

Women in science: Public health education and promotion 2022

Edited by

Melody Goodman, Shazia Qasim Jamshed, Sunjoo Kang
and Rosemary M. Caron

Published in

Frontiers in Public 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 978-2-8325-2461-9
DOI 10.3389/978-2-8325-2461-9

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

Women in science: Public health education and promotion 2022

Topic editors

Melody Goodman — New York University, United States

Shazia Qasim Jamshed — Sultan Zainal Abidin University, Malaysia

Sunjoo Kang — Yonsei University, Republic of Korea

Rosemary M. Caron — University of New Hampshire, United States

Citation

Goodman, M., Jamshed, S. Q., Kang, S., Caron, R. M., eds. (2023).

Women in science: Public health education and promotion 2022.

Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-2461-9

Table of contents

05	Editorial: Women in science: Public Health Education and Promotion 2022 Rosemary M. Caron, Shazia Qasim Jamshed, Melody S. Goodman and Sunjoo Kang
08	Magnitude and Determinant Factors of Herbal Medicine Utilization Among Mothers Attending Their Antenatal Care at Public Health Institutions in Debre Berhan Town, Ethiopia Getu Engida Wake and Girma Wogie Fitie
20	Attitudes to Cannabis Use and Public Prevention Information Among Young Adults: A Qualitative Interview Study With Implications for Prevention Practice Pia Kvillemo, Anna K. Strandberg and Johanna Gripenberg
33	Physicians' Response and Preparedness of Terrorism-Related Disaster Events in Quetta City, Pakistan: A Qualitative Inquiry Fazal Ur Rehman Khilji, Zil-e-Huma, Nosheen Sikander Baloch, Maryam Shoaib, Zaffar Iqbal, Abdul Raziq, Nabila Sadaf, Syed Ainuddin, Sajjad Haider, Fahad Saleem, Qaiser Iqbal, Tanveer Hussain, Asfandiyar Ayaz and Rabia Ishaq
43	Determinants of observing health protocols related to preventing COVID-19 in adult women: A qualitative study in Iran Javad Yoosefi Lebni, Saeede Pavee, Mandana Saki, Arash Ziapour, Ahmad Ahmadi and Mehdi Khezeli
55	Research trends of mesenchymal stem cells application in orthopedics: A bibliometric analysis of the past 2 decades Zhibo Deng, Fenqi Luo, Yuan Lin, Jun Luo, Dianshan Ke, Chao Song and Jie Xu
69	Public awareness and use of 997 emergency medical service phone number during the COVID-19 pandemic Duaa Aljabri and Hissah Albinali
76	Status and influencing factors of medication literacy among Chinese caregivers of discharged children with Kawasaki disease Yingzi Zhang, Xiuqiong Wang, Jianghui Cai, Yanfeng Yang, Yiling Liu, Yeling Liao, Yanhong Zhou, Baoqin He, Wen Wen, Qian Zhuang and Yonghong Lin
84	Evidence-based core information for health communication of tobacco control: The effect of smoking on risks of female disease Jin Liu, Yun-Yi Hao, Hui-Jia Mao, Xiang-Ju Sun, Xiao-Lu Huang, Chen-Xin Quan, Mei-Ling Cao, Shu-Ting Wei, Xue-Zheng Jin and Yi-Bo Wu

- 97 **Discontinuation of long acting reversible contraceptive use and its determinants among women in Ethiopia: Systematic review and meta-analysis**
Natnael Atnafu Gebeyehu, Kirubel Dagnaw Tegegne, Gebyaw Biset, Dagne Addisu Sewuyew, Biresaw Wassihun Alemu and Alemker Mola Yitayew
- 110 **Barriers to gender equity for female healthcare academicians and researchers in Pakistan: Is it still an issue?**
Madeeha Malik, Azhar Hussain, Ayisha Hashmi, Hamza Saeed, Hafsa Azhar and Aqsa Sajjid Abbasi
- 120 **Potential and weak links in the management of tuberculosis by Pakistani private pharmacy staff**
Fatima Balquis, Muhammad Farhan Sohail, Huma Hamid, Waseem Ullah, Amer Hayat Khan and Gul Shahnaz



OPEN ACCESS

EDITED AND REVIEWED BY

Christiane Stock,
Charité – Universitätsmedizin Berlin, Germany;
Humboldt-Universität zu Berlin, Germany

*CORRESPONDENCE

Rosemary M. Caron
✉ rosemary.caron@unh.edu

RECEIVED 11 April 2023

ACCEPTED 17 April 2023

PUBLISHED 04 May 2023

CITATION

Caron RM, Jamshed SQ, Goodman MS and
Kang S (2023) Editorial: Women in science:
Public Health Education and Promotion 2022.
Front. Public Health 11:1204113.
doi: 10.3389/fpubh.2023.1204113

COPYRIGHT

© 2023 Caron, Jamshed, Goodman and Kang.
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: Women in science: Public Health Education and Promotion 2022

Rosemary M. Caron^{1*}, Shazia Qasim Jamshed^{2,3},
Melody S. Goodman⁴ and Sunjoo Kang⁵

¹Department of Health Management and Policy, Master of Public Health Program, College of Health and Human Services, University of New Hampshire, Durham, NH, United States, ²Faculty of Pharmacy, Universiti Sultan Zainal Abidin, Kuala Terengganu, Terengganu, Malaysia, ³Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan, ⁴Department of Biostatistics, School of Global Public Health, New York University, New York, NY, United States, ⁵Department of Global Health and Disease Control, Master of Infectious Disease Control Program, Graduate School of Public Health, Yonsei University, Seoul, Republic of Korea

KEYWORDS

women in science, public health, education, health promotion, research

Editorial on the Research Topic

Women in science: Public Health Education and Promotion 2022

To highlight the significant contributions of women to fulfilling the public health mission, this Research Topic features scholarly contributions in the field of Public Health Education and Promotion. This theme is intentionally broad in scope, and sought varied research contributions initiated by women. This editorial provides an overview of the key findings of the papers published in the Research Topic on “*Women in science—Public Health Education and Promotion 2022*.” The types of articles received in response to this Research Topic are summarized below.

1. Original research

Cannabis use has been shown to increase the risk of health issues and social problems (1, 2). Kvillemo et al. examined young adults’ attitudes toward cannabis use and prevention in Sweden. Participants were recruited through purposeful sampling, and semi-structured, in-depth interviews were conducted using a video platform. The experience of risks with cannabis use varied among the informants who based their risk perception on knowledge received from teachers, authorities, and media. Multi-component drug prevention programs should be implemented, combining a fact-based focus on risks, and delivered by credible and relatable messengers.

Herbal medicine is the most widely used form of traditional medicine. Although there is insufficient data on the safety of herbal medicine, local herbal products are recommended by healthcare professionals in sub-Saharan African countries during pregnancy (3–5). Wake and Fitie assessed the determinants of herbal medicine utilization among pregnant women in Ethiopia. Data were collected via in-person interviews administered using a semi-structured questionnaire. Pregnant women who did not possess an education beyond primary school were more likely to consume herbal medicine during pregnancy in comparison to study participants who possessed a college-level, or higher form of education. Those study participants who had smaller monthly family incomes were more likely to use herbal

medicine during pregnancy compared to those pregnant women who had greater monthly family incomes. The authors recommended that healthcare providers should discuss and create awareness about the benefits and complications of herbal medicine utilization during pregnancy.

In another example of health services education and utilization, [Balquis et al.](#) identified the quality and storage status of fixed-dose combination antituberculosis drugs and awareness regarding multi-drug-resistant tuberculosis (MDR-TB) among pharmacy staff in Pakistan. The authors noted that the poor control of TB and MDR-TB incidence were closely related to diagnosis time, supply of TB medication, provision of counseling, and implementation of the national TB program. Furthermore, the majority of the pharmacy staff lacked information regarding MDR-TB, and few TB patients had access to the national TB program. The authors concluded that timely identification of TB patients, quality management, and sustainable logistics on essential medication could decrease the MDR-TB incidence rate.

Other research from Pakistan conducted by [Malik et al.](#) examined the perception of female healthcare academicians about gender equity and related barriers by implementing a qualitative study design in health professions education. A semi-structured interview encompassing gender equity as an issue, perceived traits, professional relationship with male colleagues, and representation in leadership positions explored the participants' experiences. The participants discussed the level of support and harassment at the workplace, and salary disparity as barriers inhibiting gender equity. Recommendations included the development of policies to advocate for female recruitment, advancement, and equity in the workplace.

Terrorism-related disasters (TRDs) are a rampant challenge globally and impose an unexpected burden on healthcare services that requires adequate preparedness. Considering the high incidence of TRDs in Pakistan and scarcity of information on its management, this qualitative study was designed to evaluate TRD response and preparedness of physicians. [Khilji et al.](#) noted that although physicians were prepared professionally and psychologically for dealing with a TRD, they identified critical barriers for the mitigation of TRDs, including lack of disaster-related curricula, training, and resources.

Accessing healthcare services during emergency situations was further examined in the work by [Aljabri and Albinali](#). The Saudi Red Crescent Authority operates Emergency Medical Services (EMS) via the dedicated call number 997 and "Asefny" mobile application. The authors evaluated public awareness and use of the EMS phone number and compared EMS response times between requests made via the 997 phone number and "Asefny" mobile application during the COVID-19 lockdown. A cross-sectional survey was distributed through online platforms and identified several factors that may affect awareness and use of the EMS number, such as gender, location, nationality, education level, having children, and having a chronic illness. The study also found differences in the modes of requesting EMS, with the use of the "Asefny" mobile application being more prevalent than the 997 number.

[Lebni et al.](#) examined women's adherence to COVID-19 health protocols in Iran. Purposeful and snowball sampling were used to

reach the participants, and semi-structured, in-person interviews were conducted. The authors recommended that it is essential to have a precise understanding of a society's customs and culture to develop effective, multi-faceted interventions targeting individual, environmental, and social factors.

Kawasaki disease (KD) is an acute, self-limited febrile illness of unknown cause that predominantly affects children <5 years of age and is now recognized as a leading cause of acquired heart disease in children in developed countries (6). [Zhang et al.](#) examined medication literacy among Chinese caregivers of discharged children with KD. Factors associated with medication literacy were higher education levels, higher income, and longer duration of hospitalization. Caregivers with shorter duration of hospitalization and lower education levels and income should be targeted for medication literacy improvement. The authors proposed that effective communication between caregivers and healthcare providers, comprehensible education materials, training to improve nursing knowledge, and regular follow-ups are methods to improve medication literacy among KD caregivers.

2. Systematic review

[Gebeyehu et al.](#) conducted a meta-review to identify the determinants of Ethiopian women's discontinuance of long-acting reversible contraceptives. The side effects were the priority reason for discontinuing long-acting contraceptive methods. Predictive factors on women's decision to stop using contraceptives were service dissatisfaction, and the desire to become pregnant.

[Liu et al.](#) conducted a systematic review of evidence relevant to tobacco control to improve the effectiveness of health communication. The authors also developed and evaluated tailored health education messages for tobacco control based on target audience input. The authors concluded that the promotion of public health literacy among international populations could contribute to reducing tobacco use and related health issues.

A third systematic review conducted by [Deng et al.](#) examined the use of mesenchymal stem cells (MSC) in the field of orthopedics to determine trends and potential areas for future development. The main areas of MSC research included the source of MSCs, *in vitro* experiments, the differentiation process of MSCs, and use of MSCs in knee disease treatment. The authors noted that potential research areas include tissue engineering and uses in orthopedic disease.

Conclusion

The research highlighted herein demonstrates the many contributions women are making in the field of public health education and promotion globally and thus, comprises the Women in Public Health Education and Promotion, 2022, collection.

Author contributions

RC led the planning and writing of the editorial. All authors contributed to the writing and review process for the editorial.

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

1. Solowij N, Grenyer BF. Are the adverse consequences of cannabis use age-dependent? *Addiction*. (2002) 97:1083–6. doi: 10.1046/j.1360-0443.2002.00243.x
2. Van Ours JC, Williams J. Cannabis use and its effects on health, education and labor market success. *J Econ Surv*. (2015) 29:993–1010. doi: 10.1111/joes.12070
3. World Health Organization (WHO). *Traditional Medicine -September 1996 (No. 134) [fact sheet]*. (2021) 1996:8–9. Available online at: <http://www.nzdl.org/cgi-bin/library?e=d-00000-00---off-0cdl-00-0--0-10-0--0--0direct-10--4-----0-0l-11-en-50--20-about-00-0-1-00-0--4--0-0-11-10-0utfZz-810&cl=CL1.242&d=HASH017a3b463ffbce1010e805c>=1> (accessed April 10, 2023).
4. Fan T-P, Briggs J, Liu L, Lu A, Jan van der G, Xu A. The art and science of traditional medicine part 1: TCM today-a case for integration of traditional medicine. *Sci Adv*. (2014) S1–S24.
5. World Health Organization (WHO). *Traditional Medicine Strategy 2014-2023*. (2013). Available online at: https://apps.who.int/iris/bitstream/handle/10665/92455/9789241506090_eng.pdf (accessed April 10, 2023).
6. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. (2017) 135:e927–99. doi: 10.1161/CIR.0000000000000484



Magnitude and Determinant Factors of Herbal Medicine Utilization Among Mothers Attending Their Antenatal Care at Public Health Institutions in Debre Berhan Town, Ethiopia

Getu Engida Wake* and Girma Wogie Fitie

Department of Midwifery, Institute of Medicine and Health Science, Debre Berhan University, Debre Berhan, Ethiopia

OPEN ACCESS

Edited by:

Sunjo Kang,
Yonsei University, South Korea

Reviewed by:

Eneyew Melkamu,
Jimma University, Ethiopia
HAI BA MAI,
Hue University, Vietnam

*Correspondence:

Getu Engida Wake
getuengida3030@gmail.com

Specialty section:

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

Received: 24 February 2022

Accepted: 29 March 2022

Published: 29 April 2022

Citation:

Wake GE and Fitie GW (2022)
Magnitude and Determinant Factors
of Herbal Medicine Utilization Among
Mothers Attending Their Antenatal
Care at Public Health Institutions in
Debre Berhan Town, Ethiopia.
Front. Public Health 10:883053.
doi: 10.3389/fpubh.2022.883053

Background: World health organization defined herbal medicines as the practice of herbs, herbal materials, herbal preparations, and finished herbal products. Globally women are the primary utilizer of herbal medicine and even they consume it during their pregnancy period. The World health organization reported that the majority of the global population used traditional medicine. This study aimed to assess the magnitude and determinant factors of herbal medicine utilization among pregnant mothers attending their antenatal care at public health institutions in Debre Berhan town, Ethiopia.

Methodology: Institution-based cross-sectional study was conducted among pregnant mothers who attended their antenatal care at public health institutions in Debre Berhan town, Ethiopia from 12 February 2021 to 12 April 2021. A systematic random sampling method was used to get selected pregnant mothers. Epi data version 3.1 and SPSS version 25 were used for data entry and analysis, respectively. P -value ≤ 0.05 was used as a cut point of statistical significance in multivariable binary logistic regression.

Results: A total of 422 pregnant mothers were included with a 100% response rate and 277 (65.6%) of them used an herbal medicine during their current pregnancy. Educational level up to primary school [AOR 2.21, 95% CI: 1.17 – 4.18], monthly family income of <2,800 ETB [AOR 1.72, 95% CI: 1.01–2.92], and lack of awareness of the complication of herbal medicine utilization [AOR 10.3, 95% CI: 6.27–16.92] were determinant factors of herbal medicine utilization.

Conclusion: The utilization of herbal medicine among pregnant mothers in this study is high and almost all of them did not disclose their utilization of herbal medicine to their healthcare providers. The ministry of health should integrate traditional medicine with conventional medicines. Midwives and obstetricians should openly discuss regarding benefits and complications of herbal medicine utilization for those pregnant mothers during their antenatal care counseling sessions as routine care.

Keywords: herbal, traditional medicine, utilization, Ethiopia, mothers

INTRODUCTION

Traditional medicine is defined as the ways of protecting and restoring health that existed before the arrival of modern medicine (1). It is underestimated part of healthcare that finds in almost every country in the world (2). Traditional medicine has been being used in the maintenance of health and the prevention, diagnosis, improvement, or treatment of physical and mental illness (3). According to the WHO, herbal medicine is defined as the practice of herbs, herbal materials, herbal preparations, and finished herbal products (4), and they are derived from plant parts such as leaves, stems, flowers, roots, and seeds (5). Globally in the previous decade, there has been revived need and interest in the use of traditional medicine (6). The WHO estimated that 80% of the global population used traditional and complementary medicine as primary healthcare (3). The utilization of traditional medicine has maintained its global popularity and it varies from country to country (1). In Asian countries, the consumption of traditional medicine ranges from 40% in China to 65% in India (1, 7). Similarly in European countries utilization of traditional medicine accounts for 31% in Belgium, 49% in France, and 70% in Canada (7).

Approximately 80% of the population in Africa used traditional medicine (6), and evidence indicated that in sub-Saharan African countries (SSA) the prevalence of traditional medicine utilization among pregnant mothers was between 25 and 65% (8). Even though there is insufficient data on the safety of herbal medicine utilization during pregnancy (9), local herbal products were being recommended by healthcare professionals in sub-Saharan African countries (SSA) for different health-related problems during pregnancy (10). Herbal medicines toxicity can be related to a lack of proper standardization, absence of quality control, and adulteration of herbal products with other pharmaceutical drugs and potentially toxic substances. Hence utilization of some unstudied herbal medicines with unknown pharmacologic activity can end up in adverse health outcomes for some vulnerable groups such as older adults, children, and pregnant women and their fetuses (11–13).

According to the results of some kinds of literature, overutilization of herbal medicine during pregnancy is associated with different maternal and child adverse health outcomes such as preterm birth, cesarean birth, low birth weight, vaginal bleeding during pregnancy, maternal and neonatal morbidity and mortality, different congenital anomalies such as cleft lip, hypoplastic left heart syndrome, inguinal hernia, hydronephrosis, duplicate renal pelvis, fetal ductus arteriosus constriction, trisomy 18, and different form of maternal gastrointestinal complaints (14, 15). Globally women are the primary utilizer of herbal medicine (HM), and even they consume different herbal medicine during the pregnancy period (16). The consumption of herbal medicine among pregnant

and childbearing mothers ranges from 7 to 55% (17), and this difference depends on the consumer's geographic location, ethnicity, culture, traditions, and social status (16). Accordingly, utilization of herbal medicine among pregnant mothers was 34% in Australia (18), 50% in European Union (19, 20), and 6–9% in the USA and Canada, respectively (21, 22). Herbal products are believed a safe and natural alternative to conventional drugs among pregnant mothers and are used for the treatment of non-life treating conditions such as nausea and constipation (23). Globally, herbal medicine is available over the counter which makes them very accessible for utilization despite its health consequence when self-prescribed by pregnant women (24).

Many studies had revealed that pregnant women used different types of herbal medicine and the most commonly used herbal medicines were ginger (*Zingiber officinale* Roscoe), Chamomile (*Matricaria chamomilla* L.), peppermint (*Mentha piperita* L.), Echinacea (*Echinacea purpurea* L.), cranberry (*Vaccinium oxycoccus* L. and *Vaccinium macrocarpum* L.), garlic (*Allium sativum* L.), raspberry (*Rubus idaeus* L.), valerian (*Valeriana officinalis* L.), fenugreek (*Trigonella foenum-graecum* L.), fennel (*Foeniculum vulgare* Mill.), herbal blends, and teas, namely, green and black teas [*Camellia sinensis* (L.) Kuntze](25–27). Pregnant mothers use herbal medicine for mother or child-health-related problems and the most commonly reported indications for utilization of herbal medicines were nausea, vomiting, urinary tract infections (UTIs), preparation or facilitation of labor, cold, gastrointestinal problems, improvement of fetal outcomes and prevention of miscarriage, anxiety, health maintenance, and edema (26, 27). Moreover, pregnant mothers consume herbal medicines due to their easy accessibility, assumed better efficacy compared to modern medicine, traditional/cultural belief, and low cost of herbal medicines compared to conventional medicine (28, 29).

Some evidence from Australia and Kenya showed that older and married pregnant mothers with low economic status, low educational level, and those who had nausea, and vomiting were the most utilizers of herbal medicine (29–32). Another literature has also found that herbal medicine use during pregnancy was determined by some factors such as higher maternal age, lower educational level of the spouse, poor pregnancy outcomes, previous herbal medicine utilization large family size, self-employment, unemployment, and rural residence in addition to previously mentioned factors (33).

Nearly 80% of the Ethiopian population uses traditional medicine (34). The consumption of herbal medicines in Ethiopia is not only common but also culturally accepted and acknowledged (35). Evidence indicated that the practice of herbal medicine in Ethiopia ranges from 40.6% in Harar to 73.6% in Hosanna (36, 37). The cultural acceptability of healers and local pharmacopeia, the relatively low cost of traditional medicine, and difficult access to modern health facilities were some of the reasons for herbal medicines utilization in Ethiopia (38). The majority of the pregnant mothers are unaware of the possible maternal and fetal complications of herbal medicine utilization (29, 39), and those pregnant mothers and breastfeeding women are vulnerable to harmful effects of herbal medicines consumption since the appropriate dosages

Abbreviations: ANC, antenatal care; AOR, adjusted odds ratio; CI, confidence interval; COR, crude odds ratio; ETB, Ethiopian Birr; HCP, healthcare professionals; HMs, herbal medicine; HMU, herbal medicine utilization; OR, odds ratio; SPSS, Statistical Package for Social Sciences; SSA, sub-Saharan African; TM, traditional medicine; USA, United State of America; WHO, world health organization.

of herbal medicines and safety are not well established (40). The study of prevalence and determinants of herbal medicine utilization among pregnant mothers is a current public health concern in many developing countries including Ethiopia. In addition, even though some studies were conducted in Ethiopia, there is a scarcity of data on the magnitude and determinants of herbal medicine utilization among pregnant women. Therefore, this study aimed to assess the magnitude and determinant factors of herbal medicine utilization among mothers attending their antenatal care visit at public health institutions in Debre Berhan town Ethiopia.

METHODS

Study Design and Study Period

An institutional-based cross-sectional study was conducted from 12 February 2021 to 12 April 2021.

Study Setting and Participants

The study was conducted in Debre Berhan town, which is one of the 13 zones of the Amhara regional state. Debre Berhan town is located 130 km to the north of Addis Ababa city. It is found at an altitude of 2,850 m from sea level with a temperature ranging from 13 to 28°C. The town has nine kebele (seven kebele has an urban population while two of the kebeles have both urban and rural populations). Regarding the number of health institutions, the town has one comprehensive referral hospital, two private hospitals, three public health centers, nine health posts, and 18 private clinics. Pregnant women who came to attend antenatal care at public health institutions in Debre Berhan town during the study period were our study population.

Inclusion and Exclusion Criteria

Pregnant women who came for antenatal care visits at public health institutions in Debre Berhan town during the data collection period were included, while pregnant mothers who were seriously sick, who could not come to public health institutions and be unable to respond during the data collection time were excluded from the study.

Sample Size Determination, Sampling Technique, and Procedure

The sample size was determined using a single population proportion formula based on the assumption of 95% CI, 5% margin of error, and 48.6% prevalence of herbal medicine utilization (41).

$$N = \frac{(Z \alpha/2)^2 * P * (1 - P)}{d^2}$$

Where;

n = the actual sample size

Z = the standard normal deviation at 95% CI; =1.96

P = proportion of herbal medicine utilization

d = margin of error that can be tolerated, 5% (0.05)

$$n = \frac{(1.96)^2 * 0.486 * (1 - 0.486)}{(0.05)^2} = 383.$$

By considering a 10% of non-response rate ($n = 39$, the final sample size become ($N = 422$) pregnant mothers.

There are a total of four public health institutions in Debre Berhan town that provide focused antenatal care and we included all four public health institutions. The numbers of pregnant mothers who visited the public health institutions which were surveyed from each health institution were allocated proportionally based on the expected number of pregnant mothers who visited the public health institutions for the study period and the estimation was made depending on the number of pregnant mothers who visited each health institution for the last 2 months. The proportional allocation was calculated using the following formula:

$$nj = n/N * Nj$$

Where:

nj = Sample size of the j th health institution

n = total sample size

Nj = number of pregnant mothers who visited the j th health institution in the last 2 months.

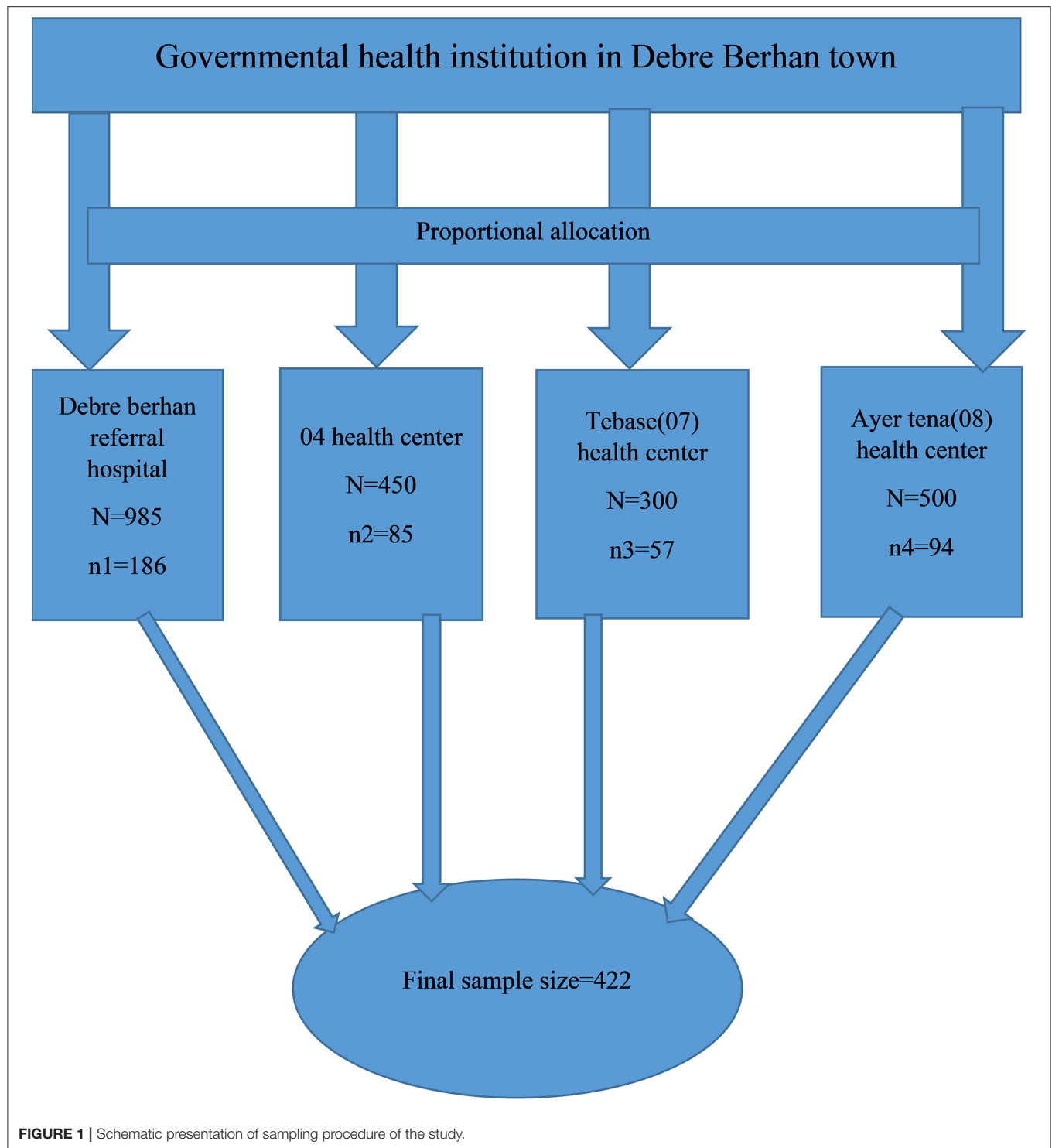
N = Total number of pregnant mothers who visited all public health institutions in the last 2 months. Lastly, study participants were selected systematically ($k = 5$) based on the order of pregnant mothers who come to antenatal care rooms at health institutions until the required sample size was obtained $K = 2235/422 = 5^{\text{th}}$ (Figure 1).

Operational and Definition of Terms

- Herbal medicine use: refers to using the seeds, berries, roots, leaves, bark, or flowers of a plant for medicinal purposes.
- Herbal medicine utilization in current pregnancy: respondents were labeled as herbal medicine users if they have taken herbal medicine *via* any route of administration during the current pregnancy period. Routine meal preparations and nutrients such as food additives were excluded.
- Knowledge was measured using four items prepared to assess it. Study participants were asked the knowledge-related questions and value one was given for correct answers and value zero was given for those incorrect answers. Then respondent's score was dichotomized as sufficient knowledge or insufficient knowledge after the total score was computed by summing up all the items together.
- Sufficient in knowledge: Study participants who answered equal to or greater than the mean values of knowledge-related questions.
- Insufficient knowledge: Study participants who answered less than the mean values of knowledge-related questions.

Methods of Data Collection Tool, Procedure, and Quality Control

Data were collected by face-to-face interviews administered using a semi-structured questionnaire. Five-degree pharmacy and two adult nursing masters were recruited as data collectors and supervisors, respectively. The data collection tool was developed from different published literature and slight modification was made to the questions to make them in line with the



objective of our study (35–37, 41). The questionnaires were designed in the English language, translated into Amharic, and back to the English language for consistency of collected data. Twenty-six items were included in the final questionnaire divided into three sections. The first section covered data regarding sociodemographic and pregnancy-related information

such as age, marital status, ethnicity, educational status of the mother, employment status, religion, monthly income, parity, presence or absence of ANC visiting history, presence or absence of health problems not related to gestation, trimester of pregnancy and distance from the health facility. The second section aimed at assessing the knowledge level of herbal

medicine among pregnant mothers and it was assessed by a series of questions such as whether they have heard about herbal medicine or not, the types of herbal medicine they knew, information about the complication of herbal medicine utilization and types of complications of herbal medicine utilization they knew. The third section was used to collect data concerning the level of herbal medicine utilization among pregnant mothers, source of information regarding herbal medicine, presence or absence of discussion with their healthcare providers about herbal medicine utilization, and satisfaction level of pregnant mothers toward utilization of herbal medicine. The utilization of herbal medicine among pregnant mothers was assessed by different questions such as the utilization of herbal medicines during pregnancy, reason of use among herbal medicine utilizer, type of herbal medicine used, the purpose of herbal medicine utilization, trimester of herbal medicine utilization, source of information about herbal medicine use and any untoward effects faced during their utilization of herbal medicines.

To maintain data quality, data collectors were given training for 2 days about the overall research objective including data collection procedures, tools, and how to fill data. In addition, the questionnaire was pretested in 10% of the sample size in Ataye hospital 3 weeks before the actual data collection period, and necessary amendments such as language clarity and appropriateness of the tools were done based on the findings of the pretest before the actual data collection time. Collected data were reviewed and checked for completeness and consistency by supervisors and the principal investigator daily.

