have anti-inflammatory properties, thereby alleviating the detrimental effects of the cytokine storm in COVID-19. Lastly, women tend to have less comorbidities than men, due to healthier lifestyles and the protective effects of estrogen.

COVID-19 AND PREGNANCY

Pregnancy is a unique physiological condition with changes in the endocrine system (e.g., high levels of cortisol, progesterone and estrogen), cardiovascular system (e.g., increased cardiac output, decreased systemic vascular resistance, higher blood volume) and respiratory system (e.g., swelling of upper respiratory tract, elevated diaphragm, lower total lung capacity, hyperventilation) (229, 230). Considering COVID-19, physiologically elevated basal oxygen consumption levels, a predisposition to developing lung edema and dyspnea, as well as hypercoagulability are all relevant during pregnancy (231–234).

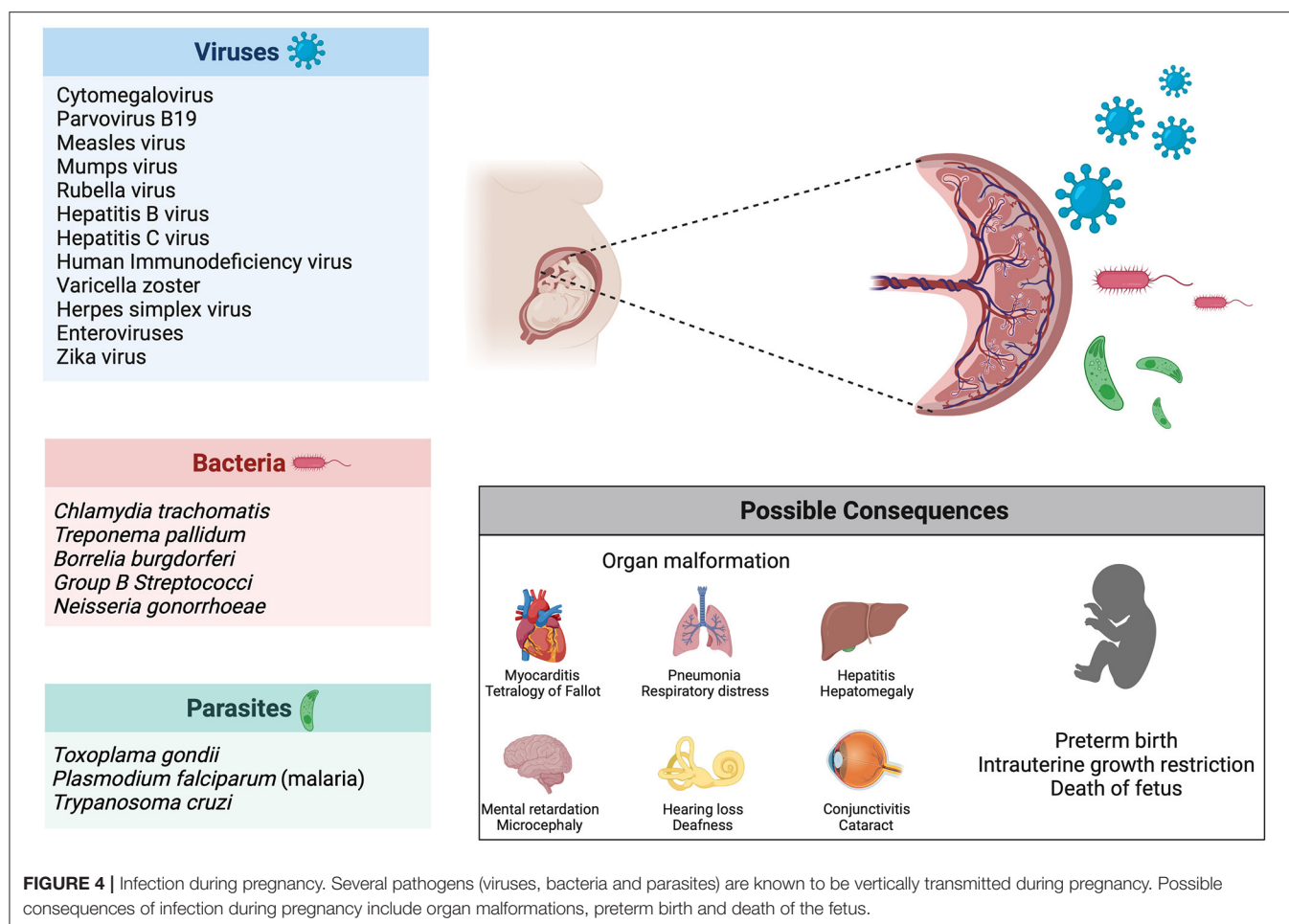
According to a meta-analysis from Di Toro et al. which included 1,100 pregnancies, most pregnant women infected with SARS-CoV-2 had uncomplicated clinical courses with frequent symptoms being fever and cough, pneumonia was prevalent in 89% of the cases (235). They further found an ICU admission rate of 8% and 5 maternal deaths, implying that pregnant women do not face worse outcomes than non-pregnant women. Other studies have also found pregnant COVID-19 patients to have similar clinical characteristics and disease outcomes as non-pregnant women (236, 237). Conversely, higher admission rates to ICU and a higher risk for more severe COVID-19 cases was reported among pregnant compared with non-pregnant patients (238–240). Advanced maternal age, comorbidities such as diabetes mellitus, hypertension, low socioeconomic status as

well as obesity have all been identified as possible risk factors for maternal death from COVID-19 (241).

The current pandemic has resulted in the requirement to transform and adapt healthcare services for pregnant women in high-risk groups including women with gestational diabetes mellitus (GDM) or diabetes mellitus. GDM is the most common medical complication of pregnancy and affects 10% of pregnancies globally. Those diagnosed with this condition are at higher risk for a severe COVID-19 infection due to predisposing factors such as hyperglycemia, obesity and hypertension (242). Critically, the most common underlying conditions of pregnant women with SARS-CoV-2 that were hospitalized for severe disease were pre-pregnancy BMI ≥ 30 kg/m² (41.7%) and diabetes mellitus (Type 2) (12.5%) (243). An interplay of several pathophysiological mechanisms is thought to increase the risk of an unfavorable course and a worse prognosis for patients with GDM. In general, diabetes or insulin resistance reduces T cell function leading to an impaired immune response. This results in the global cellular dysfunction underlying a variety of symptoms associated with diabetes, including a higher risk of respiratory infections (244). Moreover, it has been indicated that some COVID-19 patients develop a diabetes-like syndrome (245). Taken together, these factors could lead to poor pregnancy outcomes including pre-term labor, neonatal admissions to ICU or still birth. Therefore, several healthcare guidelines from the NIH (USA), STIKO/Robert Koch Institute (Germany) and the RCOG (UK) have emphatically expressed the urgency for pregnant women (diabetic and/or obese) to be vaccinated.

Commonly reported neonatal complications are preterm birth, premature rupture of membranes and fetal distress, while intrauterine growth restriction, miscarriage and death are rare events (246, 247). The high cesarean section rate (85%) among COVID-19 positive women is noteworthy, despite COVID-19 not posing a contraindication for vaginal delivery (235). Possibly, improved infection control during labor explains the preference for C-section, however, vaginal fluids were repeatedly tested were negative for SARS-CoV-2, indicating low risk for intrapartum transmission (246, 247).

Vertical transmission describes the process of ante-, peri- or postnatal mother-to-child transmission of infectious agents (248). The focus of this review will be on vertical transmission before birth, meaning *in utero* infection of the fetus. Several bacteria, viruses and parasites are known to cause congenital infection, the most common one being the cytomegalovirus (CMV) (249). The consequences of these infections depend on the pathogens, with some causing fetal death (e.g., parvovirus B19, mumps virus, rubella virus) and others leading to malformations or organ defects (e.g., Chlamydia trachomatis, Treponema pallidum, CMV, Toxoplasma gondii) (250). Another determinant of teratogenicity is the time of infection: the rubella virus causes cerebral, cardiac, ophthalmic and auditory defects when infection occurs in the first trimester of pregnancy (during organogenesis), whereas the fetus is most vulnerable to the hemolytic effect of parvovirus B19 and subsequent hydrops fetalis during the second trimester, due



to heightened hematopoiesis in the fetal liver (Figure 4) (250, 251).

While SARS-CoV-2 can be passed from mother to infant through respiratory droplets during labor or in the postnatal period, the question of *in utero* transmission remains unresolved (252). Infection rates among neonates born to COVID-19 positive mothers are low (6%), however, cases of early-onset COVID-19 exist with infants testing positive *via* nasopharyngeal swabs within 12 h postpartum (235, 253). Further, antibodies against SARS-CoV-2 identified in newborns shed additional light on the possibility of prenatal vertical transmission (254, 255). In contrast to IgG, which is subject to physiological transplacental transfer and therefore could originate from maternal blood, elevated levels of IgM indicate infection of the fetus *in utero*, as IgM usually does not cross the placental barrier (256). Nevertheless, inflammatory processes can affect the placental barrier and result in altered transfer of immunoglobulin (257). Thus, elevated IgM levels in neonates are no definite proof for *in utero* transmission of SARS-CoV-2.

Furthermore, in a study from Hecht et al. SARS-CoV-2 RNA was detected in the syncytiotrophoblast and cytotrophoblast of placentas from COVID-19 positive mothers (258). This

demonstrates that SARS-CoV-2 can infect the placenta, however, it does not definitely confirm vertical transmission. Further, these women were tested (positive for COVID-19) peripartum, limiting the insights into late pregnancy infection.

A potential way for vertical transmission of SARS-CoV-2 during pregnancy is *via* ACE2. As reviewed above, ACE2 is expressed in fetal and maternal tissues during pregnancy and most amply so in the early stages (77–81, 88, 89). Strong co-expression of ACE2 and TMPRSS2, necessary for cleavage of the spike protein, at the maternal-fetal-interface was reported by some studies (78, 259). In contrast, when examining expression patterns of ACE2 and TMPRSS2 in placentas, Pique-Regi et al. only found negligible co-transcription, especially compared to receptors for Zika virus and CMV, both known to cause congenital infections (260). While ACE2 was repeatedly shown to be present in endometrial and placental tissues, research on TMPRSS2 is inconclusive (258, 260, 261). It should be noted that low expression of TMPRSS2 does not necessarily equal low risk of SARS-CoV-2 infection. Other proteases have been suggested to provide an alternate pathway for viral cell entry, such as TMPRSS4, furin or cathepsin L (94). Notably, TMPRSS4 is expressed alongside ACE2 in the endometrium and, akin

to ACE2, increases toward the window of implantation (261). Furthermore, TMPRSS4 has the capacity of facilitating cell entry of SARS-CoV-2, thus, making it a candidate for promoting vertical transmission (262).

Another option for *in utero* transmission of SARS-CoV-2 while omitting ACE2 is through infected blood cells. While viremia in COVID-19 exists, only low levels of SARS-CoV-2 RNA are detectable in blood of infected patients (263, 264). When studying the full-term placenta from a COVID-19 positive mother whose newborn was also tested positive, Facchetti et al. showed that viral proteins and RNA were present in numerous fetal and maternal cells (265). Of particular interest is the finding that fetal monocytes were infected with SARS-CoV-2, thus, providing a potential vehicle for vertical transmission.

When interpreting results regarding vertical transmission, it must be considered that most studies solely include mothers tested positive for COVID-19 during the third trimester or peripartum and little attention has been devoted to early pregnancy. Recently, Valdespino-Vázquez et al. examined placental and fetal tissues from a miscarriage during the first trimester of a COVID-19 positive patient (266). They found viral proteins and RNA as well as hyper-inflammation present in both the placenta and the fetal organs (266). As organogenesis occurs in early pregnancy, infection during this crucial time would have detrimental effects on the fetal outcome. Additionally, a case report on a first trimester COVID-19 infection indicated, not only that SARS-CoV-2 persists in the placenta, but it also infected the amniotic fluid and fetal membranes (267). Strikingly, while the mother remained asymptomatic, her unborn succumbed to hydrops fetalis and death (267). Therefore, more research on COVID-19 and its effects on early pregnancy is urgently needed.

Indeed, vertical transmission is not the only way a pathogen can harm an unborn infant. Firstly, SARS-CoV-2 is known to cause placental damage, including maternal and fetal vascular malperfusion, decidual arteriopathy, intervillous thrombi as well as inflammation (e.g., villitis, intervillitis, chorioamnitis) (268–270). Abnormal ACE2 expression caused by SARS-CoV-2 infection in both decidua and placenta could potentially impair key physiological processes, such as placentation and vascularization during pregnancy (271). Hence, dysregulation of RAS could play a critical role in developing preeclampsia-like placental pathology, COVID-19 associated miscarriages and still births. Placental impairment leads to compromised fetal supply of oxygen and nutrients with subsequent complications, such as intrauterine growth restriction or miscarriage, independent of vertical transmission (272). Remarkably, placental pathology exists even in mild or asymptomatic cases of COVID-19 (273, 274).

Aside from locally impacting the placenta, COVID-19 is a systemic disease and the maternal immune response can result in fetal injury (250). Being subjected to an inflammatory milieu, can damage the lungs and brain of the developing fetus (250). Likewise, maternal fever and upper respiratory infection, both characteristics of COVID-19, are linked to congenital heart disease (275). Deleterious effects of the

cytokine storm induced by SARS-CoV-2 are not confined to the pregnant woman but could also affect the fetus, possibly resulting in multi-organ failure and ultimately fetal demise (276).

Of equal importance are psychological implications of the ongoing pandemic, such as higher rates of depression and anxiety among pregnant women, which might impact health and well-being of both mother and child (277, 278). Psychological stress is a known risk factor for miscarriage, especially during early pregnancy, which might be linked to elevated cortisol levels (279, 280). Furthermore, the pandemic lead to hampered access to pre- and postnatal care services, possibly contributing to underdiagnosis of complications (281). Interestingly, pregnant women were found to be at lower risk for depressive symptoms in comparison to non-pregnant women and mothers delivering during the COVID-19 pandemic had reduced risk of postpartum-depression than before the pandemic (282, 283). This points to substantial psychological resilience among expectant mothers.

In general, gravid patients present certain challenges to medical treatment. As mentioned above, pregnant women exhibit edema and swelling in the upper respiratory tract, thereby complicating endotracheal intubation (229). Moreover, pregnancy has implications on medication used to treat COVID-19 and vice versa; for example, Favipiravir, an antiviral drug used against COVID-19, should not be administered during pregnancy, and for magnesium sulfate, used for prophylaxis and treatment of preeclampsia, dosage adjustment is required in COVID-19 patients (284, 285).

While vaccination is seen as a promising way to resolve the COVID-19 pandemic, pregnant women were not included in clinical trials and, accordingly, a lack of evidence exists regarding safety and efficacy of COVID-19 vaccines in pregnancy (286). This not only resulted in differing recommendations from national and international organizations regarding vaccination against SARS-CoV-2 during pregnancy, but also in confusion and low acceptance among pregnant women (287, 288). Very recently, evidence about the safety and effectiveness of COVID-19 vaccines for pregnant women is emerging. Preliminary data indicates that vaccination against COVID-19 during pregnancy and lactation is safe regarding maternal side effects, female fertility as well as pregnancy and neonatal outcomes (289, 290). Based on 35,691 volunteers during or shortly before pregnancy, participants did not report any adverse side effects among pregnant women who received mRNA COVID-19 vaccines either from Pfizer/BioNTech or Moderna (290). It was demonstrated for COVID-19 mRNA vaccines that not only an immune response could be elicited in pregnant and lactating women but also that the antibodies could be passed onto their infants through the umbilical cord blood and breast milk (291–294). Given the ongoing pandemic, further research is urgently needed to provide reliable recommendations for the vaccination of pregnant and lactating women.

CONCLUDING REMARKS AND FUTURE PERSPECTIVES

This review describes the impact of COVID-19 on non-pregnant and pregnant women. Its aim is to explore why the SARS-CoV-2 infection affects men more severely than women and bringing knowledge about genetic, endocrine and exogenous factors together. Different ways of how COVID-19 can harm pregnant mothers and neonates are discussed and currently available data on the possibility of vertical transmission is summarized. This review intends to connect the pathophysiology of COVID-19 to the physiology of pregnancy, decidualization and RAS.

While knowledge on COVID-19 is increasing rapidly, a lack of evidence for the impact on pregnancy remains. Although the currently available data shows that non-pregnant and pregnant women seem to be less affected in terms of severity and mortality, little is known about the long-term effects of viral infection on the fetus. Vertical transmission seems to be rare, but neither is the possibility of *in utero* transmission excluded, nor are the effects of the maternal immune response on the unborn fully understood. Considering the therapeutic obstacles that the pandemic poses on pregnant COVID-19 patients, further research is needed to improve maternal and fetal management.

Notably, a major part of research on COVID-19 and pregnancy focuses explicitly on the third trimester, resulting in a lack of knowledge concerning adverse effects and vertical transmission during early pregnancy. With new SARS-CoV-2 variants emerging, continuous effort is required to shed light on their consequences for pregnancy as well as lactation. Furthermore, pregnant women should not be excluded in future clinical trials for COVID-19 vaccines and therapies. Scientific progress will enable doctors and

health workers to provide evidence-based treatments for pregnant women.

AUTHOR CONTRIBUTIONS

AL, MS, and JR performed information retrieval and/or analyzed data. MS, YS, and SB provided intellectual input, resources, and funding. AL wrote the original draft of the manuscript and drew the figures. The presented work here is used in MD thesis of AL. All authors reviewed the manuscript and approved of submission.

FUNDING

This work was supported by funding to MS intramural funds of Tübingen University the IZKF (2510-0-0) and by the Margarete von Wrangell (MvW 31-7635.41/118/3) habilitation scholarship co-funded by the Ministry of Science, Research and the arts (MWK) of the state of Baden-Württemberg and by the European Social Funds. AL is supported by the Tübingen Medical faculty Interdisziplinäres Promotionskolleg Medizin program (2021-1-02). To YS and MS the Ferring COVID-19 Investigational Grants in Reproductive Medicine and Maternal Health (RMMH) and we also thank the Open Access Publishing Fund of Tuebingen University. The funders played no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

ACKNOWLEDGMENTS

All figures were created with BioRender.com. **Figure 2** was adapted from Renin-Angiotensin System by BioRender.com.

REFERENCES

- Wang C, Horby PW, Hayden FG, Gao GF, A. novel coronavirus outbreak of global health concern. *Lancet*. (2020) 395:470–3. doi: 10.1016/S0140-6736(20)30185-9
- WHO. WHO COVID-19 Dashboard Genova(2020). Available online at: <https://covid19.who.int/> (accessed October 30, 2021).
- Ghebreyesus T. WHO Director-General's opening remarks at the media briefing on COVID-19. (2020). Available from: <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020> (accessed March 11, 2020)
- Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. *Am J Reprod Immunol*. (2010) 63:425–33. doi: 10.1111/j.1600-0897.2010.00836.x
- Somerville LK, Basile K, Dwyer DE, Kok J. The impact of influenza virus infection in pregnancy. *Future Microbiol*. (2018) 13:263–74. doi: 10.2217/fmb-2017-0096
- Silasi M, Cardenas I, Kwon JY, Racicot K, Aldo P, Mor G. Viral infections during pregnancy. *Am J Reprod Immunol*. (2015) 73:199–213. doi: 10.1111/aji.12355
- Ochoa-Bernal MA, Fazleabas AT. Physiologic events of embryo implantation and decidualization in human and non-human primates. *Int J Mol Sci*. (2020) 21. doi: 10.3390/ijms21061973
- Critchley HOD, Maybin JA, Armstrong GM, Williams ARW. Physiology of the Endometrium and Regulation of Menstruation. *Physiol Rev*. (2020) 100:1149–79. doi: 10.1152/physrev.00031.2019
- Brosens JJ, Parker MG, McIndoe A, Pijnenborg R, Brosens IA. A role for menstruation in preconditioning the uterus for successful pregnancy. *Am J Obstet Gynecol*. (2009) 200:615.e1–6. doi: 10.1016/j.ajog.2008.11.037
- Clancy KB. Reproductive ecology and the endometrium: physiology, variation, and new directions. *Am J Phys Anthropol*. (2009) 140 Suppl 49:137–54. doi: 10.1002/ajpa.21188
- Gellersen B, Brosens JJ. Cyclic decidualization of the human endometrium in reproductive health and failure. *Endocr Rev*. (2014) 35:851–905. doi: 10.1210/er.2014-1045
- Suthaporn S, Jayaprakasan K, Thornton JG, Walker KF, Castellanos M, May S, et al. Evaluating the influence of progesterone concentration and time of exposure on in vitro endometrial decidualisation. *Mol Cell Endocrinol*. (2021) 528:111242. doi: 10.1016/j.mce.2021.111242
- Roberts DK, Parmley TH, Walker NJ, Horbelt DV. Ultrastructure of the microvasculature in the human endometrium throughout the normal menstrual cycle. *Am J Obstet Gynecol*. (1992) 166:1393–406. doi: 10.1016/0002-9378(92)91611-D
- Gellersen B, Brosens IA, Brosens JJ. Decidualization of the human endometrium: mechanisms, functions, and clinical perspectives. *Semin Reprod Med*. (2007) 25:445–53. doi: 10.1055/s-2007-991042

15. Ng SW, Norwitz GA, Pavlicev M, Tilburgs T, Simón C, Norwitz ER. Endometrial decidualization: the primary driver of pregnancy health. *Int J Mol Sci.* (2020) 21. doi: 10.3390/ijms21114092
16. Okada H, Tsuzuki T, Murata H. Decidualization of the human endometrium. *Reprod Med Biol.* (2018) 17:220–7. doi: 10.1002/rmb2.12088
17. Sachs L, Shelesnyak MC. The development and suppression of polyploidy in the developing and suppressed deciduoma in the rat. *J Endocrinol.* (1955) 12:146–51. doi: 10.1677/joe.0.0120146
18. Sroga JM, Ma X, Das SK. Developmental regulation of decidual cell polyploidy at the site of implantation. *Front Biosci.* (2012) 4:1475–86. doi: 10.2741/s347
19. Tan J, Kan A, Hitkari J, Taylor B, Tallon N, Warraich G, et al. The role of the endometrial receptivity array (ERA) in patients who have failed euploid embryo transfers. *J Assist Reprod Genet.* (2018) 35:683–92. doi: 10.1007/s10815-017-1112-2
20. Kimber SJ. Molecular interactions at the maternal-embryonic interface during the early phase of implantation. *Semin Reprod Med.* (2000) 18:237–53. doi: 10.1055/s-2000-12562
21. Achache H, Revel A. Endometrial receptivity markers, the journey to successful embryo implantation. *Hum Reprod Update.* (2006) 12:731–46. doi: 10.1093/humupd/dml004
22. Sharma S, Godbole G, Modi D. Decidual control of trophoblast invasion. *Am J Reprod Immunol.* (2016) 75:341–50. doi: 10.1111/aji.12466
23. Weimar CH, Macklon NS, Post Uiterweer ED, Brosens JJ, Gellersen B. The motile and invasive capacity of human endometrial stromal cells: implications for normal and impaired reproductive function. *Hum Reprod Update.* (2013) 19:542–57. doi: 10.1093/humupd/dmt025
24. Grewal S, Carver J, Ridley AJ, Mardon HJ. Human endometrial stromal cell rho GTPases have opposing roles in regulating focal adhesion turnover and embryo invasion *in vitro*. *Biol Reprod.* (2010) 83:75–82. doi: 10.1095/biolreprod.109.080630
25. Grewal S, Carver JG, Ridley AJ, Mardon HJ. Implantation of the human embryo requires Rac1-dependent endometrial stromal cell migration. *Proc Natl Acad Sci U S A.* (2008) 105:16189–94. doi: 10.1073/pnas.0806219105
26. Teklenburg G, Salker M, Molokhia M, Lavery S, Trew G, Aojanpong T, et al. Natural selection of human embryos: decidualizing endometrial stromal cells serve as sensors of embryo quality upon implantation. *PLoS ONE.* (2010) 5:e10258. doi: 10.1371/journal.pone.0010258
27. Brosens JJ, Salker MS, Teklenburg G, Nautiyal J, Salter S, Lucas ES, et al. Uterine selection of human embryos at implantation. *Sci Rep.* (2014) 4:3894. doi: 10.1038/srep03894
28. Koot YE, Teklenburg G, Salker MS, Brosens JJ, Macklon NS. Molecular aspects of implantation failure. *Biochim Biophys Acta.* (2012) 1822:1943–50. doi: 10.1016/j.bbdis.2012.05.017
29. Cha J, Sun X, Dey SK. Mechanisms of implantation: strategies for successful pregnancy. *Nat Med.* (2012) 18:1754–67. doi: 10.1038/nm.3012
30. Damsky C, Sutherland A, Fisher S. Extracellular matrix 5: adhesive interactions in early mammalian embryogenesis, implantation, and placentalization. *FASEB J.* (1993) 7:1320–9. doi: 10.1096/fasebj.7.14.8224605
31. Iwahashi M, Muragaki Y, Ooshima A, Yamoto M, Nakano R. Alterations in distribution and composition of the extracellular matrix during decidualization of the human endometrium. *J Reprod Fertil.* (1996) 108:147–55. doi: 10.1530/jrf.0.1080147
32. Erlebacher A. Immunology of the maternal-fetal interface. *Annu Rev Immunol.* (2013) 31:387–411. doi: 10.1146/annurev-immunol-032712-100003
33. Yang F, Zheng Q, Jin L. Dynamic function and composition changes of immune cells during normal and pathological pregnancy at the maternal-fetal interface. *Front Immunol.* (2019) 10:2317. doi: 10.3389/fimmu.2019.02317
34. Bulmer JN, Williams PJ, Lash GE. Immune cells in the placental bed. *Int J Dev Biol.* (2010) 54:281–94. doi: 10.1387/ijdb.082763jb
35. Sojka DK, Yang L, Yokoyama WM. Uterine natural killer cells. *Front Immunol.* (2019) 10:960. doi: 10.3389/fimmu.2019.00960
36. Brighton PJ, Maruyama Y, Fishwick K, Vrljicak P, Tewary S, Fujihara R, et al. Clearance of senescent decidual cells by uterine natural killer cells in cycling human endometrium. *Elife.* (2017) 6. doi: 10.7554/eLife.31274
37. Bonney EA. Alternative theories: Pregnancy and immune tolerance. *J Reprod Immunol.* (2017) 123:65–71. doi: 10.1016/j.jri.2017.09.005
38. Ticconi C, Pietropolli A, Di Simone N, Piccione E, Fazleabas A. Endometrial immune dysfunction in recurrent pregnancy loss. *Int J Mol Sci.* (2019) 20. doi: 10.3390/ijms20215332
39. Collins MK, Tay CS, Erlebacher A. Dendritic cell entrapment within the pregnant uterus inhibits immune surveillance of the maternal/fetal interface in mice. *J Clin Invest.* (2009) 119:2062–73. doi: 10.1172/JCI38714
40. Tirado-González I, Freitag N, Barrientos G, Shaikly V, Nagaeva O, Strand M, et al. Galectin-1 influences trophoblast immune evasion and emerges as a predictive factor for the outcome of pregnancy. *Mol Hum Reprod.* (2013) 19:43–53. doi: 10.1093/molehr/gas043
41. Chang RQ, Li DJ, Li MQ. The role of indoleamine 2,3-dioxygenase in normal and pathological pregnancies. *Am J Reprod Immunol.* (2018) 79:e12786. doi: 10.1111/aji.12786
42. Sagrillo-Fagundes L, Bienvenue-Pariseault J, Legembre P, Vaillancourt C. An insight into the role of the death receptor CD95 throughout pregnancy: guardian, facilitator, or foe. *Birth Defects Res.* (2019) 111:197–211. doi: 10.1002/bdr2.1470
43. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong JC, Turner AJ, et al. Angiotensin-converting enzyme 2: SARS-CoV-2 receptor and regulator of the renin-angiotensin system: celebrating the 20th anniversary of the discovery of ACE2. *Circ Res.* (2020) 126:1456–74. doi: 10.1161/CIRCRESAHA.120.317015
44. Hamming I, Cooper ME, Haagmans BL, Hooper NM, Korstanje R, Osterhaus AD, et al. The emerging role of ACE2 in physiology and disease. *J Pathol.* (2007) 212:1–11. doi: 10.1002/path.2162
45. Donoghue M, Hsieh F, Baronas E, Godbout K, Gosselin M, Stagliano N, et al. A novel angiotensin-converting enzyme-related carboxypeptidase (ACE2) converts angiotensin I to angiotensin 1–9. *Circ Res.* (2000) 87:E1–9. doi: 10.1161/01.RES.87.5.e1
46. Wang K, Gheblawi M, Oudit GY. Angiotensin converting enzyme 2: a double-edged sword. *Circulation.* (2020) 142:426–8. doi: 10.1161/CIRCULATIONAHA.120.047049
47. Li Y, Zhou W, Yang L, You R. Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor. *Pharmacol Res.* (2020) 157:104833. doi: 10.1016/j.phrs.2020.104833
48. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol.* (2004) 203:631–7. doi: 10.1002/path.1570
49. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty.* (2020) 9:45. doi: 10.1186/s40249-020-00662-x
50. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *Jama.* (2020) 324:782–93. doi: 10.1001/jama.2020.12839
51. Patel VB, Zhong JC, Grant MB, Oudit GY. Role of the ACE2/Angiotensin 1–7 axis of the renin-angiotensin system in heart failure. *Circ Res.* (2016) 118:1313–26. doi: 10.1161/CIRCRESAHA.116.307708
52. Crackower MA, Sarao R, Oudit GY, Yagil C, Kozieradzki I, Scanga SE, et al. Angiotensin-converting enzyme 2 is an essential regulator of heart function. *Nature.* (2002) 417:822–8. doi: 10.1038/nature00786
53. Bindom SM, Lazartigues E. The sweeter side of ACE2: physiological evidence for a role in diabetes. *Mol Cell Endocrinol.* (2009) 302:193–202. doi: 10.1016/j.mce.2008.09.020
54. Shiota A, Yamamoto K, Ohishi M, Tatara Y, Ohnishi M, Maekawa Y, et al. Loss of ACE2 accelerates time-dependent glomerular and tubulointerstitial damage in streptozotocin-induced diabetic mice. *Hypertens Res.* (2010) 33:298–307. doi: 10.1038/hr.2009.231
55. Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, et al. Angiotensin-converting enzyme 2 protects from severe acute lung failure. *Nature.* (2005) 436:112–6. doi: 10.1038/nature03712

56. Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, et al. COVID-19 and comorbidities: deleterious impact on infected patients. *J Infect Public Health*. (2020) 13:1833–9. doi: 10.1016/j.jiph.2020.07.014
57. Cheng H, Wang Y, Wang GQ. Organ-protective effect of angiotensin-converting enzyme 2 and its effect on the prognosis of COVID-19. *J Med Virol*. (2020) 92:726–30. doi: 10.1002/jmv.25785
58. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med*. (2020) 76:14–20. doi: 10.1016/j.ejim.2020.04.037
59. Wang H, Yang P, Liu K, Guo F, Zhang Y, Zhang G, et al. SARS coronavirus entry into host cells through a novel clathrin- and caveolae-independent endocytic pathway. *Cell Res*. (2008) 18:290–301. doi: 10.1038/cr.2008.15
60. Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. *Nat Commun*. (2020) 11:1620. doi: 10.1038/s41467-020-15562-9
61. Sarzani R, Giulietti F, Di Pentima C, Giordano P, Spannella F. Disequilibrium between the classic renin-angiotensin system and its opposing arm in SARS-CoV-2-related lung injury. *Am J Physiol Lung Cell Mol Physiol*. (2020) 319:L325–L36. doi: 10.1152/ajplung.00189.2020
62. Amraei R, Rahimi N. COVID-19, Renin-Angiotensin System and Endothelial Dysfunction. *Cells*. (2020) 9. doi: 10.3390/cells9071652
63. D'Ardes D, Boccatonda A, Rossi I, Guagnano MT, Santilli F, Cipollone F, et al. COVID-19 and RAS: unravelling an unclear relationship. *Int J Mol Sci*. (2020) 21. doi: 10.3390/ijms21083003
64. Rossi GP, Sanga V, Barton M. Potential harmful effects of discontinuing ACE-inhibitors and ARBs in COVID-19 patients. *eLife*. (2020) 9:e57278. doi: 10.7554/eLife.57278
65. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med*. (2020) 8:e21. doi: 10.1016/S2213-2600(20)30116-8
66. Sriram K, Insel PA. Risks of ACE inhibitor and ARB usage in COVID-19: evaluating the evidence. *Clin Pharmacol Ther*. (2020) 108:236–41. doi: 10.1002/cpt.1863
67. Fosbøl EL, Butt JH, Østergaard L, Andersson C, Selmer C, Kragholm K, et al. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with COVID-19 diagnosis and mortality. *Jama*. (2020) 324:168–77. doi: 10.1001/jama.2020.11301
68. Flacco ME, Acuti Martellucci C, Bravi F, Parruti G, Cappadona R, Mascitelli A, et al. Treatment with ACE inhibitors or ARBs and risk of severe/lethal COVID-19: a meta-analysis. *Heart*. (2020) 106:1519–24. doi: 10.1136/heartjnl-2020-317336
69. Patoulias D, Katsimardou A, Stavropoulos K, Imprialos K, Kalogirou MS, Doumas M. Renin-angiotensin system inhibitors and COVID-19: a systematic review and meta-analysis. Evidence for significant geographical disparities. *Curr Hypertens Rep*. (2020) 22:90. doi: 10.1007/s11906-020-01101-w
70. Reynolds HR, Adhikari S, Pulgarin C, Troxel AB, Iturrate E, Johnson SB, et al. Renin-angiotensin-aldosterone system inhibitors and risk of Covid-19. *N Engl J Med*. (2020) 382:2441–8. doi: 10.1056/NEJMoa2008975
71. Hippisley-Cox J, Young D, Coupland C, Channon KM, Tan PS, Harrison DA, et al. Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 83 million people. *Heart*. (2020) 106:1503–11. doi: 10.1136/heartjnl-2020-317393
72. Yang G, Tan Z, Zhou L, Yang M, Peng L, Liu J, et al. Effects of angiotensin II receptor blockers and ACE (angiotensin-converting enzyme) inhibitors on virus infection, inflammatory status, and clinical outcomes in patients with COVID-19 and hypertension: a single-center retrospective study. *Hypertension*. (2020) 76:51–8. doi: 10.1161/HYPERTENSIONAHA.120.15143
73. Fernández-Atucha A, Izaguirre A, Fraile-Bermúdez AB, Kortajarena M, Larrinaga G, Martínez-Lage P, et al. Sex differences in the aging pattern of renin-angiotensin system serum peptidases. *Biol Sex Differ*. (2017) 8:5. doi: 10.1186/s13293-017-0128-8
74. Xie X, Chen J, Wang X, Zhang F, Liu Y. Age- and gender-related difference of ACE2 expression in rat lung. *Life Sci*. (2006) 78:2166–71. doi: 10.1016/j.lfs.2005.09.038
75. Dalpiaz PL, Lamas AZ, Caliman IF, Ribeiro RF, Abreu GR, Moyses MR, et al. Sex hormones promote opposite effects on ACE and ACE2 activity, hypertrophy and cardiac contractility in spontaneously hypertensive rats. *PLoS ONE*. (2015) 10:e0127515. doi: 10.1371/journal.pone.0127515
76. Chadchan SB, Popli P, Maurya VK, Kommagani R. The SARS-CoV-2 receptor, angiotensin-converting enzyme 2, is required for human endometrial stromal cell decidualization[†]. *Biol Reprod*. (2021) 104:336–43. doi: 10.1093/biolre/iaaa211
77. Marques FZ, Pringle KG, Conquest A, Hirst JJ, Markus MA, Sarris M, et al. Molecular characterization of renin-angiotensin system components in human intrauterine tissues and fetal membranes from vaginal delivery and cesarean section. *Placenta*. (2011) 32:214–21. doi: 10.1016/j.placenta.2010.12.006
78. Weatherbee BAT, Glover DM, Zernicka-Goetz M. Expression of SARS-CoV-2 receptor ACE2 and the protease TMPRSS2 suggests susceptibility of the human embryo in the first trimester. *Open Biol*. (2020) 10:200162. doi: 10.1098/rsob.200162
79. Valdés G, Neves LA, Anton L, Corthorn J, Chacón C, Germain AM, et al. Distribution of angiotensin-(1-7) and ACE2 in human placentas of normal and pathological pregnancies. *Placenta*. (2006) 27:200–7. doi: 10.1016/j.placenta.2005.02.015
80. Valdés G, Corthorn J, Bharadwaj MS, Joyner J, Schneider D, Brosnihan KB. Utero-placental expression of angiotensin-(1-7) and ACE2 in the pregnant guinea-pig. *Reprod Biol Endocrinol*. (2013) 11:5. doi: 10.1186/1477-7827-11-5
81. Li M, Chen L, Zhang J, Xiong C, Li X. The SARS-CoV-2 receptor ACE2 expression of maternal-fetal interface and fetal organs by single-cell transcriptome study. *PLoS ONE*. (2020) 15:e0230295. doi: 10.1371/journal.pone.0230295
82. Levy A, Yagil Y, Bursztyn M, Barkalifa R, Scharf S, Yagil C. ACE2 expression and activity are enhanced during pregnancy. *Am J Physiol Regul Integr Comp Physiol*. (2008) 295:R1953–61. doi: 10.1152/ajpregu.90592.2008
83. Morgan T, Craven C, Ward K. Human spiral artery renin-angiotensin system. *Hypertension*. (1998) 32:683–7. doi: 10.1161/01.HYP.32.4.683
84. Irani RA, Xia Y. Renin angiotensin signaling in normal pregnancy and preeclampsia. *Semin Nephrol*. (2011) 31:47–58. doi: 10.1016/j.semnephrol.2010.10.005
85. Irani RA, Xia Y. The functional role of the renin-angiotensin system in pregnancy and preeclampsia. *Placenta*. (2008) 29:763–71. doi: 10.1016/j.placenta.2008.06.011
86. Verdonk K, Visser W, Van Den Meiracker AH, Danser AH. The renin-angiotensin-aldosterone system in pre-eclampsia: the delicate balance between good and bad. *Clin Sci (Lond)*. (2014) 126:537–44. doi: 10.1042/CS20130455
87. Merrill DC, Karoly M, Chen K, Ferrario CM, Brosnihan KB. Angiotensin-(1-7) in normal and preeclamptic pregnancy. *Endocrine*. (2002) 18:239–45. doi: 10.1385/ENDO:18:3:239
88. Bloise E, Zhang J, Nakpu J, Hamada H, Dunk CE, Li S, et al. Expression of severe acute respiratory syndrome coronavirus 2 cell entry genes, angiotensin-converting enzyme 2 and transmembrane protease serine 2, in the placenta across gestation and at the maternal-fetal interface in pregnancies complicated by preterm birth or preeclampsia. *Am J Obstet Gynecol*. (2021) 224:298.e1–e8. doi: 10.1016/j.ajog.2020.08.055
89. Neves LA, Stovall K, Joyner J, Valdés G, Gallagher PE, Ferrario CM, et al. ACE2 and ANG-(1-7) in the rat uterus during early and late gestation. *Am J Physiol Regul Integr Comp Physiol*. (2008) 294:R151–61. doi: 10.1152/ajpregu.00514.2007
90. Wang Y, Pringle KG, Sykes SD, Marques FZ, Morris BJ, Zakar T, et al. Fetal sex affects expression of renin-angiotensin system components in term human decidua. *Endocrinology*. (2012) 153:462–8. doi: 10.1210/en.2011-1316
91. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. (2020) 395:565–74. doi: 10.1016/S0140-6736(20)30251-8
92. Samudrala PK, Kumar P, Choudhary K, Thakur N, Wadekar GS, Dayaramani R, et al. Virology, pathogenesis, diagnosis and in-line treatment of COVID-19. *Eur J Pharmacol*. (2020) 883:173375. doi: 10.1016/j.ejphar.2020.173375