Methods of Data Entry and Analysis

The collected data was cleaned, coded, and entered into Epidata version 3.1 and exported to statistical package for social science (SPSS) version 25 for analysis. Bivariable logistic regression was used to identify the determinant factors of herbal medicine utilization among pregnant mothers. Variables with a significant association in the bivariable analysis were entered into a multivariable binary logistic regression

TABLE 1 | Distribution of study participants by sociodemographic characteristics and their respective chi-square test at public health institutions in Debre Berhan town, Ethiopia, 2021 ($n = 422$).

Variable	Category	Herbal medicine utilization				chi-square (χ^2)	p-value
		No		Yes			
		Frequency	Percent	Frequency	Percent		
Age	<20	12	8.3	31	11.2	1.06	0.59
	20–30	96	66.2	173	62.5		
	>30	37	25.5	73	26.4		
Religion	Orthodox	104	71.7	225	81.2	5.74	0.06
	Muslim	29	20	32	16.6		
	Protestant	12	8.3	20	7.2		
Ethnicity	Amhara	139	95.9	261	94.2	0.55	0.76
	Oromo	5	3.4	13	4.7		
	Tigre	1	0.7	3	1.1		
Marital status	Married	125	86.2	240	86.6	0.98	0.81
	Single	12	8.3	26	9.4		
	Divorced	4	2.8	7	2.5		
	Windrowed	4	2.8	4	1.4		
Educational status	Illiterate	12	8.3	36	13.0	13.896	0.003
	Primary school	18	12.4	66	23.8		
	Secondary school	47	32.4	85	30.7		
	College and above	68	46.9	90	32.5		
Employment status	Government employee	49	33.8	86	31.0	1.65	0.44
	Self-employee	63	43.4	138	49.8		
	Unemployed	33	22.8	53	19.1		
Average monthly income	<2800	52	35.9	155	56.0	16.01	0.001
	2800–4800	44	30.3	52	18.8		
	>4800	49	33.8	70	25.3		
Parity	Null	72	49.65	124	44.76	3.06	0.22
	1–2 children	56	38.62	103	37.18		
	3–4 children	17	11.72	50	18.05		
The complication of herbal medicine utilization	no	44	30.3	228	82.3	112.18	0.001
	yes	101	69.7	49	17.3		

Knowledge of pregnant mothers towards herbal medicine

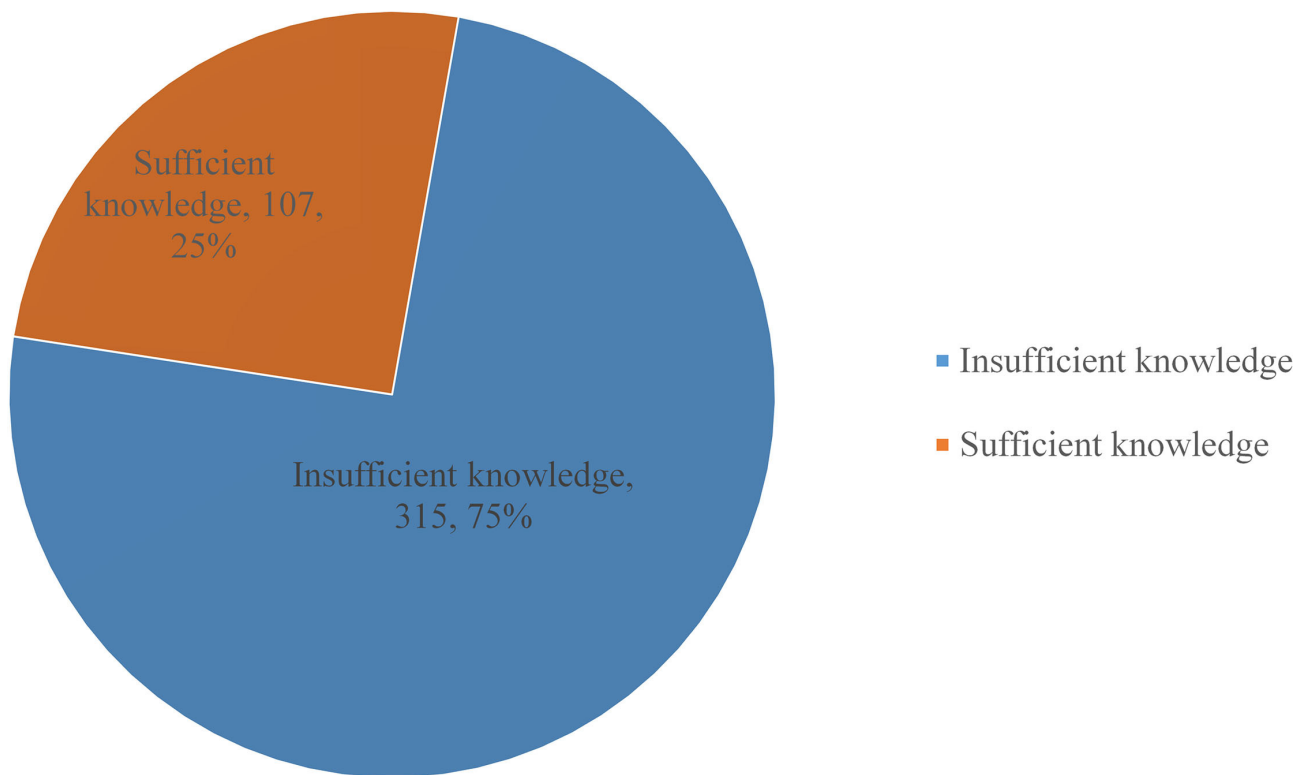


FIGURE 2 | Knowledge of pregnant mothers toward herbal medicine among mothers who visited governmental health institutions for antenatal care in Debre Behan town, Ethiopia.

analysis to assess the determinant factors of herbal medicine utilization among pregnant mothers and P -values <0.2 and 0.05 were considered statistically significant for bivariable and multivariable binary logistic regression, respectively. The overall results were presented in texts, tables, and figures.

RESULTS

Sociodemographic Characteristics of Study Participants

A total of 422 pregnant mothers were involved with a response rate of 100%. The mean age and average monthly family income of the study participants were 28 years old and 3,264 Ethiopian Birr (ETB), respectively. Almost all of them were Amhara and the majority of them were Orthodox religious followers (Table 1).

Knowledge and Practice of Pregnant Mothers Toward Herbal Medicine Utilization

Of the total study participants, 420 (99.5%) respondents heard about herbal medicine from different sources and

150 (35.5%) knew about complications of herbal medicine utilization (Figure 2).

Of the total study participants, more than half of them used an herbal medicine during their current pregnancy. Among study participants who used herbal medicine in the current pregnancy, 163 used it during the first trimester of pregnancy. The most common source of information about herbal medicine was families followed by media (Table 2).

Types and Indications of Herbal Medicine Used During the Current Pregnancy

Of all respondents who stated that they had used an herbal medicine during their current pregnancy, the most commonly used herbal medicines were Ginger (*Zingiber officinale* Roscoe), Damakesse (*Ocimum lamiifolium*) followed by Tenadam (Fringed rue) (Figure 3). The common indications for the utilization of herbal medicine during current pregnancy were common cold and headache (Figure 4).

Factors Associated With Herbal Medicine Utilization Among Pregnant Mothers

Bivariable and multivariable binary logistic regression were conducted to examine the determinant factors of herbal medicine

TABLE 2 | Study participant's characteristics toward herbal medicine utilization at public health institutions in Debre Berhan town, Ethiopia, 2021 ($n = 422$).

Variables	Frequency	Percent (%)
Herbal medicine use during the current pregnancy		
No	145	34.4
Yes	277	65.6
Source of information of herbal medicine ($n = 277$)		
Family members	182	65.7
Healthcare professionals	19	6.9
Media (internet, television, radio, book)	76	27.4
Trimester		
First trimester	163	58.8
Second trimester	88	31.8
Third trimester	26	9.4
Reasons for herbal medicine use ($n = 277$)		
Family, tradition, or culture	177	63.9
Belief in the effectiveness of herbal medicines	131	47.3
Herbal medicines are cheap and accessible	115	41.5
Treatment of other medical problems	16	5.8
Reason for not using herbal medicines among non-users ($n = 145$)		
Lack of belief in the benefits of herbs	22	15.2
Afraid the side effect	60	41.4
Didn't get sick during gestation	63	43.4
Discuss with HCPs about herbal medicine use ($n = 422$)		
No	397	94.1
Yes	25	5.9
Side effects from herbal medicine use ($n = 277$)		
No	218	78.7
Yes	59	21.3
Satisfaction with herbal medicine use ($n = 277$)		
Very satisfied	60	21.7
Partially satisfied	152	54.9
Not satisfied	65	23.5

HCPs, healthcare professionals.

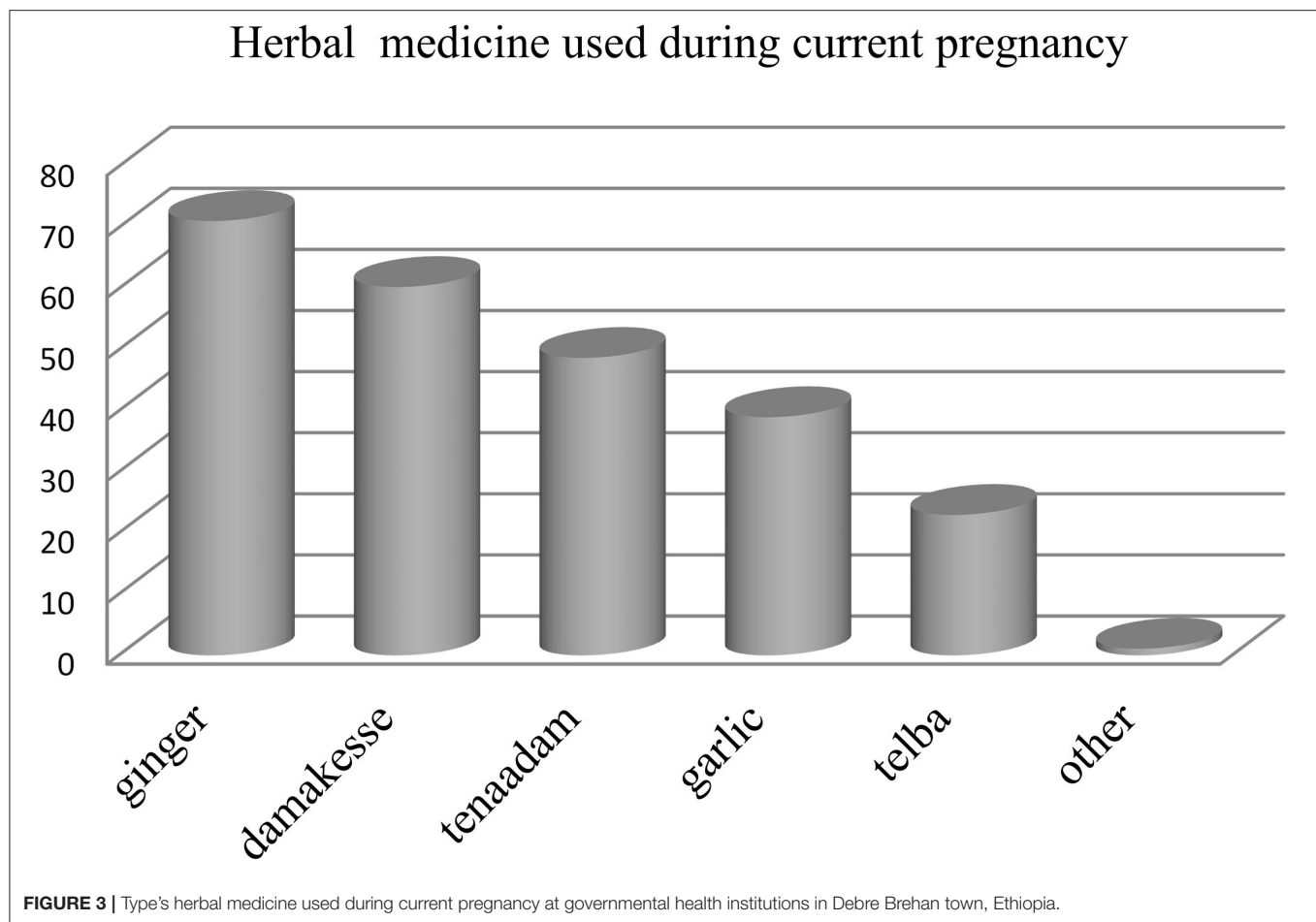
utilization among pregnant mothers. In bivariable logistic regression variables such as educational level of pregnant mothers, average monthly income of the family, absence of ANC visit, presence of health problems not related to gestation, lack of discussion of herbal medicine utilization with healthcare professionals, knowledge level of pregnant mothers toward herbal medicine, and lack of awareness of complication of herbal medicine utilization were significantly associated with pregnant mothers herbal medicine utilization. But in multivariable binary logistic regression, only three variables (educational level, average monthly family income, and absence of awareness of complications of herbal medicine utilization) were significantly associated with the practice of herbal medicine among pregnant mothers. Thus, those pregnant mothers whose educational level was till primary school were 2 times more likely to consume herbal medicine during current pregnancy in comparison to study participants whose educational level was college and above [AOR: 2.21, 95% CI:1.17–4.18]. Those study participants who had a monthly family income of <2,800 Ethiopian Birr (ETB)

were almost 2 times more likely to use herbal medicine during current pregnancy compared to those pregnant mothers who had a monthly family income of >4,200 Ethiopian Birr (ETB) [AOR: 1.72, 95% CI: 1.01–2.92]. Moreover, pregnant mothers who lacked awareness of complications of herbal medicine utilization were 10 times more likely to use herbal medicine during their pregnancy in comparison to studying participants who had awareness of complications of herbal medicine utilization [AOR: 10.3, 95% CI: 6.27–16.92] (Table 3).

DISCUSSION

This study aimed to assess the utilization of herbal medicine and its determinant factors among mothers attending their antenatal care visit at public health institution in Debre Berhan town, Ethiopia. This study found that the prevalence of utilization of herbal medicine during the current pregnancy was 65.6%. This finding is in line with the results of a study conducted in Zimbabwe (69.5%) (42), and lower than the result of a study conducted in Hosanna, Ethiopia (73.1%) (37). Moreover, this finding is higher than the finding of a study conducted in Nekemte hospitals, Ethiopia (50.4%) (35), public hospital of Harar, Ethiopia (40.6%) (36), University Gondar referral and teaching hospital, Ethiopia (48.6%) (41). This difference might be associated with the difference in sample size and study setting (some of them were conducted only in hospitals and other was community-based study). Besides this difference might be related to cultural differences across the regions of the country. Again this finding is higher than the results of the study conducted in Iran (48.4%) (43), Uganda (20%) (44), Tanzania (10.9%) (45), and Ghana (52.7%) (46). This difference might be related to cultural/belief variations across the countries, geographical differences, accessibility and affordability of herbal medicines, and methodological deference of the study such as study design, sample size, study setting, and included population.

Our study indicated that the most commonly used herbal medicine during the current pregnancy was ginger (71.1%). This finding is consistent with the results of a study conducted in Alexandria Egypt (32), Nekemte hospital, Ethiopia (35), and the University of Gondar referral and teaching hospital, Ethiopia (41). The similarity of this finding with the finding of a study conducted in Ethiopia might be associated with socio-cultural similarity and easy accessibility of herbs (ginger) all over the regions of Ethiopia and the study population of our study was similar to the study conducted in Alexandria Egypt. But this finding is different from the finding of two studies conducted in Iran (43, 47) which indicated sour orange and Ammi as commonly used herbal medicine, respectively. This difference could be attributed to socio-cultural differences and differences in types of herbal availability across the countries. Our study reported that the most common indication for herbal medicine utilization during the current pregnancy was the common cold (53.30%). This finding is in line with the report of a study conducted in a public hospital in Harar, Ethiopia, and the University of Gondar referral and teaching hospital, Ethiopia, respectively (36, 41). But the current finding is different from the

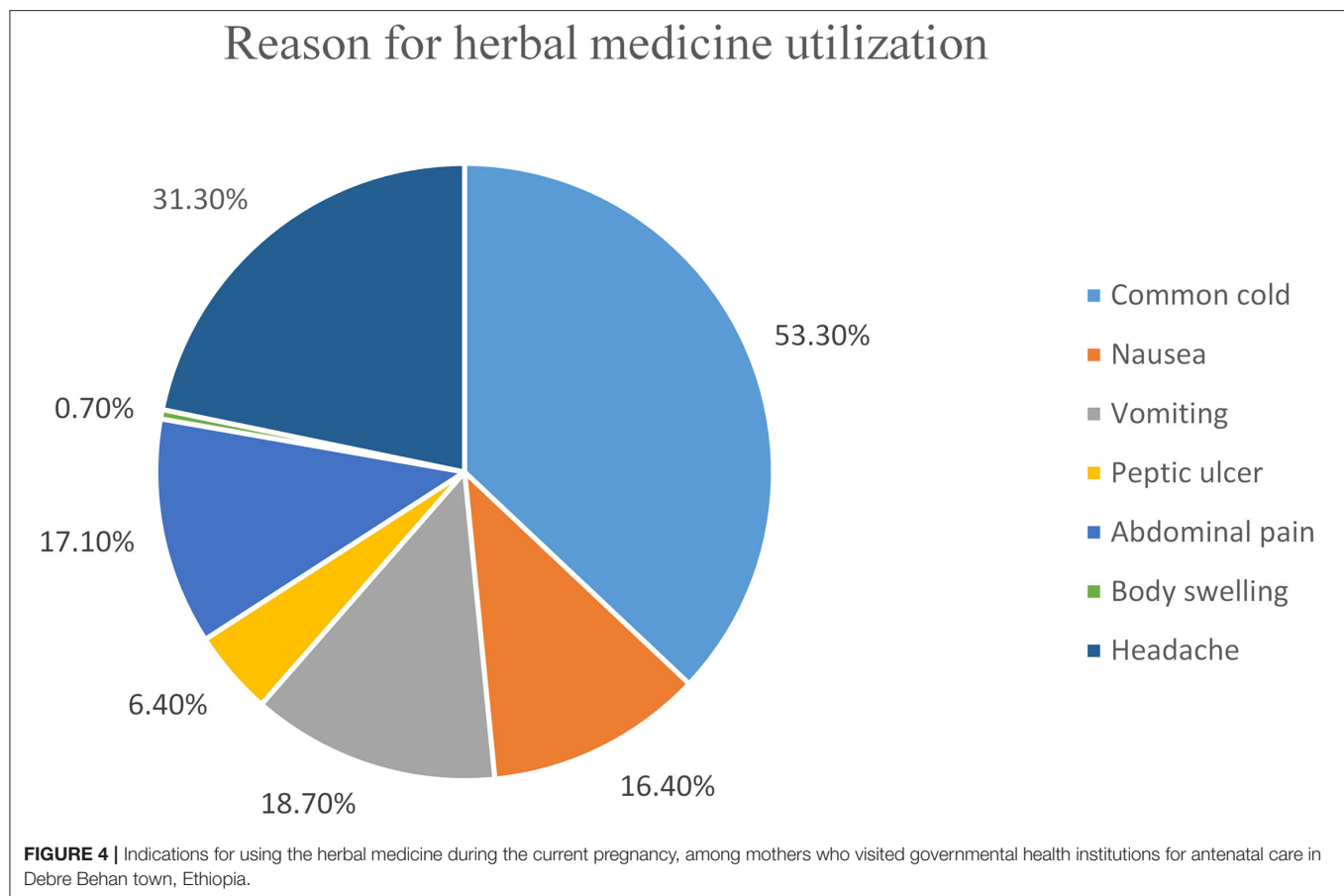


results of a study conducted in Iran (43) and Malaysia (48) which indicated promotion of fetal health and facilitation of labor as the common indication for herbal medicine utilization, respectively.

More than half (59%) of pregnant mothers used herbal medicine in the first trimester of pregnancy and this finding is in line with the results of a study conducted in Nekemte hospital, Ethiopia (35), University of Gondar referral and teaching hospital, Ethiopia (41), and Iran (47). This consistency could be because many minor complications of pregnancy take place at the early stage of pregnancy and pregnant mothers took those herbal medicines to alleviate those minor problems. But this finding is different from the study conducted in Iran (43) and Malaysia (48), and both studies reported that the majority of study participants used herbal medicine in the third trimester of pregnancy. In our study, only (6%) of pregnant women disclosed utilization of herbal medicine during current pregnancy to their healthcare providers. This finding is in line with the result of a study conducted at the University of Gondar referral and teaching hospital, Ethiopia (41) and northern Uganda (44). This similarity might be because of the fear of pregnant mothers that healthcare providers might disagree with the idea and practice of herbal medicine during pregnancy if they disclosed the information to their healthcare providers (49).

Those pregnant mothers with a primary educational level were two times more likely to use herbal medicine during current pregnancy as compared to those who had an educational status of college and above. This finding is in line with the result of studies conducted in Hosanna, Ethiopia, and the University of Gondar referral and teaching hospital, Ethiopia (37, 41). The possible explanation is that those educated pregnant mothers could have information about the efficacy of modern or conventional medicine over herbal medicine. Again those educated pregnant mothers might have better information about the bad consequences of herbal medicine utilization during pregnancy and tend to use less traditional medicine in comparison to their counterparts.

Those pregnant mothers who had low average monthly income were almost 2 times more likely to use herbal medicine during their current pregnancy compared to their counterparts. This finding is in line with the results of studies conducted in the University of Gondar referral and teaching hospital, Ethiopia (41), Tanzania (45), and Ghana (46). Probably those pregnant mothers who were found in the lower socioeconomic class could have not afforded the cost of modern medicine and herbal medicine was more accessible and affordable for



them to utilize when health-related problems happened. Those pregnant mothers who had no awareness of complications of herbal medicine utilization were 10 times more likely to use herbal medicine in comparison to pregnant mothers who had awareness of complications of herbal medicine utilization during their pregnancy and which is the new finding of this study. Probably lack of adequate information or knowledge on the complication of herbal medicine utilization exposed those pregnant mothers to utilize herbal medicine during their pregnancy. According to different pieces of evidence, herbal medicine utilization in some of the sub-Saharan African countries was associated with cultural and religion (50, 51) which is different from our study result which indicated the absence of a significant association between herbal medicine utilization and culture and religion of study participants. This might be associated with the difference in the ratio of traditional healers and healthcare professionals to the population in some sub-Saharan African countries. The ratio of traditional healers to the population in sub-Saharan Africa is 1:500, whereas the ratio of medical doctors to the population is 1:40,000 (52). Contrary to the above, there were large numbers of health extension workers in the community of Ethiopia which created adequate awareness of herbal medicine utilization during pregnancy.

LIMITATIONS OF THE STUDY

The cause and effect relationship of the predictor variables with the level of pregnant mother herbal medicine utilization was not determined because of the cross-sectional nature of the study design. Besides, the study did not address the attitude of pregnant mothers toward the utilization of herbal medicine and the study did not assess the amount of herbal medicine the mother used.

CONCLUSION

The utilization of herbal medicine among pregnant mothers in this study was high. The most commonly used herbal medicines were ginger (*Zingiber officinale* Roscoe), Damakesse (*Ocimum lamiifolium*), and Tenadam (*Fringed rue*). Common cold and headache were the common indications for utilization of herbal medicine during the current pregnancy period. Furthermore, educational level, average monthly family income, and absence of awareness of the complication of herbal medicine utilization were determinant factors of herbal medicine utilization among pregnant mothers. Governmental and non-governmental health institutions should promote traditional medicine practitioners to work together with

TABLE 3 | Bivariable and multivariable binary logistic regression analysis for factors associated with utilization of herbal medicine among pregnant mothers at public health institutions in Debre Berhan town, Ethiopia, 2021 ($n = 422$).

Variables	Using herbal medicine				
	Yes	No	COR(95%CI)	AOR(95%CI)	P-value
Educational status					
Illiterate	36	12	2.27(1.10, 4.68)	1.72(0.79, 3.74)	0.169
Primary school	66	18	2.77(1.51, 5.09)	2.21(1.17, 4.18)*	$\leq 0.015^*$
Secondary school	85	47	1.37(0.85, 2.19)	1.22(0.74, 2.02)	0.431
College & above	90	68	1	1	
Average monthly family Income					
<2800	155	52	2.09(1.28, 3.38)	1.72(1.01, 2.92)*	$\leq 0.045^*$
2800–4200	52	44	0.83(0.48, 1.42)	0.78(0.44, 1.37)	0.381
>4200	70	49	1	1	
Discuss with HCPs about HMU					
No	257	140	0.46(0.17, 1.25)	0.43(0.15, 1.23)	0.115
Yes	20	5	1	1	0.68
Do you have ANC?					
No	65	24	1.55(0.92, 2.59)	1.76(0.96, 3.23)	0.105
Yes	212	121	1	1	
Presence of health problems not related to gestation					
No	259	141	0.41(0.14, 1.23)	0.39(0.13, 1.21)	
Yes	18	4	1	1	
Level of knowledge					
Sufficient	62	45	1	1	
Insufficient	215	100	1.56(0.99, 0.45)	1.55(0.97, 2.47)	0.070
Awareness of HMU complication					
No	228	44	10.68(6.68–17.10)	10.3(6.27–16.92)*	$\leq 0.001^*$
Yes	49	101	1	1	

AOR, Adjusted odds ratio; HCPs, healthcare professions; HMU, herbal medicine user; COR, Crude odds ratio; CI, confidence interval; *, significantly associated value.

modern medicine practitioners. Healthcare providers should openly discuss and create awareness about the benefit and complications of herbal medicine utilization during pregnancy giving special attention to those pregnant mothers who had a low educational level, low monthly family income and for those pregnant mothers who had no awareness of the complication of herbal medicine utilization during their antenatal counseling session as routine care. Again we recommend further research to be conducted by addressing the experience of herbal medicine use among users and providers through qualitative approaches.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

Ethical clearance was obtained from the research and ethical review board of Debre Berhan University, institute of medicine and health science (Ref. No. IHRRCB-020/04/2021). The letter

of permission from the ethical review board and midwifery department was submitted to all governmental health institutions in Debre Berhan town. Besides, a letter of permission which was obtained from all four governmental health institutions in Debre Berhan town was submitted to each health institution's maternal and child health unit department. Lastly, informed written consent was obtained from pregnant mothers before data collection.

AUTHOR CONTRIBUTIONS

GW and GF: conceptualization, formal analysis, writing-original draft preparation, writing-review and editing, and funding acquisition. GW: methodology, data curation, and visualization. GF: software and supervision. All authors contributed to the article and approved the submitted version.

ACKNOWLEDGMENTS

We would like to thank all study participants, data collectors, supervisors, and all health workers of governmental health institutions in Debre Berhan town for their cooperation.