93. Zhang YZ, Holmes EC, A. Genomic Perspective on the Origin and Emergence of SARS-CoV-2. *Cell*. (2020) 181:223–7. doi: 10.1016/j.cell.2020.03.035
94. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. (2021) 19:141–54. doi: 10.1038/s41579-020-00459-7
95. Wang MY, Zhao R, Gao LJ, Gao XF, Wang DP, Cao JM. SARS-CoV-2: structure, biology, and structure-based therapeutics development. *Front Cell Infect Microbiol*. (2020) 10:587269. doi: 10.3389/fcimb.2020.587269
96. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*. (2003) 426:450–4. doi: 10.1038/nature02145
97. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. (2020) 579:270–3. doi: 10.1038/s41586-020-2012-7
98. Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, et al. Structural basis of receptor recognition by SARS-CoV-2. *Nature*. (2020) 581:221–4. doi: 10.1038/s41586-020-2179-y
99. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. (2020) 181:271–80.e8. doi: 10.1016/j.cell.2020.02.052
100. Stadnytskyi V, Bax CE, Bax A, Anfinrud P. The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. *Proc Natl Acad Sci U S A*. (2020) 117:11875–7. doi: 10.1073/pnas.2006874117
101. Tang S, Mao Y, Jones RM, Tan Q, Ji JS, Li N, et al. Aerosol transmission of SARS-CoV-2? Evidence, prevention and control. *Environ Int*. (2020) 144:106039. doi: 10.1016/j.envint.2020.106039
102. Abd EW, Eassa SM, Metwally M, Al-Hraishawi H, Omar SR. SARS-CoV-2 transmission channels: a review of the literature. *MEDICC Rev*. (2020) 22:51–69. doi: 10.37757/MR2020.V22.N4.3
103. Chen Y, Chen L, Deng Q, Zhang G, Wu K, Ni L, et al. The presence of SARS-CoV-2 RNA in the feces of COVID-19 patients. *J Med Virol*. (2020) 92:833–40. doi: 10.1002/jmv.25825
104. Li D, Jin M, Bao P, Zhao W, Zhang S. Clinical characteristics and results of semen tests among men with coronavirus disease 2019. *JAMA Netw Open*. (2020) 3:e208292. doi: 10.1001/jamanetworkopen.2020.8292
105. Groß R, Conzelmann C, Müller JA, Stenger S, Steinhart K, Kirchhoff F, et al. Detection of SARS-CoV-2 in human breastmilk. *Lancet*. (2020) 395:1757–8. doi: 10.1016/S0140-6736(20)31181-8
106. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med*. (2020) 172:577–82. doi: 10.7326/M20-0504
107. McAloon C, Collins Á, Hunt K, Barber A, Byrne AW, Butler E, et al. Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. *BMJ Open*. (2020) 10:e039652. doi: 10.1136/bmjopen-2020-039652
108. Salzberger B, Buder F, Lampl B, Ehrenstein B, Hitzentbichler F, Holzmann T, et al. Epidemiology of SARS-CoV-2. *Infection*. (2021) 49:233–9. doi: 10.1007/s15010-020-01531-3
109. Singanayagam A, Patel M, Charlett A, Lopez Bernal J, Saliba V, Ellis J, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. *Euro Surveill*. (2020) 25. doi: 10.2807/1560-7917.ES.2020.25.32.2001483
110. Walsh KA, Jordan K, Clyne B, Rohde D, Drummond L, Byrne P, et al. SARS-CoV-2 detection, viral load and infectivity over the course of an infection. *J Infect*. (2020) 81:357–71. doi: 10.1016/j.jinf.2020.06.067
111. Widders A, Broom A, Broom J. SARS-CoV-2: the viral shedding vs infectivity dilemma. *Infect Dis Health*. (2020) 25:210–5. doi: 10.1016/j.idh.2020.05.002
112. Cevik M, Bamford CGG, Ho A. COVID-19 pandemic—a focused review for clinicians. *Clin Microbiol Infect*. (2020) 26:842–7. doi: 10.1016/j.cmi.2020.04.023
113. Liu X, Liu C, Liu G, Luo W, Xia N. COVID-19: Progress in diagnostics, therapy and vaccination. *Theranostics*. (2020) 10:7821–35. doi: 10.7150/thno.47987
114. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. (2020) 382:1708–20. doi: 10.1056/NEJMoa2002032
115. Adil MT, Rahman R, Whitelaw D, Jain V, Al-Taani O, Rashid F, et al. SARS-CoV-2 and the pandemic of COVID-19. *Postgrad Med J*. (2021) 97:110–6. doi: 10.1136/postgradmedj-2020-138386
116. Spinato G, Fabbri C, Polesel J, Cazzador D, Borsetto D, Hopkins C, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. *Jama*. (2020) 323:2089–90. doi: 10.1001/jama.2020.6771
117. Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. *Jama*. (2020) 324:603–5. doi: 10.1001/jama.2020.12603
118. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol*. (2021) 93:1013–22. doi: 10.1002/jmv.26368
119. Berlin DA, Gulick RM, Martinez FJ. Severe COVID-19. *N Engl J Med*. (2020) 383:2451–60. doi: 10.1056/NEJMcp2009575
120. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. (2020) 8:420–2. doi: 10.1016/S2213-2600(20)30076-X
121. Calabrese F, Pezzuto F, Fortarezza F, Hofman P, Kern I, Panizo A, et al. Pulmonary pathology and COVID-19: lessons from autopsy. The experience of European Pulmonary Pathologists. *Virchows Arch*. (2020) 477:359–72. doi: 10.1007/s00428-020-02886-6
122. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur Radiol*. (2020) 30:4381–9. doi: 10.1007/s00330-020-06801-0
123. Wan S, Li M, Ye Z, Yang C, Cai Q, Duan S, et al. CT manifestations and clinical characteristics of 1115 patients with coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Acad Radiol*. (2020) 27:910–21. doi: 10.1016/j.acra.2020.04.033
124. Lai CC, Ko WC, Lee PI, Jean SS, Hsueh PR. Extra-respiratory manifestations of COVID-19. *Int J Antimicrob Agents*. (2020) 56:106024. doi: 10.1016/j.ijantimicag.2020.106024
125. Magadam A, Kishore R. Cardiovascular Manifestations of COVID-19 Infection. *Cells*. (2020) 9. doi: 10.3390/cells9112508
126. Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, et al. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. (2020) 5:667–78. doi: 10.1016/S2468-1253(20)30126-6
127. Orsini A, Corsi M, Santangelo A, Riva A, Peroni D, Foidelli T, et al. Challenges and management of neurological and psychiatric manifestations in SARS-CoV-2 (COVID-19) patients. *Neurol Sci*. (2020) 41:2353–66. doi: 10.1007/s10072-020-04544-w
128. Rahi MS, Jindal V, Reyes SP, Gunasekaran K, Gupta R, Jaiyesimi I. Hematologic disorders associated with COVID-19: a review. *Ann Hematol*. (2021) 100:309–20. doi: 10.1007/s00277-020-04366-y
129. Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 cytokine storm; what we know so far. *Front Immunol*. (2020) 11:1446. doi: 10.3389/fimmu.2020.01446
130. Felsenstein S, Herbert JA, McNamara PS, Hedrich CM. COVID-19: Immunology and treatment options. *Clin Immunol*. (2020) 215:108448. doi: 10.1016/j.clim.2020.108448
131. Blanco-Melo D, Nilsson-Payant BE, Liu WC, Uhl S, Hoagland D, Möller R, et al. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. *Cell*. (2020) 181:1036–45.e9. doi: 10.1016/j.cell.2020.04.026
132. Keam S, Megawati D, Patel SK, Tiwari R, Dhama K, Harapan H. Immunopathology and immunotherapeutic strategies in severe acute respiratory syndrome coronavirus 2 infection. *Rev Med Virol*. (2020) 30:e2123. doi: 10.1002/rmv.2123
133. Melenotte C, Silvin A, Goubet AG, Lahmar I, Dubuisson A, Zumla A, et al. Immune responses during COVID-19 infection. *Oncoimmunology*. (2020) 9:1807836. doi: 10.1080/2162402X.2020.1807836
134. Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging

- pathogenesis and therapy concepts. *J Leukoc Biol.* (2020) 108:17–41. doi: 10.1002/JLB.3COVR0520-272R
135. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) Outbreak in China: summary of a report of 72 314 cases from the chinese center for disease control and prevention. *Jama.* (2020) 323:1239–42. doi: 10.1001/jama.2020.2648
 136. Pollard CA, Morran MP, Nestor-Kalinowski AL. The COVID-19 pandemic: a global health crisis. *Physiol Genomics.* (2020) 52:549–57. doi: 10.1152/physiolgenomics.00089.2020
 137. Yasuhara J, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: a systematic review. *Pediatr Pulmonol.* (2020) 55:2565–75. doi: 10.1002/ppul.24991
 138. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* (2020) 395:1054–62. doi: 10.1016/S0140-6736(20)30566-3
 139. Zhang B, Zhou X, Qiu Y, Song Y, Feng F, Feng J, et al. Clinical characteristics of 82 cases of death from COVID-19. *PLoS ONE.* (2020) 15:e0235458. doi: 10.1371/journal.pone.0235458
 140. Edler C, Schröder AS, Aepfelbacher M, Fitzek A, Heinemann A, Heinrich F, et al. Dying with SARS-CoV-2 infection-an autopsy study of the first consecutive 80 cases in Hamburg, Germany. *Int J Legal Med.* (2020) 134:1275–84. doi: 10.1007/s00414-020-02317-w
 141. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *Bmj.* (2020) 369:m1966. doi: 10.1136/bmj.m1966
 142. de Leeuw AJM, Oude Luttikhuis MAM, Wellen AC, Müller C, Calkhoven CF. Obesity and its impact on COVID-19. *J Mol Med.* (2021) 99:1–17. doi: 10.1007/s00109-021-02072-4
 143. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. *Jama.* (2020) 323:2052–9. doi: 10.1001/jama.2020.6775
 144. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19: focus on severity and mortality. *Front Public Health.* (2020) 8:152. doi: 10.3389/fpubh.2020.00152
 145. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ.* (2020) 11:29. doi: 10.1186/s13293-020-00304-9
 146. Raifman MA, Raifman JR. Disparities in the population at risk of severe illness from COVID-19 by race/ethnicity and income. *Am J Prev Med.* (2020) 59:137–9. doi: 10.1016/j.amepre.2020.04.003
 147. Karmakar M, Lantz PM, Tipirneni R. Association of social and demographic factors with COVID-19 incidence and death rates in the US. *JAMA Netw Open.* (2021) 4:e2036462. doi: 10.1001/jamanetworkopen.2020.36462
 148. Kumar A, Arora A, Sharma P, Anikhandi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr.* (2020) 14:535–45. doi: 10.1016/j.dsx.2020.04.044
 149. Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol.* (2020) 8:813–22. doi: 10.1016/S2213-8587(20)30272-2
 150. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. *J Diabetes Sci Technol.* (2020) 14:813–21. doi: 10.1177/1932296820924469
 151. Holman N, Knighton P, Kar P, O'Keefe J, Curley M, Weaver A, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol.* (2020) 8:823–33. doi: 10.1016/S2213-8587(20)30271-0
 152. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. *Cell Metab.* (2020) 31:1068–77.e3. doi: 10.1016/j.cmet.2020.04.021
 153. Agarwal S, Schechter C, Southern W, Crandall JP, Tomer Y. Preadmission diabetes-specific risk factors for mortality in hospitalized patients with diabetes and coronavirus disease 2019. *Diabetes Care.* (2020) 43:2339–44. doi: 10.2337/dc20-1543
 154. Cariou B, Hadjadj S, Wargny M, Pichelin M, Al-Salameh A, Allix I, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. *Diabetologia.* (2020) 63:1500–15. doi: 10.1007/s00125-020-05180-x
 155. Yu B, Li C, Sun Y, Wang DW. Insulin treatment is associated with increased mortality in patients with COVID-19 and type 2 diabetes. *Cell Metab.* (2021) 33:65–77.e2. doi: 10.1016/j.cmet.2020.11.014
 156. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, et al. The impact of COPD and smoking history on the severity of COVID-19: a systemic review and meta-analysis. *J Med Virol.* (2020) 92:1915–21. doi: 10.1002/jmv.25889
 157. Portolés J, Marques M, López-Sánchez P, de Valdenebro M, Muñoz E, Serrano ML, et al. Chronic kidney disease and acute kidney injury in the COVID-19 Spanish outbreak. *Nephrol Dial Transplant.* (2020) 35:1353–61. doi: 10.1093/ndt/gfaa189
 158. Liu C, Zhao Y, Okwan-Duodu D, Basho R, Cui X. COVID-19 in cancer patients: risk, clinical features, and management. *Cancer Biol Med.* (2020) 17:519–27. doi: 10.20892/j.issn.2095-3941.2020.0289
 159. Kovalic AJ, Satapathy SK, Thuluvath PJ. Prevalence of chronic liver disease in patients with COVID-19 and their clinical outcomes: a systematic review and meta-analysis. *Hepatol Int.* (2020) 14:612–20. doi: 10.1007/s12072-020-10078-2
 160. Singh S, Khan A. Clinical characteristics and outcomes of coronavirus disease 2019 among patients with preexisting liver disease in the United States: a multicenter research network study. *Gastroenterology.* (2020) 159:768–71.e3. doi: 10.1053/j.gastro.2020.04.064
 161. Stawiski EW, Diwanji D, Suryamohan K, Gupta R, Fellouse FA, Sathirapongsasuti JF, et al. Human ACE2 receptor polymorphisms predict SARS-CoV-2 susceptibility. *bioRxiv.* (2020). doi: 10.1101/2020.04.07.024752
 162. Hussain M, Jabeen N, Raza F, Shabbir S, Baig AA, Amanullah A, et al. Structural variations in human ACE2 may influence its binding with SARS-CoV-2 spike protein. *J Med Virol.* (2020) 92:1580–6. doi: 10.1002/jmv.25832
 163. Asselta R, Paraboschi EM, Mantovani A, Duga S. ACE2 and TMPRSS2 variants and expression as candidates to sex and country differences in COVID-19 severity in Italy. *Aging.* (2020) 12:10087–98. doi: 10.18632/aging.103415
 164. Nguyen A, David JK, Maden SK, Wood MA, Weeder BR, Nellore A, et al. Human leukocyte antigen susceptibility map for severe acute respiratory syndrome coronavirus 2. *J Virol.* (2020) 94. doi: 10.1128/JVI.00510-20
 165. Wang F, Huang S, Gao R, Zhou Y, Lai C, Li Z, et al. Initial whole-genome sequencing and analysis of the host genetic contribution to COVID-19 severity and susceptibility. *Cell Discov.* (2020) 6:83. doi: 10.1038/s41421-020-00231-4
 166. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility. *Clin Infect Dis.* (2020). doi: 10.1101/2020.03.11.20031096
 167. Liu Y, Häussinger L, Steinacker JM, Dinse-Lambracht A. Association between the dynamics of the COVID-19 epidemic and ABO blood type distribution. *Epidemiol Infect.* (2021) 149:e19. doi: 10.1017/S0950268821000030
 168. Patanavanich R, Glantz SA. Smoking is associated with COVID-19 progression: a meta-analysis. *Nicotine Tob Res.* (2020) 22:1653–6. doi: 10.1093/ntr/ntaa082
 169. Huang W, Zhou H, Hodgkinson C, Montero A, Goldman D, Chang SL. Network meta-analysis on the mechanisms underlying alcohol augmentation of COVID-19 pathologies. *Alcohol Clin Exp Res.* (2021) 45:675–88. doi: 10.1111/acer.14573
 170. Bailey KL, Samuelson DR, Wyatt TA. Alcohol use disorder: a pre-existing condition for COVID-19? *Alcohol.* (2021) 90:11–7. doi: 10.1016/j.alcohol.2020.10.003
 171. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. *Brain Behav Immun.* (2020) 87:184–7. doi: 10.1016/j.bbi.2020.05.059

172. da Silveira MP, da Silva Fagundes KK, Bizuti MR, Starck É, Rossi RC, de Resende ESDT. Physical exercise as a tool to help the immune system against COVID-19: an integrative review of the current literature. *Clin Exp Med.* (2021) 21:15–28. doi: 10.1007/s10238-020-00650-3
173. Schiebinger L. Women's health and clinical trials. *J Clin Invest.* (2003) 112:973–7. doi: 10.1172/JCI19993
174. Shields KE, Lyster AD. Exclusion of pregnant women from industry-sponsored clinical trials. *Obstet Gynecol.* (2013) 122:1077–81. doi: 10.1097/AOG.0b013e3182a9ca67
175. Beery AK, Zucker I. Sex bias in neuroscience and biomedical research. *Neurosci Biobehav Rev.* (2011) 35:565–72. doi: 10.1016/j.neubiorev.2010.07.002
176. Westerman S, Wenger N. Gender differences in atrial fibrillation: a review of epidemiology, management, and outcomes. *Curr Cardiol Rev.* (2019) 15:136–44. doi: 10.2174/1573403X15666181205110624
177. Dudley JP, Lee NT. Disparities in age-specific morbidity and mortality from SARS-CoV-2 in China and the Republic of Korea. *Clin Infect Dis.* (2020) 71:863–5. doi: 10.1093/cid/ciaa354
178. Alghamdi IG, Hussain II, Almalki SS, Alghamdi MS, Alghamdi MM, El-Sheemy MA. The pattern of Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive epidemiological analysis of data from the Saudi Ministry of Health. *Int J Gen Med.* (2014) 7:417–23. doi: 10.2147/IJGM.S67061
179. Jia N, Feng D, Fang LQ, Richardus JH, Han XN, Cao WC, et al. Case fatality of SARS in mainland China and associated risk factors. *Trop Med Int Health.* (2009) 14:21–7. doi: 10.1111/j.1365-3156.2008.02147.x
180. Karlberg J, Chong DS, Lai WY. Do men have a higher case fatality rate of severe acute respiratory syndrome than women do? *Am J Epidemiol.* (2004) 159:229–31. doi: 10.1093/aje/kwh056
181. Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology.* (2003) 8:S9–14. doi: 10.1046/j.1440-1843.2003.00518.x
182. Viveiros A, Rasmuson J, Vu J, Mulvagh SL, Yip CY, Norris CM, et al. Sex differences in COVID-19: candidate pathways, genetics of ACE2, and sex hormones. *Am J Physiol Heart Circ Physiol.* (2021) 320:H296–h304. doi: 10.1152/ajpheart.00755.2020
183. Schurz H, Salie M, Tromp G, Hoal EG, Kinnear CJ, Möller M. The X chromosome and sex-specific effects in infectious disease susceptibility. *Hum Genomics.* (2019) 13:2. doi: 10.1186/s40246-018-0185-z
184. Distech CM, Berletch JB. X-chromosome inactivation and escape. *J Genet.* (2015) 94:591–9. doi: 10.1007/s12041-015-0574-1
185. Tukiainen T, Villani AC, Yen A, Rivas MA, Marshall JL, Satija R, et al. Landscape of X chromosome inactivation across human tissues. *Nature.* (2017) 550:244–8. doi: 10.1038/nature24265
186. Tipnis SR, Hooper NM, Hyde R, Karran E, Christie G, Turner AJ, et al. human homolog of angiotensin-converting enzyme. Cloning and functional expression as a captopril-insensitive carboxypeptidase. *J Biol Chem.* (2000) 275:33238–43. doi: 10.1074/jbc.M002615200
187. Chen K, Bi J, Su Y, Chappell MC, Rose JC. Sex-specific changes in renal angiotensin-converting enzyme and angiotensin-converting enzyme 2 gene expression and enzyme activity at birth and over the first year of life. *Reprod Sci.* (2016) 23:200–10. doi: 10.1177/1933719115597760
188. Wang G, Lai FM, Lai KB, Chow KM, Kwan CH, Li KT, et al. Discrepancy between intrarenal messenger RNA and protein expression of ACE and ACE2 in human diabetic nephropathy. *Am J Nephrol.* (2009) 29:524–31. doi: 10.1159/000185629
189. Sward P, Edsfieldt A, Reepalu A, Jelpsson L, Rosengren BE, Karlsson MK. Age and sex differences in soluble ACE2 may give insights for COVID-19. *Crit Care.* (2020) 24:221. doi: 10.1186/s13054-020-02942-2
190. Sama IE, Ravera A, Santema BT, van Goor H, Ter Maaten JM, Cleland JGF, et al. Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin-angiotensin-aldosterone inhibitors. *Eur Heart J.* (2020) 41:1810–7. doi: 10.1093/eurheartj/ehaa373
191. Kornilov SA, Lucas I, Jade K, Dai CL, Lovejoy JC, Magis AT. Plasma levels of soluble ACE2 are associated with sex, Metabolic Syndrome, and its biomarkers in a large cohort, pointing to a possible mechanism for increased severity in COVID-19. *Crit Care.* (2020) 24:452. doi: 10.1186/s13054-020-03141-9
192. Rahman MM, Hasan M, Ahmed A. Potential detrimental role of soluble ACE2 in severe COVID-19 comorbid patients. *Rev Med Virol.* (2021) 31:1–2. doi: 10.2139/ssrn.3729704
193. Libert C, Dejager L, Pinheiro I. The X chromosome in immune functions: when a chromosome makes the difference. *Nat Rev Immunol.* (2010) 10:594–604. doi: 10.1038/nri2815
194. Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol.* (2016) 16:626–38. doi: 10.1038/nri.2016.90
195. Invernizzi P, Pasini S, Selmi C, Gershwin ME, Podda M. Female predominance and X chromosome defects in autoimmune diseases. *J Autoimmun.* (2009) 33:12–6. doi: 10.1016/j.jaut.2009.03.005
196. Billi AC, Kahlenberg JM, Gudjonsson JE. Sex bias in autoimmunity. *Curr Opin Rheumatol.* (2019) 31:53–61. doi: 10.1097/BOR.0000000000000564
197. Akira S, Uematsu S, Takeuchi O. Pathogen recognition and innate immunity. *Cell.* (2006) 124:783–801. doi: 10.1016/j.cell.2006.02.015
198. Diebold SS, Kaisho T, Hemmi H, Akira S, Reis e Sousa C. Innate antiviral responses by means of TLR7-mediated recognition of single-stranded RNA. *Science.* (2004) 303:1529–31. doi: 10.1126/science.1093616
199. Souyris M, Cenac C, Azar P, Daviaud D, Canivet A, Grunenwald S, et al. TLR7 escapes X chromosome inactivation in immune cells. *Sci Immunol.* (2018) 3. doi: 10.1126/sciimmunol.aap8855
200. Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. *Clin Rev Allergy Immunol.* (2019) 56:308–21. doi: 10.1007/s12016-017-8648-x
201. Berghöfer B, Frommer T, Haley G, Fink L, Bein G, Hackstein H. TLR7 ligands induce higher IFN- α production in females. *J Immunol.* (2006) 177:2088–96. doi: 10.4049/jimmunol.177.4.2088
202. Torcia MG, Nencioni L, Clemente AM, Civitelli L, Celestino I, Limongi D, et al. Sex differences in the response to viral infections: TLR8 and TLR9 ligand stimulation induce higher IL10 production in males. *PLoS ONE.* (2012) 7:e39853. doi: 10.1371/journal.pone.0039853
203. Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Trans R Soc Trop Med Hyg.* (2015) 109:9–15. doi: 10.1093/trstmh/tru167
204. Garg R, Agrawal P, Gautam A, Pursnani N, Agarwal M, Agarwal A, et al. COVID-19 outcomes in postmenopausal and perimenopausal females: is estrogen hormone attributing to gender differences? *J Midlife Health.* (2020) 11:250–6. doi: 10.4103/jmh.jmh_287_20
205. Ding T, Zhang J, Wang T, Cui P, Chen Z, Jiang J, et al. Potential influence of menstrual status and sex hormones on female SARS-CoV-2 infection: a cross-sectional study from multicentre in Wuhan, China. *Clin Infect Dis.* (2021) 9:e240–8. doi: 10.1093/cid/ciaa1022
206. Pradhan A, Olsson PE. Sex differences in severity and mortality from COVID-19: are males more vulnerable? *Biol Sex Differ.* (2020) 11:53. doi: 10.1186/s13293-020-00330-7
207. Calabrese EJ. Estrogen and related compounds: biphasic dose responses. *Crit Rev Toxicol.* (2001) 31:503–15. doi: 10.1080/20014091111785
208. Gaskins AJ, Wilchesky M, Mumford SL, Whitcomb BW, Browne RW, Wactawski-Wende J, et al. Endogenous reproductive hormones and C-reactive protein across the menstrual cycle: the BioCycle study. *Am J Epidemiol.* (2012) 175:423–31. doi: 10.1093/aje/kwr343
209. Stein B, Yang MX. Repression of the interleukin-6 promoter by estrogen receptor is mediated by NF- κ B and C/EBP β . *Mol Cell Biol.* (1995) 15:4971–9. doi: 10.1128/MCB.15.9.4971
210. Florian M, Magder S. Estrogen decreases TNF- α and oxidized LDL induced apoptosis in endothelial cells. *Steroids.* (2008) 73:47–58. doi: 10.1016/j.steroids.2007.08.010
211. Straub RH. The complex role of estrogens in inflammation. *Endocr Rev.* (2007) 28:521–74. doi: 10.1210/er.2007-0001
212. Robinson DP, Hall OJ, Nilles TL, Bream JH, Klein SL. 17 β -estradiol protects females against influenza by recruiting neutrophils and increasing virus-specific CD8 T cell responses in the lungs. *J Virol.* (2014) 88:4711–20. doi: 10.1128/JVI.02081-13
213. Peretz J, Pekosz A, Lane AP, Klein SL. Estrogenic compounds reduce influenza A virus replication in primary human nasal epithelial cells derived

- from female, but not male, donors. *Am J Physiol Lung Cell Mol Physiol*. (2016) 310:L415–25. doi: 10.1152/ajplung.00398.2015
214. Chedraui P, Pérez-López FR. The severe acute respiratory syndrome due to coronavirus 2 (SARS-CoV-2) infection and the climacteric woman. *Climacteric*. (2020) 23:525–7. doi: 10.1080/13697137.2020.1837547
 215. Seeland U, Coluzzi F, Simmaco M, Mura C, Bourne PE, Heiland M, et al. Evidence for treatment with estradiol for women with SARS-CoV-2 infection. *BMC Med*. (2020) 18:369. doi: 10.1186/s12916-020-01851-z
 216. Neuhauser HK, Adler C, Rosario AS, Diederichs C, Ellert U. Hypertension prevalence, awareness, treatment and control in Germany 1998 and 2008–11. *J Hum Hypertens*. (2015) 29:247–53. doi: 10.1038/jhh.2014.82
 217. Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *Endocr Rev*. (2016) 37:278–316. doi: 10.1210/er.2015-1137
 218. Ntritsos G, Franek J, Belbasis L, Christou MA, Markozannes G, Altman P, et al. Gender-specific estimates of COPD prevalence: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis*. (2018) 13:1507–14. doi: 10.2147/COPD.S146390
 219. Cai H. Sex difference and smoking predisposition in patients with COVID-19. *Lancet Respir Med*. (2020) 8:e20. doi: 10.1016/S2213-2600(20)30117-X
 220. Erol A, Karpyak VM. Sex and gender-related differences in alcohol use and its consequences: contemporary knowledge and future research considerations. *Drug Alcohol Depend*. (2015) 156:1–13. doi: 10.1016/j.drugalcdep.2015.08.023
 221. Wennman H, Pietilä A, Rissanen H, Valkeinen H, Partonen T, Mäki-Opas T, et al. Gender, age and socioeconomic variation in 24-hour physical activity by wrist-worn accelerometers: the FinHealth 2017 survey. *Sci Rep*. (2019) 9:6534. doi: 10.1038/s41598-019-43007-x
 222. Zhang Q, Cong M, Wang N, Li X, Zhang H, Zhang K, et al. Association of angiotensin-converting enzyme 2 gene polymorphism and enzymatic activity with essential hypertension in different gender: a case-control study. *Medicine*. (2018) 97:e12917. doi: 10.1097/MD.00000000000012917
 223. Bukowska A, Spiller L, Wolke C, Lendeckel U, Weinert S, Hoffmann J, et al. Protective regulation of the ACE2/ACE gene expression by estrogen in human atrial tissue from elderly men. *Exp Biol Med (Maywood)*. (2017) 242:1412–23. doi: 10.1177/1535370217718808
 224. Gupte M, Thatcher SE, Boustany-Kari CM, Shoemaker R, Yiannikouris F, Zhang X, et al. Angiotensin converting enzyme 2 contributes to sex differences in the development of obesity hypertension in C57BL/6 mice. *Arterioscler Thromb Vasc Biol*. (2012) 32:1392–9. doi: 10.1161/ATVBAHA.112.248559
 225. Wang Y, Shoemaker R, Thatcher SE, Batifoulier-Yiannikouris F, English VL, Cassis LA. Administration of 17 β -estradiol to ovariectomized obese female mice reverses obesity-hypertension through an ACE2-dependent mechanism. *Am J Physiol Endocrinol Metab*. (2015) 308:E1066–75. doi: 10.1152/ajpendo.00030.2015
 226. De Paoli M, Werstuck GH. Role of estrogen in type 1 and type 2 diabetes mellitus: a review of clinical and preclinical data. *Can J Diabetes*. (2020) 44:448–52. doi: 10.1016/j.jcjd.2020.01.003
 227. Xu Y, Lin J, Wang S, Xiong J, Zhu Q. Combined estrogen replacement therapy on metabolic control in postmenopausal women with diabetes mellitus. *Kaohsiung J Med Sci*. (2014) 30:350–61. doi: 10.1016/j.kjms.2014.03.002
 228. Stelzig KE, Canepa-Escaro F, Schilero M, Berdnikovs S, Prakash YS, Chiarella SE. Estrogen regulates the expression of SARS-CoV-2 receptor ACE2 in differentiated airway epithelial cells. *Am J Physiol Lung Cell Mol Physiol*. (2020) 318:L1280–11. doi: 10.1152/ajplung.00153.2020
 229. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol*. (2013) 27:791–802. doi: 10.1016/j.bpobgyn.2013.08.001
 230. Kohlhepp LM, Hollerich G, Vo L, Hofmann-Kiefer K, Rehm M, Louwen F, et al. Physiological changes during pregnancy. *Anaesthesist*. (2018) 67:383–96. doi: 10.1007/s00101-018-0437-2
 231. Thornburg KL, Jacobson SL, Giraud GD, Morton MJ. Hemodynamic changes in pregnancy. *Semin Perinatol*. (2000) 24:11–4. doi: 10.1016/S0146-0005(00)80047-6
 232. Witry SW. Pulmonary edema in pregnancy. *J Obstet Gynecol Neonatal Nurs*. (1992) 21:177–84. doi: 10.1111/j.1552-6909.1992.tb02254.x
 233. Lee SY, Chien DK, Huang CH, Shih SC, Lee WC, Chang WH. Dyspnea in pregnancy. *Taiwan J Obstet Gynecol*. (2017) 56:432–6. doi: 10.1016/j.tjog.2017.04.035
 234. Thornton P, Douglas J. Coagulation in pregnancy. *Best Pract Res Clin Obstet Gynaecol*. (2010) 24:339–52. doi: 10.1016/j.bpobgyn.2009.11.010
 235. Di Toro F, Gjoka M, Di Lorenzo G, De Santo D, De Seta F, Maso G, et al. Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. *Clin Microbiol Infect*. (2021) 27:36–46. doi: 10.1016/j.cmi.2020.10.007
 236. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Maternal-Fetal Neonatal Med*. (2020) 1–4. doi: 10.1080/14767058.2020.1759541
 237. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM*. (2020) 2:100118. doi: 10.1016/j.ajogmf.2020.100118
 238. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. (2020) 370:m3320. doi: 10.1136/bmj.m3320
 239. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: Pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. *Acta Obstet Gynecol Scand*. (2020) 99:819–22. doi: 10.1111/aogs.13901
 240. Lokken EM, Walker CL, Delaney S, Kachikis A, Kretzer NM, Erickson A, et al. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome coronavirus 2 infection in Washington State. *Am J Obstet Gynecol*. (2020) 223:911.e1–e14. doi: 10.1016/j.ajog.2020.05.031
 241. Torres-Torres J, Martinez-Portilla RJ, Espino YSS, Estrada-Gutierrez G, Solis-Paredes JM, Villafan-Bernal JR, et al. Comorbidities, poverty and social vulnerability as risk factors for mortality in pregnant women with confirmed SARS-CoV-2 infection: analysis of 13 062 positive pregnancies including 176 maternal deaths in Mexico. *Ultrasound Obstet Gynecol*. (2022) 59:76–82. doi: 10.1002/uog.24797
 242. Eberle C, James-Todd T, Stichling S. SARS-CoV-2 in diabetic pregnancies: a systematic scoping review. *BMC Pregnancy Childbirth*. (2021) 21:573. doi: 10.1186/s12884-021-03975-3
 243. Sculli MA, Formoso G, Sciacca L. COVID-19 vaccination in pregnant and lactating diabetic women. *Nutr Metab Cardiovasc Dis*. (2021) 31:2151–5. doi: 10.1016/j.numecd.2021.04.012
 244. Roberts J, Pritchard AL, Treweek AT, Rossi AG, Brace N, Cahill P, et al. Why is COVID-19 more severe in patients with diabetes? The role of angiotensin-converting enzyme 2, endothelial dysfunction and the immunoinflammatory system. *Front Cardiovasc Med*. (2020) 7:629933. doi: 10.3389/fcvm.2020.629933
 245. Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol*. (2021) 17:11–30. doi: 10.1038/s41574-020-00435-4
 246. Chi J, Gong W, Gao Q. Clinical characteristics and outcomes of pregnant women with COVID-19 and the risk of vertical transmission: a systematic review. *Arch Gynecol Obstet*. (2021) 303:337–45. doi: 10.1007/s00404-020-05889-5
 247. Salem D, Katranji F, Bakdash T. COVID-19 infection in pregnant women: Review of maternal and fetal outcomes. *Int J Gynaecol Obstet*. (2021) 152:291–8. doi: 10.1002/ijgo.13533
 248. Arora N, Sadovsky Y, Dermody TS, Coyne CB. Microbial vertical transmission during human pregnancy. *Cell Host Microbe*. (2017) 21:561–7. doi: 10.1016/j.chom.2017.04.007
 249. Hughes BL, Gyamfi-Bannerman C. Diagnosis and antenatal management of congenital cytomegalovirus infection. *Am J Obstet Gynecol*. (2016) 214:B5–b11. doi: 10.1016/j.ajog.2016.02.042
 250. Adams Waldorf KM, McAdams RM. Influence of infection during pregnancy on fetal development. *Reproduction*. (2013) 146:R151–62. doi: 10.1530/REP-13-0232
 251. Lamont RF, Sobel JD, Vaisbuch E, Kusanovic JP, Mazaki-Tovi S, Kim SK, et al. Parvovirus B19 infection in human pregnancy. *Bjog*. (2011) 118:175–86. doi: 10.1111/j.1471-0528.2010.02749.x

252. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, Abbasi H, Mirjalili SR, Behforouz A, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: a review. *Fetal Pediatr Pathol.* (2020) 39:246–50. doi: 10.1080/15513815.2020.1747120
253. Capobianco G, Saderi L, Aliberti S, Mondoni M, Piana A, Dessole F, et al. COVID-19 in pregnant women: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* (2020) 252:543–58. doi: 10.1016/j.ejogrb.2020.07.006
254. Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. *Jama.* (2020) 323:1848–9. doi: 10.1001/jama.2020.4861
255. Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *Jama.* (2020) 323:1846–8. doi: 10.1001/jama.2020.4621
256. Palmeira P, Quinello C, Silveira-Lessa AL, Zago CA, Carneiro-Sampaio M. IgG placental transfer in healthy and pathological pregnancies. *Clin Dev Immunol.* (2012) 13. doi: 10.1155/2012/985646
257. Ben-Hur H, Gurevich P, Elhayani A, Avinoach I, Schneider DF, Zusman I. Transport of maternal immunoglobulins through the human placental barrier in normal pregnancy and during inflammation. *Int J Mol Med.* (2005) 16:401–7. doi: 10.3892/ijmm.16.3.401
258. Hecht JL, Quade B, Deshpande V, Mino-Kenudson M, Ting DT, Desai N, et al. SARS-CoV-2 can infect the placenta and is not associated with specific placental histopathology: a series of 19 placentas from COVID-19-positive mothers. *Mod Pathol.* (2020) 33:2092–103. doi: 10.1038/s41379-020-0639-4
259. Chen W, Yuan P, Yang M, Yan Z, Kong S, Yan J, et al. SARS-CoV-2 Entry Factors: ACE2 and TMPRSS2 Are Expressed in Peri-Implantation Embryos and the Maternal-Fetal Interface. *Engineering (Beijing).* (2020) 6:1162–9. doi: 10.1016/j.eng.2020.07.013
260. Pique-Regi R, Romero R, Tarca AL, Luca F, Xu Y, Alazizi A, et al. Does the human placenta express the canonical cell entry mediators for SARS-CoV-2? *Elife.* (2020) 9. doi: 10.7554/eLife.58716
261. Henarejos-Castillo I, Sebastian-Leon P, Devesa-Peiro A, Pellicer A, Diaz-Gimeno P. SARS-CoV-2 infection risk assessment in the endometrium: viral infection-related gene expression across the menstrual cycle. *Fertil Steril.* (2020) 114:223–32. doi: 10.1016/j.fertnstert.2020.06.026
262. Zang R, Gomez Castro ME, McCune BT, Zeng Q, Rothlauf PW, Sonnek NM, et al. TMPRSS2 and TMPRSS4 promote SARS-CoV-2 infection of human small intestinal enterocytes. *Sci Immunol.* (2020) 5. doi: 10.1126/sciimmunol.abc3582
263. Egloff C, Vauloup-Fellous C, Picone O, Mandelbrot L, Roques P. Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2. *J Clin Virol.* (2020) 128:104447. doi: 10.1016/j.jcv.2020.104447
264. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *Jama.* (2020) 323:1843–4. doi: 10.1001/jama.2020.3786
265. Facchetti F, Bugatti M, Drera E, Tripodo C, Sartori E, Cancila V, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. *EBioMedicine.* (2020) 59:102951. doi: 10.1016/j.ebiom.2020.102951
266. Valdespino-Vázquez MY, Helguera-Repetto CA, León-Juárez M, Villavicencio-Carrisoza O, Flores-Pliego A, Moreno-Verduzco ER, et al. Fetal and placental infection with SARS-CoV-2 in early pregnancy. *J Med Virol.* (2021) 93:4480–4487. doi: 10.1002/jmv.26965
267. Shende P, Gaikwad P, Gandhewar M, Ukey P, Bhide A, Patel V, et al. Persistence of SARS-CoV-2 in the first trimester placenta leading to transplacental transmission and fetal demise from an asymptomatic mother. *Hum Reprod.* (2021) 36:899–906. doi: 10.1093/humrep/deaa367
268. Resta L, Vimercati A, Cazzato G, Mazzia G, Cicinelli E, Colagrande A, et al. SARS-CoV-2 and placenta: new insights and perspectives. *Viruses.* (2021) 13. doi: 10.3390/v13050723
269. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental pathology in COVID-19. *Am J Clin Pathol.* (2020) 154:23–32. doi: 10.1093/ajcp/aqaa089
270. Sharps MC, Hayes DJL, Lee S, Zou Z, Brady CA, Almoghrabi Y, et al. A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. *Placenta.* (2020) 101:13–29. doi: 10.1016/j.placenta.2020.08.018
271. Azinheira Nobrega Cruz N, Stoll D, Casarini DE, Bertagnolli M. Role of ACE2 in pregnancy and potential implications for COVID-19 susceptibility. *Clin Sci (Lond).* (2021) 135:1805–24. doi: 10.1042/CS20210284
272. Knöfler M, Haider S, Saleh L, Pollheimer J, Gamage T, James J. Human placenta and trophoblast development: key molecular mechanisms and model systems. *Cell Mol Life Sci.* (2019) 76:3479–96. doi: 10.1007/s00018-019-03104-6
273. Hsu AL, Guan M, Johannesen E, Stephens AJ, Khaleel N, Kagan N, et al. Placental SARS-CoV-2 in a pregnant woman with mild COVID-19 disease. *J Med Virol.* (2021) 93:1038–44. doi: 10.1002/jmv.26386
274. Jaiswal N, Puri M, Agarwal K, Singh S, Yadav R, Tiwary N, et al. COVID-19 as an independent risk factor for subclinical placental dysfunction. *Eur J Obstet Gynecol Reprod Biol.* (2021) 259:7–11. doi: 10.1016/j.ejogrb.2021.01.049
275. Xia YQ, Zhao KN, Zhao AD, Zhu JZ, Hong HF, Wang YL, et al. Associations of maternal upper respiratory tract infection/influenza during early pregnancy with congenital heart disease in offspring: evidence from a case-control study and meta-analysis. *BMC Cardiovasc Disord.* (2019) 19:277. doi: 10.1186/s12872-019-1206-0
276. Joma M, Fovet CM, Seddiki N, Gressens P, Laforge M. COVID-19 and Pregnancy: Vertical Transmission and Inflammation Impact on Newborns. *Vaccines.* (2021) 9. doi: 10.3390/vaccines9040391
277. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. *J Affect Disord.* (2020) 277:5–13. doi: 10.1016/j.jad.2020.07.126
278. Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. *Am J Obstet Gynecol.* (2020) 223:240.e1–e9. doi: 10.1016/j.ajog.2020.05.009
279. Toth B, Jeschke U, Rogenhofer N, Scholz C, Würfel W, Thaler CJ, et al. Recurrent miscarriage: current concepts in diagnosis and treatment. *J Reprod Immunol.* (2010) 85:25–32. doi: 10.1016/j.jri.2009.12.006
280. Nepomnaschy PA, Welch KB, McConnell DS, Low BS, Strassmann BI, England BG. Cortisol levels and very early pregnancy loss in humans. *Proc Natl Acad Sci U S A.* (2006) 103:3938–42. doi: 10.1073/pnas.0511183103
281. Lucas DN, Bamber JH. Pandemics and maternal health: the indirect effects of COVID-19. *Anaesthesia.* (2021) 76:69–75. doi: 10.1111/anae.15408
282. Yirmiya K, Yakirevich-Amir N, Preis H, Lotan A, Atzil S, Reuveni I. Women's depressive symptoms during the COVID-19 pandemic: the role of pregnancy. *Int J Environ Res Public Health.* (2021) 18. doi: 10.3390/ijerph18084298
283. Pariente G, Wissotzky Broder O, Sheiner E, Lanxner Battat T, Mazor E, Yaniv Salem S, et al. Risk for probable post-partum depression among women during the COVID-19 pandemic. *Arch Womens Ment Health.* (2020) 23:767–73. doi: 10.1007/s00737-020-01075-3
284. D'Souza R, Ashraf R, Rowe H, Zipursky J, Clarfield L, Maxwell C, et al. Pregnancy and COVID-19: pharmacologic considerations. *Ultrasound Obstet Gynecol.* (2021) 57:195–203. doi: 10.1002/uog.23116
285. Li L, Wang X, Wang R, Hu Y, Jiang S, Lu X. Antiviral agent therapy optimization in special populations of COVID-19 patients. *Drug Des Devel Ther.* (2020) 14:3001–13. doi: 10.2147/DDDT.S259058
286. Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus disease 2019 (COVID-19) vaccines and pregnancy: what obstetricians need to know. *Obstet Gynecol.* (2021) 137:408–14. doi: 10.1097/AOG.0000000000004290
287. Giles ML, Gunatilaka A, Palmer K, Sharma K, Roach V. Alignment of national COVID-19 vaccine recommendations for pregnant and lactating women. *Bull World Health Organ.* (2021) 99:739–46. doi: 10.2471/BLT.21.286644
288. Shamshirsaz AA, Hessami K, Morain S, Afshar Y, Nassr A, Arian SE, et al. Intention to receive COVID-19 vaccine during pregnancy: a systematic review and meta-analysis. *Am J Perinatol.* (2021) 39. doi: 10.1055/a-1674-6120 [Epub ahead of print].
289. Shook LL, Fallah PN, Silberman JN, Edlow AG. COVID-19 vaccination in pregnancy and lactation: current research and gaps in understanding. *Front Cell Infect Microbiol.* (2021) 11:735394. doi: 10.3389/fcimb.2021.735394

290. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. *N Engl J Med.* (2021) 384:2273–82. doi: 10.1056/NEJMoa2104983
291. Collier AY, McMahan K, Yu J, Tostanoski LH, Aguayo R, Ansel J, et al. Immunogenicity of COVID-19 mRNA vaccines in pregnant and lactating women. *Jama.* (2021) 325:2370–80. doi: 10.1001/jama.2021.7563
292. Beharier O, Plitman Mayo R, Raz T, Nahum Sacks K, Schreiber L, Suissa-Cohen Y, et al. Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine. *J Clin Invest.* (2021) 131. doi: 10.1172/JCI154834
293. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstetr Gynecol.* (2021) 225:303.e1–e17. doi: 10.1016/j.ajog.2021.03.023
294. Butt AA, Chemaitelly H, Al Khal A, Coyle PV, Saleh H, Kaleeckal A, et al. SARS-CoV-2 vaccine effectiveness in preventing confirmed infection in pregnant women. *J Clin Invest.* (2021). doi: 10.1172/JCI153662

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Liu, Raja xavier, Singh, Brucker and Salker. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Accessing Maternal Health Care in the Midst of the COVID-19 Pandemic: A Study in Two Districts of Assam, India

OPEN ACCESS

Rashmi Padhye^{1*}, Anusha Purushotham², Maitrayee Paul³, Nilangi Sardeshpande¹, Ramnath Ballala², Shelley Dhar², Sunil Kaul³ and Renu Khanna¹

¹ Society for Health Alternatives (SAHAJ), Vadodara, India, ² Piramal Swasthya Management and Research Institute, Hyderabad, India, ³ Institute of Development Action (IDeA) - The Ant, Guwahati, India

Edited by:

Lakshmi Surya Prabha Manem,
Dr. NTR University of Health
Sciences, India

Reviewed by:

Katie Harris,
University of New South
Wales, Australia
Gloria Sclar,
Emory University, United States
Vicha Annisa Adri,
Independent Researcher, Washington,
DC, United States

*Correspondence:

Rashmi Padhye
sahajequalmeasures2030@gmail.com

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 30 July 2021

Accepted: 08 February 2022

Published: 31 March 2022

Citation:

Padhye R, Purushotham A, Paul M,
Sardeshpande N, Ballala R, Dhar S,
Kaul S and Khanna R (2022)
Accessing Maternal Health Care in the
Midst of the COVID-19 Pandemic: A
Study in Two Districts of Assam, India.
Front. Glob. Womens Health
3:750520.
doi: 10.3389/fgwh.2022.750520

Background: COVID-19 pandemic and the subsequent national lockdown in India compelled the health system to focus on COVID-19 management. Information from the field indicated the impact of COVID-19 on the provision of maternal health services. This research presents users' and providers' perspectives about the effect of the pandemic on maternal health services in select districts of Assam.

Methods: The study was undertaken to understand the status of maternal health service provision and challenges faced by 110 pregnant and recently delivered women, 38 health care providers and 18 Village Health Sanitation and Nutrition Committee members during COVID-19 pandemic. Telephonic interviews were conducted with the users identified through simple random sampling. Healthcare providers and the community members were identified purposively.

Results: Most of the interviewed women reported that they could access the health services, but had to spend out-of-pocket (for certain services) despite accessing the services from government health facilities. Healthcare providers highlighted the lack of transportation facilities and medicine unavailability as challenges in providing routine services. The study revealed high proportion of Caesarian section deliveries (42.6%, $n = 32$) and stillbirths (10.6%, $n = 8$).

Discussion: This research hypothesizes the supply-side (health system) factors and demand-side (community-level) factors converged to affect the access to maternal health services. Health system preparedness by ensuring availability of all services at the last mile and strengthening existing community-reliant health services is recommended for uninterrupted good quality and affordable maternal health service provision.

Keywords: COVID-19, maternal health, antenatal care, C-section, health services provision, expenditure on health services, stillbirth

INTRODUCTION

The onslaught of the novel coronavirus disease 2019 (COVID-19) pandemic encumbered the health systems of countries across the globe. Some countries quickly adapted with 'extensive reorganization' of the health delivery system while others struggled (1). Variations in the intensity and duration were observed across the countries in the restrictions imposed for the movement of citizens (2).

Maternal health service provisioning was disrupted in several places as an effect of lockdown policies (1, 3). The negative effect of the COVID-19 pandemic on stillbirths, neonatal mortality, intrapartum care, and Cesarean section deliveries is predicted by various studies during the pandemic (4–6).

Restriction of movement due to the lockdown, absence of public transportation and fear of contracting COVID-19 infection kept women away from seeking service. These factors led to an estimated 20–50% decrease in access to critical maternal health care services in the Asia-Pacific region (7).

In India, the first case of COVID-19 was confirmed on January 27, 2020 and cases escalated during the next 2 months. The Union Government declared a national lockdown on March 24, 2020 to contain the infection. The historically under-resourced public health system in the country struggled to cope with the additional challenges posed by the COVID-19 pandemic, which impacted the provisioning of routine health services such as immunization or antenatal care. Most of the existing health infrastructure and human resources were engaged in managing the epidemic (8). Lacunae of the public health system, such as deficits in the infrastructure and disruption of maternal and child health services, particularly antenatal services and institutional deliveries got exacerbated (9–11) during this time. A study in tertiary level health facilities in Delhi, India, observed a 7.2% increase in high-risk pregnancies and 2.5 times increase in intensive care unit (ICU) admissions for pregnant women during the pandemic. This increase may be attributed to inadequate antenatal visits and delayed health-seeking due to the nationwide lockdown and fear of contracting the virus (12).

The Accredited Social Health Activist (ASHA) program has operated in the rural areas of India since 2005. ASHAs are trained female community health volunteers linking the community to the public health system (13). ASHAs have been instrumental in reaching out to the marginalized communities in their villages and enabling their access to maternal health services (14). Another village level structure for participatory planning and action on determinants of health (15, 16) at the village level is the Village Health Sanitation and Nutrition Committee (VHSNC), initiated in 2007 for monitoring the monthly Village Health Sanitation and Nutrition Day (VHSND) and the health services, particularly maternal and child health and nutrition services (17).

With the emergence of the COVID-19 pandemic, ASHAs were assigned to pandemic-related surveillance and contact tracing (9) activities that impacted their routine maternal health-related tasks (18). At the same time, VHSNC members' lack of formal training about their responsibilities and inadequate supportive supervision and monitoring hindered them from

helping the community members during the pandemic in some places (19–21).

The present study has been conducted in Assam, which has historically performed poorly on maternal health indicators compared to other states in India. Assam has the highest Maternal Mortality Ratio (MMR) (215 per 100,000 live births in 2016–2018) (22) among the states, with only 64% of women reporting ANC registration during the first trimesters (23). One of the critical approaches to reducing maternal mortality is early identification of high-risk pregnancies (24). However, a study conducted in 2019–2020 revealed that in Assam only 7.36% of pregnancies were identified as high risk by the public health system (25).

Given these poor maternal health indicators of the state, this research was conceptualized to understand the impact of lockdown restrictions on the provisioning of maternal health services. This paper analyses the relationship between the supply-side (availability of services, skilled health care providers and infrastructure) and demand-side (barriers in accessing the health system, readiness of the patient to access the service given the higher risk of contracting the infection) (26) factors and their effect on the maternal and neonatal wellbeing during the COVID-19 pandemic in two districts of Assam.

MATERIALS AND METHODS

Study Settings

The study was conducted in two districts of Assam, Kamrup (Rural) and Darrang. The districts were selected purposively based on the presence of grassroots civil society organizations working on maternal health issues. The two components of the study included 1. a telephonic questionnaire with a cross-sectional sample of pregnant and recently delivered women and 2. a purposive sample of health care providers and VHSNC members.

Sampling Strategy and Data Collection Pregnant and Recently Delivered Women

A simple random sampling was adopted to identify pregnant women meeting all of the following inclusion criteria: (a) Have registered phone numbers (belonging to themselves or their family members) in Government of India's Reproductive Child Health (RCH) portal in Darrang or Kamrup (Rural) districts (b) Have an estimated date of delivery between March 2020 and March 2021.

The database was accessible under the Early Childhood Development (ECD) call center operational under a public private partnership between the Government of Assam and one of the research partners.

From the study population of 6396 pregnant women, a sample size of 634 [452 from Kamrup (R.) and 182 from Darrang] was determined at 95% confidence level, 10% margin of error, anticipated frequency of 85% non-response rate (**Supplementary Table 1**). The non-response rate was estimated in accordance with the response rates of the routine ECD call centre programme data.

A structured telephonic questionnaire with close ended questions was pilot tested to assess the viability and efficacy of the process. The full questionnaire was administered to 171 respondents by a 6 member-research team to assess the administrative feasibility of the study including the resources necessary, technical capabilities of the research staff and data entry/data processing procedures. After pilot testing, the final telephonic questionnaire was administered by trained research assistants between October – November 2020. At the time of the interviews, three attempts were made to contact the participants over the phone before marking ‘no response.’ The participant information sheet was shared orally and verbal informed consent was obtained from every respondent at the beginning of the telephone call, to confirm their participation in the study. Each interview on an average took 10 min. The data were captured on Microsoft Forms.

The telephonic questionnaire aimed to understand the status of maternal health service provisioning, including service utilization and out of pocket health expenditure. All the research assistants signed a non-disclosure agreement in accordance with the institutional data policy and only de-identified data were shared with the analysis team.

Health Care Providers and VHSNC Members

Staff members of the local organizations working on maternal health were trained on the interview guides. They conducted the interviews of a purposive sample of HCPs and VHSNC members from their field intervention areas. The selection was based on the availability and willingness to participate in the study, in the midst of the pandemic. All the respondents were interviewed upon seeking informed consent. Face -to-face interviews were conducted with 38 HCPs, including 15 health facility staff [13 Auxiliary Nurse Midwives (ANMs) and 2 Medical Officers (MOs)] and 23 ASHAs, and 18 VHSNC members from the two districts. They were interviewed during October and December 2020 in their villages with the help of interview guides designed to understand the effect of COVID-19 and the lockdown on the service provision (for the HCPs). VHSNC members were interviewed to understand their role, knowledge and capacity building efforts (if any) to provide access to maternal health services in their village. The average duration for the interviews was 15 min. The responses were noted by the interviewers and then translated and entered in Microsoft Excel.

Data Analysis

Microsoft Excel data outputs were used to generate data tables upon data cleaning and coding wherever required. Analysis was done using frequencies with percentages and cross tabulations (wherever possible). Further statistical analysis could not be done given- a. the small sample size and b. pre-coded answers due to the limitation of time while administering a telephonic questionnaire. For example, instead of actual expenses, they were recorded as a range. Qualitative description approach (27) was used to analyze the responses of the HCPs and the VHSNC members.

RESULTS

Experiences of Pregnant and Recently Delivered Women

Out of the 634 women contacted telephonically, 150 women answered the call, and 114 women [64 from Kamrup (R.) and 50 from Darrang] consented to participate in the study. Fifty-two respondents were contacted on their phones, whereas 62 were contacted on phones belonging to their spouse, other family members, or neighbors.

The age of the respondents ranged between 18 and 39 years with a median age of 24 years. Thirty-one respondents were under the age of 20 years whereas 11 respondents belonged to the age group 31–39 years. 83% respondents ($n = 95$) belonged to the Below Poverty Level (BPL) category. All the respondents were registered as beneficiaries under Janani Suraksha Yojana (JSY), a central government scheme which provides conditional cash assistance for institutional delivery and post-delivery care.

Antenatal Care

One hundred ten respondents accessed ANC services. 83.6% ($n = 92$) received the recommended four or more ANC visits. 39.1% ($n = 43$) respondents received all 10 services whereas 55.5% ($n = 61$) received eight to nine services from the 10 listed services (Table 1).

Although 104 women received ANC from a government health facility, 72.1% of them ($n = 75$) went to a private health facility/ laboratory for the ultrasound check-up and laboratory tests.

Delivery Care

65.8% ($n = 75$) of total respondents delivered during the reporting period. All except two had institutional deliveries. ASHAs conducted the two home deliveries. 77.3% ($n = 58$) were conducted in a government health facility.

The high proportions of stillbirths (eight stillbirths in 75 deliveries) and neonatal deaths (four neonatal deaths in 75 deliveries) (Table 1) were striking.

Post Natal Care

77.3% respondents ($n = 58$) received PNC. All except three women went to a government health facility or ASHA/ANM visited their homes for the postnatal check-up.

Expenses for Care

Services accessed from government health facilities are available for free or at a minimal monetary charge for the registration. The majority of respondents relied on government health facilities for the ANC services and no expenses were incurred by 27.3% respondents ($n = 30$). However, due to the unavailability of ultrasonography services in government health facilities, 72.1% respondents ($n = 75$) availed this service from a private health facility thus incurring out-of-pocket expenses. The details of category wise expenditure are given in Table 2.

Sixteen respondents (two home deliveries and 14 deliveries in government health facilities) did not incur any expenses for the deliveries (Table 2). For the remaining 80.8% deliveries ($n = 59$), the expenses ranged from $< ₹ 1,000$ (~14 USD) to more than

TABLE 1 | Access to ANC, delivery and PNC services for the pregnant and recently delivered women.

	Number	Percent
Respondents	114	100
Antenatal care services		
Women who received ANC [§]	110	96.4
Number of ANC visits[†]		
More than four times	60	54.5
Four times	32	29.1
less than four times	18	16.4
Number of ANC services* received by the pregnant women[†]		
All 10 services	43	39.1
8–9 services	61	55.5
5–7 services	3	2.7
<5 services	3	2.7
Place of ANC		
Government health facility [†]	104	94.6
ANC from Government health facility but ultrasound check-up and lab tests done from private health facility ^{††}	75	72.1
Private health facility	5	4.4
Home	1	1.0
Women who underwent ultrasonography as a part of ANC	81	73.6
Delivery related services		
Women who underwent deliveries [§]	75	65.8
Pregnancy outcomes^{§§}		
Live births	63	84.0
Stillbirths	8	10.6
Neonatal deaths	4	5.3
Place of delivery^{§§}		
Government health facilities	58	77.3
Private health facilities	15	20.0
Home	2	2.7
Post Natal Care services^{§§}		
Women who received PNC	58	77.3
Women who received both ANC and PNC	54	72.0

*The 10 ANC services include- 1) Urine Pregnancy Test (UPT) for confirmation of pregnancy; 2) testing for Hemoglobin (Hb) levels; 3) Blood Sugar levels; 4) checking the Blood Pressure (BP); 5) measuring Height; 6) measuring Weight; 7) Physical Examination; 8) Ultrasound check-up (USG) to check on the intrauterine growth of the fetus; 9) provision of Tetanus Toxoid (TT) Injection; and 10) Iron and Folic Acid (IFA) Tablets as per the recommended doses.

[†]The sample size used for the percent calculations is 110.

^{††}The sample size used for the percent calculations is 104.

[§]The sample size used for the percent calculations is 114.

^{§§}The sample size used for the sample size calculations is 75.

₹ 10,000 (~40 USD), with 32% respondents ($n = 24$) reporting expenses above ₹ 10,000/- and another 25.3% ($n = 19$) reporting expenses between ₹ 5,000- and ₹ 10,000/- (~70 USD- 140 USD). Major delivery-related expenses were for medicines purchase (85%, $n = 50$) and laboratory tests (61%, $n = 36$). Although all the respondents were registered as beneficiaries for cash assistance under JSY (₹ 1,400 for institutional deliveries in rural areas and ₹ 3,000 for Caesarian section deliveries), the expenses incurred are much higher than the JSY benefits for most of the respondents.

Type of Health Facility, Type of Delivery and Delivery Expenses

The proportion of Caesarian section deliveries in both government (32.8%, $n = 19$) and private health facilities (86.7%, $n = 13$) is higher than the recommended Caesarian section rate considered by the WHO (10–15%) (28). Type of health facility and type of delivery both determined the delivery expenses (Table 3).

TABLE 2 | Expenses for ANC and delivery.

	Number	Percent
Expenses incurred for ANC services[†]		
More than Rs. 1,000/-	51	46.4
Rs. 501/-Rs. 1,000/-	26	23.6
Rs. 500- Rs. 100/-	3	2.7
No expenses	30	27.3
Expenditure categories^{††}		
For ultrasound check-up	79	99
For laboratory tests	27	34
For medicines	12	15
For doctor's fees	8	10
For Transportation	8	10
Expenses incurred for deliveries[§]		
More than Rs. 10,000/-	24	32
Rs. 5,001/-Rs. 10,000/-	19	25.3
Rs. 1,001- Rs. 5,000/-	13	17.3
Less than Rs. 1,000/-	3	4
No expenses	16	21.4
Expenditure categories^{§§}		
For medicines	50	85
For laboratory tests	36	61
For doctor's fees	24	41
For transportation	22	37
For blood transfusion	20	34

[†]The sample size used for the percent calculations is 110.

^{††}The sample size used for the percent calculations is 80.

[§]The sample size used for the percent calculations is 75.

^{§§}The sample size used for the percent calculations is 59.

In the government health facilities, 76% respondents ($n = 44$) reported to have incurred expenses ranging from <₹ 1,000 (~14 USD) to more than ₹ 10,000 (~140 USD). All the deliveries in private health facilities (irrespective of the type of delivery) incurred expenses above ₹ 10,000 (~140 USD). For 9 out of 19 Caesarian section deliveries in Government health facilities, the respondents incurred expenses < ₹ 10,000 (~140 USD). Only four Caesarian section deliveries in the government health facilities incurred no expenses.

Effect of the Lockdown on Accessing Maternal Health Services

A very small number of women (7%, $n = 8$) reported challenges in accessing ANC or PNC services from health facilities due to the pandemic and the lockdown. Lack of transportation was the major challenge. Seven respondents stated that they could not avail services from their preferred government health facility due to the lockdown restrictions on travel, limited access to transport facilities, and unavailability of those particular health facilities for the delivery. Among them, three respondents delivered in a private clinic, one in a peripheral health facility, one at home and the remaining two had to travel to a higher-level health facility.

Supply Side Issues—Perceptions of Health Care Providers

It was difficult for the Health Care Providers to continue providing the services because they feared contracting the virus. However, ASHAs and ANMs made home visits and coordinated with the pregnant women and their families over the telephone whenever required.

ANMs and Medical Officers—Challenges in Service Provision

According to the health facility staff (13 ANMs and two MOs), most ANC/PNC related service provisioning was managed through home visits. The staff faced issues in traveling to the villages for home visits because of a lack of travel options to reach remote areas. Even with the additional burden of COVID-19 related activities, the ANMs and doctors kept providing ANCs.

According to the interviewed providers, the non-availability of laboratory services was one of the significant gaps in the ANC provisioning. The village-level health centers were closed for 3 months during the lockdown. Post lockdown, the Iron and Folic Acid (IFA) tablets, an essential part of the ANC services, were unavailable at the village level health centers. These were available in select health centers but reaching these facilities was also difficult due to the lack of transportation.

Six ANMs reported managing high-risk pregnancies during the lockdown through home visits and regular follow-up over the phone. In one case, the woman delivered at home with support from ASHA, without any back up support of ANM or MO.

ASHAs' Role During the Pandemic and Challenges

ASHAs were asked about pregnancy related services and the challenges therein. Eighty-nine women were registered with these 23 ASHAs during this period. Eight ASHAs reported that they could not provide any of the expected health services during this period, while 13 ASHAs reported that all 60 pregnant women registered with them missed at least one ANC/PNC during this period. These numbers mean two-thirds (60 out of the total 89) of women registered under the 23 ASHAs missed at least one ANC/PNC during the lockdown.

ASHAs expressed the need for support from the health system and the ANMs and doctors for uninterrupted provisioning of the ANC/PNC in their areas during such unprecedented situations like the COVID-19 pandemic. They also talked about the making available the necessary set up for blood tests and contact details for an ambulance to carry the patients in emergency. Owing to the unavailability of IFA tablets, ASHAs emphasized the intake of iron-rich supplementary food items to the pregnant women. However, they also expressed concerns about the disruption of livelihoods and loss of income due to the lockdown and inability to get nutritious food for pregnant women from low income groups.

The ASHAs were not aware of the VHSNC members in their villages.

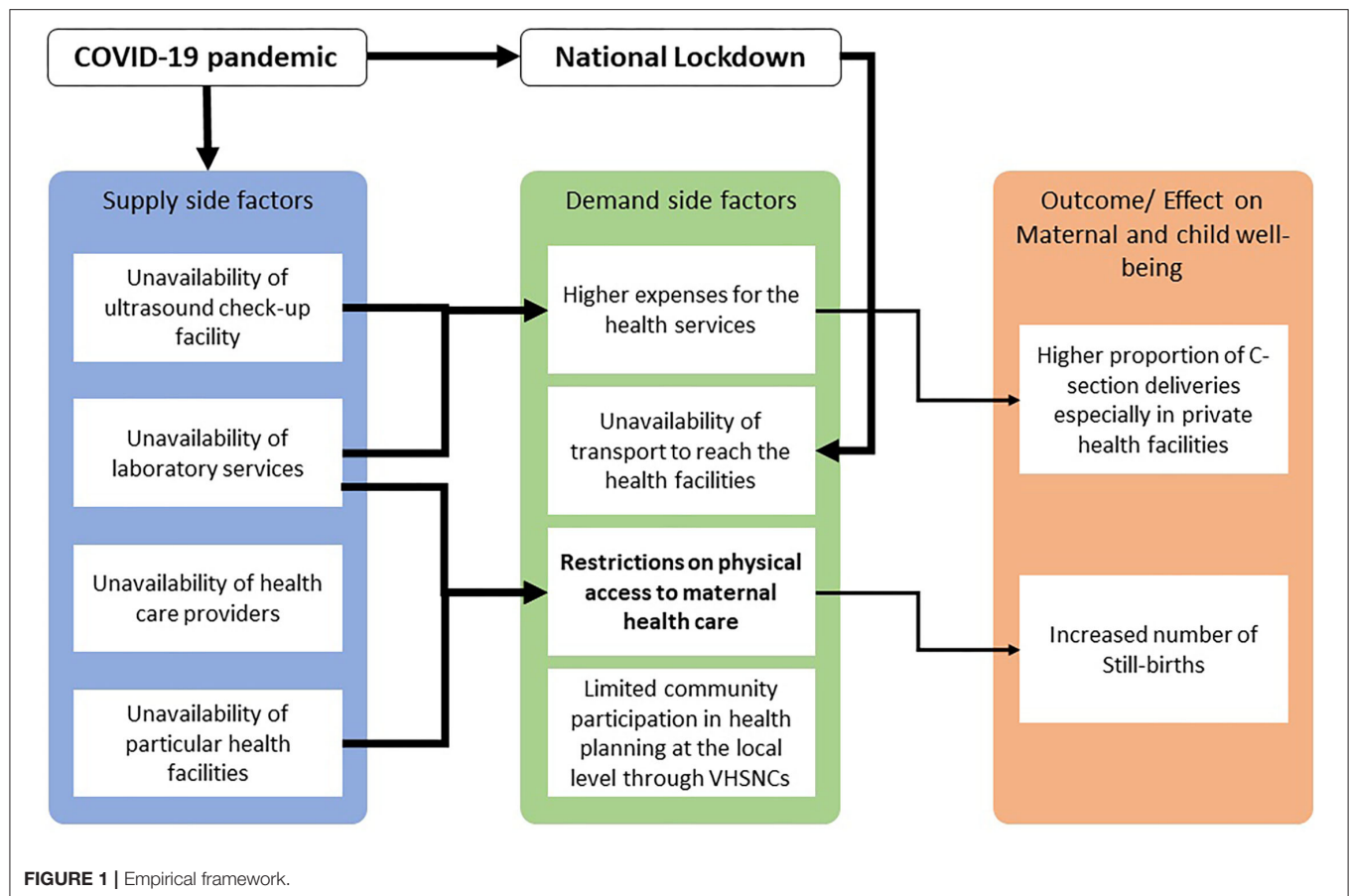
TABLE 3 | Distribution of institutional deliveries according to the type of health facility, type of delivery and expenses incurred for deliveries.

	Government health facilities [†] (n = 58)		Private health facilities [§] (n = 15)		Total* (n = 73)		
	Vaginal deliveries number (%)	C-section deliveries number (%)	Vaginal deliveries number (%)	C-section deliveries number (%)	Vaginal deliveries number (%)	C-section deliveries number (%)	Total number (%)
No expenses	10 (17.2)	4 (6.9)	0 (0.0)	0 (0.0)	10 (13.7)	4 (5.5)	14 (19.2)
Expenses below Rs. 10,000	26 (44.8)	9 (15.5)	0 (0.0)	0 (0.0)	26 (35.6)	9 (12.3)	35 (43.9)
Expenses above Rs. 10,000	3 (5.2)	6 (10.3)	2 (13.3)	13 (86.7)	5 (6.8)	19 (26.0)	24 (32.9)
Total	39 (67.2)	19 (32.8)	2 (13.3)	13 (86.7)	41 (56.2)	32 (43.8)	73 (100)

[†] The sample size used for the percent calculations is 58.

[§] The sample size used for the percent calculations is 15.

* The sample size used for the percent calculations is 73.



Challenges in Community Participation—Roles of VHSNC Members

The VHSNC members reported that in the absence of village-level outreach services during the lockdown, they could not guide the pregnant women about the health care facility for their pregnancy related health care needs. VHSNC members were not aware about their roles and responsibilities in general and, more specifically, during the COVID-19 pandemic.

The research findings from both the demand and supply side can be summarized with the help of an empirical framework

(Figure 1) that depicts the interrelations between supply-side and demand-side factors for access to maternal health services in these two districts of Assam.

DISCUSSION

COVID-19 pandemic and the subsequent lockdown changed very few things at the ground level for maternal health service delivery for these respondents. Most of the service delivery-related findings of this research are commensurate

with Health Management Information System (HMIS) data from the previous year (2019-20). In the current research, 83.6% respondents ($n = 92$) received a minimum of four ANC. HMIS data for Assam for 2019-20 (29) show similar findings, with 85.3% women receiving four or more ANCs.

One of the negative effects of the COVID-19 pandemic was unanticipated increased expenses for laboratory services and ultrasound check-up from private health facilities for respondents who had chosen a government health facility for ANC services. Unavailability of IFA tablets in village level health centres for Assam where 54.2% pregnant women are anemic (23) is also concerning.

Commensurate with both HMIS (2019-20) and NFHS-5 (2019-20) (23) findings from current research show high levels of institutional deliveries and deliveries done by the skilled birth attendants (SBAs). Despite this, it shows considerably higher proportion of stillbirths (8 from 75 deliveries) as compared to the Still Birth Rate for Assam in SRS Statistical Report 2017 (2 per 1,000 live births) (30). In addition four early neonatal deaths were also recorded from the 75 deliveries. A substantial indirect impact of COVID-19 on the perinatal outcome, including an increased rate of stillbirths, is also observed in different studies across different countries in the world, including India (6, 31, 32) but of a lesser magnitude. The rise in perinatal mortality could be linked with pandemic-related healthcare disruptions due to the movement restrictions during lockdown (3). Early identification of complications, availability of emergency obstetric services and prompt referral services help to avoid early neonatal deaths (33). Although an apparent link between the restricted physical access to the ANC and delivery services and the high levels of perinatal mortality (stillbirths and early neonatal deaths) could not be established from this research, it has underlined the need to study this further.

The reporting of Caesarian section deliveries (42.7%) is high as compared to recent state-level proportions from NFHS-5 (18.1%) and HMIS (23.5%). Also, majority of the deliveries in private health facilities (86.7%) were Caesarian section deliveries. It is well-established that the likelihood of Caesarian section delivery in a private health facility is higher than a public health facility regardless of other medical and economic factors (5, 34).

The difficulties in reaching the health facility due to lack of transportation during the pandemic are echoed in other studies for pregnant women in Panama and different states within India, viz., Chhattisgarh, Jharkhand, and Telangana (7).

ASHAs and VHSNC members are the official community representatives in the health system. The role of ASHAs in the improved utilization of ANC services, skilled birth attendance, and institutional births is highlighted in a recent study (14). Training of the local level health workers and community members would help manage primary treatment on the ground in such public health emergencies. For effective implementation of the health service delivery at

the local level, these crucial stakeholders need to work in tandem.

The research has a limitation of small sample size from a localized area. Also, the most marginalized women with no access to phones could not be covered in this research. In addition, this study has not been able to show “true effect” of the pandemic on the maternal health outcomes. This observational study provides a framework for potential linkages between the maternal health outcomes and the COVID-19 pandemic and subsequent national lockdown for future research studies to explore. More research is also recommended to determine the causes of the rise in Caesarian section deliveries and to understand the causes behind stillbirths.

In conclusion, the COVID-19 pandemic has affected women's access to maternal health services in numerous indirect ways in select areas from two districts of Assam. The health system (supply-side) factors and the community level (demand-side) factors have worked together to affect the maternal and neonatal wellbeing. Strengthening the existing health system (26), providing sustained health service delivery at different levels for essential services, including maternal health services (35) and preparing the health system to deal with unprecedented situations (7) like the COVID-19 pandemic is recommended. Assuring transportation and a safe working environment for healthcare workers is recommended. For Assam, affordable and uninterrupted good quality maternal health service provision at all levels is recommended to reduce maternal mortality and improve other maternal health indicators.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Ethics Committee at SAHAJ and Piramal Swasthya Institutional Ethics Committee. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

RP performed the data analysis and wrote the first draft of the manuscript. AP, SD, and RB prepared the study tools and coordinated the data collection of the quantitative section. MP coordinated the data collection activities on the field and supported data analysis from qualitative interviews. AP, NS, RK, and SK reviewed the first draft critically. All authors contributed to the conceptualization, study design, manuscript revision, read, and approved the submitted version.

ACKNOWLEDGMENTS

The authors of this manuscript would like to thank all the research participants for their participation and the field investigators [from DiYA Foundation, Kamrup (R.) and Manab Kalyan (Darrang)] for the efforts in the field and unconditional support through the process of data collection given the challenges of their daily lives in a pandemic situation. This work would not have been possible without them. The authors would also like to thank their respective organizations - SAHAJ,

IDEA - The Ant and PSMRI for the support throughout the study and the writing process. The authors would also like to acknowledge the financial and technical support offered by Equal Measures 2030.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fghw.2022.750520/full#supplementary-material>

REFERENCES

- Lucas DN, Bamber JH. Pandemics and maternal health: the indirect effects of COVID-19. *Anaesthesia*. (2021) 76:69–75. doi: 10.1111/anae.15408
- Frances L, Edwards J, Steven O. Governments' responses to the COVID-19 pandemic. *Int J Public Administ.* (2021). 44:879–84. doi: 10.1080/01900692.2021.1936964
- Homer CSE, Leisher SH, Aggarwal N, Akuze J, Babona D, Blencowe H, et al. Counting stillbirths and COVID 19—there has never been a more urgent time. *Lancet Global Health*. (2020) 9:E10–E11. doi: 10.1016/S2214-109X(20)30456-3
- Kumari V, Mehta K, Choudhary R. COVID-19 outbreak and decreased hospitalisation of pregnant women in labour. *Lancet Global Health*. (2020) 8:e1116–7. doi: 10.1016/S2214-109X(20)30319-3
- Bhatia M, Banerjee K, Dixit P, Dwivedi LK. Assessment of variation in cesarean delivery rates between public and private health facilities in India from 2005 to 2016. *JAMA Netw Open*. (2020) 3:e2015022. doi: 10.1001/jamanetworkopen.2020.15022
- Ashish KC, Gurung R, Kinney M, Sunny AK, Moinuddin M, Basnet O et al. Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study. *Lancet Global Health*. (2020) 8:10. doi: 10.1016/S2214-109X(20)30345-4
- Pant S, Koirala S, Subedi M. Maternal health services during COVID-19. *Euroasian J Med Sci*. (2020) 2:468–50. doi: 10.46405/ejms.v2i2.110
- Joshi A. COVID-19 pandemic in India: through psycho-social lens. *J Soc Econ Dev*. (2021) 6:1–24. doi: 10.1007/s40847-020-00136-8
- Garg S, Basu S, Rustagi R, Borle A. Primary health care facility preparedness for outpatient service provision during the COVID-19 pandemic in India: cross-sectional study. *JMIR Public Health Surveill*. (2020) 6:e19927. doi: 10.2196/19927
- Singh A, Jain P, Singh N, Kumar S, Bajpai P, Singh S et al. Impact of COVID-19 pandemic on maternal and child health services in Uttar Pradesh, India. *J Family Med Primary Care*. (2021) 10:509–13. doi: 10.4103/jfmpc.jfmpc_1550_20
- Direct and indirect effects of the COVID-19 pandemic and response in South Asia. Centre for Global Child Health. UNICEF (2021). Available online at: <https://www.unicef.org/rosa/media/13066/file/Main%20Report.pdf>
- Goyal M, Singh P, Singh K, Shekhar S, Agrawal N, Misra S. The effect of the COVID-19 pandemic on maternal health due to delay in seeking health care: experience from a tertiary center. *Int J Gynecol Obstet*. (2020) 152:231–5. doi: 10.1002/ijgo.13457
- National Health Mission. *About Accredited Social Health Activist (ASHA)*. Ministry of Health and Family Welfare, Government of India. Available online at: <http://nhm.gov.in/index1.php?lang=1&level=1&sublinkid=150&lid=226> (accessed July 29, 2021).
- Agarwal S, Curtis SL, Angeles G, Speizer IS, Singh K, Thomas JC. The impact of India's accredited social health activist (ASHA) program on the utilization of maternity services: a nationally representative longitudinal modelling study. *Hum Resour Health*. (2019) 17:68. doi: 10.1186/s12960-019-0402-4
- Sharma N, Sharma M, Jagtap D, Deshmukh A, Hegde S, Kumar A. Revamping village health sanitation and nutrition days for improved delivery of maternal and child health services at village level – experiences from a pilot phase study. *Indian J Public Health*. (2020) 64:345–50. doi: 10.4103/ijph.IJPH_444_19
- National Health Mission. *Village Health Sanitation and Nutrition Committee*. Ministry of Health and Family Welfare, Government of India. Available online at: <http://nhm.gov.in/index1.php?lang=1&level=1&sublinkid=149&lid=225> (accessed July 29, 2020).
- National guidelines for Village Health Sanitation and Nutrition Day (VHSND). *Ministry of Health and Family Welfare and Ministry of Women and Child Development, Government of India*. New Delhi (2019).
- Impact of COVID-19 on routine healthcare services and ASHAs: Bihar, Odisha, and Uttar Pradesh. MicroSave India Foundation (2020).
- Hamal M, Dieleman M, DeBrouwere V, Buning TDC. How do accountability problems lead to maternal health inequities? A review of qualitative literature from Indian public sector. *Public Health Rev*. (2018) 39:9. doi: 10.1186/s40985-018-0081-z
- Paul P, Mondal D. Maternal and child healthcare in India during COVID-19 pandemic. *Midwifery*. (2020) 92:e102865. doi: 10.1016/j.midw.2020.102865
- Srivastava A, Gope R, Nair N, Rath S, Rath S, Sinha R, et al. Are village health sanitation and nutrition committees fulfilling their roles for decentralised health planning and action? A mixed methods study from rural Eastern India. *BMC Public Health*. (2015) 16:59. doi: 10.1186/s12889-016-2699-4
- Special bulletin on maternal mortality in India 2016–18. *Sample Registration System, Office of the Registrar General, India* (2020). Available online at: <https://censusindia.gov.in/>
- National Family Health Survey (NFHS-5). India 2019–20 Assam. *International Institute of Population Sciences (IIPS) and ICF*. Mumbai: IIPS (2020).
- WHO recommendations on antenatal care for a positive pregnancy experience. World Health Organization. (2016) Available online at: <https://apps.who.int/iris/bitstream/handle/10665/250796/9789241549912-eng.pdf;jsessionid=CD633EEF7F45D33B2C075E018A85CA10?sequence=1>
- Ministry of Health and Family Welfare. *Health Management Information System - Standard Reports* (2021). Available online at: <https://hmis.nhp.gov.in/#/standardReports> (accessed January 26, 2021).
- Mehta K, Zodey S, Banerjee P, Pocius SL, Dhaliwal BK, DeLuca A, et al. Shifting research priorities in maternal and child health in the COVID-19 pandemic era in India: A renewed focus on systems strengthening. *PLoS One*. (2021) 16:e0256099. doi: 10.1371/journal.pone.0256099
- Bradshaw C, Atkinson S, Doody O. Employing a qualitative description approach in health care research. *Glob Qual Nurs Res*. (2017) 4:2333393617742282. doi: 10.1177/2333393617742282
- WHO Statement on Caesarean Section Rates. World Health Organization (2015). Available online at: https://apps.who.int/iris/bitstream/handle/10665/161442/WHO_RHR_15.02_eng.pdf;jsessionid=C7AB42990376910F0A14C2B7372B5174?sequence=1
- Health Management Information System (HMIS) 2019–20. National Health Mission. Ministry of Health and Family Welfare, Government of India. Available online at: https://nrhm-mis.nic.in/hmisreports/frmstandard_reports.aspx
- Sample Registration System Statistical Report 2017. *Office of the Registrar General and Census Commissioner, India*. Ministry of Home Affairs. Government of India. New Delhi (2017).
- Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA*. (2020) 324:705–6. doi: 10.1001/jama.2020.12746

32. COVID-19 led to rise in maternal deaths, stillbirths. The Hindu (April 02, 2021). Available online at: <https://www.thehindu.com/news/national/covid-19-led-to-rise-in-maternal-deaths-stillbirths/article34225621.ece>
33. Kakoty SD, Ahmed M, Kalita D. Causes of neonatal death and associated health seeking behaviour in Barpeta district, Assam, India: a community-based study. *Int J Commu Med Public Health*. (2016) 3:919. doi: 10.18203/2394-6040.ijcmph20163919
34. Mohanty SK, Panda BK, Khan PK, Behera P. Out-of-pocket expenditure and correlates of caesarean births in public and private health centres in India. *Soc Sci Med*. (2019) 224:45–57. doi: 10.1016/j.socscimed.2019.01.048
35. Menendez C, Gonzalez R, Donnay F, Leke RGF. Avoiding INDIRECT EFFECTS of COVID-19 on maternal and child health. *Lancet Global Health*. (2020) 2020:e863–4. doi: 10.1016/S2214-109X(20)30239-4

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial

relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Padhye, Purushotham, Paul, Sardeshpande, Ballala, Dhar, Kaul and Khanna. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



Effects of the COVID-19 Pandemic and Telehealth on Antenatal Screening and Services, Including for Mental Health and Domestic Violence: An Australian Mixed-Methods Study

Amanda Henry^{1,2,3*}, Jennifer Yang¹, Sarah Grattan³, Lynne Roberts^{2,4}, Anne Lainchbury⁵, Janani Shanthosh^{3,6}, Patricia Cullen^{7,8} and Louise Everitt^{2,9}

¹ Discipline of Women's Health, School of Clinical Medicine, UNSW Medicine and Health, University of New South Wales (NSW), Sydney, NSW, Australia, ² Department of Women's and Children's Health, St George Hospital, Sydney, NSW, Australia, ³ The George Institute for Global Health, UNSW Medicine and Health, Sydney, NSW, Australia, ⁴ St George and Sutherland Clinical School, UNSW Medicine and Health, University of New South Wales, Sydney, NSW, Australia, ⁵ Royal Hospital for Women, Randwick, NSW, Australia, ⁶ Australian Human Rights Institute, UNSW Sydney, Kensington, NSW, Australia, ⁷ School of Population Health, UNSW Sydney, Kensington, NSW, Australia, ⁸ Ngarruwan Ngadju, First Peoples Health and Wellbeing Research Centre, Australian Health Services Research Institute, University of Wollongong, Wollongong, NSW, Australia, ⁹ School of Nursing and Midwifery, Western Sydney University, Penrith, NSW, Australia

OPEN ACCESS

Edited by:

Vijay Kumar Chattu,
University of Toronto, Canada

Reviewed by:

Sarah Fredsted Villadsen,
University of Copenhagen, Denmark
Myra Betron,
Jhpiego, United States

*Correspondence:

Amanda Henry
amanda.henry@unsw.edu.au

Specialty section:

This article was submitted to
Sex and Gender Differences in
Disease,
a section of the journal
Frontiers in Global Women's Health

Received: 22 November 2021

Accepted: 04 May 2022

Published: 22 June 2022

Citation:

Henry A, Yang J, Grattan S,
Roberts L, Lainchbury A,
Shanthosh J, Cullen P and Everitt L
(2022) Effects of the COVID-19
Pandemic and Telehealth on Antenatal
Screening and Services, Including for
Mental Health and Domestic Violence:
An Australian Mixed-Methods Study.
Front. Glob. Womens Health
3:819953.
doi: 10.3389/fgwh.2022.819953

Introduction: Australian antenatal care includes specific screening and service provision for domestic and family violence (DFV) and mental health. However, the COVID-19 pandemic resulted in major care changes, including greatly expanded telehealth. Given difficulties in a safe assessment and management of disclosures via telehealth, DFV and mental health service provision might be substantially impacted. This study therefore aimed to assess COVID-19 effects on DFV and mental health screening, as well as broader service provision from the perspective of local maternity service providers.