REFERENCES

- World health organization(WHO). *Traditional Medicine -September 1996* (No. 134) [fact sheet]. (2021) 1996:8–9. Available online at: <http://www.nzd.org/cgi-bin/library?e=d-00000-00---off-0cdl-00-0---0-10-0-0-0direct-10--4-----0-0l-11-en-50--20-about--00-0-1-00-0-4---0-0-11-10-0utfZz-810&cl=CL1.242&d=HASH017a3b463ffbfce1010e805c>=1>
- Fan T-P, Briggs J, Liu L, Lu A, Jan van der G, Xu A. The art and science of traditional medicine part 1 : TCM today-a case for integration of traditional medicine. *Sci Adv.* (2014). Available from: http://www.gp-tcm.org/wp-content/uploads/2016/02/TCM_Dec_19_issue_high_resolution.pdf
- World health organization(WHO). *Traditional medicine strategy 2014-2023*. (2013). Available online at: https://apps.who.int/iris/bitstream/handle/10665/92455/9789241506090_eng.pdf
- World health organization(WHO). *Who global report on traditional and complementary medicine*. (2019). Available online at: <https://www.who.int/traditional-complementary-integrativemedicine/WhoGlobalReportOnTraditionalAndComplementaryMedicine2019.pdf>
- Bent S. Herbal medicine in the United States : review of efficacy, safety, and regulation. *J Gen Intern Med.* (2008) 23:854–9. doi: 10.1007/s11606-008-0632-y
- World health organization(WHO). *Traditional medicine strategy 2002-2005*. (2002). Available online at: <https://apps.who.int/iris/handle/10665/67163>
- World health organization(WHO). *Fifty-sixth world health assembly: traditional medicine report by the secretariat*. (2003):14–7. Available online at: <https://apps.who.int/iris/handle/10665/78244>
- Liwa AC, Smart LR, Frumkin A, Epstein HB, Fitzgerald DW, Peck RN. Traditional herbal medicine use among hypertensive patients in sub-Saharan Africa : a systematic review. *Curr Hypertens Rep.* (2014) 16:437. doi: 10.1007/s11906-014-0437-9
- Ernst E. Herbal medicinal products during pregnancy : are they safe? *Int J Obstet Gynaecol.* (2002) 109:227–35. doi: 10.1111/j.1471-0528.2002.t01-1-01009.x
- Fugh-Berman A, Lione A, Scialli AR. Do no harm : avoidance of herbal medicines during pregnancy: letters to the editor. *Obstet Gynecol.* (2005) 106:409–10. doi: 10.1097/01.AOG.0000173415.38704.0e
- Merlin LK, Mensah GK, Firempong C, Alexander K, Arnold D, Forkuo CF, et al. Toxicity and safety implications of herbal medicines used in Africa. *Intechopen.* (2019) 64–80. doi: 10.5772/intechopen.72437
- Ozioma, Josephine E-O, OANC. Herbal medicines in African traditional medicine. *Intechopen.* (2019):192–210. doi: 10.5772/intechopen.80348
- Ahmed M, Hwang JH, Hasan MA, Han D. Herbal medicine use by pregnant women in Bangladesh: a cross-sectional study. *BMC Complement Altern Med.* (2018) 18:1–9. doi: 10.1186/s12906-018-2399-y
- Muñoz Balbontín Y, Stewart D, Shetty A, Fitton CA, McLay JS. Herbal medicinal product use during pregnancy and the postnatal period: A systematic review. *Obstet Gynecol.* (2019) 133:920–32. doi: 10.1097/AOG.0000000000003217
- Illamola SM, Amaeze OU, Krepkova LV, Birnbaum AK, Karanam A, Job KM, et al. Use of herbal medicine by pregnant women: what physicians need to know. *Front Pharmacol.* (2019)10:1–16. doi: 10.3389/fphar.2019.01483
- Dugoua J. Herbal medicines and pregnancy. *J Popul Ther Clin Pharmacol.* (2010) 17:370–8.
- Tiran D. The use of herbs by pregnant and childbearing women : a risk-benefit assessment. *Complement Ther Nurs Midwifery.* (2003) 9:176–81. doi: 10.1016/S1353-6117(03)00045-3
- Frawley J, Adams J, Sibbritt D, Steel A, Broom A, Gallois C. Prevalence and determinants of complementary and alternative medicine use during pregnancy : results from a nationally representative sample of Australian pregnant women. *Aust New Zeal J Obstet Gynaecol.* (2013) 53:347–52. doi: 10.1111/ajo.12056
- Lapi F, Vannacci A, Moschini M, Cipollini F, Morsuillo M, Gallo E, et al. Use, attitudes, and knowledge of complementary and alternative drugs (CADs) among pregnant women : a preliminary survey in Tuscany. *Evid Based Complement Altern Med.* (2010) 7:477–86. doi: 10.1093/ecam/nen031
- Holst L, Wright D, Lecturer S, Haavik S, Nordeng H. Safety and efficacy of herbal remedies in obstetrics: review and clinical implications. *Midwifery.* (2011) 27:80–6. doi: 10.1016/j.midw.2009.05.010
- Moussally K, Driss Oraichi AB Herbal products use during pregnancy : prevalence and predictors. *Pharmacoepidemiol Drug Saf.* (2009) 18:454–61. doi: 10.1002/pds.1731
- Louik C, Gardiner P, Kelley K, Mitchell AA. Use of herbal treatments in pregnancy. *Am J Obs Gynecol.* (2010) 202:439.e1–439.e10. doi: 10.1016/j.ajog.2010.01.055
- Frawley J, Adams J, Steel A, Broom A, Gallois C, Sibbritt D. Women's use and self-prescription of herbal medicine during pregnancy : an examination of 1,835 pregnant women. *Women's Heal Issues.* (2015) 25:396–402. doi: 10.1016/j.whi.2015.03.001
- Geller SE. Improving the science for botanical and dietary supplements. *Altern Ther Heal Med.* (2009) 15:16–7.
- Adams J, Lui C, Sibbritt D, Broom A. Women's use of complementary and alternative medicine during pregnancy : a critical review of the literature. *Birth.* (2009) 36:237–45. doi: 10.1111/j.1523-536X.2009.00328.x
- Hall HG, Griffiths DL, McKenna LG. The use of complementary and alternative medicine by pregnant women : a literature review. *Midwifery.* (2011) 27:817–24. doi: 10.1016/j.midw.2010.08.007
- Kennedy DA, Lupattelli A, Koren G, Nordeng H. Herbal medicine use in pregnancy : results of a multinational study. *BMC Complement Altern Med.* (2013) 13:355. doi: 10.1186/1472-6882-13-355
- Gardiner P, Kemper KJ, Legedza A, Phillips RS. Factors associated with herb and dietary supplement use by young adults in the United States. *BMC Complement Altern Med.* (2007) 7:39. doi: 10.1186/1472-6882-7-39
- Mothupi MC. Use of herbal medicine during pregnancy among women with access to public healthcare in Nairobi, Kenya : a cross-sectional survey. *BMC Complement Altern Med.* (2014) 14:432. doi: 10.1186/1472-6882-14-432
- Forster DA, Denning A, Wills G, Bolger M, McCarthy E. Herbal medicine use during pregnancy in a group of Australian women. *BMC Pregnancy Childbirth women.* (2006) 6:21. doi: 10.1186/1471-2393-6-21
- Duru CB, Uwakwe KA, Chinomso NC, Mbachi II, Diwe KC. Socio-demographic determinants of herbal medicine use in pregnancy among Nigerian women attending clinics in a tertiary hospital in Imo State, South-East, Nigeria. *Am J Med Stud.* (2016) 4:1–10.
- Ibrahim Y, Fouad N, Ibrahim M, Ibrahim A. Use of herbal medicines among pregnant women attending family health centers in Alexandria. *Middle East Fertil Soc J.* (2014) 19:42–50. doi: 10.1016/j.mefs.2012.02.007
- Ahmed SM, Nordeng H, Sundby J, Aragaw YA, de Boer HJ The use of medicinal plants by pregnant women in Africa: a systematic review. *J Ethnopharmacol.* (2018) 224:297–313. doi: 10.1016/j.jep.2018.05.032
- Kassaye KD, Amberbir A, Getachew B, Mussema Y, A. historical overview of traditional medicine practices and policy in Ethiopia. *Ethiop J Health Dev.* (2006) 20:127–34. doi: 10.4314/ejhd.v20i2.10023
- Bayisa B, Tatiparthi R, Mulisa E. Use of herbal medicine among pregnant women on antenatal care at nekemte hospital, western Ethiopia. *J Nat Pharm Prod.* (2014) 9:e17368. doi: 10.17795/jjnpp-17368
- Jambo A, Mengistu G, Sisay M, Amare F, Rieder MJ, Christensen ML. Self-medication and contributing factors among pregnant women attending antenatal care at public hospitals of Harar town, Ethiopia. *Front Pharmacol.* (2018) 9:1063. doi: 10.3389/fphar.2018.01063
- Laelago T, Yohannes T, Lemango F. Prevalence of herbal medicine use and associated factors among pregnant women attending antenatal care at public health facilities in Hossana town, southern Ethiopia : a facility-based cross-sectional study. *Arch Public Heal.* (2016) 74:7. doi: 10.1186/s13690-016-0118-z
- World Bank Group. *Ethiopia: Traditional medicine and the bridge to better health*. (2001). available online at: <https://openknowledge.worldbank.org/handle/10986/10803>
- Perri D, Seely D, Mills E, Koren G. Safety and efficacy of blue cohosh (*Caulophyllum thalictroides*) during pregnancy and lactation. *Can J Clin Pharmacol.* (2008) 15:e66–73.
- Conover EA. Herbal agents and over-the-counter medications in pregnancy. *Best Pract Res Clin Endocrinol Metab.* (2003) 17:237–51. doi: 10.1016/S1521-690X(02)00102-1
- Mekuria AB, Erku DA, Gebresilassie BM, Birru EM. Prevalence and associated factors of herbal medicine use among pregnant women on antenatal care follow-up at University of Gondar referral and teaching hospital, Ethiopia : a cross-sectional study. *BMC Complement Altern Med.* (2017) 17:86. doi: 10.1186/s12906-017-1608-4

42. Mawozwa T, Nhachi C, Magwali T. Prevalence of traditional medicine use during pregnancy, at labor and for postpartum care in a rural area in Zimbabwe clinics in mother and child health. *Clin Mother Child Heal.* (2019) 16:321. doi: 10.24105/2090-7214.16.321
43. Abdollahi F, Khani S, Charati JY. Prevalence and related factors to herbal medicines use among pregnant females. *J Nat Pharm Prod.* (2018) 13:e13785. doi: 10.5812/jjnpp.13785
44. Nyeko R, Tumwesigye NM, Halage AA. Prevalence and factors associated with use of herbal medicines during pregnancy among women attending postnatal clinics in Gulu district, Northern Uganda. *BMC Pregnancy Childbirth.* (2016) 16:296. doi: 10.1186/s12884-016-1095-5
45. Fukunaga R, Morof D, Blanton C, Ruiz A, Maro G, Serbanescu F. Factors associated with local herb use during pregnancy and labor among women in Kigoma region, Tanzania, 2014–2016. *BMC Pregnancy Childbirth.* (2020) 20:122. doi: 10.1186/s12884-020-2735-3
46. Zakaria P, Abubakar L. Herbal medicine usage before and during pregnancy: a study in northern Ghana. *Int J Complement Altern Med Res.* (2018) 11:235–42. doi: 10.15406/ijcam.2018.11.00405
47. Tabatabaee M. Use of herbal medicine among pregnant women referring to Valiasr hospital in Kazeroon, Fars, South of Iran. *J Med Plants.* (2011) 10:96–108. Available online at: <http://dorl.net/dor/20.1001.1.2717204.2011.10.37.11.2>
48. Rahman AA, Sulaiman SA, Ahmad Z, Nudri W, Daud W, Hamid AM. Prevalence and pattern of use of herbal medicines during pregnancy in Tumpat district, Kelantan Malaysian. *J Med Sci.* (2008) 15:40–8. Available online at: www.ncbi.nlm.nih.gov/pmc/articles/PMC3341906
49. Nordeng H, Havnen GC. Impact of socio-demographic factors, knowledge, and attitude on the use of herbal drugs in pregnancy. *Acta Obs Gynecol Scand.* (2005) 84:26–33. doi: 10.1111/j.0001-6349.2005.00648.x
50. Batisai K. Toward an integrated approach to health and medicine in Africa. *J Soc Asp HIV/AIDS Res.* (2016) 13:113–22. doi: 10.1080/17290376.2016.1220323
51. Gakuya DW, Okumu MO, Kiama SG, Mbaria JM, Gathumbi PK, Mathiu PM, et al. Traditional medicine in Kenya: Past and current status, challenges, and the way forward. *Sci African.* (2020) 8:e00360. doi: 10.1016/j.sciaf.2020.e00360
52. Abdullahi AA. Trends and challenges of traditional medicine in Africa. *African J Tradit Complement Altern Med.* (2011) 8(5 Suppl.):115–23. Available online at: <https://doi.org/10.4314/ajtcam.v8i5s.5>

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 Wake and Fitie. 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.



Attitudes to Cannabis Use and Public Prevention Information Among Young Adults: A Qualitative Interview Study With Implications for Prevention Practice

Pia Kvillemo*, Anna K. Strandberg and Johanna Gripenberg

Stockholm Prevents Alcohol and Drug Problems (STAD), Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm Health Care Services, Stockholm, Sweden

OPEN ACCESS

Edited by:

Melody Goodman,
New York University, United States

Reviewed by:

Lucy J. Troup,
University of the West of Scotland,
United Kingdom

Darshan Singh Darshan Singh,
Universiti Sains Malaysia
(USM), Malaysia

*Correspondence:

Pia Kvillemo
pia.kvillemo@ki.se

Specialty section:

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

Received: 06 December 2021

Accepted: 23 May 2022

Published: 23 June 2022

Citation:

Kvillemo P, Strandberg AK and
Gripenberg J (2022) Attitudes to
Cannabis Use and Public Prevention
Information Among Young Adults: A
Qualitative Interview Study With
Implications for Prevention Practice.
Front. Public Health 10:830201.
doi: 10.3389/fpubh.2022.830201

Background: Cannabis use carries an increased risk of ill health and social problems, especially when initiated at a young age. Drug use is influenced by individual beliefs, knowledge, and attitudes, which are, in turn, governed by social and environmental factors. In recent years, a less restrictive attitude toward cannabis has been observed in many countries, with concerns about increased cannabis use among young people. The aim of the current study was to gain a deeper understanding of young adults' attitudes toward cannabis use and public prevention information about cannabis.

Methods: A qualitative interview study was conducted among 32 anonymous informants aged 18–29 years in the Stockholm region. Participants were recruited through purposeful sampling, and semi-structured in-depth interviews were conducted using a digital video calling platform. A qualitative content analysis of the interviews was performed to generate categories and codes for cannabis use and attitudes toward prevention information.

Results: Both cannabis users and abstainers perceived some risks with cannabis; however, for many users, the positive effects appeared to outweigh any expected harm. Furthermore, the existing public information was perceived as less credible because of an excessive focus on harm. The informants expressed a desire for neutral facts about the effects of cannabis, delivered by credible senders. Moreover, they felt that prevention information should be delivered by individuals whom young people look up to or with whom they can identify, for example, people with authority or famous people such as influencers. The informants also underlined the importance of dialogue with the target group and taking young people's experiences into account when providing information about cannabis.

Conclusion: Current risk awareness associated with cannabis use among young adults is insufficient to prevent them from using cannabis. Public prevention information should

preferably combine a fact-based focus on risks with recognition of cannabis' short-term desired effects, delivered by credible senders with authority or those with whom young people can identify.

Keywords: cannabis, youth, prevention, attitudes, intervention, law, policy, public information

INTRODUCTION

Cannabis use has been shown to increase the risk of health issues and social problems, especially in younger age groups (1–7). The general public health effects of cannabis use are still under debate, however there seem to be consensus on cannabis' association to several health problems and also that young people are vulnerable to cannabis due to a developing brain (8). Research has found that there is a link between cannabis use and schizophrenia, and that cannabis use increases the risk of premature death (9). Cannabis use has further been associated with chronic bronchitis and vascular conditions that increases the risk of cardiovascular diseases (10). In addition, cannabis use is related to negative psychological and cognitive consequences, especially among those who begin using it in adolescence (11). Cannabis negatively affects memory, language, and logical analytical ability (11, 12). Moreover, there is a risk of developing addiction, although this risk may vary depending on routes of administration, doses, forms of cannabis and setting (13). Estimations indicate that 10–20 percent of those using cannabis on a daily basis develop addiction (14) and that a ~10% of those who use cannabis even once develop an addiction (1). Prior research has repeatedly shown that low socioeconomic status is a risk factor for substance use and related problems (15, 16). However, recent research from Canada (17), the United States (18–20), Serbia (21), Switzerland (22), and Sweden (23) suggest that high socioeconomic status too is associated with excessive substance use among young people, although for other reasons, e.g., excessive pressures to achieve and isolation from parents (24).

Most countries worldwide prohibit the production, use, and distribution of cannabis for recreational use. In recent years, however, a less restrictive attitude has been observed, manifested in decriminalization, and even in legalization of production and sales (25). Various states in the USA, e.g., Alaska, Colorado, Oregon and Washington have legalized cannabis for personal use, and in Uruguay and Canada, retail and production systems were introduced in 2014 and 2018, respectively (26). In Europe, the policy on cannabis vary between countries and several of them have moved toward decriminalization of cannabis use or personal possession, e.g., Luxembourg, Croatia, Portugal and Slovenia, while the use of cannabis is still a punishable offense in Cyprus, France, Finland, Greece, Hungary, Norway and Sweden (27). In Sweden, both use and possession of cannabis is a criminal offense under the Narcotics Penal Code (28). In parallel with global liberalization of cannabis policy, people, including adolescents and young adults, report a less negative attitude toward cannabis, lowered risk awareness, and increased use (25, 29–35). When asked about reasons for using cannabis, users report a number of perceived positive effects, such as relaxation, anxiety management (35, 36), increased creativity or productivity,

facilitation of social contact (35), relief of pain, and other symptoms, especially when using cannabis for medical purposes (37, 38), and less side effects than for example when using alcohol (38, 39).

Compared to other European countries, cannabis use in the general Swedish population is still fairly low (32, 40). Estimated prevalence the last 12 months among people 15–34 years of age in Sweden 7.5%. Corresponding figures for France are 21.8%, Spain 19.1% and Germany 16.9%. However, a recent population survey in Sweden showed that 17% of women and 25% of men aged 16–29 have tried cannabis at least once (34), indicating that cannabis use among adolescents and young adults remains a public health concern. The figures also show that cannabis use appears to be slightly more common among young men than among young women. International research shows that the attitudes to cannabis policy, or laws on regulation, differ between users and non-users, which from a public information perspective is important to bear in mind. In the 1990's, Skretting showed that only 65% of cannabis users in Norway were in favor of prohibition of cannabis compared to 95% of non-users (41). Some years later, a study in Huston in the USA showed that 68% of drug users were in favor of legalizing cannabis, while only 33% of the non-users expressed approval (42) and in 2008, a Dutch study showed that 7% of cannabis users were found to be in favor of cannabis prohibition, compared to 50% of non-users (43).

According to the social learning theory, proposed by Albert Bandura (44), both environmental and cognitive factors interact to influence human learning and behavior, emphasizing the importance of observing, modeling, and imitating the behaviors, attitudes, and emotional reactions of others (44–50). These factors are, in turn, influenced by the social environment, including family, friends, the local community, and culture, as well as laws and associated penalties. Further, the rational choice theory states that people's behavior is based on perceptions of the expected utility of a given choice in relation to possible detriments (51, 52). The perception of risks has been shown to play an important role in cannabis use (53–55). However, knowledge about potential harm alone has been insufficient in preventing cannabis use (55, 56). In a recent survey of 1,161 active athletes, Zieger et al. (56) found that attitudes mediated the relationship between knowledge and cannabis use. In another European study of 86,107 students aged 15–16 years, Piontek et al. (49) similarly highlighted the importance of personal attitudes for cannabis use, based on the finding that the immediate social situation, for example, friends' behavior, was associated with cannabis use. The importance of friends' behavior for substance use was also supported in a recent qualitative interview study among affluent Swedish students aged 15–19, which showed that social availability of the substance

and a desire to fit in at parties was a central motive for substance use (57).

Although a lot of research on mental health promotion interventions, including interventions related to substance use, has been carried out (58), technical advances and new generations of young people continuously growing up, make updated knowledge on the best way to effectively raise risk awareness and reduce positive attitudes toward cannabis among young people necessary (55, 59). Children and adolescents in Western countries are often exposed to substance use prevention intervention programs in school, which is strategic from a public health perspective, since all children attend school (60–64). In Sweden, providing educational information about illicit drugs is mandatory in primary and secondary schools, but the schools are free to elaborate on the teaching methods used (62–64). However, school-based prevention interventions have shown mixed results with regard to effects on cannabis use (8, 60); moreover, it remains to be clarified whether the potential effects of these programs last till adulthood (60). Evidently, school-based programs are not sufficient to prevent cannabis use in later life. Therefore, awareness campaigns and public information programs on the harmful effects of cannabis have been the cornerstones of substance use prevention among young adults who have left school; however, these have yielded questionable and sometimes adverse results (65–67). An excessive focus on the harmful consequences of drugs is perhaps one reason for the lack of desired effects (i.e., prevention of use) among the recipients of these programs (67). This might be particularly relevant in a Swedish context where the goal of the national policy on narcotics is “a society free from narcotics” (68). Information distributed from Swedish authorities and traditional print media generally portray cannabis as a potent and illegal drug contributing to social problems (69). Moreover, Swedish cannabis information symposia focus primarily on youth consumers, who are seen as particularly vulnerable to cannabis harmful consequences (69). Against this background, reasons for use, self-management or other harm reduction messages are not provided in Swedish public information on cannabis (39, 68). However, further research is needed to determine why public information on cannabis does not have the intended impact and how it should be modified to attain the desired effect, especially in the light of the international trends of deregulation and legalization of cannabis in recent years.

The decrease of legal restrictions, lowered risk awareness, and increasingly positive attitudes toward cannabis call for effective prevention measures besides, or instead of, prohibition, such as multicomponent environmental prevention programs that include effective information and communication on cannabis for the public (70). In order to carry out effective information-based prevention interventions, it is important to continuously monitor public attitudes toward cannabis use and prevention information.

The aim of the current study was to gain a deeper understanding of young adults' attitudes toward cannabis use and public prevention information. Specifically, the study aimed to answer the following questions: (1) How do young adults experience the risks associated with cannabis use? (2) Why do

young adults use or abstain from using cannabis? (3) How do young adults view information about cannabis provided by society? (4) What kind of messages do young adults think can work to prevent cannabis use? (5) Which senders do young adults think would be effective in conveying a preventive message? (6) In what ways do young adults think information about cannabis should be provided?

To the best of our knowledge, this is the first study to examine attitudes toward cannabis use in parallel with attitudes toward public prevention information among young adults in Sweden. The results can guide the development of tailored information about cannabis for young people who cannot be reached by the universal prevention interventions in school settings in countries comparable to Sweden with regard to policy and cannabis use patterns.

MATERIALS AND METHODS

A qualitative study design encompassing individual in-depth interviews with young adults aged 18–29 years was employed to answer the research questions. Qualitative content analysis of the interview material was performed after verbatim transcription.

Participants and Procedure

Purposeful sampling was used to recruit informants with varying backgrounds in terms of cannabis experience, sex, and socioeconomic background. The operationalization of cannabis experience was made by allocating informants who just tried cannabis once or a few times as well as people who were regular users in the category of “experienced” informants (tested), while those who had never tried cannabis was regarded as unexperienced (not tested). Sex was operationalized as man or woman, based on the informants' own definition. All informants chose one of these two categories when asked about their sex. The socioeconomic background was operationalized as residents in districts or municipalities with an average income of the adult population below or above the average of their respective municipality or district. Potential participants were contacted through social media (Facebook and Instagram), psychiatric clinics, the Police Authority, civil associations, and the researchers' own networks. People who were interested in participating were asked to contact the research team and were provided with information about what was required from them, that participation was anonymous, how the data were to be handled and presented, and that they could terminate their participation whenever they wanted. Informed consent was obtained and documented on tape (and later transcribed) before the interviews were conducted. The study was approved by the Swedish Ethics Review Authority (no. 2020-05669).

Semi-structured Interviews

Two of the researchers (AS and PK) carried out the interviews using a digital video calling platform, using semi-structured interview guides adapted for four categories of informants: those aged 18–25 years with and without experience of cannabis use, and those aged 26–29 years with and without experience of cannabis use. The reason for grouping the participants into

TABLE 1 | Background information about the informants.

		N	%
Age (years)	18–25	21	65.6
	26–29	11	34.4
Sex	Female	15	46.9
	Male	17	53.1
Socioeconomic status	Area income below average	14	43.8
	Area income above average	18	56.2
Experience of cannabis	Tested/user	22	68.8
	Not tested/non-user	10	31.2

these age categories were the assumption that people older than 25 years of age have probably established their own lives and are less influenced by parents as well as friends than younger people, which is partly connected the fact that the development of the brain is not complete until approximately 25 years of age (71). Thus, the interview guides directed to younger and older informants, respectively, were slightly different. The interview questions were based in social learning theory and previous research on cannabis use, covering informants' own experiences of cannabis use, perceptions of risks with use, reasons for using or abstaining from use, and attitudes to publicly disseminated information about cannabis. Some examples of the interview questions are: "Would you like to say something about your own experiences of cannabis use?", "What do you think are the reasons for using different types of cannabis?", "Do you find any health risks associated with cannabis? If yes, what are they?", and "Do you feel that you need information about cannabis? If so, what kind of information and from whom?". The interviews, which took an average of 31 minutes to complete, were recorded with the approval of the informants and transcribed verbatim. After 32 informants had been interviewed, the interviewers judged that little or no new information would be obtained by interviewing additional people and the interview process was terminated due to perceived saturation (72). Background information about the participants is presented in **Table 1**. The final group of participants included 21 cannabis testers/users and 11 abstainers, 15 women and 17 men, 21 people aged 18–25 and 11 people aged 26–29, 18 people from municipalities or districts with an average income above the current average of the municipality or district, and 14 people from areas below the corresponding average.

Content Analysis

Directed content analysis, inspired by Hsieh and Shannon (73) and Granheim and Lundman (74), was adopted to analyze the interview material. To increase the reliability of the analysis, a team-based approach was employed, involving three researchers of which two (AS and PK) worked closely together in the coding process, as described below (75). The NVivo 12 tool was used to structure the material and facilitate the analysis of the transcribed interviews. Initially, the two researchers who conducted the interviews (AS and PK) read through the transcripts repeatedly to find meaningful statements that could

TABLE 2 | An example of the content analysis.

Meaning unit	Condensed meaning unit	Code	Category
I think now when we're getting a little older, getting up to the age of 30, some of us, at least, are starting to have children and so, I think it [cannabis use] is something that is getting less and less common.	The propensity to use cannabis decreases with increasing age and as other interests and activities become important.	Competing activities or lack of interest.	Reasons to abstain.

TABLE 3 | Final coding scheme.

Categories	Risk awareness	Reasons to use	Reasons to abstain	Attitudes to public information
Codes	Knowledge	Social milieu	Negative effects or consequences	Supply and availability
	Personal observations and experience	Individual factors or needs	Competing activities or lack of interest	Messages
		Positive effects	Family (including partner)	Senders Information transfer
			Prohibition	

be grouped into preliminary categories and codes. An example of this grouping is presented in **Table 2**. The researchers were partly guided by the interview questions when looking for meaningful patterns, which according to Hsieh and Shannon (73) can be regarded as directed content analysis. With a directed approach, the analysis starts with a theory or relevant research findings as guidance for initial codes (73), which was the case in the current study. In the search for categories, information that could not be clearly linked to the interview questions was, however, also taken into account. During the coding process, the researchers discussed their findings and developed a preliminary coding scheme. Further review of the material and discussion with a third researcher (JG) generated additional revisions for categories and codes. Finally, an agreement was reached on the coding scheme presented in **Table 3**.

RESULTS

The interview material generated four categories and 13 codes. In the following sections, the results of the interviews are presented by the categories identified in the content analysis: risk awareness, reasons to use, reasons to abstain, and attitudes to public information. Furthermore, subheadings corresponding to the codes generated during the analysis are used. Participants' direct quotes are presented in italics, followed by the sex and age of the corresponding informant.

Risk Awareness

The experience of risks with cannabis use varied among the informants, but no clear difference was observed between users and non-users. Both groups appeared to base their perceptions of risks to a large extent on knowledge received from others, such as teachers in school, authorities, and *via* media. However, informants' risk awareness was also based on their observations and experiences with friends who used cannabis or their own experiences of using cannabis.

Knowledge

Most informants were aware that cannabis poses some form of health or social risks, but many lacked basic knowledge about

the drug's negative effects. Some informants reported having previously received information about risks associated with drugs in school, for example, the effects of cannabis on the brain and body, while others did not remember any cannabis-related information from school at all.

I actually have no direct memory of it [drug information in school]. We have certainly had that, but it is not something I remember. [...] I have very poor knowledge of cannabis and drugs in general.
-Female, 27 years

Informants who had tested cannabis had generally used the drug several times since their debut, and some of them did not perceive any significant risks associated with the drug, especially when using it "moderately."

I personally look at cannabis as alcohol. In the way that too much of it is absolutely not good, in the same way that too much of alcohol is not good.

-Female, 23 years

Personal Observations and Experience

Informants who had not tested cannabis based their risk awareness mainly on public information in or outside school, the media, parents' views, and observations of friends; whereas, users, including those who had only tested it once and those who regularly used it, referred to a large extent to their own experiences when speaking about perceived risks. Some participants who remembered the information provided in school found it less credible because they perceived it as exaggerated and as depicting "horror scenarios." Several participants leaned on information from acquaintances and media, and information gained from observing and communicating with friends who used cannabis, the latter leading to a higher as well as lower risk awareness.

I have seen acquaintances who overuse, and you see how it [cannabis] affects those people negatively in different ways. For example, they become quite slow, and their reactivity does not improve immediately. It does not feel like it's a positive effect, at least not in those who overuse it.

-Female, 28 years

Some informants mentioned that cannabis can lead to serious conditions, such as psychosis, and a few had themselves had unpleasant experiences related to cannabis use. One of the informants also described feelings of unreality and lasting symptoms several years after testing cannabis.

However, these were symptoms of unreality, such as perceiving the world in other ways. [...] I can still get that ... It can come a little when... comes most under stress, when I am stressed about something.

-Male, 18 years

The risk that cannabis use leads to the use of other drugs was also highlighted by several informants; one of them described his own case of drug abuse that began with his cannabis debut in his early

teens. Another informant revealed that many of her friends had actually died as a result of drug abuse, which contributed to her refraining from cannabis and other drugs.

A majority of the informants had tested cannabis, and several of them continue to use it. All the informants knew at least one person who had tested or who uses the drug frequently, and many of them, especially cannabis users, perceived that cannabis use is common in the population, primarily based on their own observations.

It [cannabis use] is common. It's very common. So the neighbor below us, they get high all the time.

-Male, 19 years

Some informants concluded, through their own experiences or observations of other people, that it is possible to combine cannabis use with work productivity, school, and other daily activities, indicating a lower perception of risk, at least in the short term.

I knew people who did it [used cannabis] regularly, every week, and at the same time did their studies very well. [...] They got an A-grade on everything. [...] So, they had A and felt great.

-Male, 20 years

Reasons to Use

The reasons for using cannabis described by the informants varied a lot, but were mostly related to the social milieu, individual factors or needs, and the positive effects of cannabis. Most of the reasons for using were reported by those who had tested or who used cannabis regularly.

Social Milieu

The social milieu seems to be important for cannabis use, especially when trying it for the first time. Several informants who had tested the drug mentioned that they had tried cannabis because it became available to them in some context.

One of my friends had lived in Canada and had smoked cannabis when he was a teenager. And it was not something I had been interested in before. But I do not know, he was part of that gang of friends and then I think he got it in some way.

-Male, 29 years

The overall impression was that young people feel that cannabis is easily accessible and they do not need to buy it themselves, because it can always be obtained through someone. Several informants reported that cannabis is used in different social contexts, and often in smaller groups. Cannabis does not appear to be a party drug that enhances a festive atmosphere; instead, it creates a relaxed atmosphere when hanging out with friends.

Yes, it is nicer in smaller groups, smaller contexts, and safer environments, when there are fewer, that is when it's nicer.

-Male, 29 years

As indicated above, some informants also considered cannabis harmless. This attitude appears to be based not only on their

own experiences, but also on discussions with people in their immediate social environment.

But I have thought about it a lot because I have not seen it as a heavy drug, or I... some people do not see cannabis as a drug at all, in my interactions. They see it as... almost like smoking a cigarette.

-Male, 24 years

Individual Factors or Needs

Several informants reported individual reasons for using cannabis, such as unwinding, relaxing, and as an aid to sleep. Some described the drug as a way to find peace, achieve a good feeling, or escape reality.

Then, it's just like this, escape reality a little, and feel relaxed. And do not think so much about what is happening. An escape, sort of.

-Female, 23 years

Another aspect of cannabis use was rooted in mental health issues, where it was used as a way of managing or reducing anxiety.

Yes, I can well imagine that it's... can have a calming effect and be nice. [...] reduce anxiety a bit.

-Female, 27 years

Another reason for using, especially for testing cannabis, was curiosity. As mentioned above, the drug use debut is not usually planned in advance, but is done in the moment when the opportunity arises.

When we were in Copenhagen, it was a fun thing. And man... I am so curious so I think it's fun to test, but I know it's really stupid too.

-Male, 24 years

Positive Effects

Some informants revealed that cannabis contributes positively to a calm and cozy atmosphere in social settings.

I have only positive experiences. I think it's much... It's much nicer and like... yes, but calmer and cozier to hang out when you have used cannabis 'rather than' alcohol, for example. It becomes much more of a... to sit at home and laugh and talk and maybe watch a movie or something like that.

-Female, 22 years

Positive effects are also experienced when users are on their own. One of the informants expressed two types of positive emotions in the following way:

I become happy and feel smart and wise and strong and want to invent something, do something fun, and take a trip. Maybe go for a walk, paint, or something. [and further] I get more tired and drowsy and so, but not in a negative way, but I get a little sleepy, a little cuddly, a little cozy. I might want to watch a movie or create something in a quiet environment. So, I get two different effects.

-Female, 19 years

Reasons to Abstain

The informants' key reasons for abstaining from cannabis use were the risks of health and social problems, such as mental illness, negative neuropsychological consequences, losing control, and a connection to (or promotion of) organized crime. The user's family or partner can also be an important factor in the decision to abstain, along with the (Swedish) legislation and penalties associated with cannabis use.

Negative Effects and Consequences

Many of the informants had heard of or observed the negative effects or consequences of cannabis, including those who had tested the drug. In some cases, negative experiences during the first time or later had led to the choice of giving up the drug, or using it less often.