Methods: Mixed-methods study of staff surveys and interviews of staff directly involved in pregnancy care (doctors, midwives, and allied health) in three Sydney (Australia) maternity units, from October 2020 to March 2021. Surveys and interviews interrogated perceived effects of the COVID-19 pandemic on delivery (ensuring required services occurred), timeliness, and quality of (a) overall maternity care and (b) DFV and mental health screening and care; and also advantages and disadvantages of telehealth. Surveys were descriptively analyzed. Interviews were conducted online, recorded, and transcribed verbatim prior to thematic analysis.

Results: In total, 17 interviews were conducted and 109 survey responses were received. Breakdown of survey respondents was 67% of midwives, 21% of doctors, and 10% of allied health. Over half of survey respondents felt the pandemic had a negative effect on delivery, timeliness, and quality of overall pregnancy care, and DFV and mental health screening and management. Perceived telehealth positives included convenience for women (73%) and reducing women's travel times (69%). Negative features included no physical examination (90%), difficulty regarding non-verbal cues (84%), difficulty if

interpreter required (71%), and unsure if safe to ask some questions (62%). About 50% felt telehealth should continue post-pandemic, but for <25% of visits. Those perceived suitable for telehealth were low-risk and multiparous women, whereas those unsuited were high-risk pregnancy, non-English speaking, and/or mental health/psychosocial/DFV concerns. “Change to delivery of care” was the central interview theme, with subthemes of impact on mental health/DFV screening, telehealth (both positive and negative), staff impact (e.g., continuity of care disruption), and perceived impact on women and partners.

Discussion: While telehealth may have an ongoing, post-pandemic role in Australian maternity care, staff believe that this should be limited in scope, mostly for low-risk pregnancies. Women with high risk due to physical health or mental health, DFV, and/or other social concerns were considered unsuited to telehealth.

Keywords: pregnancy, mental health, domestic and family violence, COVID-19, telehealth, pregnancy care

INTRODUCTION

The COVID-19 pandemic has dramatically impacted communities globally across multiple areas of life, including healthcare and access to routine care such as pregnancy care. In Australia during 2020 (first and second waves), the period this study focuses on, burden of disease secondary to COVID-19 was low on an international scale, with only 18 cases of COVID-19 in pregnancy reported in New South Wales (the study setting) in the first wave (1). However, as has been reported around the world (2), routine healthcare including antenatal care was greatly impacted in Australia, with Medicare billing for face-to-face antenatal care services declining 15% in second quarter of 2020 compared to 2019 (3).

The final impact of social isolation, lockdowns, and various restrictions to prevent the spread of COVID-19 is also still to be fully realized. These measures, as well as associated stressors such as unemployment and schooling from home, are expected to dramatically increase women's risk of domestic and family violence (DFV), (4–6) the single greatest cause of death, ill health, and disability in reproductive-age Australian women (7). Pregnant women are a vulnerable group regarding DFV, with an estimated 187,800 Australian women who have experienced violence by a current partner pregnant at some stages during the relationship and 18% of these women experiencing violence during their pregnancy (8). As well as seeing women who are actively experiencing violence during their pregnancy, maternity care providers also see women who have previously experienced intimate partner violence and who are still living with the ongoing consequences for themselves and their children.

Mental health presentations, including depression and anxiety, are also very common both during and after pregnancy. Australian and overseas studies report antenatal depression rates of approximately 10% and anxiety prevalence up to 20% in late pregnancy (9).

In general, pregnancy care is one of the times in a woman's contact with Australian healthcare services where psychosocial screening, including DFV and mental health screening, is routine and has systems in place to provide appropriate support. This

care is evidence-based and acceptable to women, allowing for risk assessment, safety planning, appropriate follow-up, and potentially decreasing post-traumatic stress disorder (PTSD) and perinatal depression as well as improving mother–child interactions (9–11).

To address DFV during the COVID-19 pandemic, the Australian government increased funding for telehealth and online support services. However, telehealth (meaning either telephone or videoconferencing/online consultation, referred to collectively as “telehealth” throughout this article) relies on women being able to speak in private and access referral pathways into community-based frontline services. Use of telehealth for the “booking-in” pregnancy visit, which is usually one of the time points for routine psychosocial screening in Australia, potentially particularly affected DFV and mental health screening. Women may not be as comfortable to disclose these issues when not in a face-to-face setting and/or may not be in a safe and private setting when booking-in from home. Accordingly, current New South Wales (NSW) Health guidelines recommend deferring DFV screening until the first face-to-face visit (12), which may be as late as 28-week gestation, delaying screening and management of any disclosures.

Although several studies have examined the overall impact of the pandemic on perinatal mental health and/or DFV, there is very limited focus on the impact of maternity systems change and its impact on screening. A rapid evidence review on women's mental health during pregnancy in the pandemic included 17 studies and found that anxiety and depressive symptoms ranged from 29.6 to 72%, more than doubled during the pandemic (12, 13). Regarding violence in pregnancy, both an Iranian and Canadian study found high levels of intimate partner violence in the early months of the pandemic (14, 15), however, neither had pre-pandemic controls for comparison.

Regarding COVID-19's impact on maternity care provision generally, a 2021 global scoping review reported that prenatal care visits decreased, healthcare infrastructure was strained, and potentially harmful policies such as increasing time between antenatal visits were instituted (16). While the replacement of in-person visits with telehealth saw some benefits, such as

increasing access to care and therefore appointment attendance rates, reducing wait times, and avoiding exposure to COVID-19, barriers identified included technical difficulties and privacy concerns. In general, management of workflow, and convenience for both staff and women, having some pregnancy care visits *via* telehealth rather than face-to-face may work very well and is likely to continue post-pandemic. It is therefore very important for maternity care services to also understand the limitations of telehealth for antenatal care, and in particular, the effect on those with complex psychosocial needs who are often experiencing broader inequities, to plan appropriate care as Australia emerges from the COVID-19 pandemic.

The aim of this study was therefore to examine, from the perspective of maternity staff, the effect of the COVID-19 pandemic on provision of maternity care in the South-Eastern Sydney Local Health District (SESLHD), Australia, particularly on the identification and management of mental health, psychosocial issues, and domestic and family violence. It also explored the implications of telehealth in antenatal care and its application moving forward.

MATERIALS AND METHODS

A mixed-methods study comprising surveys and interviews was conducted among maternity staff of SESLHD, New South Wales, Australia. In Australia, the main maternity care clinicians are registered midwives (who may or may not also have a nursing qualification), doctors, and allied health staff including social workers, physiotherapists, genetic counselors, and Aboriginal health workers. Staff were eligible if they were currently registered and practicing midwives, obstetric medical staff, or allied health staff working in the obstetric/maternity units of St George Hospital (SGH), the Royal Hospital for Women (RHW) or Sutherland Hospital (TSH), the three hospitals in SESLHD which provide pregnancy and birth care. Staff were only eligible if they had worked in SESLHD Maternity during 2019 and 2020, to allow for comparison of experiences pre-pandemic and during pandemic. For context, the three hospitals have different service capabilities and patient populations: RHW is the area's tertiary maternity referral center, performing ~3,800 births/year, with full neonatal intensive care facilities and co-located with neonatal surgical facilities and adult intensive care, and located in a high sociodemographic status area. SGH performs ~2,400 births/year, has a special care nursery (births 32 weeks and above) and full adult intensive care facilities but not neonatal intensive care, and is situated in a highly diverse sociodemographic area, with approximately half of its maternity population born overseas in a country where English is not the first language. TSH is a smaller unit, performing ~1,200 births/year, 34 weeks and above and transferring out women with major medical conditions such as preeclampsia and type 1 diabetes, and has a majority Caucasian/Australian born catchment area.

Staff Survey

An anonymous online survey (**Supplementary Material 1**) was distributed *via* staff's email to all midwifery, obstetric medical, and allied health staff providing frontline maternity care services

in SESLHD maternity facilities (RHW, SGH, TSH)—estimated to be approximately 500 staff in total. The survey included:

- demographic questions (hospital, age range, type of healthcare professional, years of experience range)
- questions about perception of the *overall* impact of the COVID-19 pandemic on delivery, timeliness, and quality of pregnancy care
- questions about pandemic impact on delivery, timeliness, and quality of (a) domestic and family violence screening and care (b) mental health screening and care
- questions about perception of telehealth (positives, negatives, women suited and not suited for telehealth, group/antenatal education impact of telehealth)

All staff were invited to participate and emailed the survey link, up to three times between November 2020 and January 2021. As not all frontline staff regularly access their NSW Health emails, flyers regarding the study were also posted in maternity staff common areas (with QR code to link to survey), and an in-service about the study given at each participating hospital to answer questions about the study and provide maternity staff with details of how to participate if they wished to do so. Completion of the survey was taken as consent to participate.

Interviews

Semi-structured interviews (**Supplementary Material 2**) were conducted with maternity healthcare staff to explore in detail their perceptions of the impact of the COVID-19 pandemic on provision of antenatal care and maternity services, with a focus on their impressions of impacts on mental health/psychosocial screening and DFV screening. Interviews were conducted after the survey distribution period; however, the survey and interview guide were developed in parallel prior to study commencement. To streamline recruitment for staff interviews, the final question of the survey asked whether staff would be interested in participating in an interview. If so, they were asked to enter contact details into the survey (with response to this question separated from response to other aspects of survey to maintain survey participant anonymity). If that did not yield an appropriate cohort of participants with representation from each hospital and each discipline, purposive sampling of initially under-represented staff occurred, *via* sending to the SESLHD emails of under-represented maternity clinician types and/or under-represented hospital maternity staff, an invitation to participate in interviews.

Potential participants were provided prior to interview with information regarding the purpose of the interviews, that participation was voluntary, and that their identity would be protected through de-identification during the transcription process and in reporting of study findings (**Supplementary Material 3**). Interviews were planned to be no longer than 1 h and to take place online (*via* zoom or Skype). Interviews were performed by study staff (SG) with no direct employment links within SESLHD/not a work colleague of the interviewees, to minimize participation or response bias due to the interviewer having a pre-existing work relationship with the interviewees. With participant consent,

the interviews were audio-recorded to allow for the ease of later transcription and coding. Interviews continued until there was representation of each of the participating hospitals and maternity care professionals (midwives, doctors, and allied health), and saturation of themes occurred.

Data Analysis

1) Surveys: Data were downloaded to SPSS (IBM SPSS Statistics for Windows, V27, Armonk, NY) and analyzed and reported using descriptive statistics (number and percentage) for closed answer questions. Where respondent subgroup size allowed (i.e., at least five in each subgroup, so that there would be no possibility of identifying individuals), then responses to questions about overall pregnancy care and specific DFV and mental health screening were analyzed by (a) hospital of practice, (b) type of maternity healthcare professional, and (c) length of time working in maternity services, with subgroup responses compared using chi-squared testing. The open-ended questions were analyzed and reported thematically.

2) Interviews: Transcripts were produced for each individual recording and initially screened by the interviewer (SG) to remove any potentially identifying details before sharing with senior authors AH and LE. Data were analyzed using the thematic approach outlined by Braun and Clarke (17) consisting of deep familiarization with the data; searching for themes; reviewing, defining and naming the themes; and finalizing the analysis. SG, AH and LE performed the analysis, each reviewing transcripts and discussing themes and subthemes until agreement was reached to validate the findings. These are illustrated by typical excerpts from participants, identified only by professional grouping (as professional grouping and hospital might inadvertently identify participants).

Ethical Approval

The studies involving human participants were reviewed and approved by South-Eastern Sydney Local Health District Human Research Ethics Committee (Ref: ETH01518/2020). The participants provided their written informed consent to participate in this study (interviews), while for anonymous survey participation, the completion of survey was taken as evidence of consent to participate.

RESULTS

Surveys

A total of one hundred and nine survey responses were received (~20% of estimated total SESLHD maternity staff): 75 from midwives (69%), 23 from medical staff (21%), and 11 from allied health (10%). As shown in **Table 1**, respondents were overwhelmingly female-identifying (97%) in keeping with the overall maternity care workforce, approximately half were aged 44 and under and half 45 or older, and TSH was slightly under-represented (9% of respondents) in comparison with its proportion of SESLHD births (~16%).

Table 2 shows the survey respondents' perception of pandemic impact on (1) delivery and (2) timeliness of overall pregnancy care, mental health screening, and domestic and

TABLE 1 | Demographic characteristics of survey respondents.

Total survey respondents	N (%), total N = 109
Primary discipline	
Midwifery	75 (69)
Antenatal care	17 (16)
Postnatal care	9 (8)
Intrapartum care	10 (9)
Midwifery Group Practice	11 (10)
CMC, CMS or CME	11 (10)
Management	4 (4)
All areas	11 (10)
Midwife, prefer not to say area	1 (1)
Medical	23 (21)
Obstetrician, work predominantly public	4 (4)
Obstetrician, work equal public and private	3 (3)
Obstetrician, work predominantly private	2 (2)
Obstetric Registrar/Resident	14 (13)
Allied Health	11 (10)
Social work	1 (1)
Physiotherapy	4 (4)
Other	6 (6)
Sex	
Female	106
Male	2
Non-binary	1
Age (years)	
<25	2 (2)
25–34	33 (30)
35–44	22 (20)
45–54	23 (21)
55 and older	27 (25)
Prefer not to say	2 (2)
Years of Experience	
5 or less	25 (23)
6–10	26 (24)
Between 11 and 15	13 (12)
16 or more	43 (39)
Prefer not to say	1 (1)
My primary affiliated public hospital:	
Royal Hospital for Women	62 (57)
St George Hospital	37 (34)
Sutherland Hospital	10 (9)

family violence screening, as well as impact on (3) quality of overall, mental health, and DFV screening and care. The proportions who viewed the pandemic as having a somewhat negative or extremely negative impact were over 50% for all categories. However, more staff rated pandemic effects on delivery ($p = 0.02$) and timeliness ($p = 0.004$) of DFV screening (but not quality of care) as *extremely* negative vs. effects on overall pregnancy care.

Regarding subgroup perceptions (**Table 3**), several statistically significant differences were noted according to hospital site.

TABLE 2 | Staff perceptions of pandemic impact on overall care and on psychosocial screening[#].

Impact on delivery	Overall pregnancy care N (%)	Mental health screening N (%)	DFV screening N (%)	P-value overall vs. mental health	P-value overall vs. DFV
Extremely negative	10 (9)	16 (15)	22 (20)	0.21	0.02
Somewhat negative	56 (51)	46 (42)	40 (37)	0.18	0.03
Neutral	29 (27)	19 (17)	22 (20)	0.39	0.26
Somewhat positive	8 (7)	10 (9)	4 (4)	0.62	0.24
Extremely positive	3 (3)	1 (1)	1 (1)	0.62	0.62
Unsure	3 (3)	17 (16)	20 (18)	0.001	<0.001
Impact on timeliness	Overall pregnancy care N (%)	Mental health screening N (%)	DFV screening N (%)	P-value overall vs. mental health	P-value overall vs. DFV
Extremely negative	8 (7)	17 (16)	23 (21)	0.06	0.004
Somewhat negative	59 (54)	43 (39)	41 (38)	0.03	0.01
Neutral	24 (22)	24 (22)	21 (19)	1.0	0.62
Somewhat positive	6 (6)	7 (6)	4 (4)	0.76	0.52
Extremely positive	0 (0)	1 (1)	1 (1)	1.0	1.0
Unsure	12 (11)	16 (15)	19 (17)	0.42	0.18
Impact on quality	Overall pregnancy care N (%)	Mental health screening and care N (%)	DFV screening and care N (%)	P-value overall vs. mental health	P-value overall vs. DFV
Extremely negative	11 (10)	6 (6)	12 (11)	0.21	0.83
Somewhat negative	60 (55)	51 (47)	44 (40)	0.22	0.03
Neutral	25 (23)	26 (24)	26 (24)	0.87	0.87
Somewhat positive	7 (6)	9 (8)	5 (5)	0.61	0.55
Extremely positive	2 (2)	2 (2)	3 (3)	1.0	1.0
Unsure	4 (4)	15 (14)	19 (17)	0.008	0.001

[#] See **Supplementary Material 1** questionnaire for examples/prompts given to staff regarding delivery, timeliness and quality of care. Bold values means statistically significant result ($p < 0.05$).

Staff at SGH (the hospital with the highest diversity population) overall had more negative perceptions about pandemic impact, particularly on the delivery, timeliness, and quality of DFV and mental health care, as well as quality (but not timeliness or delivery) of overall pregnancy care. Few significant differences were noted between the professions (midwifery, medical, and allied health), apart from a higher proportion of allied health and medical staff than midwifery staff being “not sure” about delivery, timeliness, and quality of overall care and mental health and DFV screening and care. There were no major differences in staff perceptions by years of experience.

Regarding telehealth, as shown in **Table 4**, there was a major shift in its use for pregnancy care. Over 75% of respondents reported that pre-pandemic, <10% of visits were by telehealth. During the pandemic, this shifted to only 10% stating no telehealth, with the majority (52%) stating over 10% of visits occurred by telehealth. Most respondents nominated two or more telehealth advantages, most frequently convenience for the woman (73%), reducing longer travel times for some women (69%), and reducing clinic overcrowding (62%). However, more respondents nominated multiple negative features, including inability to do physical examination (90%), difficulty picking-up non-verbal cues (84%), difficult if interpreter required (71%), and

unsure if safe to ask some questions (62%: majority noting DFV questions as unsure if safe to ask). A total of 29% felt telehealth increased inequity in pregnancy care. Regarding post-pandemic telehealth, 56% felt telehealth should definitely or probably be used for some aspects of pregnancy care, “sometimes” (10–25% of visits). Staff also felt that there were groups of women particularly suited or not suited to telehealth. Of the 64 respondents who nominated those particularly suited to telehealth, 55% nominated low-risk women, 52% multiparous women, and 34% those living further from hospital. Of 81 respondents nominating groups not suited to having any visits by telehealth, 65% were concerned regarding women with high-risk pregnancy/medical co-morbidities, 53% for non-English speaking women, and 25, 19, and 26% for women with mental health presentations, DFV issues, and other psychosocial issues, respectively.

Interviews

A total of 17 interviews were conducted (10 midwives, 3 medical staff, and 4 allied health staff). Targeted sampling *via* email invitation was required to achieve an appropriate sample due to insufficient staff indicating an interest in interview at the time of survey completion. Sufficient midwifery staff sampling was achieved with the first targeted email invitations, while a second

TABLE 3 | Staff with a negative perception of COVID-19 impact by hospital.

Very or somewhat negative impact on:	Royal Hospital for Women* N (%)	St George Hospital** N (%)	Sutherland Hospital*** N (%)	P-value
Delivery of Overall Pregnancy Care	35/62 (56)	26/37 (70)	5/10 (50)	0.31
Delivery of Mental Health screening	29/62 (47)	29/37 (78)	4/10 (40)	0.005
Delivery of DFV screening	28/62 (45)	29/37 (78)	5/10 (50)	0.008
Timeliness of Overall Pregnancy Care	35/62 (56)	26/37 (70)	6/10 (60)	0.34
Timeliness of Mental Health screening	28/62 (45)	28/37 (76)	4/10 (40)	0.008
Timeliness of DFV screening	29/62 (47)	30/37 (81)	5/10 (50)	0.003
Quality of Overall Pregnancy Care	33/62 (53)	33/37 (89)	5/10 (50)	0.001
Quality of Mental Health screening	26/62 (42)	25/37 (68)	6/10 (60)	0.047
Quality of DFV screening	25/62 (40)	27/37 (73)	4/10 (40)	0.005

*Royal Hospital for Women, Area's tertiary hospital, full maternity and neonatal facilities, high sociodemographic status area overall.

**St George Hospital, Full maternity facilities, neonatal >32 weeks facilities, high sociodemographic diversity with approximately half of maternity population born overseas in predominantly non-English speaking country.

***Sutherland Hospital, Lower risk unit, majority Caucasian Australian population.

DFV, Domestic and family violence.

TABLE 4 | Telehealth frequency pre- and during pandemic.

N (%) telehealth antenatal/pregnancy care visits	Pre-pandemic	During pandemic	P-value
None	73 (67)	11 (10)	<0.001
Occasional (<10%)	12 (11)	22 (20)	0.06
Sometimes (10–25%)	1 (1)	28 (26)	<0.001
Often (26–50%)	4 (4)	22 (20)	<0.001
Majority (over 50%)	3 (3)	7 (6)	0.20
Not sure/couldn't say	16 (15)	19 (17)	0.58

Bold values means statistically significant result ($p < 0.05$).

round of email invitations was required to achieve sufficient allied health and medical staff. After the first 14 interviews, no further new thematic areas were identified in the subsequent three interviews and therefore interviews ceased. As shown in **Figure 1**, the central theme from the interviews was the changes to delivery in care resulting from the pandemic. The major issues arising from this theme were telehealth, psychosocial/DFV considerations, perceived effects on women and partners, and effects on staff. Although positive as well as negative aspects of changes to delivery in care were nominated by staff, there was an overall sense that women's health was being sacrificed on behalf of the community, with loss of usual emphasis on woman-centered care (18). This was summarized by one midwife:

"The changes we needed to put in place were not woman-centered at all...it was governed by the needs of the greater community with COVID and the changes that we had to make." Midwife 108

Change to Delivery of Care—Telehealth

All interviewees noted the major change to delivery of care wrought by the shift away from face-to-face visits and toward telehealth. For most, telehealth was seen as an inferior albeit necessary substitute noting that lack of face-to-face appointments impacted the ability to communicate and care for women. This midwife describes what the women were saying:

"We found that women were reporting to us that they didn't feel cared for...until they had their first face-to-face appointment, and then they finally felt they were pregnant and they were being looked after." Midwife 105

One of the allied health interviewees described the difficulty of engaging on the phone:

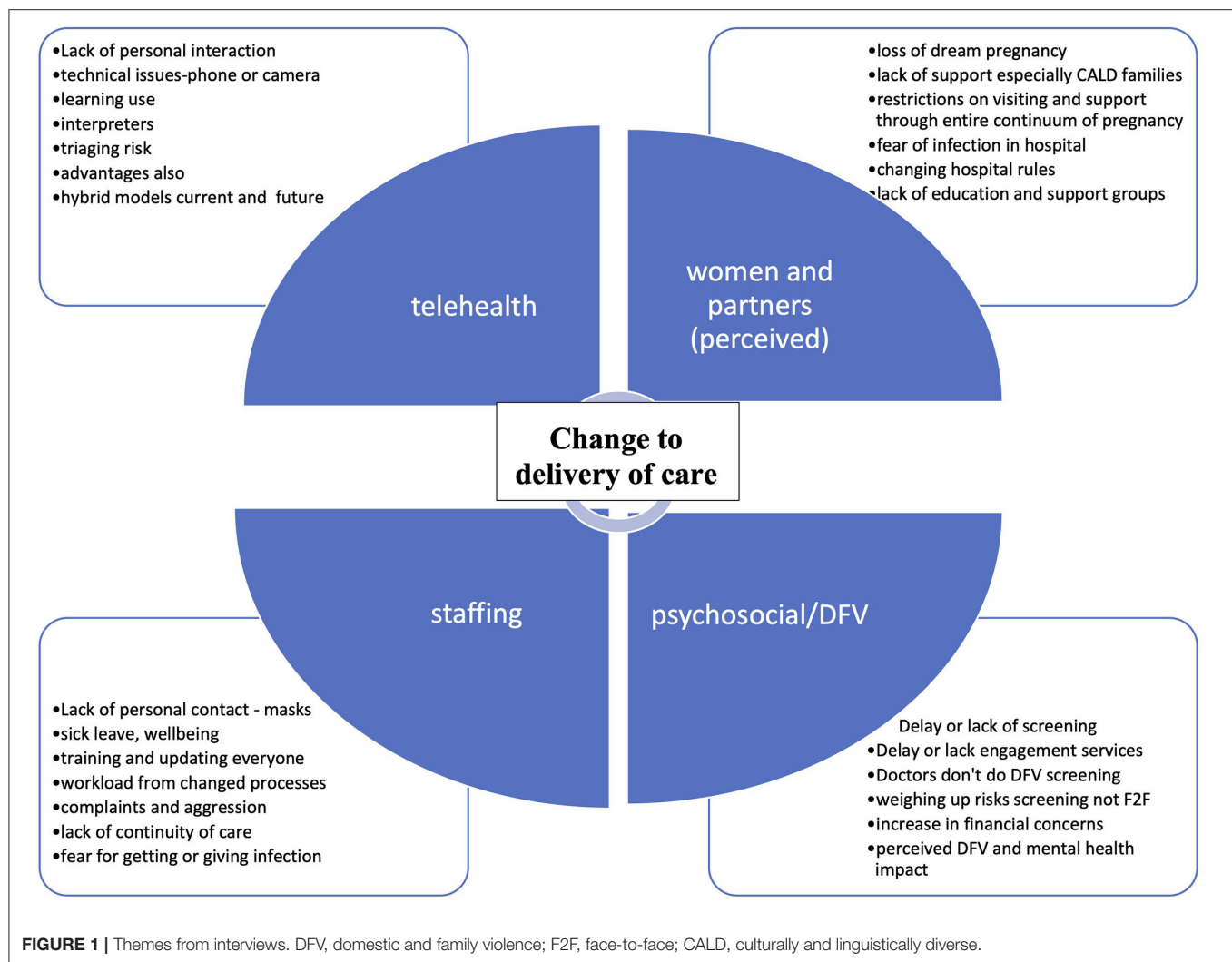
"Talking to women is so much...not just easier, but a better way to develop that rapport with someone... Talking face-to-face to somebody over the phone that doesn't really want to talk to us...it's very hard." Allied health 114

For some, this impact on effective communication with women was further impacted by technical and equipment issues. Interviewees noted the lack of appropriate equipment, meant that they could not actually work properly:

"I think it could have been good, if this organization was invested in the equipment...It took me four months to get a computer that was a laptop, and I still haven't been able to crack how to get those two apps on my desktop...so I still cannot work remotely." Midwife 102

"I didn't even have the camera on my screen until like after the events [first wave 2020]." Allied Health 114

Some recognized the potential advantages of telehealth and, however, acknowledged that it may not be appropriate for the pregnant population. One doctor described how being unable to perform physical examinations would not provide appropriate care:



"I think with the provision of a lot of telehealth services...good for cover in other areas of medicine...but antenatal care was very difficult ...because our routine check-up of a fetal heart or blood pressure can't be done over telehealth...so I don't feel as though the telehealth was able to sufficiently care for these women." Medical 107.

A midwife also felt the outcomes of care with telehealth could actually be poorer in pregnancy:

"I understand telehealth is a fantastic innovation...I can see where it has amazing value, but I think in the maternity care context, particularly in the urban setting and...high risk pregnancy...if they engage with antenatal care early, the outcomes are fantastic...whereas with telehealth it isn't the same." Midwife 109

However, for postnatal care where the woman with her baby could be seen telehealth had advantages:

"they set the whole scene up where we can see the baby and we can watch breastfeeds...we would never have been able to achieve this without telehealth." Midwife 108

Telehealth was also perceived as offering women an option of care and convenience, in particular for women living further away from hospital (one maternity unit clients not uncommonly live over 30-min drive from the hospital):

"We do a telehealth service for women who are just out of our boundary...you can reach more women or you can make things a bit more accessible to them." Midwife 101

Post-pandemic, some voiced that a hybrid model of face-to-face and telehealth would likely be adopted for some women; however, the challenge was to ensure the technology and establish criteria for who would be suitable:

"it [telehealth] would work for some and not work for others...going with the hybrid model antenatally, some women are much, much happier doing the video calls...we've seen it work so we can offer that but...we realized actually that some women still need a lot more visits and a lot more care...we have gone back to kind of normal visits for them." Midwife 104

Changes to Delivery of Care—Psychosocial and Domestic and Family Violence Screening and Care

In line with the survey results, most interview participants viewed the combination of booking visits occurring by telehealth, and face-to-face visits occurring later in gestation (and less frequently), as particularly detrimental to timely screening and care for psychosocial and DFV issues. Some women missed screening altogether, as noted by one midwife:

“..very difficult to gain the intimate information over the phone...and because we dropped some of the appointments...sometimes we didn’t get to ask these questions through the whole pregnancy. I have had a few women who went home without ever being asked.” Midwife 110

Some staff initially planned to screen *via* telehealth, so that identification of issues would not be delayed, but safety concerns precluded this:

“Because the bookings were being done on telehealth, we found it very difficult to do the DV [domestic violence] screen. In fact, we didn’t do the DV screen because one day we were doing a booking and we asked the woman is she was on her own she said ‘Yes’ and then we did the DV screen and the next thing her husband spoke... So, we then decided we had to stop.” Midwife 109

Re-instituting face-to-face visits occurred because the risks of COVID-19 were outweighed by the risks of poor psychosocial care, and staff recognized the inequity of failing to adequately provide screening and care:

“After a bit we just said, ‘Well, actually, weighing up the risks, the risk of somebody being harmed by domestic violence was higher than the risk of them actually catching COVID if they came to our hospital, and so we just started doing face-to-face appointments again...It’s our responsibility. If we’re going to screen and ask clients for information about their backgrounds, their experiences...we have to do something about it.” Allied Health 112

Many participants also recognized delaying the initial psychosocial screening *via* telehealth, even when the woman was subsequently face-to-face, meant screening may not have been done, as women were often seen by a doctor and they are not used to doing the psychosocial/DFV screen. One midwife explained:

“we might not see them until 31 weeks...GPs [general practitioners] would be seeing them in between but GPs don’t usually ask these questions, and [antenatal clinic] doctors don’t always either.” Midwife 104

Doctors also recognized that it was not something they usually did:

“very occasionally in the doctor’s clinic... the midwives will put a little sign on the file to say please complete her EDS [Edinburgh Perinatal Depression Scale], or repeat her EDS if it was sort of borderline at the previous visit or whatever, but I have to say that’s

not something we routinely do, and probably not something we do all that well, necessarily.” Medical 115

For the women, this had flow-on effects of delayed screening becoming delayed referral to services and so delay or lack of care in the window of opportunity that pregnancy provides:

“the maternity screening wasn’t happening as early...because they were doing some phone work...then for that reason they weren’t getting as many disclosures in relation to domestic violence, which then postponed our referrals...didn’t give us as much time to deal with those cases.” Allied Health 114

However, some did note an unexpected positive of restrictions, particularly partners not being allowed to come in to antenatal visits, regarding psychosocial screening:

“Sometimes it’s difficult to get a woman by herself if she’s...in a volatile relationship. And the fact that the hospital’s enforcing it means...you have that protected time with women.” Midwife 101

Another midwife felt increased disclosures occurred:

“The women were here without their husbands so we’ve had a lot more disclosure.” Midwife 110

Overall, the changed mode of appointments to telehealth, delay in asking psychosocial screening questions, and reduced face-to-face visits were perceived as impacting the care women could receive. In some cases, no or lack of screening meant opportunities were missed to provide a safe environment for women to choose to disclose DFV or psychosocial concerns and be offered appropriate supports.

Change to Delivery of Care-Perceived Effect on Women and Partners

Maternity care staff noted both practical effects of delivery of care changes and also perceived impacts on the emotional well-being of women and partners (which were in turn seen to be related to overall pandemic effects). Practical impacts on women and partners were both positive and negative from a staff perspective. An unexpected positive of the pandemic care changes was regarding postnatal care: rules not allowing visitors apart from the partner on postnatal ward meant that women got more opportunity for assistance with breastfeeding and postnatal recovery, the midwives noted:

“It is nice to not have 10 visitors in during the day so that you can do that education, get that breastfeeding embedded... sometimes people can get lost in a sea of visitors...or they don’t feel comfortable having those conversations with the midwives about perineal care...because they’ve got a room full of visitors and feel like they have to entertain and pass the baby around and that kind of thing.” Midwife 101

“Postnatally, I think the women have recovered a lot better because it’s gone back to the old days, 40 days of rest, because no one can visit them.” Midwife 108

However, restrictions antenatally, including education all switching to online, were seen as detrimental to preparation for labor, birth, and parenting. One doctor described this negative impact:

“Some things like education groups stopped running...which I think was a great shame...the maternity tours stopped running, so women, I think felt...a little bit more alienated from you know, the process of what was going to happen when they came into labor.” Medical 115

While one of the midwives noticed a change this had on fathers:

“I noticed the fathers seemed to be traumatized more about the birth experience than they used to be...the only thing I could put it down to was the fathers weren’t being permitted to come into the hospital for antenatal classes.” Midwife 102

One midwife summarized the effects of care change positives and negatives as:

“So, postnatally, definitely better. Antenatally, I think we’ll see repercussions down the track.” Midwife 108

Although some impacts on emotional well-being of changes to delivery of care were difficult to separate out from the general effects of the pandemic, there was a strong sense from staff of the negative impact of care delays, restrictions, and reduced face-to-face opportunities. These were felt to interact with general fear and health concerns around COVID-19 to further delay care.

“we spend a lot of time encouraging them to have such a low threshold to come in, but then it really became very muddy, that time of COVID [first wave], because they didn’t know what was more dangerous, coming to the hospital or staying at home, you know? So I think we did find some late presentations...that was a bit of a worry really.” Medical 115

Additionally, staff struggled with the intersection of increased need but decreased opportunities to engage with women and provide care:

“the higher incidents of DV as well as the challenges of actual engagement with clients...typically I would invite people in...they were typically coming for their antenatal appointments anyway...but there was a drop off...because they just didn’t really want to be coming in accessing healthcare...I think it’s really harmful to not deliver a service to clients that need it.” Allied Health 114.

Woman-centered care considers the woman’s individual circumstances and aims to meet the woman’s social, emotional, physical, psychological, spiritual, and cultural needs (18). The women expressed to the midwives a lack of being recognized in the changed processes:

“Just from the feedback that we’ve had from women, was that they did find it quite dehumanizing...one woman said to us that she’d lost...that sort of dream of a pregnancy that she’d had. She

said that’s been taken away from me because I’ve had no face-to-face visits; I haven’t really been able to enjoy this pregnancy.” Midwife 105

“I was noticing a high level of anxiety amongst the women, and many, many women said things to me like ‘Oh, now for the first time I feel cared about’ and they were 28 weeks pregnant.” Midwife 109

This loss of ability for women and health professionals to work in partnership affected choices, communication, and education that may have both short- and long-term health impacts for women and families post-pandemic.

Changes to Delivery of Care—Effect on Staff

Most staff reported negative perceptions of the change in care. The lack of physical contact and additional barriers to care of personal protective equipment, especially mask wearing, were seen to have impact on communication and ability to engage with women as these midwives describe:

“Wearing the masks has made it quite impersonal.” Midwife 111

“And when she’s got the mask on, I’ve got a mask on, it’s so hard to get the subtle emotion and even to show my emotion to her as well.” Midwife 110

At the same time, staff were struggling with the increased workload from changed care processes in conjunction with increased sick leave due to need to be vigilant around COVID-19 symptoms.

“There is definitely a lot more tasks and...people were taking more sick leave because they had to get swabs whereas [pre-COVID] they probably just would’ve come to work.” Midwife 101

Staff also perceived this as negatively affecting continuity of care for women:

“We’ve had more sickness with staff because you can’t just come in with a runny nose anymore...so we’ve had less staff coming in to do their clinics which means that women get less continuity.” Midwife 104

On the positive side, some staff noted that although they felt telehealth had a limited role in the maternity setting for patient care, online staff meetings were quite beneficial:

“one thing I think is great is...online applications for communication. I love them in terms of meetings...it’s very economical from a time perspective.” Midwife 109

Staff had to cope with changed practices in how they delivered their care, constantly changing restrictions and requirements while coping with the impact of the pandemic personally and in their workplace:

“on some days it was hour by hour things were changing...it was a significant workload...we all burned out by the end of last year [2020].” Midwife 101

DISCUSSION

Our mixed-methods study of three metropolitan Sydney hospitals providing maternity care found that staff perceived a major and mostly negative impact of the COVID-19 pandemic on both pregnancy care in general, and more specifically regarding screening and care for DFV and mental health issues. Although the focus of this study was primarily on pandemic impacts on psychosocial screening in pregnancy care, the interviews in particular uncovered broader themes of the overall changes to delivery of care, including telehealth. The pandemic created an immediate impact requiring changes to established delivery of models of maternity care. Women-centered care offering choice, control, and continuity was removed for both woman and the health professionals. New rapidly changing ways of working including a change to telehealth were not formally evaluated in established in maternity services or midwifery continuity of models of care, but imposed by health services as a part of pandemic response and restrictions (12). Staff had particular concern around negative impact on whether DFV screening was performed, its timeliness, and the equity of screening telehealth was acknowledged as having both positive and negative aspects, with perceived positive aspects including convenience and reduced travel time for women. Negative aspects included inability to perform physical examination, difficulty picking up non-verbal cues, issues for women requiring interpreters, and safety of asking certain questions, e.g., regarding DFV.

Changes to delivery of care saw staff express that although some telehealth would be a useful tool going forward for pregnancy care, this should still be a minority of visits and that those who were high-risk either medically or psychosocially were not suitable for any telehealth. Regarding restrictions as part of face-to-face care (mask-wearing and visitor restrictions), interviewees felt overall relatively positive about visitor restrictions, particularly for providing better immediate postnatal care. However, mask-wearing/personal protective equipment use and lack of physical contact with women were seen as further diminishing qualities of care and the major negative impacts on the personal nature of maternity care delivery. Staff were clearly concerned about the difficulties of providing woman-centered care, a central tenet of Australian pregnancy care guidelines, (18) and articulated the moral hazard of balancing perceived community needs against providing appropriate care. This echoes findings among the broader DFV Australian workforce, who have experienced increased workload but also its unrelenting, exhausting nature in addition for concern for the future: “it’s who we’re not seeing that worries me” (19). Thus, as well as for women and their families, the short- and long-term impacts for staff post-pandemic need to be considered.

In the Australian context, a number of qualitative studies have been performed to date from the perspective of midwives regarding provision of maternity care (20–22) and of women regarding their maternity care experiences (23, 24). These largely align with the more general findings of this study, with midwives reporting challenges to provision of woman-centered care (20, 22), and difficulties coping with rapid changes to care (including telehealth) and “COVID-19 causing chaos” (20–22). As in this

study, “silver linings” included the perceived positive impact of visiting restrictions on postnatal care (20, 22). The women themselves noted the impact of navigating a changing healthcare system, the impact on preparedness in pregnancy and for parenting, and facing the uncertainty of a pandemic (23, 24).

Regarding mental health and/or DFV specifically, our findings suggest that changes in maternity care delivery in Australia, with face-to-face visits later in pregnancy and fewer in number, are likely to compound the perinatal mental health and DFV impact of the pandemic, through delay in screening and care, and in some cases missed screening altogether. This issue was also noted by Hearn et al. in their study of midwives in Melbourne, Australia, who repeatedly voiced concerns around screening for family violence and noting how unsafe this was to do by telephone (21). Our findings also suggest a disparity in screening and care impacts for women from diverse backgrounds, as the unit with the highest proportion of overseas-born and non-English speaking women had a significantly higher staff perception of negative impact of the pandemic on DFV and mental health screening and care. This is also reflected in the fact that almost two times as many surveyed staff felt that telehealth increases inequities in pregnancy care vs. decreases it. This has profound implications for ensuring ongoing and timely access to DFV screening and services as part of high quality, safe, and equitable pregnancy care. Staff further explained that regarding DFV and mental health screening, deferral of screening until the woman could be seen face-to-face then resulted in delayed care for affected women and potentially missed screening and care altogether. Any increased incidence of stress and mental health disorders during the pandemic was therefore not adequately addressed (25).

Strengths and Limitations of the Study

The strengths of the study include its mixed-methods design, allowing for both breadth and depth of perception of maternity care providers. However, the decision to produce (in the interests of timely study completion) the interview guide and survey questions in parallel, rather than using survey findings to inform the interview questions, is a potential limitation. Another strength is that although many findings related to general insights on staff regarding pregnancy care, the study’s focus on the specific but extremely common issue of psychosocial screening and care during pregnancy also allowed for a deeper understanding of COVID-19 pandemic impacts in this area than would have been achieved by only a general exploration of maternity effects. Inclusion of the perspectives of allied health and medical maternity healthcare professionals in addition to those of midwives contributed to a more holistic view of maternity service provision in this area. Limitations include the geographical limitation of the work to three hospitals in a specific area of Sydney: although these hospitals do service a range of pregnant populations from low-risk through to very high risk, and with differing sociodemographic catchments, experiences of staff at these hospitals may not be the representative of the broader Australian maternity system. The lack of involvement of the women themselves also limits the conclusions that can be drawn.

Implications for Practice and Conclusion

Our study findings suggest that the adaptations to SESLHD maternity care due to the pandemic, particularly increased telehealth and reduced face-to-face visits, have some ongoing utilities for selected women and at appropriate times during the pregnancy. However, the pandemic practice of switching the “booking-in” visit to telehealth should revert to face-to-face, both to ensure that safe and appropriate psychosocial screening occurs in the first half of pregnancy, so that services for those experiencing mental health and/or DFV issues can be instituted with sufficient time to have a positive impact prior to birth. Staff perceive follow-up visits *via* telehealth to be most appropriate for those with low-risk pregnancies, who have already had children, and who live further away from the hospital. Women at high risk either because of physical health or due to mental health, DFV, and/or other social concerns are unsuitable to be seen *via* telehealth going forward. Other pandemic restrictions perceived to be positive by staff for either general care (partner only on postnatal ward/no other visitors allowed) or psychosocial/DFV screening (limited partners at antenatal visits) are not broadly sustainable on an ongoing basis. However, more restricted general (vs. partner only) visiting hours on postnatal wards may be able to be implemented to sustain postnatal care improvements.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, on reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by South-Eastern Sydney Local Health District Human

Research Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AH, LE, LR, AL, and PC: study concept and design. SG, AH, LE, LR, and AL: data acquisition. JY, SG, AH, and LE: data analysis. AH, JY, SG, LR, AL, JS, PC, and LE: data interpretation and manuscript editing. AH: manuscript drafting. All authors have approved the final submitted manuscript.

FUNDING

This research was supported by a UNSW Research COVID-19: Rapid Response Research Fund philanthropic grant. The funders had no input into the design or conduct of the research project, manuscript content or decision to publish. Patricia Cullen is funded by a NHMRC Early Career Fellowship (Grant ID: APP1158223).

ACKNOWLEDGMENTS

The authors would like to thank Dr. Lily Xu who assisted with survey distribution at one of the study hospitals.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fghw.2022.819953/full#supplementary-material>

REFERENCES

1. NSW Health. *In Focus: COVID-19 in pregnant women*. Canberra: NSW Government. (2020). Available online at: <https://www.health.nsw.gov.au/Infectious/covid-19/Documents/pregnant-women.pdf> (accessed November 20, 2021).
2. Moynihan R, Sanders S, Michaleff ZA, Scott AM, Clark J, To EJ, et al. Impact of COVID-19 pandemic on utilisation of healthcare services: a systematic review. *BMJ Open*. (2021) 11:e045343. doi: 10.1136/bmjopen-2020-045343
3. Australian Institute of Health Welfare. *Antenatal care during COVID-19, 2020*. Canberra: AIHW (2021).
4. Anurudran A, Yared L, Comrie C, Harrison K, Burke T. Domestic violence amid COVID-19. *Int J Gynaecol Obstet*. (2020) 150:255–6. eng. doi: 10.1002/ijgo.13247
5. Kofman YB, Garfin DR. Home is not always a haven: the domestic violence crisis amid the COVID-19 pandemic. *Psychol Trauma*. (2020) 12:S199–201. eng. doi: 10.1037/tra0000866
6. Women's Safety NSW. *New Domestic Violence Survey in NSW Shows Impact of COVID-19 on the Rise*. (2020). Available online at: https://www.womenssafetytynsw.org.au/wp-content/uploads/2020/04/03.04.20_New-Domestic-Violence-Survey-in-NSW-Shows-Impact-of-COVID-19-on-the-Rise.pdf (accessed November 20, 2021).
7. Australian Institute of Health Welfare. *Australia's Health 2016*. Report No.: Cat. no. AUS 199. Canberra. AIHW (2016).
8. Australian Bureau of Statistics. *Personal Safety Survey 2016*. Canberra: ABS (2016).
9. Department of Health. *Screening for Depressive and Anxiety Disorders*. (Clinical Practice Guidelines: Pregnancy Care). Canberra: Australian Government Department of Health (2019).
10. Australia's National Research Organisation for Women's Safety. *Identifying and Responding to Domestic Violence in Antenatal Care. Research to Policy and Practice*, 06/2020. Sydney: ANROWS (2020).
11. Spangaro J, Koziol-McLain J, Rutherford A, Zwi AB. “Made Me Feel Connected”: A Qualitative Comparative Analysis of Intimate Partner Violence Routine Screening Pathways to Impact. *Violence Against Women*. (2019) 26:334–58. doi: 10.1177/1077801219830250
12. NSW Health. *Guidance for Maternity and Newborn Care*. Canberra: NSW Government (2021). Available online at: <https://www.health.nsw.gov.au/Infectious/covid-19/communities-of-practice/Pages/maternity-and-newborn-care.aspx> (accessed October 21, 2021).
13. Ahmad M, Vismara L. The psychological impact of COVID-19 pandemic on women's mental health during pregnancy: a rapid evidence review. *Int J Environ Res Public Health*. (2021) 18:7112. eng. doi: 10.3390/ijerph18137112
14. Bourgault S, Peterman A, O'Donnell M. Violence against women and children during COVID-19—one year on and 100 papers. In: *A Fourth Research Round Up*. Washington, DC: Center for Global Development (2021). (accessed April 12, 2021).

15. Naghizadeh S, Mirghafourvand M, Mohammadirad R. Domestic violence and its relationship with quality of life in pregnant women during the outbreak of COVID-19 disease. *BMC Pregnancy Childbirth*. (2021) 21:88. doi: 10.1186/s12884-021-03579-x
16. Kotlar B, Gerson E, Petrillo S, Langer A, Tiemeier H. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. *Reprod Health*. (2021) 18:10. doi: 10.1186/s12978-021-01070-6
17. Clarke V, Braun V. *Successful Qualitative Research: A Practical Guide for Beginners*. London: Sage (2013).
18. Department of Health. 2 *Providing Woman-Centred Care*. Canberra: (Clinical Practice Guidelines: Pregnancy Care); Australian Government Department of Health (2019).
19. Baffsky R, Beek K, Wayland S, Shanthosh J, Henry A, Cullen P. "The real pandemic's been there forever": qualitative perspectives of domestic and family violence workforce in Australia during COVID-19. *BMC Health Serv Res*. (2022) 22:1–17. doi: 10.1186/s12913-022-07708-w
20. Bradfield Z, Hauck Y, Homer CSE, Sweet L, Wilson AN, Szabo RA, et al. Midwives' experiences of providing maternity care during the COVID-19 pandemic in Australia. *Women Birth*. (2022) 35:262–71. doi: 10.1016/j.wombi.2021.02.007
21. Hearn F, Biggs L, Wallace H, Riggs E. No one asked us: Understanding the lived experiences of midwives providing care in the north west suburbs of Melbourne during the COVID-19 pandemic: an interpretive phenomenology. *Women Birth*. (2021). eng. doi: 10.1016/j.wombi.2021.09.008. [Epub ahead of print].
22. Stulz VM, Bradfield Z, Cummins A, Catling C, Sweet L, McInnes R, et al. Midwives providing woman-centred care during the COVID-19 pandemic in Australia: a national qualitative study. *Women Birth*. (2021). eng. doi: 10.1016/j.wombi.2021.10.006. [Epub ahead of print].
23. Atmuri K, Sarkar M, Obudu E, Kumar A. Perspectives of pregnant women during the COVID-19 pandemic: a qualitative study. *Women Birth*. (2021) 35:280–8. eng. doi: 10.1016/j.wombi.2021.03.008
24. Sweet L, Wilson AN, Bradfield Z, Hauck Y, Kuliukas L, Homer CSE, et al. Childbearing women's experiences of the maternity care system in Australia during the first wave of the COVID-19 pandemic. *Women Birth*. (2021) 98:102996. eng. doi: 10.1016/j.midw.2021.102996
25. Koyucu RG, Karaca PP. The Covid 19 outbreak: maternal mental health and associated factors. *Midwifery*. (2021) 99:103013. doi: 10.1016/j.midw.2021.103013

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Henry, Yang, Grattan, Roberts, Lainchbury, Shanthosh, Cullen and Everitt. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.



OPEN ACCESS

EDITED BY

Lauren M. Osborne,
Cornell University, United States

REVIEWED BY

Kirsty Budds,
Leeds Beckett University,
United Kingdom
Julia Riddle,
Johns Hopkins Medicine, United States

*CORRESPONDENCE

Stephanie Batram-Zantvoort
stephanie.zantvoort@uni-bielefeld.de

SPECIALTY SECTION

This article was submitted to
Women's Mental Health,
a section of the journal
Frontiers in Global Women's Health

RECEIVED 18 February 2022

ACCEPTED 15 August 2022

PUBLISHED 05 September 2022

CITATION

Batram-Zantvoort S, Wandschneider L,
Niehues V, Razum O and Miani C
(2022) Maternal self-conception and
mental wellbeing during the first wave
of the COVID-19 pandemic. A
qualitative interview study through the
lens of "intensive mothering" and "ideal
worker" ideology.
Front. Glob. Womens Health
3:878723.
doi: 10.3389/fgwh.2022.878723

COPYRIGHT

© 2022 Batram-Zantvoort,
Wandschneider, Niehues, Razum and
Miani. This is an open-access article
distributed under the terms of the
[Creative Commons Attribution License](#)
(CC BY). The use, distribution or
reproduction in other forums is
permitted, provided the original
author(s) and the copyright owner(s)
are credited and that the original
publication in this journal is cited, in
accordance with accepted academic
practice. No use, distribution or
reproduction is permitted which does
not comply with these terms.

Maternal self-conception and mental wellbeing during the first wave of the COVID-19 pandemic. A qualitative interview study through the lens of "intensive mothering" and "ideal worker" ideology

Stephanie Batram-Zantvoort*, Lisa Wandschneider,
Vera Niehues, Oliver Razum and Céline Miani

Department of Epidemiology and International Public Health, School of Public Health, Bielefeld University, Bielefeld, Germany

Mothers tended to be responsible for most of the (additional) caregiving and domestic tasks during the COVID-19 pandemic while simultaneously having to pursue their work duties. Increased role conflicts, parenting stress, and exhaustion predict adverse mental health. We aimed to examine how women referred to and made sense of dominant gender norms in their arrangements of pandemic daily life and how these beliefs impacted their maternal self-conception. Qualitative interviews with 17 women were analyzed through the lens of "intensive mothering" ideology and "ideal workers" norms, emphasizing notions of maternal guilt rising from a perceived mismatch between the ideal and actual maternal self-conception. We found that mothers' notions of guilt and their decreases in health link to dominant discourses on motherhood and intersect with "ideal worker" norms. As such, these norms amplify the burden of gendered health inequalities.

KEYWORDS

COVID-19 pandemic, women's health, self-conception, maternal guilt, public mental health, maternal wellbeing, gender norms, mothering

Introduction

The non-pharmaceutical interventions (NPIs) to contain the spread of the COVID-19-pandemic have unprecedentedly impacted the lives of families with (young) children. Closings of schools and childcare facilities, restrictions on leisure activities, and requirements to work from home called for the re-organization of household tasks, work, and childcare. Mothers tended to be responsible for most caregiving and domestic tasks before the pandemic, and their burden increased during the pandemic (1–4). Evidence shows that parenting stress and exhaustion also increased, especially for mothers of

young children (5). Consistent with pre-pandemic data, parenting stress and exhaustion were significant predictors of adverse mental health (6–8).

Adjusting to remote work from one day to the other while in parallel having (young) children to care for at home abruptly aggravated the anyhow “fragile façade of separation that allowed women to be mothers at home and transform into professionals at work” (9). This simultaneity of roles acts as a stressor that has shown to be linked to feelings of guilt when self-evaluating one’s performance as a mother and perceiving a discrepancy toward the societally dominant motherhood ideals (10, 11). Feeling ashamed about not meeting self-imposed and societal expectations of being a “good mother” seems to be a universal trait of motherhood that affects stay-at-home mothers and working mothers equally (12). The societal discourse has constructed dichotomous narratives of “good” and “bad” mothering and is accompanied by idealized criteria and unrealistically high expectations toward “good mothering,” also known as *mommy mystique* (13) or *motherhood myths* (14). It is the unattainability of this standard itself that can lead to maternal feelings of guilt (12, 14) and has been linked to adverse (mental) health outcomes, including depressive symptoms and anxiety disorders (15–17).

In the Global North, the dominant ideology of mothering “that all women are disciplined into and judged against” has first been described as *intensive mothering ideal* by sociologist Sharon Hays (10) and recurred to and evolved by various feminist scholars (17–21). *Intensive mothering* has been conceptualized as a gendered model of expectations directed toward mothers by outlining the socially most appropriate way to raise children. As such, this ideology reproduces and manifests gendered hierarchies, stereotypes, and norms (19). Intensive mothering is linked to beliefs that all relate to how mothering is conceptualized, perceived, and lived, among them *essentialism*, *fulfillment*, *child-centeredness*, *challenge*, *(intellectual) stimulation*, and *the idea that being simultaneously a caring and working mother is incompatible*.

Essentialism assumes that mothers are the most central, critical, and responsible caregivers for the child’s development and wellbeing. This, in reverse, justifies blaming mothers for their children’s adverse behaviors or developments. *Fulfillment* implies that mothers are at all times satisfied and pleased by their children and their role as a parent, and are not experiencing negative emotions or doubts. Intensive mothering expects mothers to foster their children’s cognitive, physical, and social development and organize an environment that is conducive to learning, known as *intellectual stimulation*. The child’s (presumed) needs and wishes are superior to the mother’s, leading to *child-centered* routines and interactions. This approach is pictured as *challenging* in the sense that it is natural and plausible for mothers to feel exhaustion, yet not leading to question the intensive mothering norms. Last, the intensive mothering norms ideologically *separate mothers from*

continuing or taking paid professional work. The underlying belief is that children are so special, pure, and innocent that they deserve to spend their time in the private family sphere in the presence of their mothers (10, 17). These ideals underpin the idea that ‘good mothering’ is separated from professional paid work (12, 20, 21).

The *intensive mothering ideology* interacts with and is reinforced by another influential and dominant set of norms described by scholars from the field of work sociology: the *ideal workers’ ideology*, as a substantial part of *gendered organizations* (22–24). Historically, the ideal workers’ norms have emerged from the (gendered) separation of the domestic vs. work sphere (25) as a modern phenomenon of economic and societal development after World War II (26). Until today—and despite the significantly increased female labor market participation—subliminal assumptions shape employers and workers expectations and beliefs related to workplace and family roles, favoring masculine ideal worker norms (23).

The ideal workers’ norms are constituted of three gendered assumptions: the first assumption builds upon the previously mentioned intensive mothering ideals, especially the idea that children deserve mothers who sacrifice their lives, including their careers, for their children’s goods. In other words: mothers prioritize their children over their work obligations (27). The second idea creates an image of the ideal worker who prioritizes work duties over family responsibilities, acts rationally, is fully committed to work obligations, and is strong in leadership (23). Last, the “ideal worker” equates with male employees as female workers (specifically mothers) are perceived as unable to work full-time, believed to be less committed to work, and considered more emotional than rational (23, 27).

Recent findings suggest that the *ideal worker ideology* is applied to and applied by working mothers in terms of career expectations and unwritten penalties, e.g., when women return part-time to work after their parental leave (28). This understanding of “working motherhood” intertwines with the expectations of simultaneously being involved in paid work and fulfilling all caregiving responsibilities, neither of which may be at the expense of the other (29). Conforming with the normative ideals of complementarily being the “good mother” and the “emancipated female worker” is conflicting for many, even though they may have a feminist or gender-equal self-conception (9).

More recent research suggests that women frame mothering and their “working identity” in heterogeneous ways (e.g., by delegating “intensive mothering” tasks or indicating that working leads to being “better” mothers), yet, constantly referring to ideals of “intensive mothering” (21). As such, (working) mothers repeatedly violate the “ideal mother” ideology or the “ideal worker” norms (28).

At the same time, the ideologies of “ideal worker” and “ideal parents” find their counterparts in welfare states’ policy measures that support a stereotypical male worker model

employed in full-time work over his adult life span on the one hand, and the promotion of a part-time work model for the female primary caretaker on the other hand. The still existing gender pay gap and the gendered distribution of high and low-paid occupations foster parents' negotiations about who is the primary caretaker (e.g., parental leave) and who reduces their own paid work (e.g., part-time work) (28). In Germany and other European countries, norms on masculinity and femininity are highly connected to both working and parenting ideologies and, as such, influence the decision-making processes in the phase of family formation (24): while (expectant) fathers fear disadvantages in their future careers and being perceived as non-masculine or weak, mothers (to-be) fear to be condemned as selfish (30).

During the upswing of the first COVID-19 wave, the closings of schools and childcare facilities abruptly placed families into a context of highly diverging demands (of work, childcare, schooling, and household) that had to be met contemporaneously and concurrently in time and space (5). Women, compared to men, were unequally affected by the additional loads (31) and have shown to be at higher risk of adverse mental health (32) and experiences of overburden (33). While quantitative studies provide evidence that at least some (working) mothers suffer significantly from the pandemic (34), we aim to understand better whether and, if so, how gendered norms and ideologies come into fruition as amplifiers of maternal feelings of guilt or stress. For this purpose, we apply the outlined theories as a lens that guides our further analysis, aiming to fathom how mothers negotiate the "intensive mothering ideology" and "ideal worker" norms in their sense-making. In this regard, we examine the data material through the lens of *intensive mothering* to better understand how the societally dominant mothering approach comes into play in the specific situation of a worldwide pandemic causing substantial changes in families' lives. As the *ideal workers'* ideology dominates work-related norms and identities in the Global North, we are additionally interested in how the women refer to and make sense of these norms in their interviews. Coming from a public health background, we aim to understand better maternal vulnerabilities in terms of emotional disbalance, feelings of guilt or shame, and mental health in relation to their living experiences as mothers and workers.

Materials and methods

The "Family study" is a COVID-19-specific follow-up of the BaBi birth cohort study established in 2013 in Bielefeld, North-Rhine Westphalia, Germany (35). The Babi cohort study initially explored health disparities in almost 1,000 newborns and their mothers from birth to early childhood. In our Family study, we were interested in the experiences and health of mothers of young children during the time of the first COVID-19 wave

in 2020 and the associated NPIs to contain the spread of the virus. We contacted all participants from the BaBi cohort who had previously agreed to be approached again *via* email ($n = 550$) in mid-April 2020 and about 6 weeks later through a reminder to increase participation. The participants were invited to take part in a quantitative online survey ($n = 124$), qualitative email interviews ($n = 17$), or both ($n = 17$). The study has been approved by the Ethics Committee of Bielefeld University (Ref. 2020-059).

Data collection

We refer in this present article to the qualitative data conducted *via* semi-structured, in-depth email interviews (36). Considering the strict physical distancing measures, closure of childcare facilities, and associated time pressure on the participants, we believed that email interviews would increase flexibility and give the participants more autonomy when they do the interviews (37–39).

The interview process included three waves of open questions that were identical for all participants and, from the second wave on, follow-up participant-specific questions to the answers already provided, aiming to initiate a conversation and deepen the responses. Therefore, in each round, all participants received a set of shared questions and, from round two, additional in-depth, individualized queries. Questions in the first email covered adjusting to the pandemic situation in terms of re-organizing daily life (work, childcare, household obligations) and feelings and experienced ambivalences connected to the participants' role as mothers.

The second wave included questions on the family members' health and wellbeing as well as the share of responsibility in seeking pandemic-relevant information, implementing personal protective measures, and child-orientated communication about the pandemic situation. The third wave finalized this process by asking about views on the future.

Data analysis

In previous publications on Family study findings, we explored the data through classic content analysis (40, 41). During this process of getting a sense of the data, it became apparent that narratives of "intensive mothering" ideology and "ideal worker norms" seemed to play a role in the self-conception of the women in our sample. The otherwise rather hidden normative ideas that shaped work and motherhood ideals suddenly seemed to become more prevalent and visible due to the major changes families had to face. Therefore, we re-examined the data, this time through directed content analysis. Directed content analysis allows to validate or conceptually extend existing theories (42). We aimed to identify implicit

or explicit expressions, narratives, or beliefs relating to the “intensive mothering ideology,” “ideal worker norm,” and expressions of maternal guilt in the interview material. As the emergent pandemic situation required massive adjustments from families in terms of work- and care organization, we were interested in if—and how—societal norms appeared in women’s self-conceptions concerning their role as mothers and workers. We coded the interviews according to the elements of the “intensive mothering ideology” (*essentialism and fulfillment, challenging, child-centeredness, and (intellectual) stimulation*) and the “ideal worker norm” (*women’s prioritization of children over work obligations; ideal workers’ prioritization of work over family duties and acting rationally; men’s equation with ideal worker norms*). We refrained from using the “challenge” element as an independent coding and analysis unit since the notion of challenge is running through all others aspects of the intensive mothering. The interview passages sharing the same code were carefully re-read, compared, and juxtaposed, aiming to identify shared meanings and similar (just as disparate) ways of how motherhood and work ideals channeled and became present in the women’s self-conception and approaches to work and childcare. From this circular data analysis and coding process, we derived the themes presented in the results section.

Drawing on theories for directed analysis presents a caveat, namely a tendency to identify evidence supporting the theory rather than deconstructing it (42). Being mindful of this risk, we tried to be reflective, allowing alternative or deconstructive interpretations of the data material. This has led us, for example, to identify a representation of “ideal worker” norms in the unexpected maternal self-conception of the homemaker.

To synthesize our theory-guided data analysis and place it in the context of the pandemic, we further examined our findings, looking for variations in expressions of maternal self-conception (enhancement, continuation, or deterioration) and its potential relations to maternal guilt (or the absence thereof). We reflected on whether the abrupt changes in daily life have impacted maternal self-conception and, if so, how those shifts related to “intensive mothering” ideology or “ideal worker’s norms”.

Results

Sample description

Seventeen women participated in the email interviews. Our sample is characterized by highly educated, white middle-class, cis-gender women, all living with their male partners. Most women ($n = 9$) had two children under 18 years living in their household, whereas five women had three or more children, and three women had one child. Most children visited childcare facilities before the onset of the pandemic. Only one child was in so-called “emergency childcare” during the early phase of the pandemic (“emergency care” was available only to those

children whose parents both worked in “essential” domains, e.g., health care workers, food, energy, and water supply, teachers). Four other families used emergency childcare when the access criteria were extended (Tables 1, 2). Four out of 17 women were currently out of work (homemaker, parental leave), and the remaining women worked part-time. All male partners were in work, with the majority ($n = 12$) working full-time. Overall, most interviewees drew lines of comparison between the time before the pandemic and their present situation. All women experienced significant changes in their daily lives due to the NPIs, with two trends emerging: one group expressed a positively perceived deceleration of life, while another group felt extremely stressed due to the absence of facility-based childcare and the continuation of their work duties. As to be expected, the latter group experienced a deterioration of wellbeing and mental health. In contrast, the women in the first group felt relaxed and were grateful for the extra quality time with their families.

Intensive mothering

We find miscellaneous references to the intensive mothering beliefs of essentialism, fulfillment, stimulation, child-centeredness, and the intersections of mothering and working. Both the themes “essentialist maternal identities” ($n = 8$) and “continuous responsiveness” ($n = 4$) were identified for essentialism. Feeling like a “better mother” ($n = 6$) and “fulfillment outside of mothering” ($n = 1$) refer to the narrative of fulfillment, whereas “pedagogical parenting” ($n = 5$) reflects the idea of stimulating the children’s cognitive development. Expressions of strong child-centeredness were labeled as “completely aligned with children’s needs” ($n = 2$), and the juxtapositions of mothering and working (in-home office) was visible in five interviews. Three of these felt that they could do no justice to either of them, whereas two interviewees did not experience contradictions between their identities as mothers and workers.

Essentialism I: Essentialist maternal identities

Eight interviewees see themselves as their children’s primary and most essential caregiver. This manifests in statements such as from Jane, who shares the care work with her partner. Yet she remains the responsible parent when it comes to nursing and the emotional needs of their children and “thereby take[s] over significantly more” (Jane, I: 4). Just as for Jane, Vanessa perceives herself as the parent that takes up most of the emotional and relational aspects of parenting:

“Even though my partner is currently at home more often than I am and is, therefore, more often available for the children (...), I more often take over the ‘emotional’

TABLE 1 Participants characteristics.

	<i>n</i>	valid %	mean	SD	missing (<i>n</i>)
Age	17		37.76	4.21	
Marital status					
Single	0	0.00			
Partnered/married	17	100.00			
Children (> 18) in own household					
1	3	17.65			
2	9	52.94			
3	3	17.64			
4	1	5.88			
5	1	5.88			
Facility-based childcare for children (>7) (cumulated, pre-pandemic)					
None	4	12.50			7
Childcare center	23	71.88			
Nursery	2	6.25			
Other facility	2	6.25			
Child in “emergency care” (during early phase of pandemic)*					
Yes	1	5.88			
No	16	94.12			
Hours spend on housework (pre-pandemic)			12.53	8.17	
Partners’ hours spend on housework (pre-pandemic)			5.35	3.50	
Hours spend on housework (during pandemic/ past 2 weeks)			14.06	8.61	
Partners’ hours spend on housework (during pandemic/ past 2 weeks)			7.56	4.60	1
Care hours/ week for family members (pre-pandemic)			45.65	27.56	
Partners’ care hours/ week for family members (pre-pandemic)			29.59	29.26	
Care hours/ week for family members (during pandemic/ past 2 weeks)			68.20	35.45	2
Partners’ care hours/ week for family members (during pandemic/ past 2 weeks)			48.53	37.49	2
Time spend on homeschooling (pandemic)			2.75	1.50	13
Partners’ time spend on homeschooling (pandemic)			0.33	0.58	14
Employment status					
In work	13	76.47			
Out of work	4	23.53			
Mode of employment					
Full-time					
Part-time	13	76.47			
Parental leave	2	11.76			
Not employed (e.g., home-maker, student)	2	11.76			
Marginally employed/ state benefit	0	0.00			
Employment status partner					
In work	17	100.00			
Out of work	0	0.00			
Mode of employment partner					
Full-time	12	70.59			
Part-time	4	23.53			
Not employed (e.g., home-maker, student)	0	0.00			
Marginally employed/ state benefit	1	5.88			
Essential worker					
Yes	8	53.33			2

(Continued)

TABLE 1 (Continued)

	<i>n</i>	valid %	mean	SD	missing (<i>n</i>)
No	7	46.67			
Essential worker partner					
Yes	6	35.29			
No	11	64.71			
List of professions of interviewees			Management assistant, assistant, civil servant, appraiser, controller, data analyst, information technology, teacher, psychologist, psychotherapist, language therapist, in education, student, administration		
Changes in employment situation due to pandemic					
Home-office	5	38.46			
Short-work, mandatory leave	3	23.08			
No changes	3	38.46			4

Source: Quantitative data from Family study.

*Quantitative data collection took place 2 weeks before the email interviews. In the meantime, more sectors were declared “essential,” explaining the differences in data regarding the number of children qualifying for “emergency childcare”.

tasks (e.g., conflict resolution, motivation for schoolwork) because the children (and my guilty conscience as a mother) ‘demand’ this (...)” (Vanessa, I: 7).

Vanessa is aware that their share of (parenting) tasks is unevenly distributed. Yet, she feels ambivalent since, as opposed to her mind, her “feeling” says that the division is justified or that [she] should rather take on even more tasks.” (Vanessa, I: 7). Asked about the drivers of this ambivalence, she critically evaluates her essentialist self-conception:

“(...) my ambivalence has primarily something to do with the demands I put on myself as well as dysfunctional assumptions (‘I have to be a perfect mother,’ ‘I earn less money than my partner, so I have to do more in household chores and raising children,’ ‘I can’t expect too much from my partner’)” (Vanessa, I: 7).

While for Vanessa and Jane, their greater involvement in absorbing their children’s emotional needs is perceived as unfair, they admit that they feel a great sense of responsibility that leads to more involvement compared to their partners. Here, essentialism as part of the *intensive mothering* ideology comes into play in determining Vanessa’s and Jane’s mothering practices while at least partly contradicting their attitude.

In contrast, Karen presents an essentialist idea of motherhood in unity with her maternal self-conception. She strongly values how much her younger children enjoy staying at home because, in her idea, this constantly provides them the feelings of nesting, familiarity, and safety and advances her children’s developmental growth (Karen, I: 6).

Hanna, who deliberately chose to be a stay-at-home mother to her five children, shares the love and fulfillment that Karen has articulated. She clearly expresses her satisfaction with the

fact that her and her partners’ pre-pandemic lifestyle and role-sharing seamlessly fit the pandemic situation as “what [she holds] in values and [has] practiced before is now coming to fruition”:

“We don’t have to make an excessive adjustment: being a mother at home with the children, living with them and providing a reasonable daily structure, values, encouragement and relationship skills” (Hanna, I:1).

She derives her approach to mothering as a higher divine order that corresponds to her Christian religious beliefs:

“We are of the opinion and have also made the experience that life itself and especially life in partnership and family ‘works’ most healthily, satisfactorily, happily and effectively when it is lived within the framework of a certain ‘order’ (Hanna, I: 1).

Hanna’s values firmly attach to a religious and essentialist interpretation of ‘intensive mothering’ that she understands as being present and sharing life with her children, guiding them through childhood, and imparting her beliefs and norms into their lives.

Essentialism II: Continuous responsiveness

As the ideal of being the primary carer is an integral part of a the “intensive motherhood ideology,” the concept of ongoing maternal responsiveness corresponds to this as an interactional counterpart. Due to the juxtaposition of working, self-care, and childcaring during the lockdown, most mothers in our sample experience the expectation of continuous responsiveness as a burden. For Kate, who has now been

TABLE 2 List of interviewees by name, information derived from email-interviews.

Interview ^a		Occupation	Children	Childcare situation	General impression related to overall wellbeing, mental and physical health (derived from overall email interviews)
1	Hanna	homemaker, partner: 80% full-time job, 20% self-employed	5, pregnant	At home	More relaxed, more satisfied, more cheerful, relieved, occasionally more stressed
2	Mary	part-time job as essential worker, partner: full-time job	1	Emergency childcare	Less time pressure, more balanced
3	Janine ^b	homemaker, partner: full-time job	4	At home	Some uncertainty, somewhat stressed by taking on childcare responsibilities
4	Jane	maternity leave (for expectant mothers), partner: self-employed, part-time, mainly in home-office	2, pregnant	At home	Strongly physically, nervously, and emotionally stressed, overwhelmed
5	Eve	soon starting job, partner: marginally employed/ state benefit	2	At home	More emotionally stable, more patient, emotionally in a positive mood, less daily stress
6	Karen	homemaker, partner: full-time job, currently in home office	3, pregnant	At home	More time for self-care, gratitude, calmer, more balanced
7	Vanessa	self-employed, partner: full-time, currently in home-office	2	At home	Sometimes somewhat unbalanced, experiences herself as insufficient
8	Sofie	part-time job in home-office, partner: shift work, part-time studies	2	At home	Deceleration, positive perception, and appreciation of one's situation
9	Tina	part-time essential worker, partner: self-employed	2	Emergency childcare (partially)	Less stress, deceleration, feeling happy
10	Lea	part-time essential worker, partner: full-time in home-office	2	Emergency childcare (partially)	Some family-to work-conflicts, more relaxed due to fewer appointments, exhausted but still appreciative view of time spent together with children, stronger migraines
11	Beccy ^b	part-time job in home-office, partner: full-time job (short-time working) in home-office	2	At home	Positive perception and appreciation of one's situation, home-office more stressful but fewer daily stressors
12	Dana	part-time job, partner: full-time job	1, pregnant	Emergency childcare	Hopelessness due to financial situation, worried about child's needs, high stress, psychosomatic symptoms
13	Kate	part-time job in home-office, partner: full-time job in home-office	2	At home	Highly stressed due to work and care duties, frustration, stronger migraines
14	Fiona ^b	part-time job, partially from home-office, partner: full-time job in home-office	2	Emergency childcare (partially)	Unbalanced due to daily monotony
15	Helen	home-office, partner: full-time in home-office	2	At home	Predominantly happy, sometimes irritable, grateful for the privileges of the family
16	Julie	part-time job in home-office, partner: full-time job in home-office	3	At home	High stress level, irritability, psychosomatic symptoms
17	Bianca	part-time job in home-office, partner: full-time job in home-office	1	At home	Uncertainty, more worries

^a Names do not correspond to the real names of the interviewees.

^b Not quoted in this article (as responses were too short, e.g., in a quantitative survey response style).

working and caring for the kids at home for around 9 weeks, chronic migraine attacks have increased to twice a week; she feels exhausted and has developed gastrointestinal problems. She states the relevance of self-care for her health and wellbeing. She connects her current lack of self-care to the

assumption that “mothers must always be responsive” (Kate, I: 13). Even if she rests for just a moment, her children cannot comprehend the fact that she is unavailable as they have never learned that she as a mother might be nearby but not approachable:

“And even when I take time, I often get (...) interrupted because ‘mothers always have to be approachable’. Even though we have explained to our 5-year-old that mom wants to be undisturbed from time to time, he can’t understand why he shouldn’t address me when I am in the house after all.” (Kate, I:13).

Where Kate experiences a deterioration of her physical health, Hanna notices slight decreases in her wellbeing by the fact that she is permanently present to and requested by her children. Just as Kate, she longs for a break from the continuous expectation of maternal responsiveness that reflects her reality during the pandemic. Jane, who is currently pregnant, perceives the situation as “extremely strenuous” and straining the relationship with her children. She feels that she can neither do justice to her children, as she gets quickly irritated and then reacts inappropriately or in an unfair manner, nor to her unborn child, as she does not find time to brace herself for birth and engage with her baby. She would feel relieved having “more me-time not just being a mother.” Asked about whether she feels more balanced than in the past, she replies that “overload, anger, sadness, and a guilty conscience have clearly increased,” making her feel ashamed and greatly dissatisfied as she currently experiences herself as “a mother, which [she] actually do[es] not want to be at all.” (Jane, I:4).

Julie feels challenged by the intersection of work and care duties. She thinks she would be a “better mother with more freedom to take care of the children” with fewer time constraints. Still, she also indicates that she “[misses] the time without the children, whether concentrated at work or actually alone at sports (or just alone shopping, the main thing is alone!).” (Julie, I:16).

We find that essentialism as a crucial element of the intensive mothering ideology is present in our data in how mothers perceive themselves as the most critical and responsible parent for the positive development of their children and in the actions they took to fulfill this ideal.

All women feel challenged by the (social) expectation of constant maternal attention and responsiveness they need to direct toward their children. Kate reflects how societal expectations are present in her own family dynamics while (apparently) feeling the dilemma of fulfilling these expectations at the expense of her own health. Before the pandemic started, she seemed to have established an equitable share of time for “mothering” and time for herself that is now off balance. Still trying to meet the ideal of being present and available impacts her wellbeing negatively and makes her question her mothering qualities. Jane and Julie, in contrast, make more explicit representations of feeling guilty about their current performance as a mother in depicting their actual self as non-ideal. Interestingly—and in contradiction to the ideal mothering norms of prioritizing the children’s needs over the mothers’ needs—Kate, Jane, Julie, and Hanna clarify (either explicitly or

implicitly) that first of all, they have needs that do not equal to them being mothers (e.g., having alone time) and that meeting those needs contribute to their wellbeing and emotional balance. It seems that they perceive a discrepancy between their “ideal” and the “actual” mothering self because of a lack of time in *not performing* their mother role.