I am probably one of the few people who have experienced a traumatic scenario from the first time. [...] The only thing I can do is to keep my distance from it and so. I have no problems with that now. I'm terrified of it!

-Male, 18 years

Furthermore, a couple of the informants pointed out that users' lack of ability to finance their drug use may lead to fights and physical aggression, or being forced to start selling the drug themselves.

The problem here is that you can very easily become... get into it, and get stuck. So if you don't have these financial opportunities, if you are not financially able to pay and you get stuck, then it can lead to huge catastrophic "penalties." So you can become a criminal, you can become a part of it [the dealing] and sell and buy.

-Male, 20 years

Competing Activities or Lack of Interest

Some informants expressed that they had no interest in using cannabis. This applied both to those who had tested it and those who had never used cannabis.

I have no interest in consuming cannabis, so I feel rather that it's something I want to distance myself from.

-Female, 27 years

The absence or lack of the expected effects during their cannabis debut was also presented as a reason to abstain from use.

I actually barely felt anything. It was well that you laughed a little more maybe, but I did not feel anything, I thought it was completely useless.

-Male, 24 years

Moreover, the responsibilities of raising children, work, and other competing interests and activities also contributed to cannabis use becoming less appealing with increasing age. In addition, the feeling that it is cool to use cannabis decreased as one approached the age of 30.

I think now that we are getting a little older, getting up to the age of 30, some of us are starting to have children and so on, so it's I think it [cannabis use] is something that's getting less common.

-Male, 29 years

Family or Partner

Family norms did not appear to be central to the choice of trying cannabis. In some cases, however, parents and the home environment seemed to influence abstinence from the drug, as expressed by one of the abstainers:

The whole family probably thinks it is a little tangled, sort of, if you may say so. I still understand somehow that you want to escape your problems quickly, but it feels... it's not the right way. It feels like those who take drugs may not think about the consequences. I think there are many consequences. We have not talked much about drugs at home, but it has always been a "big no no" to use drugs.

-Female, 23 years

In the case of ongoing use, a partner's demand for abstinence was also mentioned as a reason to stop using cannabis.

The reason to stop using cannabis would probably be that the girlfriend wants us [the informant and his girlfriend] to stop.

-Male, 24 years

Prohibition

The Swedish legislation prohibiting the use and handling of cannabis was reported by most informants as a prominent reason to abstain from use, and that the fact that cannabis is illegal served as a signal that it is unhealthy and dangerous to use.

In addition to the negative consequences of any stigma and sanctions associated with the ban, the ban also seems to serve as a signal that cannabis is "dangerous." It's easy to get caught and then you become addicted and then it's very difficult to stop [...] and then you can imagine that why is it [cannabis] illegal? This is probably because it is easy to get caught up in.

-Male, 21 years

Attitudes to Information

The informants provided their views on several aspects of public information about illicit drugs in general, and cannabis in particular, including supply and availability, messages, senders, and the way the messages are transferred to the target group.

Supply and Availability

Overall, the informants felt that they had not received any information about cannabis from competent authorities in the society. Only a few of them remembered the information disseminated in school, and those who had received information did not perceive it to be sufficient.

So I kind of do not think you get that much information, to be honest. It's mostly... So the school does not address anything at all, I think.

-Female, 23 years

Several informants also mentioned that information was publicly available online, for example on various authorities' websites, but young people had to search for it themselves.

If you go to an authority's website, it says [provides information on cannabis]. However, not everyone may make an active choice to go in and check.

-Female, 23 years

Sometimes, the problem was not a lack of information, but the fact that it was difficult for adults to reach out to young people, because the youth tend to ignore risks.

I do not know, I think it's difficult... or I think it's a difficult thing over all, to reach out to young people, because they think more that they are immortal and that one should not listen to adults.

-Male, 24 years

At the same time, some informants stated that there is definitely a need for more information.

Yes, it would be good... it would be good. I think there are many who do not know, or as I said, I am not a hundred percent sure about what cannabis does to you. I am not so familiar with... I have never been interested in drugs, but it... I think it's good to know about drugs.

-Male, 24 years

A few of them also mentioned that there is a taboo around conversations about cannabis and drugs in general, which may increase the risk of harm among young people.

Yes, but that it is still a bit taboo. And that we do not talk about it as much as we would need. [...] And I think there are many more who just see it like this: "Oh, that's a fun thing." So, I think very few people understand the meaning of it and the risks. Thus, the information I think can be improved.

-Female, 23 years

Messages

Some of the informants revealed a distrust toward the adult world and authorities, implying that adults emphasize the negative aspects of cannabis use and try to scare young people to prevent them from using. Such an approach can perhaps work for children and people in their early teens, according to one of the informants, but when children grow older and have friends who have tested the drug or test it themselves, they question the credibility of the information they had received. Several participants requested information in the form of valid facts and clarity about the specific effects of cannabis use, for example, the changes that take place in the body and brain when using cannabis.

Yes, I think people need information and accurate information about it. I think that this is important. It is not moralizing, and it is very clear what the negative effects are. And that's quite... yes, objective... with as good research data as possible, to show the negative effects that it can have.

-Male, 29 years

An informant also mentioned that the Swedish society's zero tolerance policy for illicit drugs creates problems in communication and a lack of transparency in information dissemination.

I think it is very difficult for authorities to seem credible in external communication if you have a form of zero tolerance for drugs. [...] I am not sure it's a problem that lies in communication, but I think it's a problem that lies in the legislation, if I am honest.

-Male, 29 years

Some informants also expressed a need for information on how to use cannabis safely, for example, how much of it can be consumed in large quantities and descriptions of what can happen on consumption.

You still want to know before you start using... When you test it, it's always good to know what you are going into.

-Female, 19 years

Some informants believed that many young people receive information and form their impressions of cannabis through music, film, television, and social media, which can lead to an incorrect or glamorized view of the drug. Artists using cannabis may be perceived as "cool" and a normalization of cannabis use may occur.

It feels like children learn more about drugs from movies. [...] All these guys who rap today and have face tattoos in videos with drugs and stuff. [...] I think young people get a completely wrong idea of drugs.

-Male, 24 years

Senders

The informants emphasized that the sender of cannabis-related information is important for the information to be perceived as credible. They indicated that they preferred someone who "knows what he or she is talking about" and someone they could look up to.

The sender I think is A and O. [...] Someone who has experience [of cannabis use], but perhaps together with a person in a lecture who is known for something, who people look up to.

-Female, 23 years

Several of the informants reiterated the fact that the best person to speak about cannabis is someone with personal experience of using, and preferably someone with whom the target group can identify, for example, a person of the same age.

I think they listen more if there is someone who is maybe 30, 35 and is a former drug addict but has gotten out of it, and that they tell about their experiences.

-Male, 24 years

One of the informants stated that everyone has the right to the same and equal information regardless of where they live and where they come from, pointing to schools as a key sender of

information related to drugs. The informants also addressed the role of parents as important in providing information about drugs, although parents are not “public senders.”

Yes, it's really the parents' responsibility. However, I think that not all parents may do so. Because I am not... I am not ethnically Swedish, and my parents may not even fully know what cannabis is specifically. So, I still think that the school should be able to take some responsibility for that really. Thus, all children from different ethnicities could learn.

-Female, 23 years

The informants also pointed out that there are advantages in employing a neutral sender with competence, that is, deep knowledge about the subject, rather than, for example, a teacher who normally teaches other subjects.

What I think is that it would have been best to bring in a neutral sender who then informs about it [cannabis]. So that it does not happen that, “Gunilla, who teaches English and Swedish, should start talking about cannabis.” If so, I think it will be like this: “Yes, but what does she know?”

-Female, 23 years

Information Transfer

An idea put forward by some of the informants was that the involvement of famous people, such as “influencers,” could be a successful alternative for reaching out with information to young people. Authorities could, for example, establish collaborations with celebrities or other people who already function as role models.

There are many influential role models. So really, maybe you can train the influencers so that they can provide good information.

-Female, 23 years

The importance of having an open dialogue when delivering information was also underlined, particularly by making young people feel that their experiences are being taken into account.

Try to enlighten more and encourage discussion among students. And maybe... Yes, and based on them and their experiences like this: “Yes, but what do you think? What do you feel then?” and have it more open.

-Female, 23 years

The informants regarded public information as a more or less realistic way to prevent people from testing cannabis, but expressed skepticism about the possibility of making regular users quit by informing them about the harmful effects.

No. I do not think so. I think you have to decide for yourself to be able to quit. It is not up to anyone else. I can only think of myself because I smoke. If someone else were to say to me “quit smoking cigarettes.” It's not like I would quit because someone says so... I know what health risks there are with smoking, and yet I continue. So, it has to come from myself if I want to quit. I think it's the same way with cannabis too.

-Female, 23 years

DISCUSSION

This study aimed to gain a deeper understanding of young adults' attitudes toward cannabis use and public prevention information about cannabis.

Summary of Results

Both cannabis users and abstainers perceived some risks with cannabis; however, for many users, the positive effects seemed to outweigh any expected harm, although both users and non-users described both positive and negative effects. Furthermore, public information was perceived as less credible by the participants because of an excessive focus on harmful effects, which they considered to be connected to the zero tolerance policy for cannabis use in Sweden. The informants expressed a desire for neutral facts about the effects of cannabis, delivered by someone with deep knowledge of the subject. Moreover, they felt that, to improve credibility, prevention information should be delivered by a sender they can look up to, or a person with whom young people can identify. The informants also stated the importance of dialogue with the target group and of taking young people's experiences into account when providing information about cannabis.

Comparison With Previous Research

The informants in this study were well aware of the risks associated with cannabis use, although several of them lacked detailed knowledge of cannabis-related effects and a few regarded cannabis as being almost harmless. To the extent that risks were recognized, they did not prevent a large number of the participants from testing cannabis or from using it regularly. Possibly the information that they received did not sufficiently emphasize the risks associated with the drug, or the target group did not care about the risks, the latter perhaps more likely since the public information on cannabis in Sweden to a large extent focus on risks (69). As mentioned by a participant, young people may believe they are “immortal” and, thereby, are almost immune to risk information. Nevertheless, cannabis use in Sweden is still less common than in many other countries (32), which may be linked to the risk of penalty on violating the Swedish ban on using or handling cannabis (28), or the perception that the ban signals dangers connected to cannabis. In the current study, about 70% of the informants reported having personal experience of cannabis use, and several of them believed that the drug was commonly used in society. A national health survey conducted by the Swedish Public Health Agency in 2018 showed that 17% of women and 25% of men aged 16–29 years had tried cannabis at least once (34), a significantly lower figure than the proportion in this study. The large number of informants with cannabis experience in the current sample could be attributed to the fact that people who have tried cannabis may be more interested in participating in a study on cannabis than people who do not have this experience. It was also a conscious strategy to include users as well as non-users in the study, in order to learn the different reasons for using and explore how users perceived prevention information, since users are more likely to influence peers who have not yet tested the drug (44–49).

It was observed that any awareness of risks, including the risk of penalty when violating the ban, did not prevent a significant proportion of young adults from testing and continuing to use cannabis. In a departure from the rational choice theory (51, 52), the perceived harm did not appear to outweigh the expected utility of using cannabis. The informants highlighted several motives for using cannabis, such as enhancing socialization with friends, increasing personal well-being, and counteracting negative feelings and mental health problems, which are reasons previously reported by young users (35, 36). The social aspect of substance use was recently highlighted in a study on Swedish students aged 15–19 years (57) in a slightly different way; among these younger individuals, peer pressure appeared to be a more prominent social motive than promoting positive experiences when hanging out with friends, whereas, the latter was emphasized more in the current study. The availability of cannabis, however, seems to be important for both adolescents and young adults when using the drug for the first time, as shown in the current study as well as the study on Swedish students (57). Since cannabis use is prohibited by the law in Sweden, the social context with peers who can provide the illegal substance, explain how to use it, and relate the expected effects may be even more important for the initiation of cannabis use among Swedish youth compared to young people in countries where cannabis can be purchased legally and information about its use and effects can be obtained easily.

Given that young adults have access to cannabis, have several reasons to use it, and perceive a number of positive effects associated with it, it is a significant challenge to prevent them from using it by providing information about its risks and harmful effects. Research suggests that presenting information alone has limited effects on behavior, and that a comprehensive perspective is more effective for substance use prevention, such as multicomponent programs where information is one of several components (65, 76). Such interventions address supply and demand, the latter being influenced by societal norms and values (70). In line with this, participants in the current study were skeptical of the fact that established cannabis users could be persuaded to stop using the drug by only informing them about the associated risks. Nevertheless, several of them actually wanted more information about cannabis, preferably, details about the effects of cannabis on the body and brain. This opinion was expressed by those who had never tried cannabis as well as those who regularly used it, the latter partly because they wanted to use the drug “safely.” Previous studies support the health benefits of self-management and protective strategies when using cannabis (39, 77–79). Whether such benefits could outweigh the results of a strict focus on risks with regard to public health in a country like Sweden, where the prevalence of cannabis still is fairly low, remains to be explored, and also which implications for information interventions such knowledge might generate. Based on our results, future studies, in any case, need to examine the possibility that preventive messages need to be formulated and directed at specific target groups rather than as a general message to the entire population.

Although the current study managed to recruit cannabis users who gladly shared their experiences (admittedly anonymously), some informants stated that the present “taboo” around

cannabis in Sweden, partly generated by the prohibition by law, counteracted a nuanced communication from the authorities, thereby impeding the credibility of public information. This view is in line with previous research, indicating that an overly one-sided focus on the harmful consequences of cannabis may impede the intended effect of the preventive message (57, 67). In congruence with the desire for nuanced information on cannabis, participants in the current study asked for a dialogue with the information provider or sender, in which their own experiences were taken into account. This aspect has previously been emphasized by Moffat et al. (80), suggesting consulting youth themselves for reality-based content in information-based cannabis prevention interventions. Additionally, research on selective prevention interventions, such as motivational interviewing to promote behavioral change in risk groups, highlighted the importance of a non-judgmental and less moralizing approach which stayed neutral to the actual behavior, including an assessment of advantages and disadvantages (81, 82). This approach may also apply to universal information prevention interventions, as supported by the current study as well as by previous research (80). Finally, the participants also highlighted the importance of a credible information provider or sender. Credibility can be gained either through having deep knowledge of the subject, an appearance of authority, or personal experience of the drug. These opinions were also shared in the interview study on Swedish students (57) with slightly younger informants. It may be debated whether people with a personal experience of substance use can be more objectively credible or helpful, but young people seem to place their trust in them. However, it is important to note that the students in the previous study (57) emphasized that the person with personal experience of using drugs should not be just anybody, for example, “a heroin addict who talked about having found Jesus,” but someone with whom they could identify. Credibility can also be increased through identification with the sender by similarity in age. In the current study, it was apparent that informants looked for reliable information from friends and acquaintances. Apart from similarities in age and life situation, friends may provide credibility through their established interpersonal relationships. Finally, the informants pointed out that famous people, such as “influencers,” can be credible senders and that public authorities should cooperate with them when communicating information about cannabis. It is unlikely that this proposal is based on influencers’ potential knowledge of cannabis, but on the fact that young people identify with them because they represent the values that the youth hold, and that they manage to establish some kind of friendship with their followers, creating a feeling of benevolence that may increase credibility (83).

Strengths and Limitations

To our knowledge, the present study is unique in that it combines interviews with Swedish young adult users and non-users, exploring their attitudes toward both cannabis use and information to prevent use. This study has several additional strengths that should be noted. First, it was based on interviews with informants representing a wide range in terms of age, sex, socioeconomic background, and experience of cannabis use, thus generating rich material highlighting many aspects of young

people's attitudes toward cannabis. Second, the research team had extensive experience of research on drug-related issues in society, including cannabis, both in terms of health and policy aspects. Two of the researchers conducted the interviews themselves, which enabled professional interviews with relevant follow-up questions as well as a deep knowledge of the material even before the qualitative content analysis began. Furthermore, a team-based analysis process was used to ensure reliability of the results. However, this study also has some limitations. The recruitment process was voluntary, which entailed a risk of distorted selection because people who wanted to participate may differ in important ways from those who did not want to participate. In the current study, there was an overrepresentation of cannabis users in relation to non-users; this was somewhat surprising in light of the strict Swedish law against cannabis, which was assumed to deter users from participating. Another limitation is the quite sparse background information about the sample, limiting the possibility to obtain a more comprehensive profile of the informants. Finally, in an interview situation, there is a risk that the interviewee may respond in a way that they believe the researcher expects them to (42).

CONCLUSION

Current risk awareness associated with cannabis use among young adults is insufficient to prevent actual cannabis use. Therefore, multicomponent drug prevention programs, where information is one of the components or strategies, should be implemented, combining a firm and fact-based focus on risks with recognition of cannabis' short-term desired effects, delivered by credible senders with authority or those with whom young adults can identify.

DATA AVAILABILITY STATEMENT

The data are available from the Centre for Psychiatry Research, a collaboration between the Karolinska Institutet and Region

Stockholm, but restrictions apply to their availability, as they were used under ethical permission for the current study, and therefore, are not publicly available. However, data are available from the authors upon reasonable request and with permission from the Centre for Psychiatry Research.

ETHICS STATEMENT

The research protocol was approved by the Swedish Ethics Review Authority and was conducted according to the principles expressed in the Declaration of Helsinki and all participants provided written informed consent.

AUTHOR CONTRIBUTIONS

PK: conceptualization, methodology, investigation, data curation, formal analysis, project administration, writing—original draft, and writing—review and editing. AKS: conceptualization, methodology, investigation, data curation, formal analysis, project administration, and writing—review and editing. JG: conceptualization, methodology, formal analysis, supervision, funding acquisition, and writing—review and editing. All authors contributed to the article and approved the submitted version.

FUNDING

This work was funded by the Stockholm Health Care Administration. The funding body had no role in the study design, data collection, analysis, data interpretation, or writing of the manuscript.

ACKNOWLEDGMENTS

We would like to thank all the participant informants for making this study possible.

REFERENCES

1. Solowij N, Grenyer BF. Are the adverse consequences of cannabis use age-dependent? *Addiction*. (2002) 97:1083–6. doi: 10.1046/j.1360-0443.2002.00243.x
2. Arria AM, Caldeira KM, Bugbee BA, Vincent KB, O'Grady KE. Marijuana use trajectories during college predict health outcomes nine years post-matriculation. *Drug Alcohol Depend*. (2016) 159:158–65. doi: 10.1016/j.drugalcdep.2015.12.009
3. Van Ours JC, Williams J. Cannabis use and its effects on health, education and labor market success. *J Econ Surv*. (2015) 29:993–1010. doi: 10.1111/joes.12070
4. Strandberg A, Skoglund C, Gripenberg JPK. Alcohol and illicit drug consumption and the association with risky sexual behaviour among Swedish youths visiting youth health clinics. *Nordisk Alkohol Nark*. (2019) 36:442–59. doi: 10.1177/1455072519845970
5. Feltmann K, Elgán TH, Strandberg AK, Kvillmo P, Jayaram-Lindström N, Grabski M, et al. Illicit drug use and associated problems in the nightlife scene: a potential setting for prevention. *Int J Environ Res Public Health*. (2021) 18:4789. doi: 10.3390/ijerph18094789
6. Strandberg AK, Elgán TH, Feltmann K, Jayaram Lindström N, Gripenberg J. Illicit drugs in the nightlife setting: changes in employee perceptions and drug use over a fifteen-year period. *Subst Use Misuse*. (2020) 55:2116–28. doi: 10.1080/10826084.2020.1793365
7. Feltmann K, Gripenberg J, Strandberg AK, Elgán TH, Kvillmo P. Drug dealing and drug use prevention – a qualitative interview study of authorities' perspectives on two open drug scenes in Stockholm. *Subst Abuse Treat Prev Policy*. (2021) 16:37. doi: 10.1186/s13011-021-00375-w
8. Donnelly J, Young M, Marshall B, Hecht ML, Saldutti E. Public health implications of cannabis legalization: an exploration of adolescent use and evidence-based interventions. *Int J Environ Res Public Health*. (2022) 19:3336. doi: 10.3390/ijerph19063336
9. Manrique-Garcia E, Zammit S, Dalman C, Hemmingsson T, Andreasson S, Allebeck P. Cannabis, schizophrenia and other non-affective psychoses: 35 years of follow-up of a population-based cohort. *Psychol Med*. (2012) 42:1321–8. doi: 10.1017/S0033291711002078
10. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med*. (2014) 370:2219–27. doi: 10.1056/NEJMra1402309

11. Crane NA, Schuster RM, Fusar-Poli P, Gonzalez R. Effects of cannabis on neurocognitive functioning: recent advances, neurodevelopmental influences, and sex differences. *Neuropsychol Rev.* (2013) 23:117–37. doi: 10.1007/s11065-012-9222-1
12. Tapert SF, Schweinsburg AD, Brown SA. The influence of marijuana use on neurocognitive functioning in adolescents. *Curr Drug Abuse Rev.* (2008) 1:99–111. doi: 10.2174/1874473710801010099
13. Schlag AK, Hindocha C, Zafar R, Nutt DJ, Curran HV. Cannabis based medicines and cannabis dependence: a critical review of issues and evidence. *J Psychopharmacol.* (2021) 35:773–85. doi: 10.1177/0269881120986393
14. Borgelt LM, Franson KL, Nussbaum AM, Wang GS. The pharmacologic and clinical effects of medical cannabis. *Pharmacotherapy.* (2013) 33:195–209. doi: 10.1002/phar.1187
15. Swift W, Coffey C, Carlin JB, Degenhardt L, Patton GC. Adolescent cannabis users at 24 years: trajectories to regular weekly use and dependence in young adulthood. *Addiction.* (2008) 103:1361–70. doi: 10.1111/j.1360-0443.2008.02246.x
16. Von Sydow K, Lieb R, Pfister H, Hofler MH, Wittchen HU. What predicts incident use of cannabis and progression to abuse and dependence? a 4-year prospective examination of risk factors in a community sample of adolescents and young adults. *Drug and Alcohol Depend.* (2002) 68:49–64. doi: 10.1016/S0376-8716(02)00102-3
17. Luthar SS, Small PJ, Ciciolla L. Adolescents from upper middle class communities: Substance misuse and addiction across early adulthood. *Dev Psychopathol.* (2018) 30:315–35. doi: 10.1017/S0954579417000645
18. Levine M. *The Price of Privilege: How Parental Pressure And Material Advantage Are Creating A Generation Of Disconnected And Unhappy Kids.* New York: Harper (2008).
19. Martin CC. High socioeconomic status predicts substance use and alcohol consumption in U. S Undergraduates. *Subst Use Misuse.* (2019) 54:1035–43. doi: 10.1080/10826084.2018.1559193
20. Patrick ME, Wightman P, Schoeni RF, Schulenberg JE. Socioeconomic status and substance use among young adults: a comparison across constructs and drugs. *J Stud Alcohol Drugs.* (2012) 73:772–82. doi: 10.15288/jsad.2012.73.772
21. Janicijevic KM, Kocic SS, Radevic SR, Jovanovic MR, Radovanovic SM. Socioeconomic factors associated with psychoactive substance abuse by adolescents in Serbia. *Front Pharmacol.* (2017) 8:366. doi: 10.3389/fphar.2017.00366
22. Charitonidi E, Studer J, Gaume J, Gmel G, Daeppen J-B, Bertholet N. Socioeconomic status and substance use among Swiss young men: a population-based cross-sectional study. *BMC Public Health.* (2016) 16:333. doi: 10.1186/s12889-016-2949-5
23. Hiltunen L. *The Pursuit of Restrained Perfection: Experiences of Ill Health Among Adolescent Girls and Boys (In Swedish).* Växjö: Linnéuniversitetet (2017).
24. Luthar SS. The culture of affluence: psychological costs of material wealth. *Child Dev.* (2003) 74:1581–93. doi: 10.1046/j.1467-8624.2003.00625.x
25. Carliner H, Brown QL, Sarvet AL, Hasin DS. Cannabis use, attitudes, and legal status in the U. S: a review. *Prev Med.* (2017) 104:13–23. doi: 10.1016/j.ypmed.2017.07.008
26. Addiction EMCeDaD. *Trends and Developments.* Luxembourg: Publications Office of the European Union (2019).
27. EMCDDA. *Cannabis Legislation in Europe. An Overview.* Luxembourg: Publications Office of the European Union (2018).
28. Ministry of Justice. *Penal Law on Narcotics [Narkotikastrafflag] (SFS 1968:64).* Stockholm: Government Offices of Sweden (1968).
29. Englund A. *Skolelevers drogvanor 2014 (School students drug habits 2014):* Centralförbundet för alkohol- och narkotikaupplysning (CAN), Stockholm: The Swedish Council for Information on Alcohol and Other Drugs (2019).
30. Schmidt LA, Jacobs LM, Spetz J. Young people's more permissive views about marijuana: local impact of state laws or national trend? *Am J Public Health.* (2016) 106:1498–503. doi: 10.2105/AJPH.2016.303153
31. Sundin E, Landberg J, Ramstedt M. Negativa konsekvenser av alkohol, narkotika och tobak - en studie med fokus på beroende och problem från andra konsumtion. CAN, editor Stockholm: CAN (2018).
32. EMCDDA. *European Drug Report 2019: Trends and Developments.* Luxembourg: Publications Office of the European Union (2021).
33. Zetterqvist ME. *Skolelevers Drogvanor 2018 (Drug Habits Among Pupils and Students) (In Swedish).* Stockholm: Centralförbundet för alkohol- och narkotikaupplysning (CAN) (2018).
34. Public Health Agency of Sweden. *Den svenska narkotikasituationen (The Swedish Drug Situation) (In Swedish)* (2021). Available online at: <https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/d/den-svenska-narkotikasituationen-2021/?pub=107044> (accessed January 25, 2022).
35. Kilwein TM, Wedell E, Herchenroeder L, Bravo AJ, Looby A. A qualitative examination of college students' perceptions of cannabis: insights into the normalization of cannabis use on a college campus. *J Am Coll Health.* (2022) 70:733–41. doi: 10.1080/07448481.2020.1762612
36. Paul B, Thulien M, Knight R, Milloy MJ, Howard B, Nelson S, et al. "Something that actually works": cannabis use among young people in the context of street entrenchment. *PLoS ONE.* (2020) 15:e0236243. doi: 10.1371/journal.pone.0236243
37. Bobitt J, Qualls SH, Schuchman M, Wickersham R, Lum HD, Arora K, et al. Qualitative analysis of cannabis use among older adults in Colorado. *Drugs Aging.* (2019) 36:655–66. doi: 10.1007/s40266-019-00665-w
38. Breyer BL, Aston ER, Gebru NM, Merrill JE. Differences in cannabis use characteristics, routines, and reasons for use among individuals with and without a medical cannabis card. *Exp Clin Psychopharmacol.* (2022). doi: 10.1037/pha0000542
39. Znoj H, Genrich G, Zeller C, Koroma D. Cannabis use, attitudes, regulation and health: survey data from an urban population of users and non-users. *J Public Health Res.* (2021) 11:2575. doi: 10.4081/jphr.2021.2575
40. EMCDDA. *Annual Report 2007: The State of the Drugs Problem in Europe.* Luxembourg: Office for Official Publications of the European Communities (2007).
41. Skretting A. Attitude of the Norwegian population to drug policy and drug-offences. *Addiction.* (1993) 88:125–31. doi: 10.1111/j.1360-0443.1993.tb02770.x
42. Trevino RA, Richard AJ. Attitudes towards drug legalization among drug users. *Am J Drug Alcohol Abuse.* (2002) 28:91–108. doi: 10.1081/ADA-120001283
43. Van der Sar R, Brouwers E, van de Goor L, Garretsen H. The opinion on Dutch cannabis policy measures: a cross-sectional survey. *Drugs.* (2011) 18:161–71. doi: 10.3109/09687637.2010.519361
44. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Adv. Behav Res Ther.* (1978) 1:139–61. doi: 10.1016/0146-6402(78)90002-4
45. Ajzen I. *Attitudes, Personality, and Behavior.* UK: McGraw-Hill Education (2005).
46. Gervilla E, Quigg Z, Duch M, Juan M, Guimarães C. Adolescents' alcohol use in botellon and attitudes towards alcohol use and prevention policies. *Int J Environ Res Public Health.* (2020) 17:3885. doi: 10.3390/ijerph17113885
47. Gerstein DR, Green LW. *Preventing Drug Abuse: What do we know?* Washington, DC: National Academies Press (US). Copyright 1993 by the National Academy of Sciences. All rights reserved (1993).
48. DiBello AM, Miller MB, Neighbors C, Reid A, Carey KB. The relative strength of attitudes versus perceived drinking norms as predictors of alcohol use. *Addict Behav.* (2018) 80:39–46. doi: 10.1016/j.addbeh.2017.12.022
49. Piontek D, Kraus L, Bjarnason T, Demetrovics Z, Ramstedt M. Individual and country-level effects of cannabis-related perceptions on cannabis use. A multilevel study among adolescents in 32 European countries. *J Adolesc Health.* (2013) 52:473–9. doi: 10.1016/j.jadohealth.2012.07.010
50. Fazio RH, Sanbonmatsu DM, Powell MC, Kardes FR. On the automatic activation of attitudes. *J Pers Soc Psychol.* (1986) 50:229–38. doi: 10.1037/0022-3514.50.2.229
51. Kotlaja MM, Carson JV. Cannabis prevalence and national drug policy in 27 countries: an analysis of adolescent substance use. *Int J Offender Ther Comp Criminol.* (2019) 63:1082–99. doi: 10.1177/0306624X18814184
52. Cornish D, Clarke R. Situational prevention, displacement of crime and rational choice theory. In: Laycock KHaG, editor. *Situational crime prevention: From theory into practice.* London: HMSO (1986).
53. Barrett P, Bradley C. Attitudes and perceived risk of cannabis use in Irish adolescents. *Ir J Med Sci.* (2016) 185:643–7. doi: 10.1007/s11845-015-1325-2
54. Martinez-Vispo C, Dias PC. Risk perceptions and cannabis use in a sample of portuguese adolescents and young adults. *Int J Ment Health Addict.* (2020) 20:595–606. doi: 10.1007/s11469-020-00392-z

55. Quinlan KJ, Valenti M, Rots G, Esrick J, Dash K. Addressing youth perceptions of harm in marijuana prevention programming. *J Appl Res Child Inform Policy Child Risk*. (2017) 8:7.
56. Zeiger JS, Silvers WS, Flegler EM, Zeiger RS. Attitudes about cannabis mediate the relationship between cannabis knowledge and use in active adult athletes. *J. Cannabis Res.* (2020) 2:18. doi: 10.1186/s42238-020-00023-3
57. Kvillemo P, Hiltunen L, Demetry Y, Carlander A-K, Hansson T, Gripenberg J, et al. How to prevent alcohol and illicit drug use among students in affluent areas: a qualitative study on motivation and attitudes towards prevention. *SATPP*. (2021) 16:83. doi: 10.1186/s13011-021-00420-8
58. Barry MM, Clarke AM, Jenkins R, Patel V, A. systematic review of the effectiveness of mental health promotion interventions for young people in low and middle income countries. *BMC Public Health*. (2013) 13:835. doi: 10.1186/1471-2458-13-835
59. Doran N, Papadopoulos A. Cannabis edibles: behaviours, attitudes, and reasons for use. *Environ Health Rev.* (2019) 62:44–52. doi: 10.5864/d2019-011
60. Norberg MM, Kezelman S, Lim-Howe N. Primary prevention of cannabis use: a systematic review of randomized controlled trials. *PLoS ONE*. (2013) 8:e53187. doi: 10.1371/journal.pone.0053187
61. Coie JD, Watt NF, West SG, Hawkins JD, Asarnow JR, Markman HJ, et al. The science of prevention. A conceptual framework and some directions for a national research program. *Am Psychol*. (1993) 48:1013–22. doi: 10.1037/0003-066X.48.10.1013
62. - Ministry of Education. *Education Act [Skollagen] (1985:1100)*. Stockholm: Government Offices of Sweden (1985).
63. The Swedish National Agency for Education. *Läroplan för grundskolan, förskoleklass och fritidshem (Curriculum for the compulsory school, preschool class and school-age educare) (revised 2018)* (In Swedish). Stockholm: The Swedish National Agency for Education (2018).
64. The Swedish National Agency for Education. *Läroplan för gymnasieskolan (Curriculum for secondary school) (In Swedish)*. Stockholm: The Swedish National Agency for Education (2011).
65. Allara E, Ferri M, Bo A, Gasparrini A, Faggiano F. Are mass-media campaigns effective in preventing drug use? A cochrane systematic review and meta-analysis. *BMJ Open*. (2015) 5:e007449. doi: 10.1136/bmjopen-2014-007449
66. Hornik R, Jacobsohn L, Orwin R, Piesse A, Kalton G. Effects of the national youth anti-drug media campaign on youths. *Am J Public Health*. (2008) 98:2229–36. doi: 10.2105/AJPH.2007.125849
67. Watson TM, Valleriani J, Hyshka E, Rueda S. Cannabis legalization in the provinces and territories: missing opportunities to effectively educate youth? *Can J Public Health*. (2019) 110:472–5. doi: 10.17269/s41997-019-00209-0
68. Ministry of Health and Social Affairs. *Continuity and Long-Term Thinking in ANDT Work* (2016). Retrieved from: <https://www.government.se/articles/2016/04/continuity-and-long-term-thinking-in-andt-work/> (accessed January 25, 2022).
69. Månsson J. *Cannabis Discourses in Contemporary Sweden. Continuity and Change Department of Social Work*. Stockholm: Stockholm University (2017).
70. Holder HD. *Alcohol and the Community: A Systems Approach to Prevention*. Cambridge: Cambridge University Press (1998).
71. Arain M, Haque M, Johal L, Mathur P, Nel W, Rais A, et al. Maturation of the adolescent brain. *Neuropsychiatr Dis Treat*. (2013) 9:449–61. doi: 10.2147/NDT.S39776
72. Weller SC, Vickers B, Bernard HR, Blackburn AM, Borgatti S, Gravlee CC, et al. Open-ended interview questions and saturation. *PLoS ONE*. (2018) 13:e0198606. doi: 10.1371/journal.pone.0198606
73. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. (2005) 15:1277–88. doi: 10.1177/1049732305276687
74. Graneheim U, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*. (2004) 24:105–12. doi: 10.1016/j.nedt.2003.10.001
75. MacQueen KM, McLellan E, Kay K, Milstein B. Codebook development for team-based qualitative analysis. *Cult Anthropol Methods J*. (1998) 10:31–6. doi: 10.1177/1525822X980100020301
76. Drack M, Apfalter W, Pouvreau D. On the making of a system theory of life: paul a weiss and ludwig von bertalanffy's conceptual connection. *Q Rev Biol*. (2007) 82:349–73. doi: 10.1086/522810
77. Pedersen ER, Hummer JF, Rinker DV, Traylor ZK, Neighbors C. Measuring protective behavioral strategies for marijuana use among young adults. *J Stud Alcohol Drugs*. (2016) 77:441–50. doi: 10.15288/jsad.2016.77.441
78. Bravo AJ, Anthenien AM, Prince MA, Pearson MR, Team MOS. Marijuana protective behavioral strategies as a moderator of the effects of risk/protective factors on marijuana-related outcomes. *Addict Behav*. (2017) 69:14–21. doi: 10.1016/j.addbeh.2017.01.007
79. Pedersen ER, Huang W, Dvorak RD, Prince MA, Hummer JF. The protective behavioral strategies for marijuana scale: further examination using item response theory. *Psychol Addict Behav*. (2017) 31:548. doi: 10.1037/adb0000271
80. Moffat BM, Haines-Saah RJ, Johnson JL. From didactic to dialogue: assessing the use of an innovative classroom resource to support decision-making about cannabis use. *Drugs*. (2017) 24:85–95. doi: 10.1080/09687637.2016.1206846
81. Miller P, Curtis A, Chikritzhs T, Toumbourou JW. *Interventions for Reducing Alcohol Supply, Alcohol Demand and Alcohol-Related Harm: Final Report*. Canberra, Australia: National Drug Law Enforcement Research Fund (NDLERF) (2015).
82. Miller WR, Rollnick S. *Motivational Interviewing: Helping People Change*. 3rd ed New York: The Guilford Press (2013).
83. Sánchez-Fernández R, Jiménez-Castillo D. How social media influencers affect behavioural intentions towards recommended brands: the role of emotional attachment and information value. *J Mark Manag*. (2021) 37:1123–47. doi: 10.1080/0267257X.2020.1866648

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 Kvillemo, Strandberg and Gripenberg. 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.



Physicians' Response and Preparedness of Terrorism-Related Disaster Events in Quetta City, Pakistan: A Qualitative Inquiry

Fazal Ur Rehman Khilji¹, Zil-e-Huma², Nosheen Sikander Baloch³, Maryam Shoaib⁴, Zaffar Iqbal⁵, Abdul Raziq⁶, Nabila Sadaf⁷, Syed Ainuddin⁸, Sajjad Haider¹, Fahad Saleem¹, Qaiser Iqbal¹, Tanveer Hussain⁸, Asfandiyar Ayaz⁸ and Rabia Ishaq^{1*}

¹ Faculty of Pharmacy and Health Sciences, University of Baluchistan, Quetta, Pakistan, ² Department of Zoology, Sardar Bahadur Khan Women's University, Quetta, Pakistan, ³ Department of Gynecology and Obstetrics, Bolan Medical College, Quetta, Pakistan, ⁴ Department of Gynecology and Obstetrics, Sandeman Provincial Hospital, Quetta, Pakistan, ⁵ Health Department Government of Balochistan, Quetta, Pakistan, ⁶ Department of Statistics, University of Balochistan Quetta, Quetta, Pakistan, ⁷ Department of Pharmacy, Sardar Bahadur Khan Womens' University, Quetta, Pakistan, ⁸ Department of Disaster Management and Development Studies, University of Balochistan, Quetta, Pakistan

OPEN ACCESS

Edited by:

Shazia Qasim Jamshed,
Sultan Zainal Abidin
University, Malaysia

Reviewed by:

Furqan Khurshid Hashmi,
Punjab University, Pakistan
Maryam Farooqui,
Qassim University, Saudi Arabia

*Correspondence:

Rabia Ishaq
rabiaishaq72@gmail.com

Specialty section:

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

Received: 04 April 2022

Accepted: 12 May 2022

Published: 27 June 2022

Citation:

Khilji FUR, Zil-e-Huma, Baloch NS, Shoaib M, Iqbal Z, Raziq A, Sadaf N, Ainuddin S, Haider S, Saleem F, Iqbal Q, Hussain T, Ayaz A and Ishaq R (2022) Physicians' Response and Preparedness of Terrorism-Related Disaster Events in Quetta City, Pakistan: A Qualitative Inquiry. *Front. Public Health* 10:912762. doi: 10.3389/fpubh.2022.912762

Background: Besides catastrophes, infrastructural damages, and psychosocial distress, terrorism also imposes an unexpected burden on healthcare services. Considerably, adequately-prepared and responsive healthcare professionals affirms effective management of terrorism-related incidences. Accordingly, the present study aimed to evaluate physicians' preparedness and response toward terrorism-related disaster events in Quetta city, Pakistan.

Methods: A qualitative design was adopted. Physicians practicing at the Trauma Center of Sandeman Provincial Hospital (SPH), Quetta, were approached for the study. We conducted in-depth interviews; all interviews were audio-taped, transcribed verbatim, and analyzed for thematic contents by a standard content analysis framework.

Results: Fifteen physicians were interviewed. The saturation was achieved at the 13th interview however we conducted another two to validate the saturation. The thematic content analysis revealed five themes and 11 subthemes. All physicians have experienced, responded to, and managed terrorism-related disaster events. They were prepared professionally and psychologically in dealing with a terrorism-related disaster. Physicians identified lack of disaster-related curricula and training, absence of a standardized protocol, recurrence of the disaster, and hostile behavior of victim's attendants during an emergency as critical barriers to effective terrorism-related disaster management. Among limitations, all respondents mentioned workspace, and resources as a foremost constraint while managing a terrorism-related disaster event.

Conclusion: Although physicians understood the abilities and had the required competencies to mitigate a terrorism-related disaster, lack of workspace and resources were identified as a potential barrier to effective disaster management. Based on the

results, we propose reconsideration and integration of the medical curriculum, particularly for terrorism-related disaster management, collaboration, and communication among various stakeholders to manage terrorism-related disaster events competently.

Keywords: physicians, response, preparedness, terrorism-related disaster events, qualitative

INTRODUCTION

Defined as “an unexpected and devastating event that exceed the coping capacity of the affected community,” disasters have existed throughout the human history (1, 2). Although, the precise prevalence of disasters is not quantifiable, it is believed that disasters occur every day somewhere in the world (3, 4). Shifting our concerns to disasters in the South Asian Region, the past 40 years have reported 1,333 disasters which resulted in 980,000 deaths. The disasters also affected 2.4 billion lives and was worth US\$ 105 billion of overall damages (5).

Parallel to the natural disasters, mankind is also faced with terrorism-related disasters (TRDs) that are a rampant challenge across the globe (6). The Global Terrorism Database (GTD) defines TRDs as “the threatened or actual use of illegal force and violence by a non-state actor to attain a political, economic, religious, or social goal through fear, coercion, or intimidation” (7). Terrorism is believed to be a leading menace to humanity (8), and since the 1970's, a rising trend of TRDs has been reported (9). Around the globe, GTD reported 156,772 TRDs from 1970 to 2015 (10). On an average of 2,000 TRD events per year reported, most attacks were executed in the Middle East and South Asia (11), which included Afghanistan and Pakistan (12).

Shifting our concerns toward Pakistan, terrorism in the country mainly originated in the Soviet-Afghan war in the 1980s (7). The September 11 attacks entirely transformed the panorama of terrorism throughout the world (13). Because of the strategic location of the country and its influential capacity regarding Afghanistan, the country is immensely affected by TRDs, and it consequently fuelled terrorism to its extreme (14–16). According to Global Terrorism Index (GTI), Pakistan was ranked 2nd in terms of 1,650 terrorist attacks, surpassing Afghanistan with 1,468 terrorist attacks in 2012. However, since then a declining trend was observed as in 2017 Pakistan counted for 7% of TRDs around the globe and further decreasing to only four attacks in 2021 (15). Terrorism is not limited to cause massive catastrophes and casualties only, but additionally, it imposes adverse effects on the financial market and economic condition globally (17). The economic growth decreases with the increase of TRDs (18) as there is an adverse relationship between Foreign Direct Investment (FDI) and terrorism (19). Correspondingly in Pakistan, the cost of counter-terrorism was US\$ 2.669 billion that increased to US\$ 17.8 billion during 2010–2011. Thus, resulted in a decrease in the investment to Gross Domestic Product (GDP) ratio and FDI inflows in the country (20). Furthermore, to combat terrorism-related activities, the Government expenditures augmented from 7.84% of GDP in the year 2005 to 11.84% of GDP in the year 2015 (7). Resultingly, this shift of resources from the productive sectors to security-related

activities made the already deprived economic condition more vulnerable (21).

In addition to economical destructions and demolitions, TRDs induce significant impacts on a health care system's capacity to act proficiently and respond effectively (22). This is true as the public healthcare system in Pakistan is scarce in terms of human resources and substantial infrastructure to accomplish the requirements of the growing population (23). According to World Health Organization (WHO), Pakistan's healthcare system lacks basic healthcare guidelines, bears the sixth minimum health expenditure to GDP ratio, and acquires only 0.6 hospital beds for every 1,000 people (24). Specifically talking about managing TRDs, research reveals that Pakistan has not adopted the recent advancements in scientific approaches of disaster management (DM) policies (25). Currently, Pakistan lacks an effective response planning system and valuable resource allocation system during TRDs (26). The higher death ratio in Pakistan during TRDs are attributed to the amplitude of collapse, lack of structured emergency medical services, increased infection rates, inadequate triaging, and deficiency in primary resuscitation services (27). Summarizing, the healthcare system of Pakistan is confronted with an overburden of TRDs upon its occurrences. Under such circumstances, it is important that health institutions and healthcare professionals are proficient, prepared, and skilled to administrate a terrorism-related incidence with restricted resources otherwise the defiantly consequences might be significantly vulnerable. Additionally, acknowledgment and consideration of preparedness and administration are imperative to overcome future disasters effectively. However, to the best of our knowledge and through extensive literature review, healthcare professionals' preparedness and response to TRDs in Pakistan is not reported in the literature. Considering the high incidence of terrorism-related events in Pakistan and scarcity of information on its management, we designed this study to evaluate the response and preparedness of healthcare professionals (physicians) toward terrorism-related events in Quetta city, Pakistan.

METHODS

Study Design and Settings

We adopted a qualitative study design (in-depth, face-to-face interviews). The flexibility of this method, including the exhaustive analysis of respondents' attitudes, experiences, and intentions, is beneficial (28, 29). Similarly, qualitative studies produce an extended range of ideas and notions to which persons carry out issues; also, the different point of view is revealed among the groups (30, 31). It is imperative to mention that the qualitative method has the edge to fill the gaps that remained undiscovered by using research-based

surveys, specifically in underdetermination areas of the research (32). Subsequently, considering the objective aspects of the current study, a qualitative design was a paramount adoption for preliminary essence anticipated to generate concepts and hypothesis that bears added potential for research compared to other models (33).

For the current study, the phenomenological approach was adopted. The rationale of adopting this approach was straight forward. Phenomenological approach in qualitative methods emphasizes experiential, lived aspects of a particular construct—that is, how the phenomenon is experienced at the time that it occurs, rather than what is thought about this experience, or the meaning ascribed to it subsequently (29).

The current study was conducted at Trauma Center Quetta (TC). The TC was established in 2016 within the premises of Sandeman Provincial Hospital Quetta (SPH-Q). The TC is a thirty-bedded facility with 24 physicians stationed to offer healthcare services that are trauma specific. The TC is well-equipped and bears the capacity to deal with all kinds of emergency conditions. The TC also provides immediate health care services round the clock and throughout the year to the victims of terrorism-related and general traumatic injuries (34).

Study Participants, Criteria, and Sampling

Registered physicians stationed permanently and practicing at the TC were approached for the interviews. Our objectives made it apparent to adopt the purposive sampling method (35). We excluded physicians on rotations, stationed at the TC as part-timers and unwilling to participate. For content analysis, we opted the saturation based approach. The theoretical saturation means that no additional data is retrievable, and the researcher can develop properties of the category. Furthermore, as same inference occurs over and over again, the researcher becomes empirically confident that a category is saturated (29).

The Interview Guide (Validation, Reliability, and Pilot Study)

A semi-structured interview guide was used for the interviews. The guide was constructed through extensive literature review (36–40), expert panel discussion, and shared experience (41–43). The guide was established with widely framed, open-ended questions that gave enough opportunities to the respondents. Parallel, physicians were provided the opportunity to illustrate their narratives and encourage sharing additional information regarding terrorism-related disaster management.

The face and content validity of the interview guide was established through a panel of experts (senior physicians) having experience in terrorism-related disaster management. Once the validity was ensured, the guide was piloted with four physicians. The pilot data analysis confirmed that the discussion topics were adequate and appropriately phrased to answer research questions and minimize validity and reliability threats. As the validity and reliability of the interview guide was ensured, it was made available for the main study (**Supplementary File**). Data and participants of the pilot study were not included in the final analysis.

Interview Procedure, Data Collection, and Analysis

The first author conducted the interviews at the TC; all participants were briefed about the study objectives before initiating the interviews. Continuously, a debriefing session was again conducted at the end of the discussion. The interviews started with an ice-breaking session. Probing questions were asked in conversations to clarify the meanings of responses and gain insight into the topic being discussed.

All interviews were audio-recorded that persisted for approximately half an hour. Along with eliciting in-depth views, the physicians were also provided the freedom to express the additional reviews and comments. During the interviews, ZI played a role as an observer while AR assisted in monitoring the field notes, facial expressions, and body language that were concomitant to audio recordings. The conducted interviews remained until the achievement of thematic saturation (44, 45). The analysis of recordings (verbatim) was carried out by the research team, followed by an informal gathering where physicians were demonstrated with finalized interview script (46). Triangulation and member check helped in establishing the credibility and contributed to trustworthiness. Parallel to triangulation, persistent observations by the research team, transferability of the data and confirmability approached were used to enhance the trustworthiness and credibility of the data analysis.

Later, physicians were asked for affirmation of correctness and clarity of words, ideas, and jargon used during the script analysis (47, 48). NVivo® was used for coding and analysis through iterations (49) and inconsistencies were cleared through mutual consensus. All emerging themes and subthemes were discussed for authenticity among the research team and presented for data inference and interpretation. Although there are various approaches to conducting thematic analysis, we adopted the process developed Braun and Clarke that followed a six-step process: familiarization, coding, generating themes, reviewing themes, defining, and naming themes, and writing up.

Ethical Approval

Institutional review board at the Faculty of Pharmacy & Health Sciences, University of Baluchistan approved the study protocol (UoB/Reg:/GSO/67). Written consent was taken from the respondents before the interviews. The physicians were introduced to the nature of the research prior to initiating the interviews. They were also made secure of the confidentiality of their responses and their right to withdraw from the study.

RESULTS

Demographic Characteristics of Physicians

The saturation was achieved on the 13th interview, but we conducted two additional interviews to validate the saturation. Fifteen physicians were interviewed out of those 9 (60%) were male. Six (40%) of the respondents had an overall experience of >10 years and 7 (46.7%) had experience of > 18 months at the TC. Eleven (73.3%) had specialization in surgery and none of

TABLE 1 | Demographic characteristics of the respondents.

Characteristics	Frequency	Percentage
Age (years)		
26–35	10	66.7
36–54	5	33.3
Gender		
Male	9	60.0
Female	6	40.0
Education		
MBBS	11	73.3
FCPS	04	26.7
Overall experience (years)		
1–5	7	46.7
6–10	2	13.3
> 10	6	40.0
Experience at trauma center (months)		
6–12	7	46.7
13–18	1	6.7
> 18	7	46.7
Current position		
MO	11	73.3
Registrar	1	6.7
PG registrar	2	13.3
Consultant	1	6.7
Specialization in disaster management		
None	15	100

the physicians were trained precisely in terms of managing or responding to disasters as shown in **Table 1**.

Thematic content analysis resulted in five major themes and 11 subthemes (**Table 2**). The themes and sub-themes are discussed as under:

Theme I: Terrorism-Related Disaster Event (Experience, Information Source, and Call-Up Mechanism)

Subtheme 1(a): Experience of Terrorism-Related Disaster Event(s)

All physicians reported experience of improvised explosive devices (IEDs), suicide attacks, mass shooting attempts on security forces, law enforcement agencies, and civilian populations. The suicide incidence of August 2016 was specifically mentioned, which occurred within SPH-Q consequent to 50 deaths.

“I was at TC when a pronounced lawyer (injured) victim of the targeted shooting was shifted to the emergency department (ED). A crowd of lawyers gathered at ED. After a little while, oh God! (appearing deep grief on his face) a tragic bomb blast occurred at the entrance of ED. Indescribable abhorrent scene converted the hospital not less than into a battlefield. After that, it was declared a suicide attack after recovering the dead body of suicide bomber.” (Physician 2, Male)

TABLE 2 | Themes and subthemes identified during data analysis.

Themes	Subthemes
Theme 1: Terrorism-related disaster event (experience, information source and call-up mechanism)	Subtheme 1(a): Experience of terrorism-related disaster event(s) Subtheme 1 (b): Disaster-related information sources and call-up mechanism
Theme 2: Response toward terrorism-based disaster event	Subtheme 2(a): Professional response Subtheme 2(b): Personal response Subtheme 2(c): Inclusive response
Theme 3: Preparedness of terrorism-related disaster	Subtheme 3(a): Current level of knowledge and familiarity of terrorism-related disaster management Subtheme 3(b): Workforce, infrastructure, and supplies Subtheme 3(c): Triage, communication, and coordination
Theme 4: Barriers toward terrorism-related disaster management	Subtheme 4(a): Safety concerns and issues Subtheme 4(b): Lack of disaster management content Subtheme 4(c): Lack of drills and hands-on training
Theme 5: Suggestions and recommendations	

Another male physician (Physician 6) commented that:

“I cannot forget the horrible incident of bomb blast followed by the mass shooting at Bethel Memorial Methodist Church in the city. It was a challenging condition for all of us.”

Subtheme 1(b): Disaster-Related Information Sources and Call-Up Mechanism

For an efficient and effective response to a disaster significantly, healthcare practitioners should promptly be informed immediately after the occurrence of a disaster. Therefore, an updated, sound, and efficient information system to respond is an essential requirement for communication across the hospital and other affiliated institutes and allied agencies. For that reason, physicians were inquired about the source of information and call-up mechanism in their institute during a terrorism related disaster event.

“We have an appropriate institutional/departmental WhatsApp group where exclusive and updated news and events are shared frequently. Moreover, national/International news networks are also a source of information regarding terrorism-related events. Likewise, Quetta is a small city soon after the occurrence of a grievous incidence; the information spreads within no time.” (Physician 3, Female)

We asked the respondents regarding the call-up mechanism contingent upon terrorism-related disaster emergencies. The

hospital administration informs all physicians of the TC about the terrorism-related incidence. Additionally, physicians are liable to report at TC within no time once they receive information about untoward news through any source. The study respondents appreciated the information and call-up system adopted by the institute in contacting the physicians during an emergent condition.

"The duty schedule is designed based on eight hourly rotational shifts; therefore, one shift always remains present on duty at TC. Off duty physicians are informed through a phone call. The mechanism of reporting is simply reasonable and useful." (Physician 9, Male)

Theme 2: Response Toward the Terrorism-Based Disaster Event

Subtheme 2(a): Professional Response

The response comprises practices and actions engaged in mitigation of concise and extended effects of a disaster. A quick and efficient response ensures instant assistance in saving precious lives, adequate medical therapy, and minimizing the collective impact of the disaster. Therefore, the comprehension response of healthcare professionals is a matter of great concern through the disaster. Relating to the responses we received, physicians were confident to respond to such terrorism-related disasters professionally and proficiently. Based on their disaster management experiences and the frequency of events they came across, according to our respondents, they feel prepared to respond to an emergent event appropriately within time.

"As soon as we receive an emergency call (or get information from any means), we ensure and supervise the arrangements along with organizing necessary equipment and allied resources at TC. We also ensure a quick check of the operation theaters, intensive care unit, wards beds, and accessibility of medicine trolleys. We provide necessary expert opinions to fulfill the gaps before the arrival of the victims." (Physician 10, Female)

Subtheme 2(b): Personal Response

In responding to a disaster, facing chaos and panic situations is a natural phenomenon. Healthcare professionals remain at risk of being exposed to trauma, which results in post-traumatic anxiety, stress, and depression. Such circumstances may lead to affect their psychosocial well-being adversely. Therefore, it is essential to understand the psychological response of physicians in such intimidating situations. Following what is being described, physicians of the current study showed a positive response, willpower, and willingness to lead to driving the team during responding and managing victims brought to the TC.

"When the victims arrive at the TC, the situation and atmosphere is indescribable. Therefore, we must lead the other healthcare professionals, allied staff, victims, and attendees of the victims professionally and ethically. We must manage the stressed and chaotic situation, and for that, we are always ready ... physically and emotionally." (Physician 4, Male)

Subtheme 2(c): Inclusive Response

Even though our study respondents were prepared, certain deficiencies were also noted during the interviews. Like other developing countries, the healthcare system of Pakistan is deprived and faced with the nonexistence of a disaster management system and response mechanism. For that reason, the physicians' response to emergencies is based on their self-experiences of countering numerous terror attacks.

"The emergency response checklists and smart response systems are theoretically familiar words. In my opinion, adopting and establishing a profound system at TC regarding response to disasters can be a great support for us. Currently, we are managing the situations on self-experiences basis without having specific operating guidelines." (Physician 5, Male)

Theme 3: Preparedness of Terrorism-Related Disaster Management

Subtheme 3(a): The Current Level of Knowledge and Familiarity of Terrorism-Related Disaster Management

Preparedness is the process of considering the potential occurrence of disaster and taking necessary action regarding filling the gaps before a disastrous event. The period of peace is an excellent opportunity to be utilized for preparation, integrated planning, organizing resources, and designing of procedures for the imminent threats and risks of disaster consequent to minimize its impacts. Evaluating the knowledge of DM among healthcare professionals is an imperative to reference to disaster-related uncertainties. During the interviews, physicians of the current study articulated sound reservations relevant to their knowledge and awareness of terrorism-related disaster management. Additionally, all the respondents confirmed that there are no training opportunities available, nor any seminars/workshops arranged that can help in improving their perceptive and knowledge of terrorism-related disaster management. In furtherance, they also stated disaster-related drills and mock exercises are beyond their imaginations.

"It is my fourth year working at TC. Since then, I have not received any formal training about terrorism-related disaster management. There is no documented informational module or written material that can help in improving relevant knowledge. We are managing terrorism-related disaster emergencies purely based on self-experiences gained from multiple encounters of terrorism-related disasters." (Physician 14, male)

Subtheme 3(b): Workforce, Infrastructure, and Supplies

The existence of a disaster management framework is another critical aspect while discussing disaster preparedness. Nevertheless, Pakistan is confronted with a poor disaster management framework, scarce health budgets, shortage of specialized healthcare professionals, and an overburdened healthcare system. Our study respondents expressed similar views when they were enquired about the availability of workforce, organizational framework, and infrastructure at TC. Though, the respondents of our study were satisfied with the medicine and supplies to some extent that are available at the TC.

"Comparative to the frequency of TRDS, we are deficient in terms of the workforce at TC. Similarly, the space is also limited. During terrorist attacks of mass casualties, we must utilize other sections of the hospital, even must shift the victims to other institutes. We do not hesitate to perform additional duties and overload ourselves because we are dedicated in our motive to saving lives on a priority basis even with limited resources." (Physician 1, Male)

During the discussion, Physician 12 (Female) added that:

"To some extent availability of medicine is satisfactory. The medicine trolleys are well prepared by pharmacists before any unwanted terrorism-related incidence. In my opinion, it may be enough to handle 80-90 victims of such event."

Subtheme 3(c): Triage, Communication, and Coordination

Triage is the process of prioritization (order of treatment) during mass disaster events. An effective triage depends on a functional and integrated command and communication system which enables in the identification of treatment priorities during the management of mass emergencies. Surprisingly, our respondents had limited knowledge of treatment orders because of poor knowledge of disaster management (as discussed above) and lack of planning and coordination within hospital departments and among different institutes.

"Triage! (Confused), soon after receiving the victims, we provide first aid and manage them according to their needs and severity. We have no protocols determinate to the treatment order. Frankly speaking, tirage is known to me, but I have no idea about its appropriate utilization." (Physician 8, Male)

Our study respondents also reported issues regarding lack of structured coordination and updated communication system. Within the TC, a traditionally acceptable coordination and communication system is existing, while; physicians had some reservations about other departments of the institute

"Patients are brought to casualty department or simultaneously to the TC in routine days. This results in a delay while managing the victims along with confusion in terms of actualization the number of casualties and prioritization (order of treatment). We can overcome such conditions through effective coordination and communication." (Physician 11, Female)

Theme 4: Barriers Toward Terrorism-Related Disaster Management

Subtheme 4(a): Safety Concerns and Issues

The chaotic and panic environment, crowd, recurrence of the terror attack at hospital setting and hostile behavior of the victim's attendees during an emergency was mentioned as a key barrier toward terrorism-related disaster management. Our respondents had serious apprehensions and presented leading reservations as they had experienced such situations earlier.

"Once a terrorism-related event occurs, the chance of secondary attack increases because of mass gathering of the crowd at TC."

Besides that, the aggressive crowd (attendees) start agitation and clamoring. It is very difficult to concentrate proper management of the victims when you have the fear of another suicide attack on your mind with the presence of an angry and hostile crowd all around." (Physician 13, Male)

Subtheme 4(b): Lack of Disaster Management Content

Lack of materials related to disaster management in the curriculum of medical education as well as during the residency training period was also stated as a barrier. The respondents stated that they had no idea or adequate understandings of disaster management when they started their medical practice. Therefore, they had only one option to follow the established practices and to perform what is being practiced at their workplace.

"The curriculum of medical education has nothing about disaster management. We are also unaware about disaster management during our residency training period. Disaster management is an important subject, and we must be informed and trained about it." (Physician 15, Male)

Subtheme 4(c): Lack of Drills and Hands-On Training

Our study respondents additionally mentioned that the lack of disaster-related training; seminars and workshops are potential barriers toward effective disaster management. Drills, mock exercises, and hands-on training sessions are essential to capacity building because as it increases the efficiency and effective management of emergencies and crisis situations.

"The institute never has arranged any disaster management seminar or workshop, considering about disaster management training remains one step ahead. In such circumstances expecting disaster drills and mock exercises are beyond the imaginations." (Physician 6, Female)

Theme 5: Suggestions and Recommendations

All physicians agreed and suggested that expansion of TC, enhancement of human resource, and increase logistics and supplies according to the requirements are needed. Furthermore, streamlining the line of instructions, provision of SOPs manual, plans, protocols, a checklist of TC, along with arranging training programs, exercises and systemically review and assessment of measures taken toward preparedness of the TC were key recommendations of the study respondents.

"We need additional space for expansion, specialized healthcare professionals along with allied staff and adequate supplies. Moreover, the administration must focus on our skills development and capacity building through regular training and exercises." (Physician 15, Female)

DISCUSSION

Terrorism-related disasters not only results in to mass casualties but also produce massive economic loss (50). The terrorism-related attacks are aimed to instigate jeopardy, in turn, certain use of unlawful turmoil and rampage to produce apprehension,

menacing, or intimidation (7). Terrorism-related attacks are not only aimed at targeting the victims but also sending a message of fear among communities (51). Hence, the population is confronted with developing a substantial number of long-term problems imposed by terrorism-related disasters (52). Data reveals that 18 - 50% of post-traumatic stress disorder (PTSD) were found prevalent among the victims of large-scale terrorism-related events (53). Besides this, terrorism is bilaterally associated with economic activity (54) and has the potential to adversely affect the economic growth (55), by marginalizing its modes of production and consumption globally (56). Additionally, the health care system is also under the siege of paramount multidimensional consequences of terrorism, even more susceptible to being a major stakeholder during its occurrence.