Fulfillment I: Feeling like a “better mother”

An approximation to the mothering ideal of fulfillment in their parental role was found in other interviewees, for example, with Tina. As all leisure activities have been canceled, Tina feels relieved due to the absence of afternoon appointments and fills this gap with fun activities like biking, hiking, or building a tipi, making her feel like a “better mother”:

“I can perform the role better. I feel like I can do more justice to being a mom. I didn’t expect to enjoy all this free time with the kids so much.” (Tina, I: 9).

Similar to Tina, Hanna and Eve see a connection between their emotional wellbeing and the quality of interactions with their children. Eve states that she has become “more patient and therefore more emotionally stable” because spending time and playing with her children does her good and makes her feel “emotionally re-charged” (Eve, I: 5). Hanna reflects that her having more leisure time leads her to view her “children better in their peculiarities and developments” (Hanna, I: 1). Just as Hanna, Karen and Lea feel profound gratitude about the closeness they currently sense with their children. Karen is grateful for the fact that she can spend “so much time with [her] children and see exactly how they develop” (Karen, I: 6). Besides her essentialist view on her providing the best conditions for her children to develop and grow, she is also completely fulfilled with and merged into her role as a mother:

“I love being a mom, and I also love being a mom around the clock all the time, like I am now in this exceptional situation” (Karen, I: 6).

Lea reflects that she can respond better now to some needs: whenever she feels challenged by her children, she reminds herself “that this time is also finite and that [she] can see it as a gift” (Lea, I:10).

Fulfillment II: Fulfillment outside of mothering

Dana and her child were in mother-child care when the NPIs were implemented; subsequently, she spent a few weeks at home. Therefore, she had a long break off work, which often made her “feel that [she] was doing little that was meaningful” as she didn’t enjoy spending most of her time exclusively with her son and “had the impression that [she] couldn’t meet his

needs" (Dana, I: 12). Now, that she continues to work and her son attends the "emergency" childcare, she feels emotionally more balanced because of the "change in daily structure" and the "task" she now has (Dana, I: 12). However, she still struggles with the sentiment of not meeting her sons' needs adequately, and, along with this, is very concerned about how she will manage two children in the future. Having her child in childcare again seems to be a relief to her as she believes that he is in good hands and receives stimuli that positively foster his development (Dana, I: 12). In her interview, Dana refers to a lot of situations where she enjoyed time with her son and family. Still, she does not relate to the ideal of being "fulfilled" through mothering, nor is she essentializing it. Instead, she locates her sense-making into her working identity and expresses how her work obligations positively influence her wellbeing.

Intellectual stimulation: Pedagogical parenting

Vanessa worries about whether she can do justice to promoting her children's needs so they do not miss out (Vanessa, I: 7). Hanna expresses her feeling of being responsible for the children's stimulation by saying that now, her children have fewer out-of-home activities, she must increasingly "provide sufficient activity opportunities (...)" (Hanna, I: 1). Sofie, whose older child is in distance learning, but does not receive material from the school, feels liable for preparing teaching material and additionally enhancing her younger daughter's cognitive progress by providing "interesting exercises, puzzles or painting tasks so that she does not feel neglected" (Sofie, I: 8). Kate feels extremely challenged by needing to perform as a teacher to her child as it opens a role conflict between her being a mother and a 'teacher'. Yet, she considers it her mission to motivate her child, although she lacks "the pedagogical and didactic skills to always act correctly according to the situation" (Kate, I: 13).

Intellectual stimulation in the sense of actively organizing an environment that fosters the child's development presents another element of 'intensive mothering ideology'. Kate, Sofie, Vanessa, and Hanna share the attitude of being responsible for their children's development by providing the required tools and learning material. While these women at least subliminally present the efforts as an additional task and somewhat a burden, Helen is enthusiastic about doing more educational work, especially "rules" and "rituals" (Helen, I: 15), for which before the pandemic, she only found time marginally or during weekends.

The analysis of the data material shows that these mothers refer to the "intensive mothering" ideal of stimulation in their educational efforts. The pandemic has re-turned this responsibility into the mothers' sphere of action as school, kindergartens, and afternoon activities have been canceled. In filling this gap, only Helen seems to rise and come closer to her "ideal" of mothering.

Child-centeredness: Completely aligned with the children's need

The motherhood ideal of child-centeredness reflects itself into planning routines, activities, and daily tasks around the (presumed) needs of the child, while the parent's needs fade to the background. Eve reveals in her interview a strongly child-centered approach to parenting, whereby she consistently speaks of herself and her husband ('we'). She describes how the closure of childcare facilities has led to the fact that they can fully accommodate their children's wishes and needs now:

"We were able to respond directly to our little daughter's wish—to become diaper-free. There was no time pressure at all. It did her an incredible amount of good. Also, it was last week when she was ready to give up the pacifier. We have time to be there for her, to accompany her." (Eve, I: 5).

Eve's use of terminology refers to her parenting approach of planning around the needs and wishes of her children. This child-centeredness is evident in her description of the pandemic-related changes as well:

"Everyday life was completely decelerated. No kids' gymnastics for the big one, no kids' gymnastics for the little one, no music classes, and no more appointments. In general, you simply have time for your children. Nothing is more important" (Eve, I: 5).

Although she says that there now is nothing more important than the time they spend with their children, her descriptions of the pre-pandemic daily life were just as child-centered since she mentioned activities exclusively for her children. The organization of everyday life around children's needs and desires continues in Eve's presentation of their day structure: all household duties, including shopping, cleaning, and cooking, happen during the children's sleeping time, whereas during the daytime, she and her partner fully concentrate on their children's wishes. A comparable child-centered parenting approach was found in Karen, whose children freely decide which parent takes up care duties for them unless her partner is in a video call and therefore, she is the only one available (Karen, I: 6).

"Our two youngest (4 and 2 years old) are still diapered and want their dad to take over when he is home. Our children decide for themselves who they need something from (...)" (Karen, I: 6).

Juxtaposition of mothering and working I: Not doing justice to both mothering and working

An inherent element of the 'intensive mothering ideology' is presented in the idea that children deserve the presence of their mothers throughout the day, reflecting the traditional notion of women being responsible for the home and men being the

breadwinners. As such, this ideal can evoke feelings of guilt or insufficiency for those alternating between the working and the family sphere. Of our participants, six out of 17 women worked at least partly in home office due to the pandemic and had not done so before. Vanessa states that the current situation leads to feeling overwhelmed and not enough, as she more strongly than ever thinks that she is not doing justice to her job- and mothering-related tasks (Vanessa, I: 7). The feeling of overload is similarly experienced by Julie, who expressed high stress as she is “torn between raising children and home office and still can’t really do justice to either side” (Julie, I: 16). Bianca deals with exhaustion and guilt as she needs to prioritize her work over her son:

“This is strenuous so that I am often very exhausted after work (...). During working hours, I often have a guilty conscience, because I would like to take care of my son more” (Bianca, I: 17).

Because of having to perform simultaneously as mothers and workers, Vanessa, Bianca, and Julie face a role conflict in deciding which of the competing demands to prioritize. Experiencing this stalemate makes these women feel doubtful, failing, and guilty.

Juxtaposition of mothering and working II: Balancing identities

A different situation is presented by Helen and Sofie, who emphasize how privileged and thankful they are for having a house, garden, and flexible working options. The different expectations toward their “mothering” and their “working” identity are experienced as less conflicting and easier to reconcile. Due to her management position, Sofie can bring her children to the office whenever she needs to be there and work from home the rest of the time. This flexibility allows her to split up her work into reasonable time slots and, in parallel, spend time with her children (Sofie, I: 8). Helen and her partner also work flexibly from home and enjoy having additional time as a family. Both women neither articulate feelings of guilt or self-doubt related to their mothering, nor do they feel overly stressed. The “intensive mothering” norms that propagate an incompatibility between being a “good” mother and participating in the labor market do not seem to affect their maternal self-conception.

References to the “ideal worker” norms

As alluded to in the previous paragraphs, we will now turn to how some interviewees implicitly referred to the “ideal worker ideology.” In five interviews, we identified three different types of references to this ideology: first, constructing the male partner

as “ideal worker” ($n = 3$), second, (failing to) constructing the “ideal worker self” ($n = 1$), and third, framing the homemaker-self within the “ideal worker” ideology ($n = 1$).

The male partner as “ideal worker”

At the time of the interview, Mary’s work had been declared as “essential,” meaning that she now can use the so-called “emergency” childcare services for the hours she is at work. The weeks before, Mary’s child was cared for at home due to the general closings of childcare facilities. While Mary and her husband for 2 weeks alternated between a morning and an afternoon shift of working and taking care of the child, Mary then took 3 weeks off, explaining that it was too challenging to work and care simultaneously:

“At the beginning, organizing childcare was the biggest challenge. It quickly became obvious to us that childcare and normal work could not be reconciled, so I took leave of absence” (Mary, I: 2).

During those 3 weeks, Mary was entirely responsible for her child, and now, that her child is back in kindergarten, she is back to work. Interestingly—and matching the male “workers ideal,” it seems unquestionable that Mary (as the mother and the one in part-time occupation) is the one taking days off from her work and returning to work now that childcare is secured again.

Such maintenance of the male ideal worker is also apparent in Lea’s interview. Lea fully has her husband’s back so he can pursue his work during regular hours. In contrast, she shifts her working hours into the early mornings, late evenings, the nap times of her younger child, and the weekends. She states that occasionally it puts pressure on her to only have disrupted time slots to work, yet she does not see a realistic possibility to change the current arrangement:

“In particular, I find the home office sometimes burdensome, because my husband works his 100% job at his desired time (...). I work reduced (...) hours (60%) and make sure that I always find time slots for it or work on the weekend. Sometimes I find that unfair (...). I would like my husband to also work on one day of the weekend and, for example, on two evenings, so that I could also work during (...) the morning. But because of his work or the (...) video conferences with colleagues, this is not so easy to implement” (Lea, I: 10).

Due to her part-time employment compared to her husband’s full-time job, Lea justifies and creates the conditions for his continuation of regular working hours. By doing so, she maintains her husband’s ideal worker status at the expense of her own work-related needs. Due to her position as a teacher, Lea will soon be allowed to use the childcare facilities. Just like

Mary, Lea justifies her children returning to kindergarten with the increase of time that she will have to spend in presence at school:

“In May [2020], the situation will probably change a bit, as I will then have more attendance time at school again. Our children will then (have to) visit the emergency care of the daycare center for these times since we cannot organize the care otherwise.” (Lea, I: 10).

Both women justify the return of their children to childcare facilities exclusively by the changes in their own work conditions. For their partners, nothing substantially (except for now working remotely) seems to have changed: their working hours are still during the day and predominantly uninterrupted. This shows that the worker ideology not only leads to the prementioned continuation of their husbands as “ideal workers” but also how they recur to this ideology by axiomatically taking the additional care hours into their sphere of responsibility by taking days off (Mary) and shifting work to the children’s sleeping times (Lea).

Kate reports a similarly disproportionate distribution of care work at her expense. While her husband works in “home office from early in the morning until the evening, [she is] from 8:30 to 14:30 (...) in the home office, while in parallel being responsible for [her] daughter’s schoolwork, entertain [her] son and [conjuring] up a lunch” (Kate, I: 13). She feels hugely stressed by the multiple and competing demands she currently experiences:

“The multi-load due to home office, homeschooling, lack of daycare, the extra demands on the household (lunch every day, more cleaning,...), the extra demands on shopping (When does it make sense in terms of time? Who looks after the children during this time?...) puts an extreme strain on me. I feel like I can’t get everything organized anymore” (Kate, I: 13).

She narrates that even before the pandemic, her husband’s job was busy, while she “only” worked part-time and “in this respect” not “yet found it unfair to be more burdened by childcare and household chores.” Since the pandemic evolved, she alone had to “compensate for the closed daycare and schools” and all “new and additional tasks” landed on her back, which she considers unfair, burdensome, and frustrating. In accordance with Mary’s and Lea’s partners’ situation, Kate’s partner continues to perform as the male ‘ideal worker’, neither having to deal with care responsibilities during his working hours nor having to piece time slots together for work. Although Kate perceives their current daily arrangement as strenuously challenging and unjust, she does not scrutinize the ‘male’ workers ideology as such. Instead, she adheres to it and therefore contributes to its maintenance. She relocates the problem of conflicting roles and responsibilities that she must comply with

(and fails to fulfill according to her interpretation) back to her area of responsibility:

“At the moment, however, I’m asking myself whether I can keep this up for much longer and whether this balancing act is even worth it. Professionally and socially, you don’t get any recognition for taking on the extra burden. Occupational development opportunities after becoming a mother are non-existent! After all, you are only available part-time and therefore only to a limited extent. No question - I still liked my job. But now the burden is simply too great. Why should I continue to take it on?” (Kate, I: 13).

This statement not only reveals her professional self-conception as not having the same “market value” after becoming a mother but also how she (and society) still perpetuate the gender system of domesticity, including its three assumptions (maternal sacrifice for the children, employers’ legitimate expectation of “ideal worker” prioritization of work over family duties, and the equation of men as “ideal workers”).

Construction (or failure) of the “ideal worker self”

In contrast to the previously displayed interviewees, Julie explains she and her partner (more or less) equally share the additional care effort. As both work remotely during the days, they established fixed times where one of them can work without interruption (in theory, yet, reality shows differently), and the other tries to work while having the main responsibility for the household and being present for the three young aged children. The division of care responsibility between Julie and her partner during the pandemic did not arise naturally. Instead, Julie claims that:

“In the second or third week of the lockdown, there was a major discussion because my mountain of tasks had steadily increased, while my husband continued to follow his usual activities, but from my point of view was better able to ignore the extra workload than I was. Since then, our split has been mostly fair – it’s a very difficult situation for all of us, but I feel we are currently a good team” (Julie, I: 16).

While Julie initially took up the pandemic childcare burden, she does not refer to the male “ideal worker” construct to justify this disparity. Instead, she traces it back to her husband’s character traits (“ability to ignore”). Yet, the “worker ideal” is also present in her interview, but in relation to herself and her employer.

Julie feels highly stressed by the lack of flexibility exhibited by her employer. Although she and her colleagues are well-equipped for home-office, the company allowed remote work during the first weeks of childcare closings only “against

crediting of days off” (Julie, I: 16). In exchange for working from home, she agreed upon fixed times of availability for calls with her team leader. These times are congruent with the slots when her husband takes the primary responsibility for their children. However, Julie claims that these agreements are “torpedoed (...) by [her] employer, by the fact that no consideration is given to [her] working hours and [she] then (...) answer[s] calls while building Lego (...)” (Julie, I: 16).

The times she agreed upon with her team leader “are not taken into account when scheduling appointments,” so they conflict again with her family responsibilities. Also, the company forced employees to take 2 weeks off in April. Julie perceived this solicitation as even more stressful because of the vacation covers she eventually had to take over as “systems had to continue to be maintained, and projects were not stopped” (Julie, I: 16). For her, the extra workload coming from colleagues being on leave was simply not manageable, which is why she took her vacation as

“single days to reduce the weekly working time and thus to be able to finish work a little earlier every day - since this hardly worked and thus I only turned days off into (unofficial) overtime, I am currently no longer willing to use this approach.” (Julie, I: 16).

Julie’s detailed account of the company shows how the “ideal worker” ideology is placed upon the employees, even if they find themselves in a family-to-job compatibility crisis. The company’s lack of concession is based upon the assumption that “ideal workers” prioritize their work obligations above the rest of their life. By claiming that Julie is no longer willing to assimilate herself to the company’s approach, she breaks with the worker-roles expectations laid upon her. She therefore constructs her company as maintaining the “ideal worker norms,” expecting their employees to adhere to this norm regardless of their personal situation. In this light, Julie constructs herself as not being able nor willing to meet the “ideal worker norm” and (as quoted before) at the same time perceives herself as ‘not being a good enough’ mother.

Framing the homemaker-self within the “ideal worker” norms

Hanna enjoys “being at home, freely dividing [her] time, and using [her] skills and strengths to benefit [her] family,” whereas her husband “enjoys his work and is happy in the provider role” (Hanna, I: 1). Accordingly, she claims that they are both satisfied “with this division/role sharing” which is “based on [their] beliefs about how [they] want to live [their] lives (...)” She pictures the gendered division of roles between them as the most functional, satisfying, and healthy system for their partnership and family. While her husband “takes the overall responsibility” and presides over the family quasi-like the “chairman of the board who is responsible and accountable,” she

perceives her role as the co-leader and manager of the operative businesses of all family-related tasks and responsibilities (Hanna, I: 1). The families’ role representation, accountabilities, and task division described by Hanna seamlessly link to terminologies and phrasing of corporate governance and management: she organizes, manages, and holds all the strands of the family together, while he represents the family to the outside world. The business metaphor continues in her self-representation as a mother managing the daily lives of her children during the pandemic:

“Due to the fact that the children have fewer playdates (...), I have to increasingly provide for activities (...). I spend a higher proportion of time in organizing new games, researching craft ideas, coordinating tasks and reward system.” (Hanna, I: 1).

Hanna feels challenged by the fact that the noise level is continuously high and says that encountering these situations requires “a more targeted use of soft skills from her” (Hanna, I: 1). She also experiences the effect of daily routine, and notices that her self-discipline has declined due to fewer external pressures. This manifests in the organization of upcoming events or appointments “like hosting guests for a birthday, doctor’s appointments, play dates” but also in daily chores (e.g., motivate children to do their chores and schoolwork). Skipping daily structures and being more relaxed about the household organization she interprets as a sign of her “laziness” and a “source of danger,” and therefore redirects her focus back to herself, the one responsible for ensuring a functioning family life (Hanna, I: 1).

Hanna’s and her partner’s roles and task divisions conform with traditional gender norms and the gender system of domesticity. Interestingly, Hanna constructs and depicts her stay-at-home mothering and homemaker obligations in a narrative congruent with the ‘ideal worker’ ideology adapted to her care-work: she is fully devoted to her job, has her areas of duty clearly in mind, leads and manages while making the best use of her skills, aiming to ensure the functioning of her family, even though this costs her strength. Hanna is not complaining about her children or her duties, even though she experiences the continuous “standby mode,” and lack of pauses during the pandemic lockdown as challenging. She reacts by bringing forward the need to more consciously use her abilities (“skill sets”) to manage strains. Throughout the interview, Hanna barely mentions conflicts between her partner’s occupational work duties and her duties as a stay-at-home mother. Instead, the challenges she perceives exclusively originate from an extension of her regular job as the primary care person for her children. While Hanna’s and her partner’s traditionally gendered role division corresponds with the ideal workers ideologies basic assumptions (female caretaker, male ‘ideal worker’), she is not explicitly perpetuating this image in

her interview, but rather holistically lives it without experiencing the burden of being torn between the two ideals of being a “good mother” and “good worker.” Nonetheless, she fills the “idealized mother norms” through an ‘ideal-workers ideology’ within her self-conceptions as a stay-at-home mother and homemaker.

Maternal self-conception and expression of maternal guilt: Continuity, improvement, deterioration

Our findings indicate that narratives of *intensive mothering* and *ideal worker* ideology are common among mothers in our sample when sharing their experiences in times of the early COVID-19 pandemic, albeit in varying nuances. Many of the participants refer to these societally dominant mothering narratives implicitly but also explicitly in some cases. Aiming to understand better how the pandemic-induced changes in daily life affect mothers’ self-conception, expressions of maternal guilt and wellbeing, we identify three groups of women. Across the above themes identified, we also focused on statements that reveal how mothers construct their “actual selves” against an “ideal self,” including their notions of maternal guilt.

The first group, composed of three working mothers (Helen, Tina, Sophie), shows an *enhancement in maternal-self-conception* as these mothers seem to achieve their internalized conception of ideal mothering. They blossom and enjoy the everyday life changes that accompanied the early phase of the pandemic. The deceleration in daily routines positively affects their mothering as they spend more time with their children, feel closer, and have grown together as a family. These positive changes affect their maternal conception in a way that makes them feel better about fulfilling their mothering role. Their interviews are phrased in an enthusiastic and balanced tone, even when mentioning challenging situations. Overall, they articulate a high sense of wellbeing and satisfaction in the absence of any statements that can be traced back to feelings of maternal guilt.

The second group of women (Hannah, Karen, Eve) is characterized by a *continuation of maternal self-perception* showing high convergence between their pre-pandemic and pandemic times notions of motherhood. Remarkably, this group is composed of the homemakers and the unemployed women. Despite strenuous circumstances, they have overall adapted smoothly to the situation. Their self-conception as mothers has not been queried as they experience (more or less) a continuation of their pre-pandemic routines. This stability can possibly be traced back to a high level of self-efficacy that was particularly present in these women’s deliberately chosen parenting approach and their value system. A continuation of maternal self-perception could also be seen in a mother (Dana) whose biggest challenge was the lack of work-related

tasks, which coincided with the closure of the kindergarten. In her interview, she does not articulate a substantial discrepancy between her ‘ideal’ and her ‘actual’ mothering beliefs. Instead, she positively values her identity as a worker, where she seems to experience (more) self-efficacy.

The third, and largest group of mothers Dana, Julie, Bianca, Kate, Vanessa, Jane, who are all working, experiences a clear deterioration in maternal self-conception. This is specifically the case for those who experience growing discrepancies between their actual self and mothering ideals, stating that they feel (more) challenged, overloaded, emotionally strained, exhausted, or physically stretched. Their expressions reflect not only poor wellbeing and mental health but also insecurities, feelings of failure, or maternal guilt concerning their performance as mothers. Some show high awareness about how (destructive) societal norms influence their mothering ideals (and, as such, their perception of failure in the light of these ideals). For these women, their currently low maternal self-esteem evolved in the context of the pandemic-induced changes, especially as most now work in home offices with no childcare. It is striking to see how outer stressors (e.g., closing of care facilities, home office) elicit role conflicts and strains and accumulate in feelings of maternal guilt.

Using the theoretical lens of *ideal worker* norms, we identify three types through which the *ideal worker* construction is evident in the self-and partner conception and at least to some extent channeled through *intensive mothering* norms. Whereas, the first type maintains the *male* ideal worker by not posing any additional care burden on the partners working time (Mary, Lea), the second type is characterized by the female failure to meet the ideal worker norms due to the employers’ inflexibility and lack of consideration for the family-specific peculiarities during the COVID-19 pandemic (Julie). Last, one woman’s construction of her homemaker self can be interpreted as an inherent adaption of the ideal worker ideology within the domestic ‘female’ sphere while at the same time protecting the ideal worker status of her husband (Hannah).

Discussion

In our analysis, we see that motherhood myths persist and are experienced as burdensome when working-, childcare, and family-related responsibilities were all transferred into the private space due to pandemic measures. We were able to make visible that mothers’ notions of guilt can be linked to dominant gendered discourses on motherhood, specifically the *intensive mothering* norms. Also, we have shown how the *ideal workers’* norm can intersect with and build upon the *intensive mothering* ideology and conceivably amplify the burden of experienced gender inequality for women in our sample. For one group, the internalization of these norms imposes a harmful self-evaluation and a deterioration of maternal self-conception. In

contrast, another group apparently seems to have reduced the gap between their “actual” and their “ideal” self. Although the latter seems positive at first glance, this evolution should not disguise that it might be the effect of the NPIs themselves (e.g., a sudden deceleration of daily routines) that makes these women feel like “better” mothers now, whereas the intensive mothering beliefs may remain as influential as before due to their dominant, hegemonial and gender-unequal character. The aim here is not to judge the group of women who experience a (positive) continuation of maternal self-conception throughout their deliberately chosen (rather traditional) family models, but rather to question why (specifically) working mothers get judged by society, in their relationships, and not least by themselves.

Our findings align with studies that showed how the NPIs affected mothers disproportionately since they were placed at the “pandemic frontline” (2, 43, 44). As in our mixed-methods analyses of the Family study, we found indications of the unequally distributed additional care work within households at the expense of the women’s mental health (reference mixed-method paper). At least for some women in our sample, these unbalanced workloads and conflicting roles are perceived as an important trigger for deteriorating mental health (e.g., increased stress levels, decreased happiness and satisfaction with oneself) and negative bodily reactions such as migraine attacks. Our findings on managing inter-role conflicts and their consequences on wellbeing are supported as a gendered phenomenon by further research as mothers during the pandemic experience role conflicts to a higher degree than fathers (45). These insights, in turn, align with evidence indicating that among mothers, both individual stress levels and parenting stress levels have significantly increased during the pandemic (46) compared to stress levels of non-parents and fathers (8, 47). At the other end of the spectrum of pandemic-related wellbeing consequences, we also found that a group of women (mainly those who do not have to manage work-family conflicts) benefited from a slower life pace and increased family time, which has also been reflected in some parts of the literature (5, 48).

So far, studies have aimed at quantifying the burden imposed on mothers by the pandemic, e.g., the number of hours spent at home and in paid employment (49), or the setbacks in productivity that have come from their commitment to the reorganization of family life (50). Our small study adds a critical in-depth analysis of socially effective and self-imposed motherhood norms, their interconnectedness with one’s professional role’s expectations, and their impact on wellbeing and mental health. Similarly, critical pieces started to emerge in personal reflections of women in the field of public health and associated disciplines, e.g., in auto-ethnographies and reflexive essays (51, 52). Most of these apply a feminist perspective criticizing the (at least partially reinforced) gender inequalities in parenting, care, and paid work during the

pandemic. As evidenced in our findings, the value of such approaches in understanding and mitigating the risks to health posed by gender norms, and exacerbated by the pandemic, cannot be ignored. They highlight the failures of yet another myth, which suggests that “women can have it all” (53), and simultaneously, the failure of policies that turn a blind eye to entrenched gender norms and relations and do not provide an environment susceptible of soothing the conflict between ideal –and socially acceptable versions of the mother and the worker.

Strengths and limitations

The qualitative study design allowed an in-depth analysis of the heterogeneous experiences of a rather homogenous group of women in terms of relationship and (high) socioeconomic status, ethnicity, age of children, place of residence, and NPIs. As the implications of the pandemic are highly context-specific, women with more diverse backgrounds and occupational statuses would possibly bring to light other stressors (e.g., fewer remote work options, financial concerns, confined housing) and diverging references to intensive mothering norms than our sample. For example, the experiences of single mothers (who represent almost 80% of single parents in Europe) (54) may differ substantially from those of our sample. As common for qualitative research, our sample size, although relatively large for such a study ($n = 17$), does not claim to give representative findings nor allows us to draw general statements. Despite this limitation and the fact that the development of our interview guide was not informed by theoretical considerations specifically targeting “intensive mothering beliefs” or “ideal worker norms” (these were recurred to in the phase of data analysis), we believe that our approach allowed to highlight crucial points of tensions in maternal self-conception that are likely to be exacerbated during the pandemic.

By using email interviews, we tried to give the participants as much autonomy as possible to answer our questions without disrupting their daily routine. Also, email interviews encourage the participant to reflect on and actively create thought processes as the interview takes place anachronously. However, they also require the participants to have certain reading and writing abilities and relatively easy access to an electronic device. Our sample only includes women who could respond to our survey and email interviews, potentially excluding those who felt even more challenged and stretched during the early pandemic phase. Most women in our sample were working from home and, as such, represented a relatively privileged group. The participants’ response behavior varied as some replied to our questions in a survey-imitating manner (short answers) instead of narrating their thoughts. About 25% of the interviewees dropped out after the second wave of responses (not replying to the third round of questions). A certain drop-out was expected, which is why we

mitigated this risk by asking the most fundamental questions in the first and second rounds of emailing.

We elaborated on the role of two influential and mutually reinforcing discourses, namely the “intensive mothering ideology” and the “ideal worker ideology.” How mothers justify their thoughts and actions by referencing these discourses shows how strongly social norms affect patterns of actions and self-conception and how their (male) partners and employers contribute to shaping those norms. It is relevant to investigate further the role of gendered norms on (mental) health and wellbeing and challenge unequally distributed expectations and responsibilities in the work- and family sphere.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, upon request.

Ethics statement

This study was reviewed and approved by the Ethics Committee of Bielefeld University (Ref. 2020-059). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SB-Z conceptualized the qualitative part of the Family study with CM and LW, and wrote the first draft of the paper. VN coded and analyzed the data with SB-Z. CM, LW, and OR provided substantial feedback on different versions

of the manuscript. All authors contributed to the final draft. All authors contributed to the article and approved the submitted version.

Funding

The present study has been conducted by the Gender Epidemiology Junior Research Group, funded by Bielefeld University. We acknowledge the financial support of the German Research Foundation (DFG) and the Open Access Publication Fund of Bielefeld University for the article processing charge.

Acknowledgments

We thank all the women who took the time to participate in this study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- Carlson DL, Petts R, Pepin JR. Changes in parents' domestic labor during the covid-19 pandemic. *SocArXiv*. (2020) 13:2020. doi: 10.31235/osf.io/jy8fn
- Motherhood and mothering during Covid-19: a gendered intersectional analysis of caregiving during the global pandemic within a Canadian context. *J Mother Stud*. (2020) 5.
- Manzo LK, Minello A. Mothers, childcare duties, and remote working under COVID-19 lockdown in Italy: cultivating communities of care. *Dialogues Hum Geogr*. (2020) 10:120–3. doi: 10.1177/2043820620934268
- Zoch G, Bächmann A-C, Vicari B. Who cares when care closes? Care-arrangements and parental working conditions during the COVID-19 pandemic in Germany. *Eur Soc*. (2020) 23:S576–88. doi: 10.1080/14616696.2020.1832700
- Calvano C, Engelke L, Di Bella J, Kindermann J, Renneberg B, Winter SM. Families in the COVID-19 pandemic: Parental stress, parent mental health and the occurrence of adverse childhood experiences—results of a representative survey in Germany. *Eur Child Adolesc Psychiatry*. (2022) 31:1–3. doi: 10.1007/s00787-021-01816-4
- Frankel LA, Kuno CB, Sampige R. The relationship between COVID-related parenting stress, nonresponsive feeding behaviors, and parent mental health. *Curr Psychol*. (2021) 1–2. doi: 10.1007/s12144-021-02333-y
- Lee SJ, Ward KP, Chang OD, Downing KM. Parenting activities and the transition to home-based education during the COVID-19 pandemic. *Child Youth Serv Rev*. (2021) 122:105585. doi: 10.1016/j.childyouth.2020.105585
- Marchetti D, Fontanesi L, Mazza C, Di Giandomenico S, Roma P, Verrocchio MC. Parenting-related exhaustion during the Italian COVID-19 lockdown. *J Pediatr Psychol*. (2020) 45:1114–23. doi: 10.1093/jpepsy/jsaa093
- Whiley LA, Sayer H, Juanchich M. Motherhood and guilt in a pandemic: Negotiating the “new” normal with a feminist identity. *Gend Work Organ*. (2021) 28:612–9. doi: 10.1111/gwao.12613
- Hays S. *The Cultural Contradictions of Motherhood*. Yale University Press (1996).
- Rotkirch A, Janhunen K. Maternal guilt. *Evol Psychol*. (2010) 8:90–106. doi: 10.1177/147470491000800108

12. Liss M, Schiffrin HH, Rizzo KM. Maternal guilt and shame: the role of self-discrepancy and fear of negative evaluation. *J Child Fam Stud.* (2012) 22:1112–9. doi: 10.1007/s10826-012-9673-2
13. Warner J. *Perfect Madness: Motherhood in the Age of Anxiety.* Riverhead Books (2005).
14. Constantinou G, Varela S, Buckby B. Reviewing the experiences of maternal guilt - the “Motherhood Myth” influence. *Health Care Women Int.* (2021) 42:852–76. doi: 10.1080/07399332.2020.1835917
15. Henderson A, Harmon S, Newman H. The price mothers pay, even when they are not buying it: mental health consequences of idealized motherhood. *Sex Roles.* (2015) 74:512–26. doi: 10.1007/s11199-015-0534-5
16. Kim S, Thibodeau R, Jorgensen RS. Shame, guilt, and depressive symptoms: a meta-analytic review. *Psychol Bull.* (2011) 137:68–96. doi: 10.1037/a0021466
17. Rizzo KM, Schiffrin HH, Liss M. Insight into the parenthood paradox: mental health outcomes of intensive mothering. *J Child Fam Stud.* (2012) 22:614–20. doi: 10.1007/s10826-012-9615-z
18. Arendell T. Conceiving and investigating motherhood: the decade’s scholarship. *J Marriage Fam.* (2000) 62:1192–207. doi: 10.1111/j.1741-3737.2000.01192.x
19. Ennis LR. *Intensive Mothering: The Cultural Contradictions of Modern Motherhood.* Demeter Press (2014).
20. Hallstein DLO. Conceiving intensive mothering. *J Mother Initiat Res Commun Involvement.* (2006) 8.
21. Christopher K. Extensive mothering. *Gend Soc.* (2012) 26:73–96. doi: 10.1177/0891243211427700
22. Acker J. Hierarchies, jobs, bodies. *Gend Soc.* (2016) 4:139–58. doi: 10.1177/089124390004002002
23. Brumley KM. The gendered ideal worker narrative. *Gend Soc.* (2014) 28:799–823. doi: 10.1177/0891243214546935
24. Williams J. *Unbending Gender.* Why family and work conflict and what to do about it. Oxford: Oxford University Press (2001).
25. McClintock-Comeaux M. Ideal worker. In: Smith V, editor. *Sociology of Work: An Encyclopedia.* SAGE Publications, Inc (2013).
26. Davies AR, Frink BD. The origins of the ideal worker: the separation of work and home in the United States from the market revolution to 1950. *Work Occup.* (2014) 41:18–39. doi: 10.1177/0730888413515893
27. Benard S, Correll SJ. Normative discrimination and the motherhood penalty. *Gend Soc.* (2010) 24:616–46. doi: 10.1177/0891243210383142
28. Lott Y, Klenner C. Are the ideal worker and ideal parent norms about to change? The acceptance of part-time and parental leave at German workplaces. *Community Work Fam.* (2018) 21:564–80. doi: 10.1080/13668803.2018.1526775
29. Güney-Frahm I. Neoliberal motherhood during the pandemic: some reflections. *Gend Work Organ.* (2020) 27:847–56. doi: 10.1111/gwao.12485
30. Klabunde A, Korn E. Parasites and raven mothers: a german-japanese comparison on (lone) motherhood. *SSRN Electron J.* (2010). doi: 10.2139/ssrn.1670591
31. Czymara CS, Langenkamp A, Cano T. Cause for concerns: gender inequality in experiencing the COVID-19 lockdown in Germany. *Eur Soc.* (2020) 23(Suppl. 1):S68–81. doi: 10.1080/14616696.2020.1808692
32. Cameron EE, Joyce KM, Delaquis CP, Reynolds K, Protudjer JLP, Roos LE. Maternal psychological distress and mental health service use during the COVID-19 pandemic. *J Affect Disord.* (2020) 276:765–74. doi: 10.1016/j.jad.2020.07.081
33. Borah Hazarika O, Das S. Paid and unpaid work during the COVID-19 pandemic: a study of the gendered division of domestic responsibilities during lockdown. *J Gend Stud.* (2020) 30:429–39. doi: 10.1080/09589236.2020.1863202
34. Yavorsky JE, Qian Y, Sargent AC. The gendered pandemic: the implications of COVID-19 for work and family. *Soc Compass.* (2021) 15:e12881. doi: 10.1111/soc4.12881
35. Spallek J, Grosser A, Holler-Holtrichter C, Doyle I-M, Breckenkamp J, Razum O. Early childhood health in Bielefeld, Germany (BaBi study): study protocol of a social-epidemiological birth cohort. *BMJ Open.* (2017) 7:e018398. doi: 10.1136/bmjopen-2017-018398
36. Adams WC. *Conducting Semi-Structured Interviews. Handbook of Practical Program Evaluation.* John Wiley & Sons (2015). p. 492–505.
37. Hawkins J. The practical utility and suitability of email interviews in qualitative research. *Qual Rep.* (2018) 23:493–501. doi: 10.46743/2160-3715/2018.3266
38. Hunt N, McHale S. A practical guide to the email interview. *Qual Health Res.* (2007) 17:1415–21. doi: 10.1177/1049732307308761
39. Meho LI. Email interviewing in qualitative research: a methodological discussion. *J Am Soc Inf Sci Technol.* (2006) 57:1284–95. doi: 10.1002/asi.20416
40. Miani C, Wandschneider L, Batram-Zantvoort S, Razum O. Covid-19 pandemic: a gender perspective on how lockdown measures have affected mothers with young children [accepted for publication]. In: Kupfer A, Stutz C, editors. *Covid, Crisis, Care, and Change? International Gender Perspectives on Re/Production, State and Feminist Transitions Dresden.* Germany: Verlag Barbara Budrich. (2022).
41. Wandschneider L, Batram-Zantvoort S, Alaze A, Niehues V, Spallek J, Razum O, et al. Self-reported mental well-being of mothers with young children during the first wave of the COVID-19 pandemic in Germany: A mixed-methods study. *Women’s Health.* (2022) 18:1–17. doi: 10.1177/1745505722114274
42. Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res.* (2005) 15:1277–88. doi: 10.1177/1049732305276687
43. Clark S, McGrane A, Boyle N, Joksimovic N, Burke L, Rock N, et al. ‘You’re a teacher you’re a mother, you’re a worker’: gender inequality during Covid-19 in Ireland. *Gend Work Organ.* (2021) 28:1352–62. doi: 10.1111/gwao.12611
44. Zamarro G, Prados MJ. Gender differences in couples’ division of childcare, work and mental health during COVID-19. *Rev Econ Househ.* (2021) 19:11–40. doi: 10.1007/s11150-020-09534-7
45. Lagomarsino F, Coppola I, Parisi R, Rania N. Care tasks and new routines for Italian families during the COVID-19 pandemic: perspectives from women. *Ital Sociol Rev.* (2020) 10:847–68A. doi: 10.13136/isr.v10i3S401
46. Babore A, Trumello C, Lombardi L, Candelori C, Chirumbolo A, Cattelino E, et al. Mothers’ and children’s mental health during the COVID-19 pandemic lockdown: the mediating role of parenting stress. *Child Psychiatry Hum Dev.* (2021) 1–3. doi: 10.1007/s10578-021-01230-6
47. Thomson KC, Jenkins E, Gill R, Richardson CG, Gagne Petteni M, McAuliffe C, et al. Impacts of the COVID-19 pandemic on family mental health in Canada: findings from a multi-round cross-sectional study. *Int J Environ Res Public Health.* (2021) 18:12080. doi: 10.3390/ijerph182212080
48. Guo J, De Carli P, Lodder P, Bakermans-Kranenburg MJ, Riem MM. Maternal mental health during the COVID-19 lockdown in China, Italy, and the Netherlands: a cross-validation study. *Psychol Med.* (2021) 1. doi: 10.1017/S0033291720005504
49. Petts RJ, Carlson DL, Pepin JR. A gendered pandemic: childcare, homeschooling, and parents’ employment during COVID-19. *Gend Work Organ.* (2021) 8:515–34. doi: 10.1111/gwao.12614
50. Lerchenmuller C, Schmallenbach L, Jena AB, Lerchenmueller MJ. Longitudinal analyses of gender differences in first authorship publications related to COVID-19. *BMJ Open.* (2021) 11:e045176. doi: 10.1136/bmjopen-2020-045176
51. Beech HH, Sutton A, Cheatham L. Parenting, privilege, and pandemic: from surviving to thriving as a mother in the academy. *Qual Soc Work.* (2021) 20:625–31. doi: 10.1177/1473325020973328
52. Bowyer D, Deitz M, Jamison A, Taylor CE, Gyengesi E, Ross J, et al. Academic mothers, professional identity and COVID-19: Feminist reflections on career cycles, progression and practice. *Gend Work Organ.* (2021) 29:309–41. doi: 10.1111/gwao.12750
53. Hewlett SA. Executive women and the myth of having it all. *Harv Bus Rev.* (2002) 80:66–73.
54. Nieuwenhuis R. *The Situation of Single Parents in the EU.* EPRS: European Parliamentary Research Service. (2020). Retrieved from: <https://policycommons.net/artifacts/1426760/the-situation-of-single-parents-in-the-eu/2041286/> (accessed August 22, 2022).