As discussed, the current study was aimed to assess the response and preparedness of physicians toward terrorism-related disaster management. We believe that the interviews extracted enough information that was able to answer the questions that were established earlier. The province of Balochistan has remained a leading victim of terrorism-related events for decades and the uncertainty turned the province into an undeclared warzone (57). Although significant reductions in terrorism-related deaths were reported across Pakistan in 2018, the number of terrorism-related deaths increased in Balochistan. Due to the strategic location of the province, the area specifically remained the worst victim of terrorism after 9/11, which fuelled the terrorism-related events (58). During this confrontation, the health care system of the province always remained at the front line in the provision of critical medical support and healthcare services to the victims of terrorism-related incidences. However, despite all the dedication, enthusiasm, and professional efforts of the healthcare system, the system of preparedness and response toward terrorism-related disasters was undefined and that was to be explored in this current study.

Respondents of the current study highlighted that financial constraints, dearth of human resources, and poor healthcare system are the major barriers to ineffective management of terrorism-related disasters. We must remember that Pakistan's economy has paid both direct and indirect costs of approximately US \$126.79 billion (7, 59) during the war against terror. Furthermore, terrorism negatively affected the flow of foreign investment, international trade, exports along with the local business in the country, which impacted lowered GDP (59). Pakistan is bearing a huge cost as government expenditures are diverted to counter-terrorism activities instead of valuable measures (54). Eventually, this diversion of expenditure overburdens the already deprived healthcare system as the policymakers are confronted with economic and financial constraints that impose restrictions on the provision of adequate healthcare services (60). However, even with all these limitations, the establishment of well-equipped TC, employment of proficient healthcare professionals, availability of logistic and medical support is evident of dedication while responding and preparing for a terrorism-related incidence.

Physicians are on the front lines while dealing with casualties or disasters (61). However, the foundation of medicine seems to

be the opposite in the case of terrorism because where physicians blindly heal, terrorists blindly kill (62). Therefore terrorism-related events require additional and sophisticated medical assistance provided by healthcare professionals specifically the physicians (63). To effectively respond to mega disasters, physicians must be prepared to handle multi-casualty incidents within their own hospitals (64). However, while managing terrorism-related disasters, physician's training may be deficient; therefore, simulated training may be required in effective and adequate preparation and enhancement of confidence to respond to terrorism-related disasters (65). This requirement is also evident from our study where the respondents agreed about the lack of training and security measures which means that they are putting their own life and the safety of the patients at risk. Focusing the training and development while dealing with terrorism related disasters, physician education and experience is of considerable significance. Understanding disaster medicine and the healthcare system response in responding to terrorism-related events should be an indispensable part of the medical curriculum. Scott and colleagues reported that medical students highlighted that they have not received adequate training to respond to disasters (66) and the same is reflected in the notion of the current study respondents.

Management of disasters and other mass casualties such as suicide bombing, IEDs, road-side bombing, and mass shooting need concrete plans. The National Association of EMS Physicians (NAEMSP) recommends a substantial role of emergency medical services (EMS) in all phases of the disaster management cycle, including preparedness, response, and recovery (61). Additionally, American Medical Association (AMA) compiled an educational framework comprising 37 target capabilities after being reviewed by stakeholders and further reviewed by National Disaster Life Support Education Consortium (NDLSEC), with interest in disaster preparedness, professional education, and curriculum development (67). The World Association of Disaster Medicine has also emphasized the need for a more scientific approach to all aspects of disaster medicine for the effective preparedness and response to terrorism-related disasters (68). The dilemmas of the response activity and chances of deficiency in preparation cannot be overlooked (69). In line to these guidelines, physicians of the current study were willing to participate in practical training rather than classroom teaching which is in accordance with the proposed literature (70). Unfortunately, respondents of the current study were unaware of such guidelines and protocols. Physicians of our study revealed that they had been provided traditional education in the classrooms; they also elaborated that they are unaware of updated and standardized strategies. Moreover, performing routine medical practices requisite to the provision of treatment to the patients, realizing updated information is least focused. Referring to the discussion, a comprehensive reconsideration of the medical education curriculum is required for integrated standardization for future physicians, as well as condensed training and continuous medical education for practicing physicians is the only way to fill the gaps and improvement in disaster management competencies. If patients are the first victims of medical error, then physicians

are termed as the “second victims” as they often experience feelings of distress, guilt, shame, and depression in response (71). The internationally accepted competency-oriented framework of physicians' education provides a thorough understanding of emergency preparedness and response, which it appeared to be missing in the current healthcare system of Pakistan.

However, our study respondents agreed that for effective management of unexpected catastrophic situations, disaster preparedness is worth of paramount significance; they also reported that, unfortunately, there is a dearth of training in the implementation of proficient disaster management. Our findings are supported by Barbosa through a survey from 224 hospital emergency departments in four North-western states, and the author identified deficiencies in preparedness involving physician training while managing terrorism-related disasters (69). It is a matter of prime concern that physicians are aware of adequate and efficient triaging, emergency management, mitigation, and rehabilitation of the victims back to their normal life. Additionally, physicians should also be trained in the provision of care, psychosocial support, and most importantly, carrying out limb, organ, and life-saving treatment to the victims. In consideration of its importance, the Office of the Assistant Secretary for Preparedness and Response (ASPR) and the Department of Defence (DoD) recommended that working together with partners to prioritize and develop examples of competency-based knowledge and skills must be included in job descriptions for public health, healthcare, behavioral health, and other national health security personnel and inter-professional health and supporting teams (72). But unfortunately, physicians, the respondents of our current study, were unaware of basic elements of disaster management such as triage principles, inter-coordination, reintegration, recuperation that are evidently ratiocinated the immediate requirement of training and development of physicians, particularly in the predicament of terrorism-related disaster management.

Physicians as the main pillar and leading arm of the health care system are required to acquire more formal education and training in both preparedness and response to be credentialed to assist (63). Revealed research recommended that disaster medicine be augmented either in the curriculum of undergraduate medical schools or in postgraduate university-based programs additionally in the continuing medical education programs (73). This enables the physicians to overcome the anarchic circumstances. Our qualitative analysis reflected the need for the incorporation of emergency/disaster medicine in the regular curriculum of medical schools in Pakistan, along with extensive disaster management training supported by the World Health Organization.

CONCLUSION

Physicians are the leading arm of the healthcare system and, as team player, has a supervisory role in managing terrorism-related disasters. The competencies, skills-set, and expertise required to deal with a terrorism-related disaster are well recognized but are deficient due to several considerations. Interpreting the

physicians' perspectives through the extracted themes revealed reconsideration and integration of standardized curriculum of medical education particularly relevant to terrorism-related disaster management. Additionally, regular training and table-top exercises for practicing physicians were also emphasized that will encourage effective and confident responses in disaster management. Finally, conferences, seminars CME programs are required to share the current experiences and to meet harmonization in the latest practices adopted globally to counter terrorism-related disasters.

LIMITATIONS

The limited information from the study settings made it hard to cross compare the data extracted from this study. Furthermore, being qualitative in nature the generalizability is always an issue. We recommend conducting a quantitative study based on the identified theme with a larger group of physicians to get a better insight of preparedness and response toward terrorism-related disaster events.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Faculty of Pharmacy and Health Sciences, University of Balochistan, Quetta. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

FK, Z-e-H, NB, and MS conducted the literature review and developed the interview protocol and the guide. FK conducted the interviews while ZI and AR monitored the process as observers. NS, SA, and SH analyzed and drafted the manuscript, which was subject to critical revision by QI, TH, AA, and RI. FS supervised the study. AA contributed in analysis, theme generation, and write up of the initial draft. All authors read and approved the final manuscript and contributed equally.

ACKNOWLEDGMENTS

The authors would like to acknowledge the physicians for their contribution to the work described in this manuscript. We would also like to thank the hospital administration for their continuous support during the interview process.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpubh.2022.912762/full#supplementary-material>

REFERENCES

- Shafiq F, Ahsan K. Knowledge management for disaster scenario: an exploratory study. *Res J Recent Sci.* (2013) 2:61–6.
- Al-Dahash H, Kulatunga U, Al-Dehesh A. Disaster response management stemming from war operation and terrorism in Iraq. In: *12th International Post-Graduate Research Conference, 10-12 June.* MediaCity (2015).
- Putra A, Petpichetchian W. Public health nurses' roles and competencies in disaster management. *Nurse Media J Nurs.* (2011) 1:1–14. doi: 10.14710/nmjn.v1i1.742
- Nofal A, Alfayyad I, Khan A, Al Aseri Z, Abu-Shaheen A. Knowledge, attitudes, and practices of emergency department staff towards disaster and emergency preparedness at tertiary health care hospital in central Saudi Arabia. *Saudi Med J.* (2018) 39:1123–9. doi: 10.15537/smj.2018.11.23026
- Ahmed Z. Disaster risks and disaster management policies and practices in Pakistan: a critical analysis of Disaster Management Act 2010 of Pakistan. *Int J Disaster Risk Reduct.* (2013) 4:15–20. doi: 10.1016/j.ijdr.2013.03.003
- Tolan GM, Soliman OS. An experimental study of classification algorithms for terrorism prediction. *Int J Knowl Eng.* (2015) 1:107–12. doi: 10.7763/IJKE.2015.V1.18
- Zakaria M, Jun W, Ahmed H. Effect of terrorism on economic growth in Pakistan: an empirical analysis. *Econ Res.* (2019) 32:1794–812. doi: 10.1080/1331677X.2019.1638290
- Ding F, Ge Q, Jiang D, Fu J, Hao M. Understanding the dynamics of terrorism events with multiple-discipline datasets and machine learning approach. *PLoS ONE.* (2017) 12:e0179057. doi: 10.1371/journal.pone.0179057
- Magnus D, Khan MA, Proud WG. Epidemiology of civilian blast injuries inflicted by terrorist bombings from 1970–2016. *Defence Technol.* (2018) 14:469–76. doi: 10.1016/j.dt.2018.07.014
- Santos C, El Zahran T, Weiland J, Anwar M, Schier J. Characterizing chemical terrorism incidents collected by the global terrorism database, 1970–2015. *Prehosp Disaster Med.* (2019) 34:385–92. doi: 10.1017/S1049023X19004539
- Czinkota MR, Knight G, Liesch PW, Steen J. Terrorism and international business: a research agenda. *J Int Bus Stud.* (2010) 41:826–43. doi: 10.1057/jibs.2010.12
- Edwards DS, Mcmenemy L, Stapley SA, Patel HDL, Clasper JC. 40 years of terrorist bombings—a meta-analysis of the casualty and injury profile. *Injury.* (2016) 47:646–52. doi: 10.1016/j.injury.2015.12.021
- Akhmat G, Zaman K, Shukui T, Sajjad F. Exploring the root causes of terrorism in South Asia: everybody should be concerned. *Qual Quant.* (2014) 48:3065–79. doi: 10.1007/s11335-013-9941-2
- Azhar A, Malik MN, Muzaffar A. Social network analysis of Army Public School Shootings: need for a unified man-made disaster management in Pakistan. *Int J Disaster Risk Reduct.* (2019) 34:255–64. doi: 10.1016/j.ijdr.2018.11.024
- Shahzad U, Sarwar S, Farooq MU, Qin F, USAID. official development assistance and counter terrorism efforts: pre and post 9/11 analysis for South Asia. *Socioecon Plann Sci.* (2020) 69:100716. doi: 10.1016/j.seps.2019.06.001
- Zafar H, Jawad A, Shamim MS, Memon AA, Hameed A, Effendi MS, et al. Terrorist bombings: medical response in a developing country. *J Pak Med Assoc.* (2011) 61:561–6.
- Rosenfeld JV, Mitra B, Smit DV, Fitzgerald MC, Butson B, Stephenson M, et al. Preparedness for treating victims of terrorist attacks in Australia: learning from recent military experience. *Emerg Med Australasia.* (2018) 30:722–4. doi: 10.1111/1742-6723.13091
- Shahbaz M, Shabbir MS, Malik MN, Wolters ME. An analysis of a causal relationship between economic growth and terrorism in Pakistan. *Econ Model.* (2013) 35:21–9. doi: 10.1016/j.econmod.2013.06.031
- Najaf K, Najaf R. Impact of cost of war against terrorism on the different determinants of FDI of Pakistan. *Int J Res Granthaalayah.* (2016) 4:156–68. doi: 10.29121/granthaalayah.v4.i5.2016.2691
- Rauf S, Mehmood R, Rauf A, Mehmood S. Integrated model to measure the impact of terrorism and political stability on FDI inflows: empirical study of Pakistan. *Int J Econ Finance.* (2016) 8:1–7. doi: 10.5539/ijef.v8n4p1
- Shahzad SJH, Zakaria M, Rehman MU, Ahmed T, Fida BA. Relationship between FDI, terrorism and economic growth in Pakistan: pre and post 9/11 analysis. *Soc Indic Res.* (2016) 127:179–94. doi: 10.1007/s11205-015-0950-5
- Edwards B, Issa F, Voskanyan A, Ciotton G. Counter-terrorism medicine: creating a medical initiative mandated by escalating asymmetric attacks. *Prehosp Disaster Med.* (2020) 35:595–8. doi: 10.1017/S1049023X2000103X
- Zaheer H. Blood management in disaster situations in Pakistan. *Sci Ser.* (2012) 7:1–5. doi: 10.1111/j.1751-2824.2012.01550.x
- Grossman D, Khalil U, Ray A. Terrorism and early childhood health outcomes: evidence from Pakistan. *Soc Sci Med.* (2019) 237:112453. doi: 10.1016/j.socscimed.2019.112453
- Rafiq L, Blaschke T. Disaster risk and vulnerability in Pakistan at a district level. *Geomat Nat Hazards Risk.* (2012) 3:324–41. doi: 10.1080/19475705.2011.626083
- Maqbool A, Afzal F, Razia A. Disaster mitigation in Urban Pakistan using agent based modeling with GIS. *Int J Geo Inform.* (2020) 9:203. doi: 10.3390/ijgi9040203
- Umer M, Sepah YJ, Shahpurwala MM, Zafar H. Suicide bombings: process of care of mass casualties in the developing world. *Disasters.* (2009) 33:809–21. doi: 10.1111/j.1467-7717.2009.01110.x
- Kitzinger J. Qualitative research: introducing focus groups. *Br Med J.* (1995) 311:299–302. doi: 10.1136/bmj.311.7000.299
- Berg BL, Lune H, Lune H. *Qualitative Research Methods for the Social Sciences.* Vol 5. Boston, MA: Pearson (2004).
- Krueger RA. *Focus Groups: A Practical Guide for Applied Research.* California, CA: Sage Inc ISBN: 1412969476 (2009).
- Stewart DW, Shamdasani PN. *Focus Groups: Theory and Practice.* Vol. 20. California, CA: Sage Publications (2014).
- Mullen PD, Reynolds R. The potential of grounded theory for health education research: linking theory and practice. *Health Educ Behav.* (1978) 6:280–94. doi: 10.1177/109019817800600302
- Entwistle VA, Renfrew MJ, Yearley S, Forrester J, Lamont T. Lay perspectives: advantages for health research. *Br Med J.* (1998) 316:463–6. doi: 10.1136/bmj.316.7129.463
- Shahzad F, Saleem F, Iqbal Q, Haque N, Haider S, Salman M, et al. Cross-sectional assessment of health literacy among hypertensive community of Quetta City, Pakistan. *Biomed J Sci Tech Res.* (2018) 4:1–9. doi: 10.26717/BJSTR.2018.11.002141
- Brace-Govan J. Issues in snowball sampling: the lawyer, the model and ethics. *Qual Res J.* (2004) 4:52.
- Labrague L, Hammad K, Gloe D, McEnroe-Petitte D, Fronda D, Obeidat A, et al. Disaster preparedness among nurses: a systematic review of literature. *Int Nurs Rev.* (2018) 65:41–53. doi: 10.1111/inr.12369
- Wetta-Hall R, Fredrickson DD, Ablah E, Cook DJ, Molgaard CA. Knowing who your partners are: terrorism-preparedness training for nurses. *J Continuing Educ Nurs.* (2006) 37:106–12. doi: 10.3928/00220124-20060301-03
- Rose MA, Larrimore KL. Knowledge and awareness concerning chemical and biological terrorism: continuing education implications. *J Continuing Educ Nurs.* (2002) 33:253–8. doi: 10.3928/0022-0124-20021101-05
- Veenema TG. *Disaster Nursing and Emergency Preparedness.* New York, NY: Springer Publishing Company (2018).
- Cox CW. Manmade disasters: a historical review of terrorism and implications for the future. *Online J Issues Nurs.* (2008) 13. doi: 10.3912/OJIN.Vol13No01PPT04
- Kallio H, Pietilä AM, Johnson M, Kangasniemi M. Systematic methodological review: developing a framework for a qualitative semi-structured interview guide. *J Adv Nurs.* (2016) 72:2954–65. doi: 10.1111/jan.13031
- Morris A. *A Practical Introduction to In-Depth Interviewing.* London: Sage (2015).
- Voutsina C. A practical introduction to in-depth interviewing. *Int J Res Method Educ.* (2018) 41:123–4. doi: 10.1080/1743727X.2017.1419693
- Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant.* (2018) 52:1893–907. doi: 10.1007/s11335-017-0574-8
- Nelson J. Using conceptual depth criteria: addressing the challenge of reaching saturation in qualitative research. *Qual Res.* (2017) 17:554–70. doi: 10.1177/1468794116679873
- Guest G, MacQueen KM, Namey EE. Introduction to applied thematic analysis. *Appl Them Anal.* (2012) 3:20. doi: 10.4135/9781483384436.n1

47. Anderson R. *Thematic Content Analysis (TCA). Descriptive Presentation of Qualitative Data*. (2007). Available online at: <http://rosemarieanderson.com/wp-content/uploads/2014/08/ThematicContentAnalysis.pdf> (accessed June 15, 2021).
48. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: implications for conducting a qualitative descriptive study. *Nurs Health Sci*. (2013) 15:398–405. doi: 10.1111/nhs.12048
49. Edhlund B, McDougall A. *Nvivo 12 Essentials*. Stallarholmen: FORM & KUNSKAP AB. ISBN: 1387749498 (2019).
50. Ismail A, Amjad S. Determinants of terrorism in Pakistan: an empirical investigation. *Econ Model*. (2014) 37:320–31. doi: 10.1016/j.econmod.2013.11.012
51. Möller-Leimkühler AM. Why is terrorism a man's business? *CNS Spectr*. (2018) 23:119–28. doi: 10.1017/S1092852917000438
52. Rauf A, Siddique HMA, Saleem Q, Sidra S. Terrorism and international tourism nexus: evidence from Pakistan. *Int J Econ Financial Issues*. (2020) 10:387. doi: 10.32479/ijefi.10674
53. North CS, Pfefferbaum B, Kawasaki A, Lee S, Spitznagel EL. Psychosocial adjustment of directly exposed survivors 7 years after the Oklahoma City bombing. *Compr Psychiatry*. (2011) 52:1–8. doi: 10.1016/j.comppsy.2010.04.003
54. Saleem Q, Sidra S, Rauf A, Siddique HMA. Impact of terrorism on economic growth in South Asian country. *Int J Econ Financial Issues*. (2020) 10:185. doi: 10.32479/ijefi.9699
55. Bayar Y, Gavriltea MD. Peace, terrorism and economic growth in Middle East and North African countries. *Qual Quant*. (2018) 52:2373–92. doi: 10.1007/s11135-017-0671-8
56. Mohamed H, Jebli MB, Youssef SB. Renewable and fossil energy, terrorism, economic growth, and trade: evidence from France. *Renew Energy*. (2019) 139:459–67. doi: 10.1016/j.renene.2019.02.096
57. Niaz B, Hassan A, Irtaza S. Role of media in minimizing religious extremism and ethnic instability in Balochistan, Pakistan. *Glob Reg Rev*. (2020) 4:12–20. doi: 10.31703/grr.2020(V-IV).02
58. Syed SH, Saeed L, Martin RP. Causes and incentives for terrorism in Pakistan. *J Appl Security Res*. (2015) 10:181–206. doi: 10.1080/19361610.2015.1004606
59. Khan NH, Ju Y, Hassan ST. Modeling the impact of economic growth and terrorism on the human development index: collecting evidence from Pakistan. *Environ Sci Pollut Res*. (2018) 25:34661–73. doi: 10.1007/s11356-018-3275-5
60. Zaidi SA, Bigdeli M, Langlois EV, Riaz A, Orr DW, Idrees N, et al. Health systems changes after decentralisation: progress, challenges and dynamics in Pakistan. *BMJ Global Health*. (2019) 4:e001013. doi: 10.1136/bmjgh-2018-001013
61. Catlett CL, Jenkins JL, Millin MG. Role of emergency medical services in disaster response: resource document for the National Association of EMS Physicians position statement. *Prehosp Emerg Care*. (2011) 15:420–5. doi: 10.3109/10903127.2011.561401
62. Lederman Z, Voo T. Should we prioritise victims over terrorists in medical triage? *BMJ Military Health*. (2019) 165:266–9. doi: 10.1136/jramc-2018-001009
63. Kumar A, Weibley E. Disaster management and physician preparedness. *South Med J*. (2013) 106:17–20. doi: 10.1097/SMJ.0b013e3827c5c5b
64. Russo RM, Galante JM, Jacoby RC, Shatz DV. Mass casualty disasters: who should run the show? *J Emerg Med*. (2015) 48:685–92. doi: 10.1016/j.jemermed.2014.12.069
65. Pintea M, Dahl Grove D. Primary care physicians: an untapped resource for disaster response. *Curr Treat Opt Pediatr*. (2019) 5:276–83. doi: 10.1007/s40746-019-00164-5
66. Scott LA, Carson DS, Greenwell IB. Disaster 101: a novel approach to disaster medicine training for health professionals. *J Emerg Med*. (2010) 39:220–6. doi: 10.1016/j.jemermed.2009.08.064
67. Subbarao I, Lyznicki JM, Hsu EB, Gebbie KM, Markenson D, Barzansky B, et al. Consensus-based educational framework and competency set for the discipline of disaster medicine and public health preparedness. *Disaster Med Public Health Prep*. (2008) 2:57–68. doi: 10.1097/DMP.0b013e31816564af
68. Ingrassia PL, Prato F, Geddo A, Colombo D, Tengattini M, Calligaro S, et al. Evaluation of medical management during a mass casualty incident exercise: an objective assessment tool to enhance direct observation. *J Emerg Med*. (2010) 39:629–36. doi: 10.1016/j.jemermed.2009.03.029
69. Barbosa F. Emergency health care system and its role in national disasters. *J Human Insights*. (2018) 2:14–20. doi: 10.22034/jhi.2018.61425
70. Zhiheng Z, Caixia W, Jiaji W, Huajie Y, Chao W, Wannian L. The knowledge, attitude and behavior about public health emergencies and the response capacity of primary care medical staffs of Guangdong Province, China. *BMC Health Serv Res*. (2012) 12:1–9. doi: 10.1186/1472-6963-12-338
71. Gregory J, de Lepinau J, de Buyer A, Delanoy N, Mir O, Gaillard R. The impact of the Paris terrorist attacks on the mental health of resident physicians. *BMC Psychiatry*. (2019) 19:1–8. doi: 10.1186/s12888-019-2058-y
72. Burkle FM. The development of multidisciplinary core competencies: the first step in the professionalization of disaster medicine and public health preparedness on a global scale. *Disaster Med Public Health Prep*. (2012) 6:10–2. doi: 10.1001/dmp.2012.3
73. Naser WN, Saleem HB. Emergency and disaster management training: knowledge and attitude of Yemeni health professionals-a cross-sectional study. *BMC Emerg Med*. (2018) 18:1–12. doi: 10.1186/s12873-018-0174-5

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 Khilji, Zil-e-Huma, Baloch, Shoaib, Iqbal, Raziq, Sadaf, Ainuddin, Haider, Saleem, Iqbal, Hussain, Ayaz and Ishaq. 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

Melody Goodman,
New York University, United States

REVIEWED BY

Maryam Rassouli,
Shahid Beheshti University of Medical
Sciences, Iran
Bahar Khosravi,
Azarbaijan Shahid Madani
University, Iran

*CORRESPONDENCE

Ahmad Ahmadi
ahmad_ahmadi96@atu.ac.ir
Mehdi Khezeli
khezelimehdi@yahoo.com

SPECIALTY SECTION

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 15 June 2022

ACCEPTED 18 July 2022

PUBLISHED 19 August 2022

CITATION

Yoosefi Lebni J, Pavee S, Saki M,
Ziapour A, Ahmadi A and Khezeli M
(2022) Determinants of observing
health protocols related to preventing
COVID-19 in adult women: A
qualitative study in Iran.
Front. Public Health 10:969658.
doi: 10.3389/fpubh.2022.969658

COPYRIGHT

© 2022 Yoosefi Lebni, Pavee, Saki,
Ziapour, Ahmadi and Khezeli. 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.

Determinants of observing health protocols related to preventing COVID-19 in adult women: A qualitative study in Iran

Javad Yoosefi Lebni¹, Saeede Pavee², Mandana Saki³,
Arash Ziapour⁴, Ahmad Ahmadi^{5*} and Mehdi Khezeli^{6*}

¹Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran, ²Master of Tourism Planning, Department of Geography and Tourism Planning at Kharazmi University, Tehran, Iran, ³Social Determinants of Health Research Center, School of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran, ⁴Cardiovascular Research Center, Health Institute, Imam-Ali Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran, ⁵Faculty of Psychology and Educational Sciences, Allameh Tabataba'i University, Tehran, Iran, ⁶Social Development and Health Promotion Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Background: The best way to prevent COVID-19 is to observe health protocols. Therefore, identifying the reasons of following these protocols in order to plan and make intervention seems necessary. Therefore, the purpose of this study was to identify the determinants of observing health protocols related to prevention of COVID-19 among the Iranian adult women with a qualitative approach.

Method: In this qualitative study, the conventional content analysis approach was used. saturation was obtained after face-to-face semi-structured interviews with 38 women from Kermanshah who were selected through purposeful sampling and snowball sampling. Guba and Lincoln criteria were used for the strength of the research and Graneheim and Lundman method was used for its analysis.

Results: After analyzing the interviews, 5 categories, 12 subcategories and 110 initial codes were obtained. Categories and sub-categories were: 1- Individual factors (personality traits, health literacy about COVID-19); 2- Perceived risk having underlying disease in oneself and family, history of getting COVID-19 and death in close relatives; 3- Fear of the destructive consequences of the disease (concern about the economic consequences of getting the disease, concern about the treatment process); 4- Social and cultural factors (social monitoring, religious insight, ability to properly manage social interactions, impressionability from important others); 5- Environmental factors (supportive living environment, access to health and anti-infective materials).

Conclusion: Increasing the adherence of adult women to health instructions related to COVID-19 requires interventions at different levels of individual, environmental and social, and without accurate knowledge of the customs and culture of a society effective interventions cannot be established.

KEYWORDS

COVID-19, women, observing the health protocols, qualitative study, adult

Introduction

COVID-19 from China spread to other parts of the world (1, 2). Due to the ambiguous nature of this virus and its high transmission power, as well as the problems it imposes on the individual and family after infection, the most important and in fact the main way to control the disease is to eliminate the virus transmission chain (3, 4). The incidence and death rate of the disease led governments to implement a set of health protocols to prevent the disease. Depending on the situation, these protocols ranged from simple health rules such as wearing a mask to quarantine and social distancing (5). Observance of issues such as the use of masks and gloves, washing and disinfecting the hands and surfaces, maintaining proper distance and using vaccines have been mentioned as ways to prevent COVID-19 (6, 7).

In Iran, on 19 February 2020, the first definitive case of COVID-19 was announced (8) and by 19 December 2021, a total of more than 6 million people have been infected with this disease, and the death rate has reached more than 131,000 (9, 10).

In line with global warnings to break the chain of transmission, the Iranian government also implemented a variety of restrictive behaviors, such as quarantining cities and closing public centers and places, and at the same time, informed the people about various methods of preventing infection through national media and social networks (11, 12). However, despite warnings from health organizations and governments, some people did not follow health protocols because of reasons such as poverty and economic hardship (13), personal characteristics, lack of access, etc. (14). Observing health guidelines has become one of the main concerns since the outbreak of COVID-19 (15, 16), which is influenced by various physical, psychological, political, social and cultural factors (17, 18). Studies of past pandemic crises, such as influenza and SARS, have shown that factors such as perceived risk of disease, strength of transmission, death rate, and stress experienced due to the disease play an important role in the type of preventive behaviors of the general public (14). The results of Webster et al.'s (19) study showed that factors such as public awareness of disease and quarantine procedures, social norms, perceived benefits of quarantine and understanding of

disease risk, as well as practical issues such as resource depletion or financial consequences of unemployment are related to the degree of observing quarantine (19). In a study conducted in Indonesia, the variables of knowledge, personality and concern were reported as important determinants of observing health protocols related to COVID-19 (20). In a review study conducted by Shushtari et al. (17), living and working conditions, social support, trust, social norms, economic and social status, and mental health were reported to be the most important social determinants of following the COVID-19 health protocols. In another review study, environmental resources and contexts, belief in consequences, feelings, and social effects have been reported as important determinants of observing social distancing (21).

Regarding COVID-19, men have a higher rate of infection and death than women (22, 23), most studies have reported that health protocols observing in women is higher than men (24–27). This may be due to various reasons such as having enough opportunity, more access, more patience or also the general perception that women are more inclined to maintain their health than men (28). Of course, men's working conditions can also be a factor (14).

Given the importance of observing health protocols in the prevention of COVID-19, identifying the factors affecting the observance of these protocols is a necessity of any planning and intervention to protect public health. Most previous research has been done quantitatively and has examined the reasons for non-compliance with health protocols, and the reasons for compliance with health protocols has been less examined with a qualitative method, while a qualitative method can help a lot. Also, few studies have examined the reasons for observing health protocols among Iranian women. Since some Iranian women are illiterate, it is not appropriate to use a quantitative method to investigate this phenomenon. Therefore, this study aimed to explore the determinants of observing health protocols related to the prevention of COVID-19 in Iranian adult women.

Materials and methods

This study was conducted with a qualitative approach and conventional content analysis method (29) among women in

kermanshah. Participants in the study were women who had followed COVID-19 health protocols such as wearing masks, physical distance, washing hands, etc. over the past 2 months. Inclusion criteria consisted of being a woman, observing health protocols during the last 2 months and willingness to participate in the study. Exclusion criterion was an incomplete interview.

Purposeful sampling and then snowball sampling were used to reach the participants. Initially, a call was published in social media in order that those who follow the health protocols and are eligible to participate in the study tell their names and leave their phone numbers in order to be contacted to determine the time and place of the interview. Researchers attended the society and asked the women who were following health protocols, if they had fully observed health protocols in recent months, and if so, the interview would begin. At the end of the interview, the women were also asked to introduce other women who met the inclusion criteria among their friends and acquaintances, so that they could be contacted as soon as possible and the interview would be coordinated. A total of 16 women were selected through purposeful sampling and 22 women through snowball sampling. All interviews were recorded with the participants' consent, and field notes were used wherever the researcher needed them.

Semi-structured face-to-face interviews were used to collect data. The interview guide was developed to conduct the interviews; all the authors of the article designed questions to achieve the objectives of the research during three discussion sessions, then these questions were tested in interviews with three participants and after three pilot interviews, researchers corrected it during a meeting and the final interview was compiled (Table 1). All interview questions were asked of all participants, but their order depended on the participants' answers, and other minor questions were asked to complete the interview. The average duration of the interviews was 61 min, the shortest interview lasted 23 minutes and the longest one lasted 80 min. The time and place of the interviews were determined in advance with the participants and based on their opinions. Interviews were conducted in secluded public places such as parks or cultural sites such as libraries or the workplaces of some participants which were secluded and no one but the researcher and participant was present.

In order for the participants to be able to share their experiences more easily with the researcher, a female colleague with a master's degree in women studies who had sufficient experience in qualitative research methods and interviews was used. Data collection continued until theoretical saturation was reached. Saturation means when the continuation of the interview adds nothing to the research and the codes are repeated and no new code is formed, so the researcher decides not to continue the interviews (30, 31). In this study, saturation was obtained by interviewing 38 women.

Maxqda 2020 software was used for data classification and Graneheim and Lundman method was used for its analysis

TABLE 1 The guide for interview question.

Question

1	What made you observe the health protocols for preventing COVID-19?
2	Do you think that your personality had an effect on observing health protocols? Explain.
3	What do you think about health protocols and their impact on preventing COVID-19? Explain.
4	What was the most important thing that made you follow the protocols?
5	Did the words and behavior of family members, friends and other people affect your behavior? Explain.
6	Do people around you follow the health protocols like you? Explain.
7	How was your access to hygiene? Explain.

(29). Data analysis was performed by the first, second, and corresponding author of the article, with the supervision and cooperation of all authors. Thus, in the first step, immediately after each interview, the interviews were typed and saved by two members of the research team in Word 2010 software. In the second step, the text of the interviews was read and reviewed several times by the researchers to get a general understanding of the text of the interviews. In the third step, all the texts were read word for word and with great care and the codes were extracted. In the fourth step, the codes that were similar in terms of content and meaning were placed in a class and it was determined how they were related. In the fifth step, the data were placed in the main categories, which were more general and abstract than the previous classification, and the themes were extracted.

Guba and Lincoln criteria were observed to improve the quality of results (32). To increase the dependability, all contributors to the article were informed about process of analyzing and coding, and in the meetings that were held, expressed their views, and finally the names of the categories and subcategories were finalized with the approval of all authors. To increase the credibility of the study, the researchers selected participants with the greatest differences in terms of demographic characteristics to observe the principle of diversity in sampling. At the end of each interview, the researcher briefly expressed his general understanding of the participants' experiences and it should be confirmed by the participant. Also, after coding and analyzing the data, the findings of the present article were provided to 12 participants to determine whether the researchers reported their experiences correctly or not and it was confirmed after a few minor corrections. To gain Confirmability, the researchers sent data analysis and findings to 5 leading researchers in qualitative research as well as 3 people who had research experience in similar subjects to this research and, where necessary, modified them according to their opinions. In order to increase the transferability of the research, a complete

TABLE 2 Demographic information of the participants.

Variable	Group	Frequency
Age	18–30	9
	30–50	18
	Over 50	11
Education	Illiterate and elementary	7
	Junior high school and diploma	12
	Higher than diploma	19
Marital status	Single	15
	Married	18
	Divorced or widowed	5
Occupation	Housewife	14
	Self-employed	10
	Employee	7
	University student	7
History of getting COVID-19 for her and her relatives	Yes	21
	No	17

description of the whole research process was provided and the quotations of the participants were given directly and in large numbers. The research findings were also sent to 6 people who met the inclusion criteria but did not participate in the study, which was finally confirmed by them.

Ethics approval and consent to participate

To observe research ethics, the researchers considered the following issues: Ethical approval was obtained from the Kermanshah University of Medical Sciences (IR.IUMS.REC.1401.023). obtaining written consent from all participants, obtaining written consent to record the interview, introducing themselves and the necessity and objectives of the research at the beginning of each interview, observing the principles of confidentiality and maintaining the names of participants in publishing research results, determining the time and place of the interview and the desired time of cutting it by the participants, and observing the health protocols during the interview.

Results

The present study was conducted with the participation of 38 adult women in Kermanshah, whose demographic characteristics are listed in Table 2. Findings showed that most of the participants in the age range of 30 to 50 years had higher

education than diploma and were married and housewife. Also, by analyzing the data obtained from the interviews, 110 initial codes, 12 subcategories and 5 categories were obtained (Table 3).

Individual factors

The first category that was obtained was individual factors consisting of two subcategories of personality traits and having health literacy about COVID-19. In fact, part of the observance of health protocols by women was related to their personality and others to their knowledge and awareness of COVID-19.

Personality traits

Having some personality traits in people caused them to observe health behaviors more. In this study, women who felt more responsible followed health protocols more because they considered themselves responsible for their own health and that of others. Women who were kind and compassionate also followed health protocols properly. Although observing health protocols has sometimes been difficult, women who are more patient and have more hope for the future are more likely to follow them. Also, women who are less risk-averse and have a conservative personality are more likely to follow health protocols for fear of COVID-19.

“Observing the COVID-19 health protocols is related to both myself and others. Even if I am not worried about my own health, I have to wear a mask because of the health of others, which is why I always try to follow them.” (27 years old, married with a bachelor’s degree).

“I can never imagine that I could endanger anyone’s health by my negligent behavior. I can’t be so cruel. I think not following health protocols shows the peak of cruelty” (39 years old, married, bachelor’s degree).

“I’m too patient. I’ve been wearing a mask since COVID-19 came. Even at home when a guest comes, I wear a mask again. Sometimes my family tells me you’re so patient that you observe a lot.” (48 years old, married, under diploma).

“I love my life and I do not want to die, so I wear a mask and I do not go to crowded places” (22 years old, single with a bachelor’s degree).

Having health literacy about COVID-19

In fact, most participants had comprehensive information on various aspects of COVID-19 and had obtained this information from a variety of sources, not just one source of information. Participants who had good information about all aspects of COVID-19, such as how to transmit and prevent COVID-19, how to observe social distance, and how to use masks and other health supplies, were more observant.

TABLE 3 Codes, categories and subcategories obtained from interviews with participating women.

Categories	Subcategories	Codes
Individual factors	Personality traits Health literacy about COVID-19	Responsibility, compassion, conservatism, patience, hope Proper knowledge of COVID-19, proper knowledge on the ways of transmitting and preventing COVID-19, proper knowledge on how to observe social distancing, proper knowledge on how to use masks and other health supplies
Perceived risk	Having underlying disease in oneself and family History of getting COVID-19 and death in close relatives	Asthma, diabetes, cancer, kidney disease, heart disease and so on History of COVID-19 in family, history of COVID-19 among friends and colleagues, history of COVID-19 in neighbors and relatives
Fear of the destructive consequences of the disease	Concern about the economic consequences of getting the disease Concern about the treatment process	High cost of disease treatment, high cost of medical tests, job loss Prolonged treatment, endangering other family members, disrupting her life and other family members
Social and cultural factors	Social supervision Religious insight Ability to properly manage social interactions Impressionability from important others	Worry about others criticizing for not observing, worry about others distancing from them if they do not follow protocols, being stigmatized as uncultured To be responsible for one's own body, to consider endangering one's own health as a sin, to consider endangering the health of others as a sin To reduce face-to-face communication and make more use of telephone communication, to use social media for communication, to use social media for social and cultural events To follow the advice of celebrities, to follow the advice of religious clerics, to follow the advice of prominent doctors, to follow the advice of nurses and important people
Environmental factors	Supportive living environment Access to health and anti-infective materials	Sensitivity of other family members to observe protocols, observance of health protocols by apartment building residents, observance of health protocols by most colleagues Adequate access to masks and gloves, adequate access to alcohol

"I tried to increase my knowledge in this field from the early outbreak, so in addition to following scientific news, I collected information on various websites, and sometimes I even used English sources, so I knew what a bad disease we were facing, which made me pay more attention" (50 years old, married with under diploma education).

"My husband works in the health office and he passed on good information to us, so I tried to follow all the health protocols" (33 years old, married, higher than a diploma).

"I wear both masks and gloves and I always use alcohol. I haven't traveled since COVID-19 came because I know that not following any of these things will make me much more likely to

get infected and my life and my family life will be in danger." (51 years old, married with elementary education).

"I try not to go to crowded places at all, or every time I go I put on two masks and When I get in a taxi or bus, I immediately roll down the windows so that there is air flow, because I know that if there is no air flow, I might get infected." (29 years old, single with a bachelor's degree).

Perceived risk

People who feel more at risk for COVID-19 are more likely to observe health protocols. This fear increases with a history of

underlying disease in the individual and family members. Also, if one of her close relatives gets COVID-19 and she observes the treatment process, she feels fearful, which causes her to follow health protocols more.

Having an underlying disease in herself and her family

Some participants, due to having a dangerous underlying illness in themselves or their family members, considered themselves obliged to follow health protocols. In fact, it can be said that they feel more fearful due to having an underlying disease and that made them more observant.

"I have diabetes, so I'm very scared of COVID-19 and I always try to observe because I know I will die if I get it." (61 years old, widow, illiterate).

"My mother has asthma and her lungs are very weak. If she gets COVID-19, it is very dangerous for her, so I try to be very careful and observant so that nothing bad happens." (37 years old, single with a diploma).

"My mother-in-law has cancer and lives with us. Because of her I have to pay a lot of attention and be very observant so that, God forbid, nothing bad happens to her" (27 years old, married with a bachelor's degree).

"My father is on dialysis and if he gets COVID-19 it is not clear what will happen to him, so I and other family members try to be very observant so that nothing bad happens" (21 years old, single with a diploma).

History of COVID-19 in close relatives

History of COVID-19 in close relatives and observing the life of these people after getting it and the difficulties they experienced caused the participating women to express that by observing such an experience, they feel more at risk and follow health protocols better. Also, people who experienced COVID-19 death in close relatives and family felt more at risk and observed the protocols more than others.

"My father took COVID-19, he got very bothered, our lives were disrupted for a few weeks. Frankly speaking, after my father became ill, I was very scared and I observed more" (35 years old, single with a bachelor's degree).

"At first I thought that COVID-19 was not dangerous for me, but when I saw that our neighbor had taken COVID-19 and was being bothered by it a lot, I was scared and tried to observe more." (65 years old, divorced, illiterate).

"One or two of my friends and colleagues took COVID-19 and went to the brink of death, and one of them died. When I found out that my colleague was dead, I was very worried and I have been observing more since that day." (44 years old, married with a bachelor's degree).

Fear of the destructive consequences of the disease

This category on the one hand refers to the economic consequences of COVID-19 and on the other hand is concerned about the process of treatment of the disease that may endanger the health of associates and disrupt their lives.

Concerns about the economic consequences of getting the disease

Getting COVID-19 in Iran is associated with high economic costs, and families with a COVID-19 patient have to spend a lot of money on a daily basis. Also, with getting this disease and deprivation of work, people's income decreases, so some participants stated that they followed COVID-19 health protocols for fear of the economic consequences of it.

"If I get covid-19, I have to stay home until I die, because they say the cost is too high, so I try to observe a lot not to get infected." (27 years old, single with a bachelor's degree).

"I am a hairdresser. If I take COVID-19, I have to stay home for at least a few weeks and my job is closed, so I have to be very observant in order not to lose my job" (42 years old, divorced with a bachelor's degree).

"I observe because I know the cost of medical tests, etc. is too high. Also, because public hospitals do not have the capacity, I have to go to a private hospital where overnight expenses are the same as my husband's a month income" (37 years old, married with a master's degree).

Social and cultural factors

Social and cultural factors were one of the important determinants of observing health protocols by participants. Part of these social factors were related to social pressures that required a person to observe health protocols, part to the religious views of individuals about their own health and the health of others. Proper management of social interactions and being influenced by important others were other social and cultural factors.

Social monitoring

In Iranian society, someone who does not follow health protocols, especially the use of masks, is usually reprimanded by the public, and others may distance themselves from him or criticize him for not observing health protocols properly. Most participants stated that they followed health protocols for fear of being rejected or warned by others. In fact, non-compliance with health protocols in society causes others to label the wrongdoer

as a silly person, and this issue causes some people to observe health protocols to avoid such labels.

"I get very upset that someone criticizes me, so I always try to follow health protocols so that no one nags at me" (32 years old, married with a master's degree).

"If I see that someone does not follow the health protocols, I distance myself from them and do not talk to them, and since I do not want anyone to treat me like this, I try to follow the health protocols as much as I can." (67 years old, married, illiterate).

"In the bus, anyone who does not wear a mask is labeled a thousand times, and I really give people the right. I do not want anyone to think that I do not have understanding and wisdom, so I try to wear a mask" (55 years old, married with a bachelor's degree).

"There is a friend of mine who does not believe in wearing a mask at all, etc. Other friends label her a thousand times." (47 years old, widow, under diploma).

Religious insight

Religious people consider themselves responsible for their own health and the health of others, and consider any harm to their own health and the health of others a sin. According to these people, non-observance of health protocols is an example of intentional harm to oneself and others because it endangers health and this is a sin, so they try to observe health protocols as much as they can in order to avoid sin.

"God has given us a body which we have to take care of, and if we are not careful we have sinned" (38 years old, married with a master's degree).

"Just as drug use is a sin and endangers health, not observing protocols is just as, and perhaps more, a sin because it endangers the health of others in addition to one's own health" (41 years old, married with a master's degree).

"If I do not follow the protocols and cause someone else to get COVID-19, I have committed a great sin, so I always try to observe it for the sake of others" (29 years old, single with a bachelor's degree).

"When I know that not wearing a mask endangers the health of others, I convince myself to wear a mask even if I am bothered, because if I cause the health of others to be endangered, I have committed a sin and I will be punished in the Hereafter" (40 years old, single, under diploma).

Ability to properly manage social interactions

Iranian culture is based on stable social relationships, so that most Iranians visit close relatives during the week, which can be dangerous during COVID-19 prevalence. While the ability to properly manage these interactions can be very helpful,

some participants tried to fill this gap by reducing face-to-face communication and making more use of telephone and virtual communication, and by holding various social events in virtual space, they were could observe health protocols.

"My main concern about not following health protocols was related to attending various events that I tried to participate in them in through virtual space as much as possible" (39 years old, married with a bachelor's degree).

"I did not attend any ceremonies from the beginning of COVID-19. I called and congratulated or offered my condolences wherever necessary." (29 years old, single with a bachelor's degree).

"During COVID-19 period, I did not attend all the birthday parties and various anniversary ceremonies, etc. We made it through virtual space." (44 years old, married with a bachelor's degree).

Impressionability from important others

There are always some people in individuals' lives who play a decisive role in shaping behavior. For this reason, in the face of COVID-19, some participants stated that they had tried to follow health protocols, following the statements of some celebrities, clerics, prominent doctors, nurses and other important people in life. And perhaps in the absence of such people, the rate of compliance with health protocols would be lower than before.

"When I saw celebrities wearing masks and holding their weddings in private, I learned to follow health protocols" (44 years old, married with a bachelor's degree).

"Many of our religious scholars have told us to observe health protocols. Well, we have to follow their instructions" (42 years old, divorced, under diploma).

"Doctors have been very bothered during these 2 years. When I see they want us to observe. The least we can do is to be careful about our behavior" (35 years old, single with a doctorate).

"Many nurses have lost their lives in order to maintain our health. The only thing they ask us to do is to observe more. I try to do it because of them" (57 years old, married with a bachelor's degree).

Environmental factors

Environmental factors consisting of two sub-categories of supportive living environment and access to health and anti-infective materials were other determinants of health protocols. In fact, if people are in an environment where most people follow the protocols and also have access to the necessary health materials, the rate of compliance with the protocols will increase, as most

participants stated that most people in their environment were sensitive to health protocols and they have had sufficient access to hygienic materials such as glove, masks, etc., and this has led to their encouragement to observe health protocols.

Supportive living environment

Most of the participants stated that other family members followed the health protocols and were sensitive to their behavior, which led them to observe more. Also, some people considered the observance of health protocols by colleagues and neighbors as the reason for their observance.

“My mother reminds me every day to put on a mask and wear gloves when I go out, which makes me very self-conscious” (37 years old, single, with PhD degree).

“In our apartment building, from the early time the COVID-19 came, we took a washing liquid and put it in the yard, and we required all people to wash their hands with water and liquid when they come from the outside, and they do not have the right to take off their masks until they reach their apartment. These made me become more sensitive to the observance of health protocols” (62 years old, married with a diploma).

“Many families do not care and they go to party every day, but our family is not like that. We have observed a lot during these 2 years. When I see that we observe that much at home, I also try to observe it outside as much as I can.” (27 years old, married with a bachelor's degree).

“Most of my colleagues follow the protocols, and when I see them, I observe. If they did not observe them, I would not observe them.” (44 years old, married with a bachelor's degree).

Access to hygienic and anti-infective materials

Adequate access to hygienic materials causes other people not to use the lack of materials as an excuse not to observe health protocols, and this issue itself can affect the observance of health protocols.

“We have several packages of masks in different designs and colors at home. I have no problem accessing the masks.” (32 years old, married with a master's degree).

“I have both hand sanitizer and surface sanitizer for each of my children. I check every time they go out to take them.” (39 years old, married with a bachelor's degree).

“I always put a mask and alcohol in my bag to use whenever I need.” (27 years old, single with a bachelor's degree).

Discussion

The aim of this study was to explore the determinants of observing health protocols related to the prevention of COVID-19 in Iranian adult women with a qualitative approach. The results showed that the observance of health protocols by women is affected by various factors, some of which are related to the personality of individuals and others to the social factors and behaviors of others and the social environment in which they live.

Individual factors consisting of personality traits and having health literacy about COVID-19 was one of the important determinants of observing health protocols by women. In fact, women who felt more responsible for their own health and that of others around them were more likely to follow health protocols. In Ningsih et al. (33) study, a significant relationship was found between social responsibility and observance of health protocols. Also, due to the dangerous conditions of COVID-19, women who had a conservative personality followed health protocols better to avoid getting COVID-19. And because observing health protocols was sometimes really difficult and tedious, women who were patient were more inclined to follow health protocols. This finding is consistent with the research of Soleimanvandi Azar et al. (14) conducted in Iran because in their research, laziness and impatience were reported as one of the most important reasons for not wearing masks and observing other health protocols. In the research of Sari and Fawzi (20) personality traits have also been reported as one of the important determinants of compliance with health protocols.

Having a health literacy about COVID-19 was another determinant of women's observance of health protocols. In most studies, health literacy in the field of COVID-19 has been reported as one of the most important reasons for compliance or non-compliance with health protocols (34–36). In fact, the more people know about prevention methods and how to follow health protocols, the more they are encouraged to follow these protocols.

Perceived risk, consisting of two subcategories of underlying disease in oneself and family, as well as a history of COVID-19 and death in close relatives, was one of important determinants of women's observing health protocols. This finding was in line with the 2021 Plohl and Musil study (37). Also in Wise et al. (38) research, understanding the risk and understanding the economic and health effects of COVID-19 have been reported as factors affecting the observance of COVID-19 health protocols. Because the incidence and death from COVID-19 were higher in people with the underlying disease, women who had such diseases or a family member of theirs had, felt more at risk and tried to follow health protocols. They also felt more at risk when they saw the conditions of people with COVID-19 or their death, and tried to observe health protocols. In a study conducted in Italy, susceptibility of risk

of contracting COVID-19 disease was significantly associated with observing health protocols related to the prevention of COVID-19 (25).

Another important finding of the study was the fear of the destructive consequences of COVID-19. In the study of Harper et al. (39), fear and anxiety about COVID-19 played an important role in influencing hygienic behaviors such as hand washing and social distancing. The expenses of COVID-19 patients in Iran were sometimes very high due to shortages of medical supplies, and the families of the patients had to pay a lot of money, and the disease itself caused people to stay away from working conditions for weeks or even months. This issue put a lot of economic pressure on the family, therefore, COVID-19 in Iran would lead to a lot of economic pressure on families, so some participants observed protocols to prevent these costs.

Concern about the disease treatment process was another determinant of women's adherence to health protocols. In fact, in addition to the economic cost of COVID-19, the length of the treatment process and the risk to other family members and disruption of their lives caused women to observe health protocols. In the study of Webster et al. (19), understanding the risk of disease has been reported as one of the important determinants of adhering to health protocols.

Social and cultural factors were another new and interesting finding in this study and showed that the health behavior of individuals is affected by the cultural and social context of societies and to intervene more effectively in this field, cultural and social components must be considered. In the study of Indrayathi et al. (40), social norms have been mentioned as one of the determinants of compliance with health protocols. In most researches on the observance or non-observance of health protocols related to COVID-19 social and cultural factors have been reported as one of the important determinants (17, 41).

Social monitoring was one of the important determinants of women's adherence to health protocols, which was one of the new and significant findings in this study. When most people in the environment follow health protocols and a person ignores these protocols, it causes other people in the community to warn that person and look at him negatively and stigmatize them and show with their behaviors that they would not like to communicate with them. In fact, it can be said that by turning health behaviors into a social norm, people accept it more easily and there is no need for government inspectors to implement it, but it is inspected and controlled by the people themselves (18). Therefore, it seems that in order to observe health protocols more, people can be encouraged more by creating more social supervision, rather than legislation and legal punishment.

Religious insight was another important determinant of health protocols. Religious people consider themselves responsible for their own health and even that of others, and according to the rules of Islam, which is the most common religion in Iran, harming their own health and the health of others is forbidden and punishable. Therefore, most women considered not following health protocols as harming their

own health and the health of others, so they tried to follow these protocols as much as possible. In general, various studies have shown that during the COVID-19 pandemic, the number of religious practices increased and most people prayed or performed religious acts to end COVID-19 (42). Yoosefi lebni et al. 2021 in a study conducted among housewives in Iran during the COVID-19 period reported that women resorted to religious practices such as praying, supplication, etc. to relieve the anxiety caused by the COVID-19 outbreak (43). However, in some communities, religious people may describe quarantine laws or other health protocols as anti-religious because they stay them away from mass religious practices, so they may not follow these protocols (44). Of course, due to the religious context of Iranian society, clerics were also effective in observing health protocols because they invited people from different forums to observe health protocols (45).

Another new and interesting finding in this study was the ability to properly manage social interactions, which was one of the important determinants of observing health protocols. In fact, this finding showed that even in communities where there are a lot of family interactions, COVID-19 expansion can be prevented with proper management of these interactions. Expanding the use of social media for communication can be a good alternative to real communication, so it is suggested that health officials and planners facilitate and accelerate the use of virtual communication in society. In societies like Iran, where people still have extensive contact with close and distant relatives, observing health protocols such as social distancing and quarantine had become a problem, and the cases of COVID-19 increased whenever there were special social ceremonies. In a study conducted by Soleimanvandi Azar et al. (14). In Iran, they reported that social customs are one of the main obstacles to compliance with health protocols in Iran. In another study conducted among Iranian women, the use of social media was reported as one of the alternative solutions for real communication in the COVID-19 period (43).

Impressionability from important others was another important finding in this study. In any society, some people learn by looking at the lifestyles of those who are important to them or try to behave like them. Now these important others may come from every stratum and guild in society (such as artists, clerics, footballers, prominent doctors, Etc.). Various studies have reported the effect of celebrities in encouraging people to follow COVID-19 protocols (46, 47).

Environmental factors including a supportive living environment and access to health and anti-infective materials was another determinant of observing health protocols. When in a community in living and working places, most people follow health protocols and are sensitive to the behavior of others and feel responsible, other people in that community are encouraged to follow health protocols. Research by Coroiu et al. (26) also showed that people's health behaviors to prevent COVID-19 are influenced by the behavior of other people living in the community, that is, when people see that most

people observe health protocols, they are encouraged to observe the protocols.

Access to sanitary and anti-infective materials was another determinant of compliance with health protocols. In most previous researches, lack of access or difficult access to health and anti-infective materials has been reported as one of the main reasons for not observing health protocols (14, 48, 49).

Strengths and limitations of the study

This study is one of the few studies that qualitatively seeks to identify the determinants of observing health protocols related to COVID-19 among Iranian adult women, which can provide new and first-class information to health and social planners so that they can intervene to increase people's adherence to health protocols. There were some limitations in this study. One of the main limitations was that some participants were reluctant to do the interview due to fear of getting COVID-19. The researchers obtained their consent by explaining the conditions of the interview and the full observance of health protocols such as the use of masks, gloves, etc. during the interview. The willingness of the participants as well as the observance of some social customs caused the researchers to use a trained and experienced woman in the field of interviews and qualitative research to conduct interviews.

Conclusion

The results showed that women observe health protocols under the influence of various factors such as individual factors, perceived risk, fear of the destructive consequences of the disease, social and cultural factors and environmental factors. Therefore, increasing the adherence of adult women to the health instructions related to COVID-19 requires interventions at different levels. At the individual level, it seems necessary to promote health literacy about COVID-19, to strengthen their sense of responsibility for their own health and the health of others, to increase the feeling of fear of getting COVID-19, and to show the consequences of getting it in the media, in order to encourage people to follow protocols more. At the social level, strengthening and cultivating more social monitoring to control the behavior of people who do not follow health protocols, using the capacity of religious clerics and celebrities to encourage people to observe health protocols, and training and instructing to better manage social interactions are seemed necessary. At the environmental level, it appears necessary to provide and make available health supplies to the public so that they can observe health protocols without any worries or restrictions.

Data availability statement

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Kermanshah University of Medical Sciences (IR.IUMS.REC.1401.023). The patients/participants provided their written informed consent to participate in this study.

Author contributions

JY, MK, and AA were responsible for the study conceptualization and led the paper's writing. JY and AZ conducted the literature review and assisted in writing the paper. SP and AA performed the analysis, assisted in interpreting the data, and writing the paper. JY and MS assisted with the interpretation of the results and drafting programmatic implications and responsible for the data collection and coordination of the study. AZ co-led the conceptualization, supervised all aspects of writing the paper, and provided extensive comments on the manuscript. All authors were responsible for the study. All authors have read and approved the final manuscript.

Funding

This study received funding from Kermanshah University of Medical Sciences (4010279). The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication.

Acknowledgments

We are grateful to the Deputy for Research and Technology, Kermanshah University of Medical Sciences, for co-operating in this research. The authors would like to thank all the participants who patiently participated.