OPEN ACCESS

EDITED BY

Vijay Kumar Chattu,
University of Toronto, Canada

REVIEWED BY

Rubeena Zakar,
University of the Punjab, Pakistan
Russell Kabir,
Anglia Ruskin University, United Kingdom

*CORRESPONDENCE

Mekasha Getnet Demeke
✉ mekashagetnet@gmail.com

SPECIALTY SECTION

This article was submitted to Maternal Health, a section of the journal Frontiers in Global Women's Health

RECEIVED 24 June 2022

ACCEPTED 20 December 2022

PUBLISHED 07 February 2023

CITATION

Demeke MG and Shibeshi ET (2023) Intimate partner violence against women of reproductive age and associated factors during COVID-19 pandemic in Northern Ethiopia, 2021: A community-based cross-sectional study.

Front. Glob. Womens Health 3:977153.
doi: 10.3389/fgwh.2022.977153

COPYRIGHT

© 2023 Demeke and Shibeshi. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Intimate partner violence against women of reproductive age and associated factors during COVID-19 pandemic in Northern Ethiopia, 2021: A community-based cross-sectional study

Mekasha Getnet Demeke^{1*} and Ehtemariam Tefera Shibeshi²

¹Department of Nursing, College of Health Sciences, Debre Berhan University, Debre Berhan, Ethiopia,

²Department of Public Health, College of Health Sciences, Debre Berhan University, Debre Berhan, Ethiopia

Background: Intimate partner violence (IPV) is a major public health concern that affects more than one-third of all women globally. Assessing the prevalence of intimate partner violence and associated factors during the COVID-19 pandemic in various localities is crucial for intervention actions. So far, a few studies have been done in Ethiopia during the current COVID-19 pandemic.

Objective: This study aimed to assess the prevalence of intimate partner violence in women of reproductive age and associated factors during the COVID-19 pandemic in Debre Berhan town, Ethiopia, 2021.

Methodology: A community-based cross-sectional study was done. A total of 809 ever-partnered women of reproductive age were selected randomly via a multistage sampling method. Crude and adjusted odds ratios (AOR) with the resulting 95% confidence interval (CI) were used to verify the strength of associations. Significant associations were declared at p -values <0.05 .

Result: Among the 796 women who successfully participated in the study, 337 (42.3%) experienced at least one type of intimate partner violence. Prevalence of psychological, physical, and sexual violence was 35.3% (281), 15.3% (122), and 15.2% (121), respectively. Multivariate analysis revealed that women with no formal education [AOR (95% CI): 3.66 (1.91–6.98)], having no own income [AOR (95% CI): 1.78 (1.24–2.56)], and attitude of IPV were acceptable [AOR (95% CI): 4.02 (1.33–12.14)]; a male partner with no formal education [AOR (95% CI): 3.06 (1.53–6.14)], with “level of religious beliefs” [weak—AOR (95% CI): 4.17 (1.45–12.03); and medium—AOR (95% CI): 1.64 (1.13–2.39)], who is alcoholic [AOR (95% CI): 5.91 (4.03–8.67)], and with smoking habits [AOR (95% CI): 2.04 (1.10–3.77)] and >5 [AOR (95% CI): 1.83 (1.01–3.39)] was significantly associated with the presence of intimate partner violence.

Conclusion and recommendation: This study revealed a high prevalence of IPV in the study participants. The high intimate partner violence prevalence was due to multiple factors, thus demanding empowering women and tailored health education for male partners.

KEYWORDS

COVID-19 pandemic, intimate partner, reproductive age, violence, gender-based violence

Abbreviations

AOR, adjusted odds ratio; CI, confidence interval; COR, crude odds ratio; GBV, gender-based violence; IPV, intimate partner violence; SPSS, Statistical Package for Social Sciences; WHO, World Health Organization

1. Introduction

Gender-based violence (GBV) is any brutality directed at an individual based on their sex, gender identity, or socially defined ways of maleness and femaleness (1–3). Both men and women can experience GBV; however, the rates among women are severely higher (1–4). Thus, violence against women is the primary form of GBV, a major public health problem, and a fundamental violation of women's human rights (1–5). It includes any violent acts such as threats, coercion, and denial of liberty against women (5–7). The actor of violence against women can be anyone, irrespective of their relationship with the victim, whereas the main perpetrators are male partners including husbands, fiancées, or ex-partners, often referred to as intimate partners (5–8).

Intimate partner violence (IPV) is the insidious form of violence against women, which includes physical, sexual, and emotional types of violence (6–10). It has been known that IPV can cause lifelong mental, physical, and reproductive health problems (7, 11–13). Women who experience IPV also risk further conflicts with others and develop social disorders (11–14).

Intimate partner violence occurs among women in developed and developing countries, in all settings, socioeconomic, religious, and cultural groups, without restrictions (1–3). It is estimated that over 35% of women worldwide have experienced IPV at some point in their lives (8–10). In that, nearly 33% of women in a relationship reported having experienced either physical and/or sexual abuse (5–8). However, the rate as well as types of IPV vary across regions, countries, and also among localities within a country (7).

About 27% of women in European and western Pacific regions and 30% of women in South America reported IPV (7–10, 15). The prevalence of IPV was typically high in women across African countries (16–18). For instance, about 50% of women in Côte d'Ivoire experienced IPV (19).

Likewise, a high prevalence of sexual (59%) and physical (49%) violence was reported in women in Ethiopia (7). Evidencing, IPV is a major public health concern affecting the physical, sexual, mental, and social well-being of the women in the country (13, 20–22).

Intimate partner violence increases during conflicts and pandemics (16, 17). During pandemics, people are forced to perform firm protective actions; thus, their normal lifestyles are likely to be changed (23, 24). As the global pandemic of coronavirus (COVID-19) spreads across continents and communities, governments of nearly all countries globally force their people to respond with strict preventive actions such as staying at home, keeping social distance, etc. (20, 24).

A finding from Tajikistan showed that the prevalence of physical, emotional, and sexual violence was 23.2%, 15.5%, and 1.7%, respectively. In this study, the educational level and alcohol-drinking status of husbands were significantly associated with intimate partner violence (71).

The COVID-19 pandemic and the demand for spouses to stay at home can aggravate differences and open up unsettled issues, rising emotive to deficiencies and minor mistakes (25, 26). This pandemic has also been believed to increase risk factors such as alcohol use (25). In acute cases, with a lack of awareness and skills to resolve conflicts, IPV is aggravated and worsens in partners with emotional divorce (25, 27). As well, quarantine, fear of infection, the chaos of social networks,

reduced access to health and social services, distress, misinformation, income shortage, financial loss, job loss, and limited social support are likely to raise risks of IPV in the pandemic (25–27). This evidence is supported by a study done in Tajikistan, which stated that intimate partner violence is significantly associated with no or primary educational status and husbands who have alcohol-drinking habits (71).

The government of Ethiopia also affirmed to take several actions since the first cases of COVID-19 were identified in the country (28). As a result, the normal lifestyle of the people across different parts of Ethiopia has been affected notably due to the protective actions, fear of infection, and other socioeconomic effects, which might lead to an increase in the prevalence of IPV in different parts of the country. Different strategies were implemented as prevention measures like homestay, physical distance, washing hands with water and soap, and wearing facemasks (20, 24). Thus, this study aimed to assess the prevalence of IPV in women of reproductive age and the associated risk factors in Debre Berhan town in Ethiopia during the COVID-19 pandemic.

2. Methods and materials

2.1. Study area

This study was conducted in Debre Berhan, North Shoa Zone of Amhara Region, Ethiopia. Debre Berhan is located about 120 km northeast of the capital city, Addis Ababa, of the country. The town is among the fast-growing cities in Ethiopia. It has a total population of 113,693 (69). Currently, the town has 14 Kebele administrations, among which 9 are urban and the rest are recently included rural kebeles. According to the information obtained from the North Shoa Zone Health Department, there are a total of about 26,663 households in Debre Berhan, which are unevenly distributed throughout the 14 Kebele administrations.

2.2. Study design and period

A community-based cross-sectional study design was utilized to assess the prevalence of intimate partner violence in women of reproductive age and associated risk factors in Debre Berhan. The study was conducted from February to April 2021 G.C.

2.3. Source population

All women of reproductive age living in Debre Berhan in 2021 G.C were the source population for the present study (Table 1).

2.4. Study population

Women of reproductive age living in the selected six kebeles of Debre Berhan, namely, Kebele 2, Kebele 3, Kebele 7, Kebele 8, Atakilt, and Zanjira, were the study population for the present study from which the participant women of reproductive age were selected directly.

TABLE 1 Number of households in each of the kebeles of Debre Berhan, 2021 G.C.

SN	Name of kebele	Locality	HHs per kebele	HHs and kebeles per locality		Remark
1	Kebele 1	Urban	982	22,775 HHs	9 kebeles	
2	Kebele 2	Urban	3,431			Selected
3	Kebele 3	Urban	2,619			Selected
4	Kebele 4	Urban	3,654			
5	Kebele 5	Urban	2,968			
6	Kebele 6	Urban	2,350			
7	Kebele 7	Urban	1,052			Selected
8	Kebele 8	Urban	2,794			Selected
9	Kebele 9	Urban	2,925			
10	Atakilt	Rural	1,569	3,888 HHs	5 kebeles	Selected
11	Zanjira	Rural	578			Selected
12	Chole	Rural	335			
13	Faji	Rural	764			
14	Genet	Rural	642			
Total	26,663	26,663	14	6 kebeles		

HH, household.

Source: The data were obtained from the North Shoa Zone Health Department, Debre Berhan, Ethiopia, 2021.

2.5. Inclusion and exclusion criteria

2.5.1. Inclusion criteria

Women of reproductive age who are ever-partnered and living in the selected Kebele during the COVID-19 pandemic since the onset of the COVID-19 pandemic until the data collection period were eligible for this study.

2.5.2. Exclusion criteria

Women of reproductive age who are never-partnered and not living in the selected Kebele during the COVID-19 pandemic and whose partners are not physically with them since the onset of the COVID-19 pandemic until the data collection period were not eligible for this study.

2.6. Sample size determination

The sample size for the present study was calculated in harmony with the study objectives using the following two ways. First, the sample size for the prevalence of intimate partner violence (the first objective) was calculated using the single population proportion formula and basic assumptions as shown below:

$$n = \frac{Z^2 \frac{\alpha}{2} pq}{d^2}$$

where

- n = desired sample size

- confidence level considered is 95%
- Z = standard normal deviate at 95% confidence level (1.96)
- P = proportion of IPV prevalence of 24.6% taken from a study conducted previously in Aksum town, northern Ethiopia (20)
- $q = 1 - P$ ($1 - 0.246$) = 0.754
- d = degree of accuracy desired 5% (0.05).
 ✓ The minimum possible sample size was ≈ 285 .
 ✓ A design effect of 2 was used: $285 \times 2 = 570$.

Thus, the total sample size calculated considering the 24.6% IPV prevalence was 570 women.

Second, the sample size calculated considering the second objective (regarding the associated factors) was calculated by taking significantly associated factor variables from previous studies that were conducted in Ethiopia and elsewhere (20, 22, 30, 43) by using Epi Info version 7 software *via* the cross-sectional study option, as shown in Table 2.

As shown in Table 2, most of the calculated sample sizes regarding the associated risk factor variables (the second objective of this study) were smaller than the sample size calculated regarding the first objective of this study, equal to 570. However, the sample sizes calculated regarding the age and occupation of the male partners equal to 735 and 610, respectively, were larger than the sample size calculated regarding the first objective of this study (Table 2).

Accordingly, the sample size calculated based on the age of the male partner (equal to 735) was assumed to be optimal for both objectives of this study. Finally, an estimated nonresponse rate of 10% was considered (i.e., $735 \times 0.10 = 73.5 \approx 74$), and the final sample size determined for the present study was equal to $735 + 74 = 809$ women of reproductive age.

2.7. Sampling procedure

In this study, a stratified multistage sampling technique was applied. In the first stage, kebeles (primary sampling units) were selected randomly by a lottery method. At this stage, all of the 14 kebeles in the town were stratified into urban and rural kebeles to have an unbiased allocation of samples between the two localities. After that, nearly half of the kebeles in each of the two localities, which means four of the nine urban kebeles and two of the five rural kebeles, were selected randomly by the lottery method.

In the second stage, households (secondary sampling units) were selected by a systematic random sampling method among the households in each of the six eligible kebeles. At this stage, the list of residents in the respective kebele was used as a sampling frame, while a sampling interval “ K ” was calculated by dividing the number of total households available in a given kebele by the sample size allotted for the kebele.

Finally, one ever-partnered woman of reproductive age was selected per household. In the cases of households where two or more ever-partnered women of reproductive age were available, one of the available ever-partnered women of reproductive age was selected randomly by the lottery method using rolled sheets of “zeros” and “one.” However, in the cases of households where no ever-partnered woman of reproductive age was available, data collectors moved to the next (+1) household until they arrived at a household where an eligible woman was available.

TABLE 2 Sample size calculation based on factor variables to assess IPV prevalence among women of reproductive age during the COVID-19 pandemic in Debre Berhan, 2021 G.C.

Variables	CI	Power	Unexposed: exposed ratio	IPV prevalence in exposed	IPV prevalence in unexposed	OR	Sample size
Women-related factors							
Age	95	80	0.08	33.2%	7.7%	5.95	380
Occupation	95	80	0.31	45.2%	30.8	1.85	511
Education	95	80	0.48	26.5%	12.7%	2.47	324
Pregnancy status	95	80	5.25	87.2%	28.1%	17.4	40
Acceptance of IPV	95	80	0.49	45.6%	21.4%	3.08	143
Relationship status	95	80	7.68	66.1%	33.8%	3.81	174
Male partner-related factors							
Age	95	80	0.89	30.9%	21.7%	1.61	735
Occupation	95	80	1.89	28.9%	40.1%	1.65	610
Education	95	80	2.4	47.3%	32.9%	1.83	427
Alcohol use	95	80	0.85	53.3%	19%	4.87	64
Smoking	95	80	0.05	82.1%	35.1%	8.5	118

CI, confidence interval; OR, odds ratio; IPV, intimate partner violence.

Above all, to ensure an unbiased allotment of samples between rural and urban localities and within the selected kebeles in each locality, numbers of final study units (women of reproductive age) were allotted proportionally to size. Accordingly, using the outlined sampling procedure explained thus far in the text and depicted in the diagram presented beneath, a total of 809 ever-partnered women of reproductive age were enrolled for the present study (Figure 1).

2.8. Data collection technique and procedure

Data collection was carried out by using a structured questionnaire set concerning intimate partner violence and the associated factors. The types of intimate partner violence were classified into physical, sexual, and emotional violence, and queries

conforming to each type of violence were prepared based on the WHO instrument on violence against women (5). To assess the associated factors, questions regarding women-related, male partner-related, and family-related variables were prepared in line with the conceptual framework outlined in advance (Figure 2).

Finally, each participant ever-partnered woman of reproductive age was asked to complete the questionnaire with the necessary information, either administered by herself or with the help of an interviewer, in accordance with her education status and preference for the procedure.

2.9. Variables of the study

2.9.1. Dependent variables

Ø The dependent variable for the present study was any type of IPV.

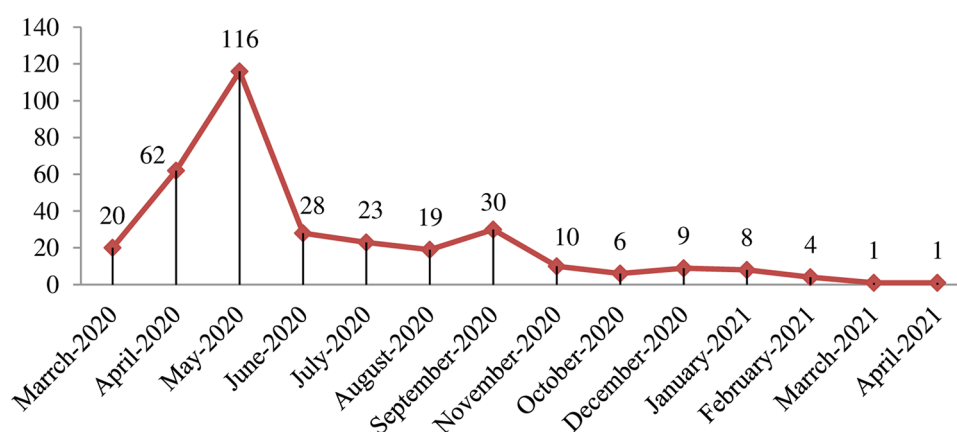


FIGURE 1

Conceptual framework for factors affecting intimate partner violence against women of reproductive age.

2.9.2. Independent variables

Independent variables for the present study are as follows:

- **Women-related factors:** Age, education, occupation, own income, relationship status, religion, access to media (TV/radio), pregnancy status, and acceptance of IPV.
- **Male partner-related factors:** Age, education, occupation, own income, religious belief (level of attitude rated by the woman), alcohol consumption habit, and smoking habit.
- **Family-related factors:** Family size, number of children, presence of extended family, and monthly family income.

2.10. Operational definitions

- **Acceptance of IPV:** It refers to the attitude or principle of a woman toward the cultural or societal thought of “intimate partner violence is acceptable.”
- **Emotional violence:** It refers to verbal acts such as insults, belittling, humiliation, intimidation like destroying things, threats of harm, and threats to take away children (5).
- **Extended family:** It includes any family member other than the biological (adopted) children of the couple, such as grandparents, parents, uncles, aunts, sisters, brothers, or relatives of the male partner or the woman (47).
- **Intimate partner violence absent:** A woman has not experienced all of the three types of violence (i.e., physical, sexual, and

emotional violence) by her intimate partner during the COVID-19 pandemic (i.e., from March 20, 2020, until the data collection period) (5).

- **Intimate partner violence present:** A woman has experienced at least one of the three types of violence (i.e., physical, sexual, and emotional violence) by her intimate partner during the COVID-19 pandemic (i.e., from March 20, 2020, until the data collection period) (5).
- **Intimate partner violence:** Any form of physical, sexual, and emotional violence against women by an intimate partner (5).
- **Intimate partner:** The male partner of the woman in a couple, either her husband (legal or illegal), a fiancée, a boyfriend, or any male sexual partner, who cohabits with the woman (5).
- **Physical violence:** It refers to any of the acts such as slapping, hitting, kicking, and beating against the victim woman by her intimate partner (5).
- **Presence of own income:** The presence of any regular means of income belonging to each individual in a couple (i.e., the woman and the male partner each) (43).
- **Religious belief of male partner:** It refers to the level of attitude or principle of the male partner toward religious faiths, which was measured as rated by the mouth of the woman in rating words, such as weak, medium, and strong.
- **Sexual violence:** It refers to acts including forced sexual intercourse and other forms of sexual bullying against the victim woman by her intimate partner (5).

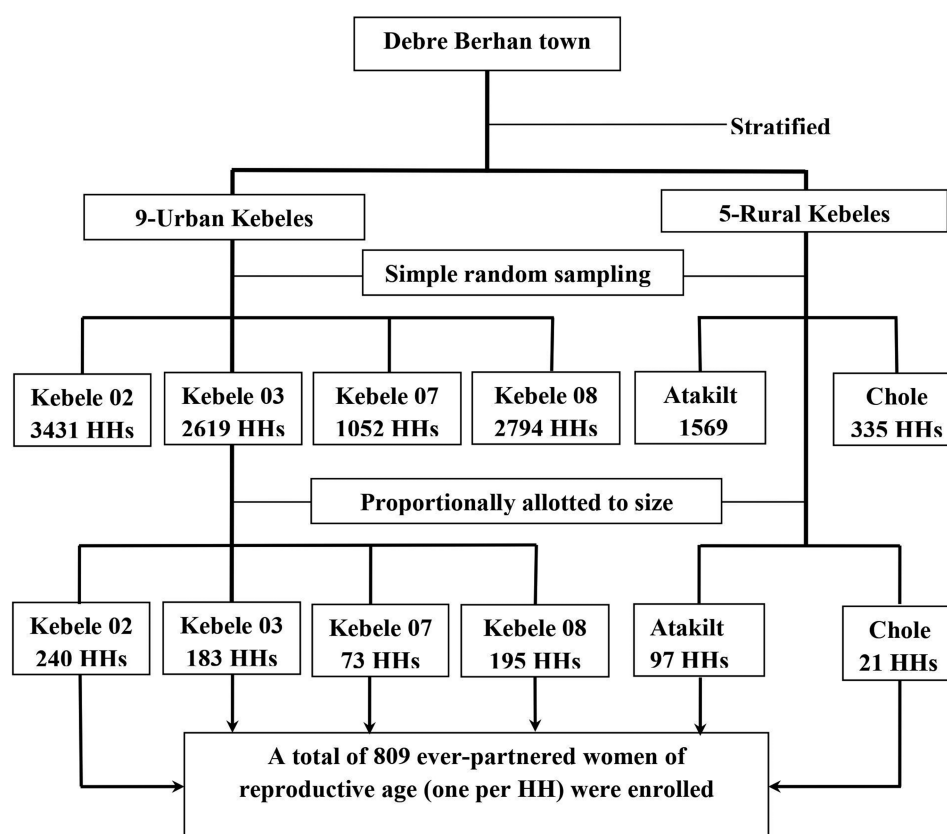


FIGURE 2

Schematic representation of the sampling procedure of ever-partnered women of reproductive age in Debre Berhan town.

2.11. Data quality control

To ensure data quality, training was given to data collectors and supervisors for 1 day. The questionnaire was administered in Amharic (native language). Before the actual data collection, the questionnaire was tested by taking 5% of the total sample size among women of reproductive age in Debre Sina town. On-spot checks, re-interviewing, and checking completed questionnaires and quality of recordings were done *via* daily supervision by field supervisors. In addition, training was given to all data collectors and supervisors for 2 days before the actual data collection.

2.12. Data processing and analysis

Data were entered in Epi.Data Version 4.2 software, while further statistical analyses were done using Statistical Package for Social Sciences (SPSS) version 24. Descriptive statistics were used to describe the prevalence of IPV and sociodemographic characteristics of the study participants in percentages and frequencies. A binary logistic regression model, with bivariate and multivariate analyses, was used to verify the association of each independent variable with the dependent variable.

In the modeling process, first, bivariate logistic regression analysis was performed to detect the association of each independent variable with the dependent variable using a crude odds ratio (COR), 95% confidence interval (CI), and *P*-value. Then, all independent variables with *P*-values ≤ 0.25 in the bivariate analysis were selected and entered in the multivariate logistic regression analysis, while independent variables suspected for collinearity/multicollinearity (coefficients = 0.8) with other variables were excluded (70). Finally, in the multivariate logistic regression analysis, the strength of associations of each independent variable with the dependent variable was verified using an adjusted odds ratio (AOR) and 95% CI. Associations were declared significant at *P*-value < 0.05 .

2.13. Ethical consideration

Ethical clearance and approval were obtained from the Institutional Review Board of the Institute of Health Science and Medicine, College of Health Science, Debre Berhan University, which was further communicated to zonal and town health departments/offices and to the selected Kebele administrations. Verbal consent was obtained from each participant woman. The names of the study participants were not taken, all the necessary data were collected and registered based on unique codes of women given by the study, and thus all information was kept confidential.

3. Results

3.1. Sociodemographic characteristics of the study participants

A total of 796 women successfully participated in the study, giving a response rate of 98.4%. Of the 796 study participant women, 332 (41.7%), 368 (46.2%), and 96 (12.1%) were in the age groups of

18–28, 29–38, and 39–45 years, respectively. The age of the male partners of the study participant women ranged from 20 to 68 years. About 115 (14.4%) of women and 77 (9.7%) of male partners were illiterate. The majority of the study participant women (584,

TABLE 3 Sociodemographic characteristics of the study participant women and their male partners and families in Debre Berhan, Ethiopia, 2021 (*n* = 796).

Variable	Category	Frequency	Percentage
Age of woman (years)	18–28	332	41.7
	29–38	368	46.2
	39–45	96	12.1
Woman education	No formal education	115	14.4
	Primary education	216	27.1
	Junior education	145	18.2
	Secondary education	139	17.5
	Diploma and above	181	22.7
Woman occupation	Farmer	14	1.8
	Manual worker	87	10.9
	Housewife	335	42.1
	Trader/Pettit-trade	210	26.4
	Govt./NGO employee	150	18.8
Woman religion	Orthodox	622	78.1
	Muslim	126	15.8
	Others	48	6.0
Relationship status	Married	584	73.4
	Unmarried	212	26.6
Residence	Rural kebeles	115	14.4
	Urban kebeles	681	85.6
Age of male partner (years)	20–30	246	30.9
	31–40	402	50.5
	41–68	148	18.6
Male partner education	No formal education	77	9.7
	Primary education	199	25.0
	Junior education	123	15.5
	Secondary education	149	18.7
	Diploma and above	248	31.2
Male partner occupation	Farmer	71	8.9
	Manual worker	182	22.9
	Trader/Pettit-trade	227	28.5
	Govt./NGO employee	316	39.7
Family size	3 and below	265	33.3
	4–5	300	37.7
	6 and above	231	29.0
Presence of children	Yes	676	84.9
	No	120	15.1

73.4%) were married, 676 (84.9%) had at least one child, and 681 (85.6%) were living in urban kebeles (Table 3).

3.2. Prevalence of intimate partner violence in the study participants

Among the 796 study participant women of reproductive age in Debre Berhan, 337 (42.3%) were experiencing at least one type of violence by an intimate partner during the COVID-19 pandemic (Table 4). The prevalence of any form of intimate partner violence in women of reproductive age during the COVID-19 pandemic was 38.3% (44) among women living in rural kebeles and 43% (293) among women living in urban kebeles (Table 4). Also, the overall prevalence of each of the three types of violence, psychological, physical, and sexual violence, in the study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic was 35.3% (281), 15.3% (122), and 15.2% (121), respectively (Table 4).

Regarding co-occurrence of two or more types of violence, about 72 (9%) of the study participant women were experiencing psychological and physical violence, 27 (3.4%) were experiencing

psychological and sexual violence, 2 (0.3%) were experiencing physical and sexual violence, and 43 (5.4%) of the study participants were experiencing all types of violence (psychological, physical, and sexual violence) by an intimate partner during the COVID-19 pandemic (Table 4). However, about 193 (24.3%) of the study participants of reproductive age were experiencing only one type of violence (Table 4). In more detail, about 139 (17.5%) of the study participants were experiencing only psychological violence, 5 (0.6%) were experiencing only physical violence, and 49 (6.2%) were experiencing only sexual violence by intimate partners (Table 4).

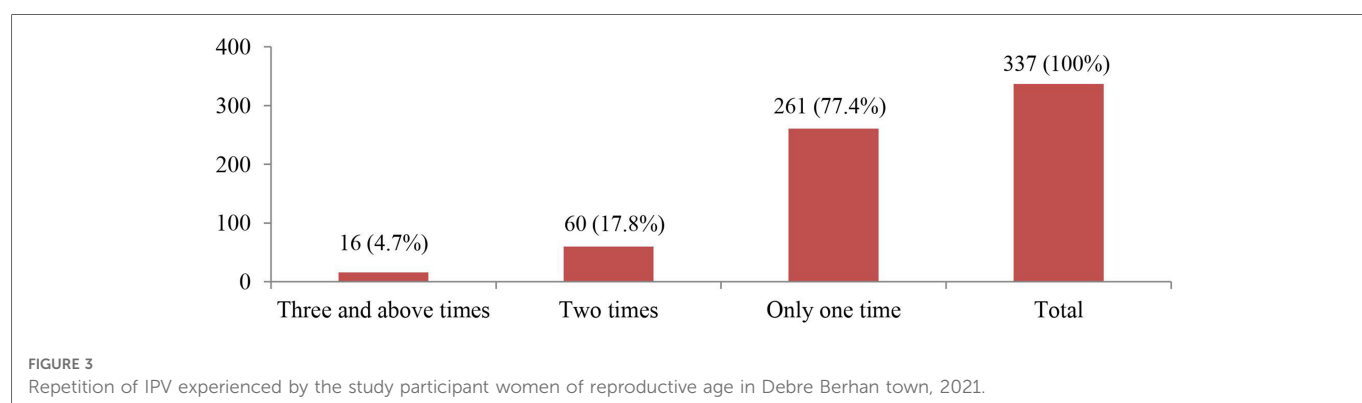
Regarding violence repetition on each participant woman across the depth of the study during the pandemic era, among the total of 337 participant women who were experiencing at least one type of IPV, 16 (4.7%) were experiencing violence three and more times, 60 (17.8%) of them were experiencing two times, and the remaining 261 (77.4%) women were experiencing violence only once in the 14 months this study has addressed (Figure 3).

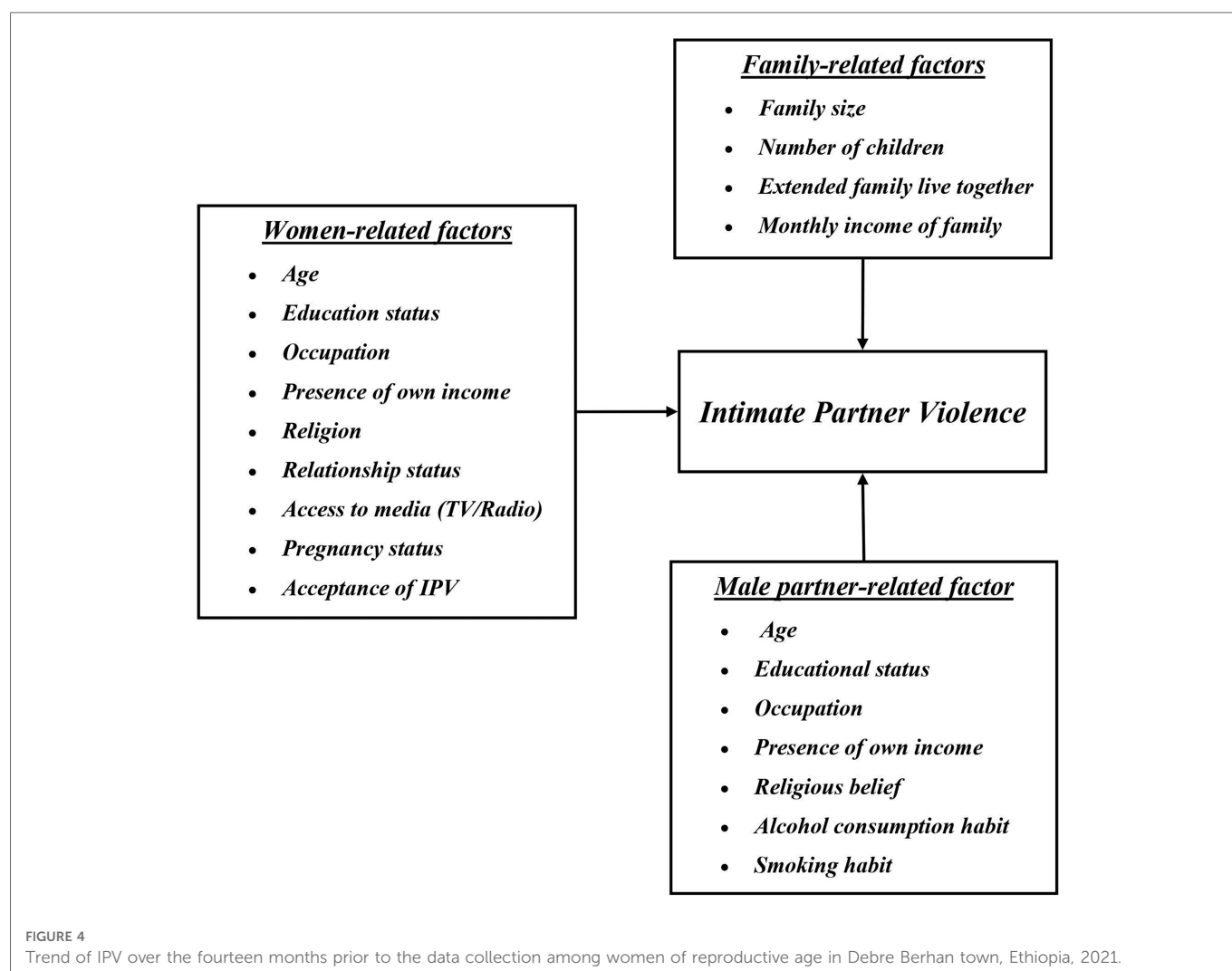
The trend of at least one type of IPV among the study participant women of reproductive age over the 14 months prior to the data collection during the pandemic varied considerably (Figure 4). In the first 3 months of the pandemic, the occurrence of IPV had an

TABLE 4 Prevalence of intimate partner violence in women of reproductive age in Debre Berhan, Ethiopia, 2021 ($n = 796$).

Type of violence	Total No. (%)	Residence kebeles		P-value
		Rural No. (%)	Urban No. (%)	
Psychological violence only	139 (17.5)	22 (19.1)	117 (17.2)	0.621
Physical violence only	5 (0.6)	0 (0.0)	5 (0.7)	0.025
Sexual violence only	49 (6.2)	4 (3.5)	45 (6.6)	0.110
Psychological + physical violence	72 (9.0)	10 (8.7)	62 (9.1)	0.886
Psychological + sexual violence	27 (3.4)	2 (1.7)	25 (3.7)	0.172
Physical + sexual violence	2 (0.3)	0 (0.0)	2 (0.3)	0.157
Psychological + physical + sexual violence	43 (5.4)	6 (5.2)	37 (5.4)	0.924
Overall psychological violence	281 (35.3)	40 (34.8)	241 (35.4)	0.900
Overall physical violence	122 (15.3)	16 (13.9)	106 (15.6)	0.638
Overall sexual violence	121 (15.2)	12 (10.4)	109 (16.0)	0.080
Any IPV (at least one type of IPV) present	337 (42.3)	44 (38.3)	293 (43.0)	0.332
No IPV present	459 (57.7)	71 (61.7)	388 (57.0)	0.332

IPV, intimate partner violence.





increasing trend, with 116 of the total 337 victims experiencing it in May 2020, and the least occurrences of 1 case of IPV occurred during March and April 2021 (Figure 4).

3.3. Associated risk factors for intimate partner violence against women

3.3.1. Bivariate logistic regression analysis of associated factors for IPV

The bivariate logistic regression analysis results of the woman-related factors of IPV among the study participant women of reproductive age in Debre Berhan revealed that variables such as the age, education status, own income, and attitude of the woman toward the acceptability of IPV were significantly associated with the presence of any IPV. In addition, according to the bivariate logistic regression analysis results of the male partner-related associated factors, the age, education status, occupation, religious belief, and alcohol-drinking and smoking habits of the male partner showed statistically significant association with the presence of any IPV (Table 6).

In addition to the bivariate logistic regression analyses presented above, a multivariate logistic regression analysis was

done for the selected association factor variables for IPV with P -values ≤ 0.25 in the bivariate analysis. Accordingly, the multivariate logistic regression analysis showed that the woman-related factor variables, such as woman's education status of no formal education, primary education, and junior education, showed significant association with the presence of any IPV as evidenced in the results from the AOR with 95% CI with P -values of less than 0.001 (AOR = 3.66, 95% CI: 1.91–6.98; AOR = 3.52, 95% CI: 2.04–6.07; and AOR = 3.35, 95% CI: 1.87–6.02), respectively (Tables 5, 8). As well, the risk factor variables such as woman's own income (AOR = 1.78; 95% CI: 1.24–2.56; P -value < 0.001), with woman's attitude on IPV acceptance (AOR = 4.02; 95% CI: 1.33–12.14; P -value < 0.05), showed significant association with the presence of any IPV (Table 8).

Likewise, the multivariate logistic regression analysis results showed that the male partner-related factor variables such as lack of formal education (AOR = 3.06; 95% CI: 1.53–6.14; P -value < 0.001), weak (AOR = 4.17; 95% CI: 1.45–12.03; P -value < 0.001) and medium levels of religious belief (AOR = 1.64; 95% CI: 1.13–2.39; P -value < 0.05), alcohol-drinking habit of the male partner (AOR = 5.91; 95% CI: 4.03–8.67; P -value < 0.001), and smoking habit (AOR = 2.04; 95% CI: 1.10–3.77; P -value < 0.05) of the male

TABLE 5 Bivariate logistic regression analysis of the association of woman-related factors with IPV among women of reproductive age in Debre Berhan town, 2021 (*n* = 796).

Variable	Category	Any IPV		COR (95% CI)	P-value
		No Fr (%)	Yes Fr (%)		
Age of woman (years)	18–28	209 (63.0)	123 (37.0)	0.42 (0.27–0.67)	0.000
	29–38	210 (57.1)	158 (42.9)	0.54 (0.34–0.85)	0.008
	39–45	40 (41.7)	56 (58.3)	1	
Woman education	No formal education	44 (38.3)	71 (61.7)	7.24 (4.25–12.33)	0.000
	Primary education	97 (44.9)	119 (55.1)	5.50 (3.46–8.74)	0.000
	Junior education	75 (51.7)	70 (48.3)	4.19 (2.54–6.89)	0.000
	Secondary education	95 (68.3)	44 (31.7)	2.08 (1.24–3.49)	0.006
	Diploma and above	148 (81.8)	33 (18.2)	1	
Woman occupation	Farmer	9 (64.3)	5 (35.7)	0.73 (0.23–2.27)	0.583
	Manual worker	46 (52.9)	41 (47.1)	1.17 (0.69–1.98)	0.571
	Housewife	188 (56.1)	147 (43.9)	1.02 (0.69–1.51)	0.911
	Trader/Pettit-trade	131 (62.4)	79 (37.6)	0.79 (0.52–1.21)	0.276
	Govt./NGO emp.	85 (56.7)	65 (43.3)	1	
Woman religion	Others	30 (62.5)	18 (37.5)	0.85 (0.46–1.55)	0.590
	Muslim	65 (51.6)	61 (48.4)	1.32 (0.90–1.94)	0.152
	Orthodox	364 (58.5)	258 (41.5)	1	
Residence	Rural kebeles	71 (61.7)	44 (38.3)	0.82 (0.55–1.23)	0.339
	Urban kebeles	388 (57.0)	293 (43.0)	1	
Relation status	Unmarried	118 (55.7)	94 (44.3)	1.12 (0.81–1.54)	0.491
	Married	341 (58.4)	243 (41.6)	1	
Woman has own income	No	203 (51.8.)	189 (41.2)	1.61 (1.21–2.14)	0.001
	Yes	256 (63.4)	148 (36.6)	1	
Woman access to media	No	33 (50.8)	32 (49.2)	1.35 (0.82–2.25)	0.242
	Yes	426 (58.3)	305 (41.7)	1	
Pregnancy status	Pregnant	58 (55.2)	47 (44.8)	1.12 (0.74–1.69)	0.589
	Not pregnant	401 (58.0)	290 (42.0)	1	
Woman attitude on IPV	Acceptable	6 (24.0)	19 (76.0)	4.51 (1.78–11.42)	0.001
	Not acceptable	453 (58.8)	328 (41.2)	1	

IPV, intimate partner violence; COR, crude odds ratio; CI, confidence interval.

partner showed significant association with the presence of any IPV (Tables 6, 8).

Regarding the family-related risk factor variables, the multivariate logistic regression analysis results showed that the family size of four to five members (AOR = 1.73; 95% CI: 1.03–2.92; *P*-value < 0.05) and family size of more than five members (AOR = 1.83; 95% CI: 1.01–3.39; *P*-value < 0.05) showed significant association with the presence of any IPV (Tables 7, 8). In contrast, factors such as the age of the woman, the age of the male partner, occupation of the male partner, and the presence of children did not show significant association with the presence of any IPV, considering *P*-values of < 0.05, regardless of the level of association each of these variables showed in the bivariate analysis (Tables 7, 8).

3.3.2. Analysis of risk factors associated with each of the three types of violence

In addition to the analyses of the risk factors associated with the presence of any IPV (at least one of the three types of violence) as presented above, the present study also attempted to analyze risk factors associated with each of the three types of violence psychological, physical, and sexual violence separately. Similar statistical procedures were applied. The separate analysis results are explicitly presented in the **supplementary annex 5**.

At the same time, analysis results for the factors that had significant association with each type of violence are presented in the text and a table herewith. Accordingly, the education status of women below a diploma, a woman with the occupation of farmer

TABLE 6 Bivariate logistic regression analysis of the association of male partner-related factors with IPV among women of reproductive age in Debre Berhan, 2021 (*n* = 796).

Variable	Category	Any IPV		COR (95% CI)	P-value
		No Fr (%)	Yes Fr (%)		
Age of male partner (years)	20–30	154 (62.6)	92 (37.4)	0.54 (0.36–0.81)	0.003
	31–40	235 (58.5)	167 (41.5)	0.64 (0.44–0.93)	0.020
	41– 68	70 (47.3)	78 (52.7)	1	
Male partner education	No formal education	25 (32.5)	52 (67.5)	5.08 (2.93–8.81)	0.000
	Primary education	90 (45.2)	109 (54.8)	2.96 (2.00–4.38)	0.000
	Junior education	73 (59.3)	50 (40.7)	1.67 (1.07–2.63)	0.026
	Secondary education	95 (63.8)	54 (36.2)	1.39 (0.90–2.14)	0.136
	Diploma and above	176 (71.0)	72 (29.0)	1	
Male partner occupation	Farmer	37 (52.1)	34 (47.9)	1.61 (0.96–2.70)	0.074
	Manual worker	93 (51.1)	89 (48.9)	1.67 (1.16–2.42)	0.006
	Trader/Pettit-trade	128 (56.4)	99 (43.6)	1.35 (0.95–1.92)	0.090
	Govt./NGO employee	201 (63.6)	115 (36.4)	1	
Male partner own income	No	23 (46.9)	26 (53.1)	1.59 (0.89–2.83)	0.119
	Yes	436 (58.4)	311 (41.6)	1	
Religious belief of the male partner	Weak	7 (23.3)	23 (76.7)	7.36 (3.04–17.78)	0.000
	Medium	255 (53.0)	226 (47.0)	1.98 (1.46–2.70)	0.000
	Strong	197 (69.1)	88 (30.9)	1	
Alcoholic habit of the male partner	Yes	77 (28.8)	190 (71.2)	6.41 (4.63–8.88)	0.000
	No	382 (72.2)	147 (27.8)	1	
Smoking habit of the male partner	Yes	20 (24.4)	62 (75.6)	4.95 (2.92–8.38)	0.000
	No	439 (61.5)	275 (38.5)	1	

IPV, intimate partner violence; COR, crude odds ratio; CI, confidence interval.

and housewife, a woman with no own income, a woman with the thought that IPV is acceptable, a male partner without formal education, and a male partner with alcohol-drinking habit were significant predictors of psychological violence (**Table 9**).

Likewise, a woman with an education below diploma, a woman without income, and male partners with alcohol-drinking and smoking habits were the significant predictors of physical violence (**Table 9**). Also, a woman with junior education, no own income, thought of IPV as acceptable, and no access to media, male partners without formal education, strong religious beliefs, and smoking habits, and larger family sizes were the main predictors of sexual violence (**Table 9**).

4. Discussion

Investigation of the prevalence of IPV in women of reproductive age and associated factors in various localities of a given country, particularly during emergencies, including pandemics, is vital for intervention strategies. Accordingly, the present study assessed the prevalence of IPV in women of reproductive age and associated factors in Debre Berhan during the COVID-19 pandemic.

The present study revealed a high overall prevalence of IPV (42.3%) in the study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic. This figure was significantly higher than the overall prevalence of IPV (24.6%) revealed by a previous study conducted in Aksum town, Ethiopia, during the COVID-19 pandemic (20). This finding was also significantly higher compared with 29%, 30%, 37.1%, and 37.5% lifetime prevalence of IPV in women of reproductive age reported in the Amhara region (29), nationwide (30), Debre Tabor town (47), and in the Tigray district (22), respectively, before the pandemic. The present finding was equivalent to the overall IPV prevalence of 40%–50% in Brazil during the COVID-19 pandemic (25), 48% lifetime IPV prevalence in Saudi Arabia (43), and 40.9%–45.2% in Zimbabwe (46). The disparities observed in the overall prevalence of IPV among studies might be due to variations in sociodemographic characteristics of the study participant women, education status of the male partners, addiction status of the male partner, family-related risk factors, duration of data collection periods, and variations in reactions of the communities to the pandemic.

In addition, the present study revealed the highest prevalence of psychological violence (35.3%) among all three forms of IPV,

TABLE 7 Bivariate logistic regression analysis of the association of family-related factors with IPV among women of reproductive age in Debre Berhan, 2021 (*n* = 796).

Variable	Category	Any IPV		COR (95% CI)	P-value
		No Fr (%)	Yes Fr (%)		
Family size	≤3	179 (67.5)	86 (32.5)	1	
	4–5	167 (55.7)	133 (44.3)	1.66 (1.18–2.34)	0.004
	≥ 6	113 (48.9)	118 (51.1)	2.17 (1.51–3.13)	0.000
Presence of children	Yes	372 (55.0)	304 (45.0)	2.15 (1.40–3.31)	0.000
	No	87 (72.5)	33 (27.5)	1	
Number of children	None	87 (72.5)	33 (27.5)	1	
	Single	128 (64.3)	71 (35.7)	1.46 (0.89–2.40)	0.132
	2–4	238 (51.5)	224 (48.5)	2.48 (1.60–3.85)	0.000
	≥5	6 (40.0)	9 (60.0)	3.96 (1.31–11.98)	0.015
Extended family living together	Present	211 (54.5)	176 (45.5)	1.29 (0.97–1.70)	0.081
	Not present	248 (60.6)	161 (39.4)	1	
Monthly family income in ETB	≤1,000	67 (56.8)	51 (43.2)	0.76 (0.34–1.70)	0.505
	1,001–3,500	175 (59.3)	120 (40.7)	0.69 (0.32–1.46)	0.326
	3,501–6,000	138 (58.2)	99 (41.8)	0.72 (0.34–1.54)	0.392
	6,001–10,000	64 (55.2)	52 (44.8)	0.81 (0.36–1.82)	0.613
	>10,000	15 (50.0)	15 (50.0)	1	

IPV, intimate partner violence; COR, crude odds ratio; CI, confidence interval; ETB, Ethiopian birr.

followed by physical (15.3%) and sexual (15.3%) violence. Regarding the ranks within the three types of violence, the present study finding was consistent with results from previous studies conducted in Ethiopia and elsewhere (15, 20, 43). Concerning the prevalence of each of the three types of violence, psychological, physical, and sexual violence, the present study found higher prevalence of IPV in each of the respective types of violence than those revealed by a study done in Aksum town, Ethiopia (20) and a study conducted in Vitória, State of Espírito Santo, Brazil (15). In contrast to the present findings of the prevalence of each of the three types of IPV, higher lifetime prevalence of psychological (48.5%), physical (34.8%), and sexual (16.8%) violence was reported by a study done in Saudi Arabia before the COVID-19 pandemic (43).

In addition to the understanding of the overall prevalence of any IPV and each of the three types of violence, a systematic investigation of the significant factors associated with the presence of IPV is fundamental for enhanced intervention strategies. For that reason, the present study also tried to assess the factors associated with the presence of any IPV (at least one type of violence).

According to the results of the present study, the women-related factors such as woman's education status, own income, and attitude toward acceptance of IPV were strongly associated with the presence of any IPV among women of reproductive age in Debre Berhan.

The chance of having at least one type of IPV was about 3.7 times higher in women who have no formal education, 3.5 times higher in women who have primary education, and 3.4 times higher in women who have junior education compared with the women who have a diploma or above. The present finding on the significant association of lower education status of a woman with the presence

of IPV was consistent with the findings of previous studies done in several parts of Ethiopia (29, 30, 48) and elsewhere (15). This might be due to the lower awareness of less educated women to refuse IPV and guard themselves by the law or other ways.

Regarding the other woman-related factors that showed significant association with the presence of any IPV among the present study participants, the likelihood of experiencing at least one type of IPV was about 1.8 times higher among women who reported they lacked income compared with the women who reported having their own income. The present finding on the significant association of the lack of own income of women with the presence of any IPV was consistent with the findings of previous studies done in Ethiopia (30), Zimbabwe (46), and Brazil (15). This might be due to the fact that women who are economically dependent on male partners or are not self-reliant have insufficient capacity to defend themselves from such troubles.

The attitude of women regarding the acceptability of IPV is the most important women-related risk factor that showed a strong significant association with the presence of any IPV. Given that, the chance of experiencing at least one type of IPV was about four times higher among women who reported IPV as acceptable compared with those women who reported IPV as not acceptable. This finding was in agreement with the findings of previous studies conducted on women in Ofla district (22), Debre Tabor town, Ethiopia (66), and Uganda (65). This might be related to the fact that women who think IPV is acceptable are less likely to refuse violence against them by male partners, which might further enable male partners to view the violence they do against women partners as a normal act rather than a taboo.

TABLE 8 Bivariate and multivariate logistic regression analysis of the association of selected risk factors with IPV among women of reproductive age in Debre Berhan, 2021 (*n* = 796).

Variable	Category	OR (95% CI)	
		Crude	Adjusted
Age of woman (years)	18–28	0.42 (0.27–0.67)**	0.88 (0.38–2.04)
	29–38	0.54 (0.34–0.85)**	0.90 (0.44–1.82)
	39–45	1	1
Woman education	No formal education	7.24 (4.25–12.33)**	3.66 (1.91–6.98)**
	Primary education	5.50 (3.46–8.74)**	3.52 (2.04–6.07)**
	Junior education	4.19 (2.54–6.89)**	3.35 (1.87–6.02)**
	Secondary education	2.08 (1.24–3.49)**	1.79 (0.97–3.28)
	Diploma and above	1	1
Woman has own income	No	1.61 (1.21–2.14)**	1.78 (1.24–2.56)**
	Yes	1	1
Woman access to media	No	1.35 (0.82–2.25)	0.98 (0.51–1.88)
	Yes	1	1
Woman attitude on IPV	Acceptable	4.51 (1.78–11.42)**	4.02 (1.33–12.14)*
	Not acceptable	1	1
Age of the male partner (years)	20–30	0.54 (0.36–0.81)**	1.03 (0.48–2.21)
	31–40	0.64 (0.44–0.93)*	0.88 (0.48–1.61)
	41–68	1	1
Male partner education status	No formal education	5.08 (2.93–8.81)**	3.06 (1.53–6.14)**
	Primary education	2.96 (2.00–4.38)**	1.46 (0.85–2.50)
	Junior education	1.67 (1.07–2.63)*	0.93 (0.51–1.68)
	Secondary education	1.39 (0.90–2.14)	0.91 (0.52–1.61)
	Diploma and above	1	1
Male partner occupation	Farmer	1.61 (0.96–2.70)	0.50 (0.24–1.02)
	Manual worker	1.67 (1.16–2.42)**	0.95 (0.56–1.62)
	Trader/Pettit-trade	1.35 (0.95–1.92)	0.76 (0.48–1.22)
	Govt./NGO employee	1	1
Male partner has own income	No	1.59 (0.89–2.83)	1.82 (0.85–3.92)
	Yes	1	1
Religious belief of the male partner	Weak	7.36 (3.04–17.78)**	4.17 (1.45–12.03)**
	Medium	1.98 (1.46–2.70)**	1.64 (1.13–2.39)*
	Strong	1	1
Alcohol habit of the male partner	Yes	6.41 (4.63–8.88)**	5.91 (4.03–8.67)**
	No	1	1
Smoking habit of the male partner	Yes	4.95 (2.92–8.38)**	2.04 (1.10–3.77)*
	No	1	1
Family size	3 and below	1	1
	4–5	1.66 (1.18–2.34)**	1.73 (1.03–2.92)*
	6 and above	2.17 (1.51–3.13)**	1.85 (1.01–3.39)*
Presence of children	Yes	2.15 (1.40–3.31)**	1.39 (0.74–2.61)
	No	1	1

(continued)

TABLE 8 Continued

Variable	Category	OR (95% CI)	
		Crude	Adjusted
Number of children ^a	No child	1	—
	Single child	1.46 (0.89–2.40)	—
	2–4 children	2.48 (1.60–3.85)**	—
	≥5 children	3.96 (1.31–11.98)*	—
Extended family living together	Present	1.29 (0.97–1.70)	1.05 (0.70–1.59)
	Not present	1	1

IPV, intimate partner violence; OR, odds ratio; CI, confidence interval.

^aVariable(s) not included in the multivariate analysis due to collinearity with other variable(s).*Significant at $P < 0.05$; **Significant at $P < 0.01$.

In the same way, the present study revealed the male partner-related risk factor variables, such as low educational status, poor religious beliefs, alcohol consumption, and smoking habit of male partners, were significantly associated with the presence of any IPV.

The odds of having at least one type of IPV were about 3.1 times higher in women whose partners have no formal education than women whose male partners have a diploma or above. The present finding regarding the significant association of lower education status of male partners with the presence of IPV against women was in harmony with the findings of previous studies done in Brazil (15, 67), Sudan (45), and Ethiopia (29). This might be due to a poorer tendency to handle conditions that may lead to violence among less educated male partners.

The likelihood of experiencing at least one type of IPV was about 4.2 times and 1.6 times higher in women whose male partners have weak and medium levels of religious beliefs, respectively, compared to women whose male partners have strong religious beliefs. Even if there are theoretical frames that showed the connection between the level of religious beliefs with the attitude of male partners toward taking violent actions against women, empirical evidence reporting the significance of the association of the variable with the occurrence of IPV is rare.

The chance of experiencing at least one type of IPV among women whose male partners have alcohol consumption habits was about 5.9 times higher than women whose male partners are nonalcoholic. The present study finding on the significant association of alcohol consumption habits of male partners with the presence of IPV against women was consistent with previous studies done in Brazil (15, 67), Nigeria (31), Sudan (45), and different parts of Ethiopia (22, 29, 48).

The odds of having at least one type of IPV in women whose male partners have smoking habits were about two times higher than their counterparts. The present finding on the significant association of the smoking habit of male partners with the presence of IPV against women was consistent with the finding of a previous study done elsewhere (67). The significant associations of the above drug use habits of male partners with the presence of any IPV can be explained by the effect the chemicals in the aforesaid drugs can cause on the functioning of the brain of users and by the social and economic consequences of drug addiction.

TABLE 9 Bivariate and multivariate logistic regression analyses of the association of factors with each type of IPV among women of reproductive age in Debre Berhan, 2021 ($n = 796$).

Variable	Category	Violence		P-value	COR (95%CI)	P-value	AOR (95% CI)
		No	Yes				
Psychological violence							
Woman education	No formal education	59	56	0.000	5.66 (3.25–9.84)	0.001	3.26 (1.66–6.38)
	Primary education	109	107	0.000	5.85 (3.57–9.59)	0.000	4.92 (2.73–8.87)
	Junior education	89	56	0.000	3.75 (2.20–6.39)	0.000	3.28 (1.76–6.13)
	Secondary education	103	36	0.011	2.08 (1.19–3.66)	0.028	2.07 (1.08–3.96)
	Diploma and above	155	26	1		1	
Woman occupation	Farmer	13	1	0.066	0.15 (0.02–1.14)	0.001	0.02 (0.01–0.20)
	Labor worker	51	36	0.303	1.33 (0.77–2.29)	0.052	0.47 (0.22–1.01)
	Housewife	213	122	0.710	1.08 (0.72–1.62)	0.004	0.38 (0.20–0.74)
	Trader/petit-trade	140	70	0.792	0.94 (0.61–1.47)	0.373	0.77 (0.44–1.36)
	Govt./NGO employee	98	52	1		1	
Woman has own income	No	280	124	0.006	1.51 (1.13–2.02)	0.000	2.79 (1.71,4.56)
	Yes	235	157	1		1	
Male partner education	No formal education	34	43	0.000	3.56 (2.09–6.06)	0.033	2.13 (1.06–4.28)
	Primary education	109	90	0.000	2.33 (1.56–3.46)	0.639	1.14 (0.66–1.99)
	Junior education	86	37	0.432	1.21 (0.75–1.95)	0.316	0.73 (0.39–1.35)
	Secondary education	103	46	0.317	1.26 (0.80–1.97)	0.427	0.79 (0.43–1.42)
	Diploma and above	183	65	1		1	
Alcohol habit of the male partner	Yes	98	169	0.000	6.42 (4.64–8.88)	0.000	6.31 (4.30–9.27)
	No	417	112	1		1	
Physical violence							
Woman education	No formal education	92	23	0.000	8.80 (3.24–23.91)	0.007	4.49 (1.52–13.31)
	Primary education	169	47	0.000	9.79 (3.80–25.21)	0.001	5.66 (2.05–15.65)
	Junior education	117	28	0.000	8.42 (3.16–22.44)	0.001	6.17 (2.15–17.70)
	Secondary education	120	19	0.001	5.57 (2.03–15.33)	0.002	5.44 (1.85–16.00)
	Diploma and above	176	5	1		1	
Woman has own income	No	323	69	0.080	1.42 (0.96–2.09)	0.020	1.76 (1.09–2.84)
	Yes	351	53	1		1	
Alcohol habit of the male partner	Yes	177	90	0.000	7.90 (5.09–12.24)	0.000	5.58 (3.46–8.99)
	No	497	32	1		1	
Smoking habit of the male partner	Yes	42	40	0.000	7.34 (4.50–11.99)	0.000	4.46 (2.51–7.95)
	No	632	82	1		1	
Sexual violence							
Woman education	No formal education	87	28	0.000	4.53 (2.20–9.35)	0.194	1.77 (0.76–4.17)
	Primary education	180	36	0.003	2.82 (1.42–5.59)	0.377	1.43 (0.65–3.13)
	Junior education	115	30	0.000	3.67 (1.81–7.47)	0.005	3.19 (1.42–7.14)
	Secondary education	124	15	0.188	1.70 (0.77–3.77)	0.447	1.41 (0.58–3.44)
	Diploma and above	169	12	1		1	
Woman has own income	No	355	49	0.015	1.63 (1.10–2.42)	0.001	2.21 (1.37–3.57)

(continued)

TABLE 9 Continued

Variable	Category	Violence		P-value	COR (95%CI)	P-value	AOR (95% CI)
		No	Yes				
Woman access to media	Yes	320	72	1		1	
	No	47	18	0.004	2.34 (1.31–4.18)	0.007	2.83 (1.33–6.02)
	Yes	628	103	1		1	
Attitude of women toward IPV	Acceptable	13	12	0.000	5.61 (2.49–12.61)	0.000	7.35 (2.76–19.62)
	Not acceptable	662	109	1		1	
Male partner education	No formal education	50	27	0.000	7.34 (3.72–14.47)	0.000	4.90 (2.13–11.25)
	Primary education	162	37	0.000	3.10 (1.69–5.70)	0.387	1.40 (0.65–3.02)
	Junior education	105	18	0.018	2.33 (1.16–4.70)	0.759	1.14 (0.50–2.60)
	Secondary education	127	22	0.012	2.35 (1.21–4.60)	0.419	1.39 (0.63–3.08)
	Diploma and above	231	17	1		1	
Religious belief of the male partner	Weak	19	11	0.000	6.92 (2.93–16.37)	0.018	3.41 (1.24–9.37)
	Medium	393	88	0.000	2.68 (1.64–4.38)	0.001	2.46 (1.42–4.29)
	Strong	263	22	1		1	
Smoking habit of the male partner	Yes	53	29	0.000	3.70 (2.24–6.12)	0.003	2.48 (1.35–4.55)
	No	622	92	1		1	
Family size	≤3	237	28	1		1	
	4–5	254	46	0.095	1.53 (0.93–2.53)	0.039	2.08 (1.04–4.17)
	≥ 6	184	47	0.003	2.16 (1.30–3.59)	0.003	3.01 (1.44–6.29)

IPV, intimate partner violence; COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval.

Regarding the family-related risk factor variables, the present study revealed that family size was the only association factor significantly associated with the presence of any IPV among the present study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic.

Accordingly, the chances of having at least one type of IPV were about 1.7 and 1.8 times higher among women with family sizes of 4–5 and above 5, respectively, compared with those with a family size of less than 4. This finding of the present study can be explained by the resource and other economic issues or limitations often linked to a large family size, which might aggravate the occurrence of IPV (47). However, empirical evidence that revealed the significant association of the risk factor with the presence of IPV is rare. The study was done by using standardized questionnaires, assessing IPV specifically during the COVID-19 pandemic, and using a wider time frame to collect data, including ever-partnered rather than ever-married women. However, the present study has not supported the quantitative finding with qualitative triangulation.

5. Recommendations and conclusions

The present study revealed a high overall prevalence of IPV in the study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic, which evidences a major public health significance that needs critical attention. The high overall prevalence of any IPV in the study participants proves that about

nine of every twenty women of reproductive age in the town are at risk of experiencing at least one of the three types of IPV during the COVID-19 pandemic.

Regarding the prevalence of each of the three types of IPV in women, the present study disclosed that psychological violence was the most prevalent type of IPV, followed by physical and sexual violence, among the study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic. The study showed that about 7 of every 20 women of reproductive age in the town are at risk of having psychological violence, about 3 of every 20 women of reproductive age in the town are at risk of having physical violence, and about 3 of every 20 women of reproductive age in the town are at risk of experiencing sexual violence by an intimate partner during the COVID-19 pandemic.

Statistical analyses revealed that the high prevalence of any IPV in the study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic was significantly associated with multiple risk factors related to women, male partners, and families. The woman-related risk factors of woman's lower educational status, lack of own income, and attitude toward IPV as acceptable; the male partner-related risk factors of male partner's lower educational status, poor religious beliefs, and alcohol-drinking and smoking habits; and the family-related risk factors of large family size were significantly associated with the presence of any IPV among the present study participant women of reproductive age in Debre Berhan during the COVID-19 pandemic.

Based on the main findings of the present study, the following recommendations have been given to the respective bodies.

In making decisions and in planning to tackle the problem of IPV in the long run, policymakers should take into account the need to address the main risk factors significantly predicting the presence of any IPV. As a result, ways to improve the educational status of girls (women), empower women economically, and provision of tailored health education programs regarding the miss-thoughts of women, such as the attitude of accepting IPV, should be devised. Policymakers should also make ways of identifying and tackling the coexisting consequences such as IPV in settings where pandemics are occurring.

In addition, whenever policymakers are working on future attempts to recover some of the social, economic, and health impacts of the COVID-19 pandemic across communities, they should also take into account the high prevalence of IPV against women in different parts of Ethiopia, including the present study area, Debre Berhan, and the long-lasting effect that IPV causes on its victims.

The North Shoa Zone and Debre Berhan health offices should work in collaboration with other sectors that are working on gender-related issues in the zone and the town regarding various issues related to women empowerment and family planning and also work toward the diffusion of information and concepts on the existing laws that may help the women to protect themselves from violent acts of male partners.

Further researchers should conduct prevalence studies in different localities of the country where data regarding the prevalence of IPV and associated risk factors during the current COVID-19 pandemic are not available. In addition, future researchers should also try to integrate qualitative study methods and more specific variables that can directly measure the impact of the COVID-19 pandemic (or future pandemics) on each of the study units.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Debre Berhan University, IRB. The patients/participants provided their written informed consent to participate in this study.

References

1. Unite Nations. Declaration on the elimination of violence against women, UN General Assembly. Geneva: United Nations (1993). p. 1–2. Available at: <http://www.un.org/documents/ga/res/48/a48r104.htm> (Accessed December 25, 2020).
2. Russo NF, Pirolot A. Gender-based violence concepts, methods, and findings. *Ann NY Acad Sci.* (2006) 1087(2006):178–205. doi: 10.1196/annals.385.024
3. Hosain M, McAlpine A. *Gender-based violence research methodologies in humanitarian settings: An evidence review and recommendations.* Cardiff: Elrha (2017).
4. Swedish International Development Cooperation Agency. *Preventing and responding to gender-based violence: expressions and strategies.* Stockholm: SIDA (2015). ISBN: 978-91-586-4251-5.
5. García-Moreno C, Jansen HAFM, Ellsberg M, Heise L, Watts C. *WHO multi-country study on women's health and domestic violence against women: initial results on prevalence, health outcomes and women's responses.* Geneva: World Health Organization (2005).
6. World Health Organization. *Understanding and addressing violence against women.* Geneva: WHO (2012).

Acknowledgments

The authors acknowledge Debre Berhan University, College of Health Science, Department of Public Health for providing them with this opportunity to research into their area of interest. The authors extend their gratitude to the study participant women for their willingness to take part in this study and genuinely provide the necessary information. Also, the authors express their heartfelt thanks to the data collectors and supervisors, who unreservedly devoted and completed their duty in the data collection process.

Author contributions

Conceptualization, investigation, methodology, and writing—original draft: ETS. Project administration, software, supervision, validation, visualization, and writing—review and editing: MGD. Data curation, formal analysis, and resources: MGD and ETS. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fgwh.2022.977153/full#supplementary-material>.

7. World Health Organization. *Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence*. Geneva: WHO (2013).
8. World Health Organization. *Violence against women: key facts*. Geneva: World Health Organization (2017). p. 29. Available at: <https://www.who.int/newsroom/factsheets/detail/violenceagainst-women> (Accessed November 23, 2020).
9. Miller E, McCaw B. Intimate partner violence. *N Engl J Med.* (2019) 2019 (380):850–7. doi: 10.1056/NEJMr1807166
10. Bott S, Guedes A, Ruiz-Celis AP, Mendoza JA. Intimate partner violence in the Americas: a systematic review and reanalysis of national prevalence estimates. *Rev Panam Salud Publica.* (2019) 43:e26. doi: 10.26633/RPSP.2019.26
11. Vives-Cases C, Ruiz-Cantero MT, Escriba-Aguir V, Miralles JJ. The effect of intimate partner violence and other forms of violence against women on health. *J Public Health (Oxf).* (2011) 33(1):15–21. doi: 10.1093/pubmed/fdq101
12. Beydoun HA, Beydoun MA, Kaufman JS, Lo B, Zonderman AB. Intimate partner violence against adult women and its association with major depressive disorder, depressive symptoms and postpartum depression: a systematic review and meta-analysis. *Soc Sci Med.* (2012) 75(6):959–75. doi: 10.1016/j.socscimed.2012.04.025
13. Ellsberg M, Jansen HAFM, Heise L, Watts CH, Garcia-Moreno C. Intimate partner violence and women's physical and mental health in the WHO multi-country study on women's health and domestic violence: an observational study. *Lancet.* (2008) 371 (9619):1165–72. doi: 10.1016/S0140-6736(08)60522-X
14. Bonomi AE, Thompson RS, Anderson M, Reid RJ, Carrell D, Dimer JA, et al. Intimate partner violence and women's physical, mental, and social functioning. *Am J Prev Med.* (2006) 30(6):458–66. doi: 10.1016/j.amepre.2006.01.015
15. Leite FMC, Amorim MHC, Wehrmeister FC, Gigante DP. Violence against women, Espírito Santo, Brazil. *Rev Saúde Pública.* (2017) 51(33):4–5. doi: 10.1590/S1518-8787.2017051006815
16. Swiss S, Jennings PJ, Aryee GV, Brown GH, Jappah-Samukai RM, Kamara MS, et al. Violence against women during the Liberian civil conflict. *JAMA.* (1998) 279 (8):625–9. doi: 10.1001/jama.279.8.625
17. Hossain M. Evaluation of a violence prevention intervention and lessons for future research in conflict settings: Working with men to prevent violence against women—a community survey, cluster randomised controlled trial and nested cohort study in Côte d'Ivoire (2015).
18. Muluneh MD, Stulz V, Francis L, Agho K. Gender based violence against women in sub-Saharan Africa: a systematic review and meta-analysis of cross-sectional studies. *Int J Environ Res Public Health.* (2020) 17:903. doi: 10.3390/ijerph17030903
19. Gupta J, Falb K, Kpebo D, Annan J. Abuse from in-laws and associations with attempts to control reproductive decisions among rural women in Cote d'Ivoire: a cross-sectional study. *BJOG.* (2012) 119(9):1058–66. doi: 10.1111/j.1471-0528.2012.03401.x
20. Gebrewahd GT, Gebremeskel GG, Tadesse DB. Intimate partner violence against reproductive age women during COVID-19 pandemic in northern Ethiopia 2020: a community-based cross-sectional study. *Reprod Health.* (2020) 17(152):3–4. doi: 10.1186/s12978-020-01002-w
21. Girmay A, Mariye T, Bahrey D, Hailu B, Iyasu A, G/medhin G, et al. Intimate partner physical violence and associated factors in reproductive age married women in Aksum Town, Tigray, Ethiopia 2018, and community based study. *BMC Res Notes.* (2019) 12(1):627. doi: 10.1186/s13104-019-4615-3
22. Adhena G, Oljira L, Dessie Y, Hidru HD. Magnitude of intimate partner violence and associated factors among pregnant women in Ethiopia. *Hindawi Adv Public Health.* (2020) 2020:1682847. doi: 10.1155/2020/1682847
23. United Nations Women. COVID-19 and violence against women and girls: addressing the shadow pandemic. Policy Brief No. 17. New York: UN-Women (2020). Available at: www.unwomen.org (accessed 2020)
24. Evans DP. COVID-19 and violence: a research call to action. *BMC Women's Health.* (2020) 20(249):2–5. doi: 10.1186/s12905-020-01115-1
25. Sharifi F, Larki M, Roudsari RL. COVID-19 outbreak as threat of violence against women. *J Midwifery Reprod Health.* (2020) 8(3):2376–9. doi: 10.22038/JMRH.2020.16036
26. Alon TM, Olmstead-Rumsey J, Doepeke M, Tertilt M. *The impact of COVID 19 on gender equality: working paper national bureau of economic research*. Massachusetts: Cambridge University (2020).
27. Bradbury-Jones C, Isham L. The pandemic paradox: the consequences of COVID-19 on domestic violence. *J Clin Nurs.* (2020) 2020(29):2047–49. doi: 10.1111/jocn.15296
28. Federal Ministry of Health and Ethiopian Public Health Institute. *COVID-19 prevention and control quarantine and border control implementation guide*. Addis Ababa: MOH, EPHI (2020).
29. Alebel A, Kibret GD, Wagnew F, Tesema C, Ferede A, Petrucca P, et al. Intimate partner violence and associated factors among pregnant women in Ethiopia: a systematic review and metaanalysis. *Reprod Health.* (2018) 15(196):2–7. doi: 10.1186/s12978-018-0637-x
30. Chernet AG, Cherie KT. Prevalence of intimate partner violence against women and associated factors in Ethiopia. *BMC Womens Health.* (2020) 20(22):5–7. doi: 10.1186/s12905-020-0892-1
31. Oche OM, Adamu H, Abubakar A, Aliyu MS, Dogondaji AS. Intimate partner violence in pregnancy: knowledge and experiences of pregnant women and controlling behavior of male partners in Sokoto, Northwest Nigeria. *Hindawi Int J Reprod Med.* (2020) 2020:7626741. doi: 10.1155/2020/7626741
32. Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: relevance for HIV prevention in hyperendemic countries of Southern Africa. *AIDS.* (2008) 2008(4): S73–86. doi: 10.1097/01.aids.0000341778.73038.86
33. Reynolds DL, Garay JR, Deamond SL, Moran MK, Gold W, Styra R. Understanding compliance and psychological impact of the SARS quarantine experience. *Epidemiol Infect.* (2008) 136(9):997–1007. doi: 10.1017/S0950268807009156
34. Rose C. Plague and violence in early modern Italy. *Renaissance Q.* (2018) 2018 (71):1000–35. doi: 10.1086/699602
35. Sabbatani S, Fiorino S. The Antonine plague and the decline of the roman empire. *Infez Med.* (2009) 2009(17):261–75.
36. Silverman JG, Decker MR, Sagurto N, Balaiah D, Raj A. Intimate partner violence and HIV infection among married Indian women. *J Am Med Assoc.* (2008) 2008 (300):703–10. doi: 10.1001/jama.300.6.703
37. Hawryluck L, Gold WL, Robinson S, Pogorski S, Galea S, Styra R. SARS control and psychological effects of quarantine, Toronto, Canada. *Emerg Infect Dis.* (2002) 2004(10):1206–12. doi: 10.3201/eid1007.030703
38. Van Gelder N, Peterman A, Potts A, O'Donnell M, Thompson K, Shah N, et al. COVID-19: reducing the risk of infection might increase the risk of intimate partner violence. *EClinicalMedicine.* (2020) 2020(21):1–2. doi: 10.1016/j.eclinm.2020.100348
39. Waksman RD, Blank D. The importance of domestic violence in times of COVID-19. *Residência Pediátrica.* (2020). doi: 10.25060/residpediatr-2020.v10n2-414
40. Mazza M, Marano G, Lai C, Janin L, Sani G. Danger in danger: interpersonal violence during COVID-19 quarantine. *Psychiatry Res.* (2020) 2020(289):1–3. doi: 10.1016/j.psychres.2020.113046
41. Mittal S, Singh T. Gender-based violence during COVID-19 pandemic: a mini-review. *Front Glob Womens Health.* (2020) 1(4):4–5. doi: 10.3389/fghw.2020.00004
42. Elghossain T, Bott S, Akik C, Obermeyer CM. Prevalence of intimate partner violence against women in the Arab world: a systematic review. *BMC Int Health Hum Rights.* (2019) 19(29):2–4. doi: 10.1186/s12914-019-0215-5
43. Wali R, Khalil A, Alattas R, Foudah R, Meftah I, Sarhan S. Prevalence and risk factors of domestic violence in women attending the national guard primary health care centers in the western region, Saudi Arabia, 2018. *BMC Public Health.* (2020) 20:239. doi: 10.1186/s12889-020-8156-4
44. Falb KL, Annan J, Kpebo D, Gupta J. Reproductive coercion and intimate partner violence among rural women in Côte d'Ivoire: a cross-sectional study. *Afr J Reprod Health.* (2014) 18(4):61.
45. Ali AA, Yassin K, Omer R. Domestic violence against women in eastern Sudan. *BMC Public Health.* (2014) 14:1136. doi: 10.1186/1471-2458-14-1136
46. Iman'ishimwe Mukamana J, Machakanja P, Adjei NK. Trends in prevalence and correlates of intimate partner violence against women in Zimbabwe, 2005–2015. *BMC Int Health Hum Rights.* (2020) 20(2):3–7. doi: 10.1186/s12914-019-0220-8
47. Azanaw KA, Gelagay AA, Lakew AM, Teshome DF. Physical violence and associated factors among housemaids living in Debre-Tabor Town, northwest Ethiopia: does employer alcohol intake increase housemaid violence? *Hindawi Int J Reprod Med.* (2019) 2019:8109898. doi: 10.1155/2019/8109898
48. Girmay A, Mariye T, Bahrey D, Hailu B, Iyasu A, G/medhin G, et al. Intimate partner physical violence and associated factors in reproductive age married women in Aksum Town, Tigray, Ethiopia 2018, and community based study. *BMC Res Notes.* (2019) 12:627. doi: 10.1186/s13104-019-4615-3
49. Palermo T, Peterman A. Undercounting, overcounting, and the longevity of flawed estimates: statistics on sexual violence in conflict. *Bull World Health Org.* (2011) 2011 (89):924–26. doi: 10.2471/BLT.11.089888
50. Campbell AM. An increasing risk of family violence during COVID-19 pandemic: strengthening community collaborations to save lives. *Foren Sci Int.* (2020) 2020(2):1–2. doi: 10.1016/j.fsir.2020.100089
51. Peterman P, O'Donnell T, Shah O-P, Van Gelder N. *Pandemics and violence against women and children. CGD working paper 528*. Washington, DC: Center for Global Development (2020).
52. Menéndez C, Lucas A, Munguambe K, Langer A. Ebola crisis: the unequal impact on women and children's health. *Lancet Global Health.* (2015) 2015(3):e130. doi: 10.1016/S2214-109X(15)70009-4
53. John N, Casey SE, Carino G, McGovern T. Lessons never learned: crisis and gender based violence. *Dev World Bioeth.* (2020) 2020(20):65–8. doi: 10.1111/dewb.12261
54. Sikira A, Urassa JK. Linking the twin pandemics: gender based violence and HIV in Serengeti district, Mara, Tanzania. *Int Asian Soc Sci.* (2015) 2015(5):324–34. doi: 10.18488/journal.1/2015.5.6/1.6.324.334
55. Davies SE, Bennett BA. Gendered human rights analysis of Ebola and Zika: locating gender in global health emergencies. *Int Affairs.* (2016) 2016(92):1041–60. doi: 10.1111/468-2346.12704
56. Lee SM, Kang WS, Cho AR, Kim T, Park JK. Psychological impact of the 2015 MERS outbreak on hospital workers and quarantined hemodialysis patients. *Compr Psychiatry.* (2018) 2018(87):123–7. doi: 10.1016/j.comppsy.2018.10.003

57. Campbell JC. Health consequences of intimate partner violence. *Lancet*. (2002) 2002(359):1331–6. doi: 10.1016/S0140-6736(02)08336-8
58. Schneider D, Harknett K, McLanahan S. Intimate partner violence in the great recession. *Demography*. (2016) 2016(53):471–505. doi: 10.1007/s13524-016-0462-1
59. Nie W. The origin of quarantine. *Global Partners Educ*. (2015) 2015(5):24–31. <http://www.gpejournal.org/>
60. Kagi J. Crime rate in WA plunges amid coronavirus social distancing lockdown measures. ABC News (2020). Available at: <https://www.abc.net.au/news/2020-04-08/coronavirus-shutdown-sees-crime-ratedrop-in-wa/12132410> (Accessed December 22, 2020).
61. Zhang J, Lu H, Zeng H, Zhang S, Du Q, Jiang T, et al. The differential psychological distress of the populations affected by the COVID-19 pandemic. *Brain Behav Immunity*. (2020) 2020(87):49–50. doi: 10.1016/j.bbi.2020.04.031
62. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychology impact of quarantine and how to reduce it. *Lancet*. (2020) 2020 (395):912–20. doi: 10.1016/S0140-6736(20)30460-8
63. Hatchimonji JS, Swendiman RA, Seamon MJ, Nance ML. Trauma does not quarantine: violence during the COVID 19 pandemic. *Ann Surg*. (2020) 2020(272):e53–4. doi: 10.1097/SLA.0000000000003996
64. Straus HE, Guonjian EH, Christian E, Roberts RR. Assessment of intimate partner violence abuse ratings by recently abused and never abused women. *BMC Womens Health*. (2020) 20:181. doi: 10.1186/s12905-020-01043-0
65. Kouyoumdjian FG, Calzavara LM, Bondy SJ, O'Campo P, Serwadda D, Nalugoda F, et al. Risk factors for intimate partner violence in women in the Rakai Community Cohort study, Uganda, from 2000 to 2009. *BMC Public Health*. (2013) 13:566. doi: 10.1186/1471-2458-13-566
66. Muche AA, Adekunle AO, Arowojolu AO. Gender-based violence among married women in Debre Tabor Town, Northwest Ethiopia: a qualitative study. *Afr J Reprod Health*. (2017) 21(4):102–9. doi: 10.29063/ajrh2017/v21i4.11
67. Leite FMC, Luis MA, Amorim MHC, Macie ELN, Gigante DP. Violence against women and its association with the intimate partner's profile: a study with primary care users. *Rev Bras Epidemiol*. (2019) 22:E190056. doi: 10.1590/1980-549720190056
68. Capaldi DM, Knoble NB, Shortt JW, Kim HK. A systematic review of risk factors for intimate partner violence. *Partner Abuse*. (2012) 3(2):231–80. doi: 10.1891/946-6560.3.2.231
69. FDR Ethiopia CSA. *Population projection of Ethiopia for all regions at wereda level from 2014 to 2017*. Addis Ababa: Central Statistical Agency (2013).
70. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. (2008) 3(17):1–8. doi: 10.1186/1751-0473-3-17
71. Vinnakota D, Parsa AD, Sivasubramanian M, Mahmud I, Sathian B, Kabir R. Intimate partner violence and pregnancy termination among Tajikistan women: evidence from nationally representative data. *Women*. (2022) 2(2):102–14. doi: 10.3390/women2020012

Frontiers in Global Women's Health

Highlights physical and mental health problems
women face around the world

Advances our understanding of the health
issues for women globally, especially in low-
middle income countries. It aligns with the UN
Sustainable Development Goals and promotes
physical and mental wellbeing for women.

Discover the latest Research Topics

[See more →](#)

Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact



Frontiers in Global Women's Health