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

1. Delshad Noghabi A, Yoshany N, Mohammadzadeh F, Javanbakht S. Predictors of COVID-19 preventive behaviors in Iranian population over 15 years old: an application of health belief model. *J Mazandaran Univ Med Sci.* (2020) 30:13–21.
2. Roser M, Ritchie H, Ortiz-Ospina E, Hasell J. Coronavirus disease (COVID-19)-statistics and research. Our World in Data. Available online at: <https://ourworldindata.org/coronavirus#citation> (accessed March 10, 2020).
3. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *Lancet Glob Health.* (2020) 8:e488–e96. doi: 10.1016/S2214-109X(20)30074-7
4. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA.* (2020) 323:1406–7. doi: 10.1001/jama.2020.2565
5. Brouard S, Vasilopoulos P, Becher M. Sociodemographic and psychological correlates of compliance with the COVID-19 public health measures in France. *Can J Polit Sci.* (2020) 53:253–8. doi: 10.1017/S0008423920000335
6. Zorriehzahra MJ, Dadar M, Ziarati M, Seidgar M, Hassantabar F, Ghasemi M, et al. A perspective on the origin of COVID-19 and its epidemic situation in Iran and the world. *J Marine Med.* (2020) 2:41–52. doi: 10.30491/2.1.2
7. Control CfD, Prevention. *Interim Clinical Guidance For Management Of Patients With Confirmed 2019 Novel Coronavirus (2019-nCoV) Infection.* (2020). Available online at: <https://stacks.cdc.gov/view/cdc/89980> (accessed February 12, 2020).
8. Mokhayeri Y, Mohammadi R, Aghaali M, Nikbakht R, Taherpour N, Nakhaeizadeh M. Estimation of the basic reproduction number (0) of the COVID-19 epidemic in Iran. *Med J Islamic Republic Iran.* (2020) 34:95. doi: 10.34171/mjiri.34.95
9. *Coronavirus Updates.* (2021). Available online at: www.worldometers.info
10. Ritchie H, Mathieu E, Rod s-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, et al. Coronavirus pandemic (COVID-19). Our World in Data. Available online at: <https://ourworldindata.org/covid-vaccinations?country=JPN~USA> (accessed March 5, 2020).
11. Zandifar A, Badrfam R. Iranian mental health during the COVID-19 epidemic. *Asian J Psychiatr.* (2020) 51:101990. doi: 10.1016/j.ajp.2020.101990
12. Tuite AR, Bogoch II, Sherbo R, Watts A, Fisman D, Khan K. Estimation of coronavirus disease 2019 (COVID-19) burden and potential for international dissemination of infection from Iran. *Ann Internal Med.* (2020) 172:699–701. doi: 10.7326/M20-0696
13. Wright AL, Sonin K, Driscoll J, Wilson J. Poverty and economic dislocation reduce compliance with COVID-19 shelter-in-place protocols. *J Economic Behav Organ.* (2020) 180:544–54. doi: 10.1016/j.jebo.2020.10.008
14. SoleimanvandiAzar N, Irandoost SF, Ahmadi S, Xosravi T, Ranjbar H, Mansourian M, et al. Explaining the reasons for not maintaining the health guidelines to prevent COVID-19 in high-risk jobs: a qualitative study in Iran. *BMC Public Health.* (2021) 21:1–15. doi: 10.1186/s12889-021-10889-4
15. Zitek EM, Schlund RJ. Psychological entitlement predicts noncompliance with the health guidelines of the COVID-19 pandemic. *Person Individ Differ.* (2021) 171:110491. doi: 10.1016/j.paid.2020.110491
16. Nejhadadgar N, Togholi R, Yoosefi Lebni J, A Melca I, Ziapour A. Exploring the barriers in maintaining the health guidelines amid the COVID-19 pandemic: a qualitative study approach. *Inquiry.* (2022) 59:1–11. doi: 10.1177/00469580221100348
17. Shushtari ZJ, Salimi Y, Ahmadi S, Rajabi-Gilan N, Shirazikhah M, Biglarian A, et al. Social determinants of adherence to COVID-19 preventive guidelines: a comprehensive review. *Osong Public Health Res Perspect.* (2021) 12:346. doi: 10.24171/j.phrp.2021.0180
18. Young SD, Goldstein NJ. Applying social norms interventions to increase adherence to COVID-19 prevention and control guidelines. *Prev Med.* (2021) 145:106424. doi: 10.1016/j.ypmed.2021.106424
19. Webster RK, Brooks SK, Smith LE, Woodland L, Wessely S, Rubin GJ. How to improve adherence with quarantine: rapid review of the evidence. *Public Health.* (2020) 182:163–9. doi: 10.1016/j.puhe.2020.03.007
20. Sari DK, Fawzi A. Determinants of compliance with the implementation of the COVID-19 health protocol in the community of Kediri City. *J Nurs Pract.* (2021) 5:189–95. doi: 10.30994/jnp.v5i1.171
21. Noone C, Warner NZ, Byrne M, Durand H, Lavoie KL, McGuire BE, et al. A scoping review of research on the determinants of adherence to social distancing measures during the COVID-19 pandemic. *Health Psychology Rev.* (2021) 15:350–70. doi: 10.1080/17437199.2021.1934062
22. Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. *JAMA Network Open.* (2020) 3:e205619-e. doi: 10.1001/jamanetworkopen.2020.5619
23. Sharma G, Volgman AS, Michos ED. Sex differences in mortality from COVID-19 pandemic: are men vulnerable and women protected? *Case Reports.* (2020) 2:1407–10. doi: 10.1016/j.jaccas.2020.04.027
24. Pollak Y, Dayan H, Shoham R, Berger I. Predictors of non-adherence to public health instructions during the COVID-19 pandemic. *Psychiatry Clin Neurosci.* (2020) 74:602–4. doi: 10.1111/pcn.13122
25. Carlucci L, D'ambrosio I, Balsamo M. Demographic and attitudinal factors of adherence to quarantine guidelines during COVID-19: the Italian model. *Front Psychol.* (2020) 11:559288. doi: 10.3389/fpsyg.2020.559288
26. Coroiu A, Moran C, Campbell T, Geller AC. Barriers and facilitators of adherence to social distancing recommendations during COVID-19 among a large international sample of adults. *PLoS ONE.* (2020) 15:e0239795. doi: 10.1371/journal.pone.0239795
27. Rundle CW, Presley CL, Militello M, Barber C, Powell DL, Jacob SE, et al. Hand hygiene during COVID-19: recommendations from the American contact dermatitis society. *J Am Academy Of Dermatol.* (2020) 83:1730–7. doi: 10.1016/j.jaad.2020.07.057
28. Amodan BO, Bulage L, Katana E, Ario AR, Fodjo JNS, Colebunders R, et al. Level and determinants of adherence to COVID-19 preventive measures in the first stage of the outbreak in Uganda. *Int J Environ Res Public Health.* (2020) 17:8810. doi: 10.3390/ijerph17238810
29. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today.* (2004) 24:105–12. doi: 10.1016/j.nedt.2003.10.001
30. Yoosefi Lebni J, Khorami F, Ebadi Fard Azar F, Khosravi B, Safari H, Ziapour A. Experiences of rural women with damages resulting from an earthquake in Iran: a qualitative study. *BMC Public Health.* (2020) 20:1–13. doi: 10.1186/s12889-020-08752-z
31. Van Rijnsoever FJ. (I can't get no) saturation: a simulation and guidelines for sample sizes in qualitative research. *PLoS ONE.* (2017) 12:e0181689. doi: 10.1371/journal.pone.0181689
32. Lincoln YS, Lynham SA, Guba EG. Paradigmatic controversies, contradictions, and emerging confluences, revisited. *Sage Handbook Qualitative Res.* (2011) 4:97–128.
33. Ningsih OS, Eka AR, Danal PH. Factors predicting adolescents' compliance on Covid-19 prevention protocols. *Indonesian Nurs J Educ Clin.* (2020) 6:55–63. doi: 10.24990/injec.v6i1.365
34. Liem A, Wang C, Wariyanti Y, Latkin CA, Hall BJ. The neglected health of international migrant workers in the COVID-19 epidemic. *Lancet Psychiatry.* (2020) 7:e20. doi: 10.1016/S2215-0366(20)30076-6
35. Fridman I, Lucas N, Henke D, Zigler CK. Association between public knowledge about COVID-19, trust in information sources, and adherence to social distancing: cross-sectional survey. *JMIR Public Health Surveill.* (2020) 6:e22060. doi: 10.2196/22060
36. Xu Y, Lin G, Spada C, Zhao H, Wang S, Chen X, et al. Public knowledge, attitudes, and practices behaviors towards coronavirus disease 2019

(COVID-19) during a national epidemic—China. *Front Public Health*. (2021) 9:227. doi: 10.3389/fpubh.2021.638430

37. Plohl N, Musil B. Modeling compliance with COVID-19 prevention guidelines: the critical role of trust in science. *Psychol Health Med*. (2021) 26:1–12. doi: 10.1080/13548506.2020.1772988

38. Wise T, Zbozinek TD, Michelini G, Hagan CC, Mobbs D. Changes in risk perception and self-reported protective behaviour during the first week of the COVID-19 pandemic in the United States. *Royal Soc Open Sci*. (2020) 7:200742. doi: 10.1098/rsos.200742

39. Harper CA, Satchell LP, Fido D, Latzman RD. Functional fear predicts public health compliance in the COVID-19 pandemic. *Int J Mental Health Addict*. (2021) 19:1875–88. doi: 10.1007/s11469-020-00281-5

40. Indrayathi PA, Januraga PP, Pradnyani PE, Ward PR, Gesesew HA. Perceived social norms as determinants of adherence to public health measures related to COVID-19 in Bali, Indonesia. *Front Public Health*. (2021) 9:269. doi: 10.3389/fpubh.2021.646764

41. Khalatbari-Soltani S, Cumming RC, Delpierre C, Kelly-Irving M. Importance of collecting data on socioeconomic determinants from the early stage of the COVID-19 outbreak onwards. *J Epidemiol Community Health*. (2020) 74:620–3. doi: 10.1136/jech-2020-214297

42. Osei-Tutu A, Affram AA, Mensah-Sarbah C, Dzokoto VA, Adams G. The impact of COVID-19 and religious restrictions on the well-being of Ghanaian Christians: the perspectives of religious leaders. *J Relig Health*. (2021) 60:2232–49. doi: 10.1007/s10943-021-01285-8

43. Yoosefi Lebni J, Irandoost SF, Xosravi T, Ahmadi S, Ziapour A, Soofizad G, et al. Explaining the problems faced by Iranian housewives during the COVID-19 quarantine period, and their adaption strategies: a qualitative study. *Womens Health*. (2021) 17:17455065211063291. doi: 10.1177/17455065211063291

44. DeFranza D, Lindow M, Harrison K, Mishra A, Mishra H. Religion and reactance to COVID-19 mitigation guidelines. *Am Psychol*. (2020) 76:744–54. doi: 10.31234/osf.io/zvyc2

45. Yoosefi Lebni J, Ziapour A, Mehedi N, Irandoost SF. The role of clerics in confronting the COVID-19 crisis in Iran. *J Relig Health*. (2021) 60:2387–94. doi: 10.1007/s10943-021-01295-6

46. Lebni JY, Irandoost SF, Mehedi N, Sedighi S, Ziapour A. The role of clerics in confronting the COVID-19 crisis in Iran. *J Relig Health*. (2021) 60:2387. doi: 10.1017/dmp.2020.498

47. Leng HK, Phua YXP. Athletes as role models during the COVID-19 pandemic. *Manag Sport Leisure*. (2022) 27:163–7. doi: 10.1080/23750472.2020.1762330

48. Asemahagn MA. Factors determining the knowledge and prevention practice of healthcare workers towards COVID-19 in Amhara region, Ethiopia: a cross-sectional survey. *Trop Med Health*. (2020) 48:1–11. doi: 10.1186/s41182-020-00254-3

49. Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair allocation of scarce medical resources in the time of COVID-19. *New England J Med*. (2020) 382:2049–55. doi: 10.1056/NEJMs2005114



OPEN ACCESS

EDITED BY
Melody Goodman,
New York University, United States

REVIEWED BY
Fan Huang,
Guangzhou University of Chinese
Medicine, China
Mingke Wang,
Naval Medical Center, China

*CORRESPONDENCE
Jie Xu
jiexud@126.com

†These authors have contributed
equally to this work

SPECIALTY SECTION
This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 17 August 2022
ACCEPTED 07 September 2022
PUBLISHED 26 September 2022

CITATION
Deng Z, Luo F, Lin Y, Luo J, Ke D,
Song C and Xu J (2022) Research
trends of mesenchymal stem cells
application in orthopedics: A
bibliometric analysis of the past 2
decades.
Front. Public Health 10:1021818.
doi: 10.3389/fpubh.2022.1021818

COPYRIGHT
© 2022 Deng, Luo, Lin, Luo, Ke, Song
and Xu. This is an open-access article
distributed under the terms of the
[Creative Commons Attribution License
\(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

Research trends of mesenchymal stem cells application in orthopedics: A bibliometric analysis of the past 2 decades

Zhibo Deng [†], Fenqi Luo[†], Yuan Lin, Jun Luo, Dianshan Ke, Chao Song and Jie Xu*

Department of Orthopedics, Fujian Clinical Research Center for Spinal Nerve and Joint Diseases, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou, China

Background: Bibliometric analysis and visualization tools were used to determine the development trend of mesenchymal stem cells (MSCs) in orthopedics in the past 20 years, so as to guide researchers to explore new directions and hotspots in the field in the future.

Methods: In the Web of Science Core Collection, all articles about the application of MSCs in orthopedics from 2002 to 2021 were searched. The qualitative and quantitative analysis was performed based on Web of Science and CiteSpace software.

Results: A total of 2,207 articles were retrieved. After excluding non-article articles such as review and letter and non-English language articles, 1,489 articles were finally included. Over the past 2 decades, the number of publications on the application of MSCs in orthopedic diseases increased. Among them, the United States, China, Japan and the United Kingdom have made significant contributions in this field. The most productive institution was Shanghai Jiao Tong University. *Journal of Orthopedic Research* published the largest number of publications. The journal with the highest citation frequency was *Experimental Hematology*. The authors with the highest output and the highest citation frequency on average were Rochy S. Tuan and Scott A. Rodeo, respectively. "Mesenchymal stem cell", "in vitro" and "Differentiation" were the top three keywords that appeared. From the keyword analysis, the current research trend indicates that the primary research hotspots of MSCs in orthopedics are the source of MSCs, *in vitro* experiments and the differentiation of MSCs into bone and cartilage. The frontiers of this field are the combination of MSCs and platelet-rich plasma (PRP), the treatment of knee diseases such as osteoarthritis, osteogenic differentiation, and the application of biological scaffolds combined with MSCs.

Conclusion: Over the past 2 decades, the application of MSCs in orthopedic diseases has received increasing attention. Our bibliometric analysis results provide valuable information and research trends for researchers in the field to understand the basic knowledge of the field, identify current research hotspots, potential collaborators, and future research frontiers.

KEYWORDS

mesenchymal stem cell, orthopedics, bibliometric analysis, hotspot, Web of Science

Introduction

Mesenchymal stromal/stem cells (MSCs) are non-hematopoietic adult stem cells derived from mesoderm (1). It can be found in bone marrow, fat, synovium, tonsil, peripheral blood, amniotic fluid, umbilical cord blood and other tissues (2). It has the potential of self-replication, self-division, self-renewal, and multidirectional differentiation, to repair tissues and maintain their homeostasis (3, 4). In addition to the powerful immunomodulatory properties to regulate neighboring cells and enhance tissue repair ability, MSCs can also differentiate into resident cells to replace damaged tissues (5). Therefore, it plays a key role in tissue healing and regenerative medicine.

At present, MSCs have been proved to be able to treat a variety of diseases, such as hematological diseases, cardiovascular system diseases, digestive system diseases, nervous system diseases, autoimmune diseases and other diseases (6). In addition, MSCs have been proved to have the potential ability to differentiate into bone, cartilage, tendon, ligament, muscle, fat and other cells (7). Meanwhile, MSCs have good immunomodulatory activity and paracrine ability (8), which can synthesize and release cytokines, stimulate progenitor cell proliferation, inhibit cell apoptosis, and promote tissue repair. They are the seed cells with the most promising clinical application in regenerative medicine (9), and have been widely used in the treatment of orthopedic diseases (10), especially for sports injury diseases, such as cartilage injury, meniscus injury, cruciate ligament injury, achilles tendon rupture, rotator cuff injury, etc (11). Bibliometrics is a tool to evaluate published articles through mathematical and statistical methods, and bibliometrics analysis has been widely used in various medical disciplines. It enables beginners to intuitively, systematically and comprehensively understand the development process and hot trends of a particular field (12). CiteSpace is a software that visualizes information to present and identify new trends. The software can display the structural relations and evolution rules of a research field for beginners from different dimensions and levels in the way of knowledge map (13). At the same time, the software is easy to obtain, easy to operate and readable, so it has been widely used in bibliometrics analysis and other fields.

At present, the research in this field of MSCs in orthopedic diseases mainly focuses on the mechanism research and clinical observation, but there is a lack of clear combing in the hotspot trend and intuitive structure display. This study intends to analyze the application of MSCs in orthopedic diseases in the past 20 years through bibliometrics analysis. The authors, publishing institutions, keywords and other elements are presented in the form of knowledge map, so as to comprehensively understand the research background of MSCs in the treatment of orthopedic diseases, predict the future

development trend and hotspots, and provide reference for further related research.

Methods

Data collection and search strategy

Considering that Web of Science (WoS) is an important academic database in the world and is often used in bibliometric analysis (14, 15), we chose the WoS core collection database as the literature source. The time period of the search was 2002–2021. The search strategies were as follows: TS = (mesenchymal stem cell* OR MSC* OR bone marrow stromal stem cell* OR mesenchymal stromal cell* OR bone marrow stromal cell* OR mesenchymal progenitor cell*) AND TS= (orthopedic* OR orthopedics department OR Clinical orthopedic* OR Bone science OR orthopedic*). A total of 2,207 studies were retrieved, and only 1,521 articles were exported for records and cited references in the format of plain text files. All data used in this work were downloaded from public databases, therefore did not require ethics committee approval or informed consent. Detailed retrieval strategy is listed in Table 1.

Statistical analysis

Information including annual publications and journal distributions was obtained from the WoS database. The chart of annual publications was generated using Microsoft Excel 2019. Then, the data was imported into CiteSpace (5.8R3), and 1,489 records were retained after removing duplications. “Time Slicing” was set for one per slice from 2002 to 2021. All the options in “Term Source,” “pathfinder,” “pruning sliced networks,” and “Pruning the merged network” in pruning were selected. Country, institutions, journal and keywords in node types were selected to perform co-occurrence analysis, respectively. Besides, the node “Keyword” was used for cluster analysis. In the co-occurrence maps, the size of nodes represents the degree of co-occurrence or the frequency of citation, and the connection between nodes represents the cooperation and co-occurrence relationship. It is worth noting that nodes with high frequency and high centrality are the critical points in the field, and therefore these are also the core of our study (13).

Results

Annual publication outputs and trends

As shown in Figure 1, a total of 2,207 literatures were retrieved. We only included articles and English language

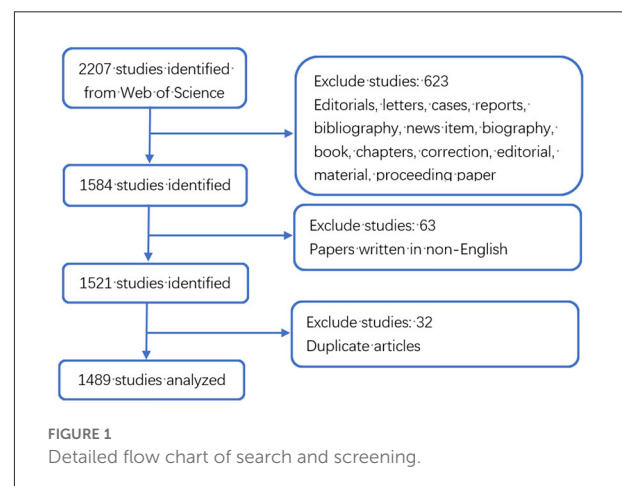
TABLE 1 Data sources and flow of retrieval strategy.

Content

Data sources	Web of Science Core Collection		
Publication date	1 January 2002–31 December 2021		
Languages	English only		
Document type	Article only		
Search strategy			
	#1	139,289	TS = (mesenchymal stem cell* OR MSC* OR bone marrow stromal stem cell* OR mesenchymal stromal cell* OR bone marrow stromal cell* OR mesenchymal progenitor cell*)
	#2	44,985	TS = (orthopedic* OR orthopedics department OR Clinical orthopedic* OR Bone science OR orthopedic*)
	#3	2,207	#1 AND #2
	#4		Document types: (Article)
	#5		Language: (English)
	#6	1,521	#1 AND #2 AND #3 AND #4 AND #5

documents, and finally the remaining 1,521 publications retained a total of 1,489 articles after excluding duplicate articles. It is known that the research in the field of MSCs in orthopedic diseases mainly focuses on basic scientific researches and clinical researches. As shown in Figure 2, according to the annual distribution of publications, with year as the abscissa and number of publications as the ordinate, the continuous exploration of MSCs in orthopedics is visually presented. It can be seen that the number of publications in 2004 was the lowest, with 22. The highest was 136 in 2019. The research period can be divided into two stages: from 2002 to 2004, the number of annual publications showed a downward trend, and from 2004 to 2019, the number of annual publications showed a gradual upward trend. Since 2019, there has been a slow decline in the research results of MSCs in orthopedic diseases worldwide, which may be related to the COVID-19 pandemic, as it leads to a decline in scientific research productivity. In 2002, the reason for the sudden increase in publications was considered a breakthrough in stem cell basic research. Since 2010, there have been more than 70 articles published annually, indicating that MSCs have always been a research hotspot in the treatment of orthopedic diseases, and a stable research environment has been formed.

To better study the dynamics change of MSCs in orthopedics over the past 20 years, we divided the period into two periods based on the 10-year period. The two periods were the 2002–2011 period and 2012–2021 period, as shown in Table 2. there were 577 publications in the first period (2002–2011), while there were 912 publications in the second period (2012–2021), an increase of 158%. This increasing trend is also reflected in the other variables considered in the table. In terms of authors, the first period involved 2,596 scholars, while the second period had a total of 4,847 authors. This means that with the development of MSCs in the field of orthopedics, increasing scholars began to pay attention to this field and published relevant research



results. As for journals, the number of journals increased from 169 in the first period to 275 in the second period, an increase of 163%. In terms of countries, there were only 39 countries in the first period and 63 countries in the second period, representing an increase of 162%. This means that about a third of the countries worldwide are involved in MSCs research in the field of orthopedics. It is worth noting that the sample recorded a total of 66,498 citations over the time frame analyzed, for a total average of 44.66 citations per article. The average number of citations per article in the first period was 77.27 times, but only 24.03 times in the second period. Considering that the publications of the second period were published recently, the cumulative number of citations was still small. Whether there is a lack of representative articles in the second period, it still needs a certain amount of time to accumulate the citations and then analyze again.

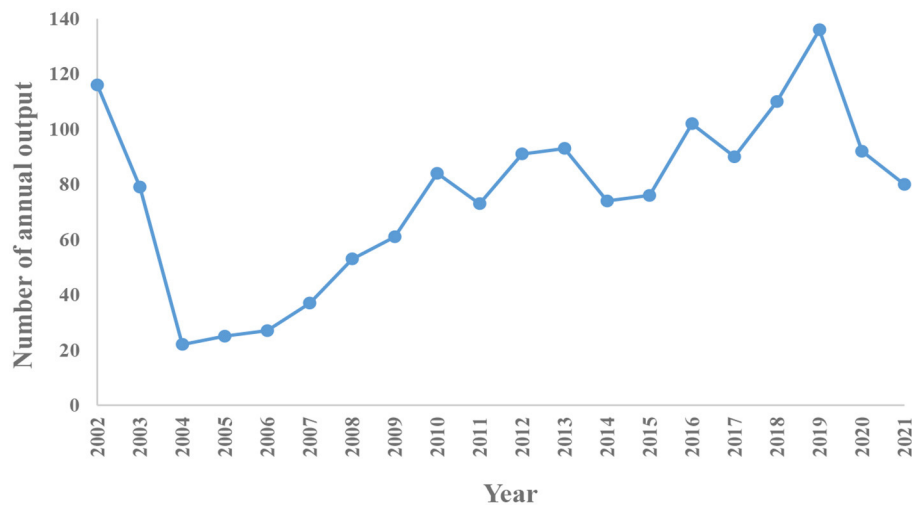


FIGURE 2

The annual number of publications and trends on MSCs in orthopedics between 2002 and 2021.

TABLE 2 Comparison of the major characteristics of the two periods (2002–2011 and 2012–2021).

Period	Articles	Authors	Journals	Countries	Citations	Average citations
2002–2011	577	2,596	169	39	44,583	77.27
2012–2021	912	4,847	275	63	21,915	24.03
Total	1,489	675	369	103	66,498	44.66

Analysis of countries

The 1,489 articles came from 65 different countries or regions. Among them, The United States (USA) (553) was the most productive country, China (230) was the second, and Japan (134) was the third. England (120) was the fourth and Germany (109) was the fifth. The top 5 countries with total citations were USA (33,025), England (6,384), Japan (6,209), Italy (5,953) and China (5,515). As can be shown in Figure 3, although USA had the largest number of publications, its publications had gradually declined in recent years. Publications of other countries, such as England and Germany, increased with each year. Although the Netherlands was not in the top 5 in terms of the number of publications and the total number of citations, the average number of citations was the highest. For the average citation times of each article, the top 5 countries were Netherlands (73.15), Italy (67.65), France (62.47), USA (59.72), Switzerland (54.56).

Analysis of institutions

A total of 1,711 institutions have participated in the research of MSCs in orthopedics. The top six institutions for



FIGURE 3

The cooperation network map of countries related to MSCs in orthopedics from 2002–2021. Node size represents the number of output. The thicker the pink outer ring of the node, the higher the centrality.

the total number of publications were Shanghai Jiao Tong University (33), Harvard University (29), Stanford University (28), Columbia University, University of Pennsylvania (22), Mayo Clinic (22). Except the first one, the other five institutions were located in USA. Figure 4 clearly shows the close and complex collaboration between different institutions, which shows that there is still little inter-institution cooperation. While these institutions were strong in scientific research, the lack



FIGURE 4

The cooperation network map of institutions related to MSCs in orthopedics from 2002–2021.

of connectivity between nodes indicates weak collaboration between institutions. Stanford University and Hospital for Special Surgery were the most active institutions in the cooperative relationship and the most influential institutions. They were critical institutions devoted to the research of MSCs in orthopedic diseases.

Analysis of journal

As a medium for the exchange of research results, journals play a vital role in promoting cooperation and the advancement of scientific research. From 2002 to 2021, there were 51 journals devoted to MSCs in orthopedics research. Table 3 lists the top 10 journals with the most publications of MSCs in orthopedics, which are representative journals in this field. As shown in Table 3, *Journal of Orthopedic Research* published the largest number of publications of MSCs in orthopedics with 402 articles, accounting for 26.43% of the total articles, but the average cited frequency was only 46.03. Although *Biomaterials* (47) was ranked the second in terms of the number of publications, the average citation frequency of *Biomaterials* was also ranked the second (158.51). The third-most published Journal was *Journal of Tissue Engineering and Regenerative Medicine* (28). *Experimental Hematology* (25), which ranked fourth in the number of publications, was the journal with the

highest citation frequency (174.04). At the same time, the impact factors (IF) of these 10 journals are between 3.084 and 12.479. There are 6 journals with IF < 4.000, 3 journals with IF between 4.000 and 9.000, and 1 journal with IF > 10.000. The IF of *Biomaterials* (12.479) is the highest among the top 10 journals in number of publications.

Analysis of authors and cooperative relationship

By analyzing the authors of the included literature, the representative scholars and the main research population in the research field can be grasped. The 1,489 articles included a total of 7,918 authors. Table 4 lists the top 10 authors. The top three authors with the most publications were Rochy S. Tuan (13), Takeshi Muneta (12), and Ichiro Sekiya (12). Meanwhile, in terms of average citation times, the top four authors were Scott A. Rodeo (100.9), Rochy S. Tuan (74.38), Takeshi Muneta (48.42) and Ichiro Sekiya (48.42). Rochy S. Tuan (National Institutes of Health, USA), the most productive author in the field, has been focusing on basic researches such as the multilineage MSCs differentiation potential of human trabecular bone-derived cells since 2002. Figure 5 is the cooperation network map of productive authors. It can be seen that Takeshi

TABLE 3 Top 10 Journals With publications related to MSCs in orthopedics between 2002 and 2021.

Rank	Journal	Publications	Total times cited	Mean times cited	Impact factor (2020)	JCR
1	<i>Journal of Orthopedic Research</i>	402	18,503	46.03	3.494	Q1
2	<i>Biomaterials</i>	47	7,450	158.51	12.479	Q1
3	<i>Journal of Tissue Engineering and Regenerative Medicine</i>	28	645	23.04	3.963	Q2
4	<i>Experimental Hematology</i>	25	4,351	174.04	3.084	Q3
5	<i>American Journal of Sports Medicine</i>	23	1,273	55.35	6.202	Q1
6	<i>Bone</i>	23	2,048	89.04	4.398	Q2
7	<i>Biochemical and Biophysical Research Communications</i>	23	1,608	69.91	3.575	Q2
8	<i>Acta Biomaterialia</i>	22	849	38.59	8.947	Q1
9	<i>European Cells & Materials</i>	18	733	40.72	3.942	Q1
10	<i>Journal of Materials Science-Materials in Medicine</i>	18	1,790	99.44	3.896	Q2

TABLE 4 The top 10 authors in the MSCs for orthopedics ranked by publication number.

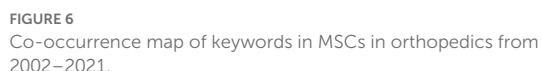
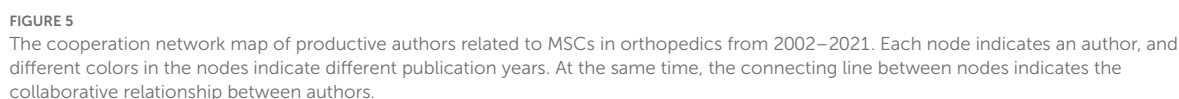
Rank	Author	No. of publications	No. of citations	Mean times cited per study
1	Rochy S. Tuan	13	967	74.38
2	Takeshi Muneta	12	581	48.42
3	Ichiro Sekiya	12	581	48.42
4	Scott A. Rodeo	10	1,009	100.9
5	Stuart B. Goodman	10	343	34.30
6	Tunku Kamarul	10	299	29.90
7	Kunikazu Tsuji	9	330	36.67
8	Peter V. Giannoudis	9	314	34.89
9	Chunfeng, Zhao	9	163	18.11
10	Norbert. Telmon	9	127	14.11

Muneta (12) and Ichiro Sekiya (12), who ranked the second and the third in the number of publications, cooperated very closely, and both of them worked in Tokyo Medical and Dental University (Japan). Both scholars devoted to the basic research of meniscal injury and osteoarthritis in knee. But on the whole, there was not much cooperation among the authors in this field, and the authors were not closely related to each other. For the further development of this field, it is suggested to strengthen the cooperation among scholars.

Analysis of keyword

Keywords represent the primary topics of published articles (16). Co-occurrence analysis of keywords can help scholars to comprehensively understand the relationship between keywords, and to analyze the relationship between various topics

in this field. Further cluster analysis is helpful for thorough analyze the research progress in this field. The lines between nodes in the co-occurrence map of keywords represent their co-occurrence relationship, and the thickness of the lines represents the number of co-occurrence times. As can be seen from Figure 6, the keywords co-occurrence analysis network consists of 457 nodes and 1,537 lines. The high-frequency and high-centrality keywords are listed in Table 5. The top 10 keywords in frequency were “mesenchymal stem cell” (649), “*in vitro*” (304), “Differentiation” (295), “Stem cell” (234), “Bone marrow” (213), “Expression” (211), “Stromal cell” (208), “Repair” (176), “Bone” (136), “Marrow stromal cell” (134). The top 10 keywords in centrality were “Tissue engineering” (0.09), “Collagen” (0.08), “Transplantation” (0.07), “Defect” (0.07), “Marrow” (0.07), “Bone marrow” (0.06), “Cell” (0.06), “Bone morphogenetic protein 2” (0.06), “Injury” (0.06), “Expression” (0.05). Keyword clustering analysis is a process to simplify keywords into a



research hotspots and trends in the field. As shown in Figure 7, the sequence number was ranked according to the size of the cluster, which divided keywords into different detailed topics. The number of nodes in each cluster was larger than 15, and the silhouette was larger than 0.8, indicating that clusters can be distinguished from each other. Keywords of MSCs in orthopedic disease can be divided into 17 clusters, in order: “differentiation” #0, “*in vitro*” #1, “subculture” #2, “Citespace” #3, “platelet-rich Plasma” #4, “bone” #5, “scaf-fold” #6, “transforming growth factor beta” #7, “bursitis” #8, “implant particles” #9, “defect” #10, “MSC” #11, “dynamic contact mechanics” #12, “cross contamination” #13, “peripheral blood” #14, “tissue repair” #15, “anti-tumor effect” #16.

Keyword timeline visualization map mainly focuses on describing the relationship between clusters and the historical span of keywords in each cluster. Nodes in the same cluster were arranged on the same horizontal line in chronological order. Time was placed at the top of the view. The closer the node was to the right, the closer it was to the present time. The research history of MSCs in orthopedics can be clarified by the analysis of the keyword timeline visualization map. As

TABLE 5 The top 10 keywords co-occurrence frequency and centrality ranking.

Rank	Keyword	Frequency	Rank	Keyword	Centrality
1	Mesenchymal stem cell	649	1	Tissue engineering	0.09
2	<i>in vitro</i>	304	2	Collagen	0.08
3	Differentiation	295	3	Transplantation	0.07
4	Stem cell	234	4	Defect	0.07
5	Bone marrow	213	5	Marrow	0.07
6	Expression	211	6	Bone marrow	0.06
7	Stromal cell	208	7	Cell	0.06
8	Repair	176	8	Bone morphogenetic protein 2	0.06
9	Bone	136	9	Injury	0.06
10	Marrow stromal cell	134	10	Expression	0.05

can be seen from Figure 8, “*in vitro*,” “differentiation,” “platelet-rich plasma,” “cross contamination” played an important role in the field, and their clustering time span was long, which showed that these clustering labels were the key research content and formed a stable research direction in the field. And “scaf-fold” and “bone” were another hot topic in recent researches. The keywords with strong bursts refer to the words that appeared frequently or were applied significantly more frequently in the short term, which can reflect the change and trend of the research direction in this field from a certain extent. The keywords were identified and analyzed using Citespace’s strong citation bursts to explore the frontier field of MSCs in orthopedic diseases. As shown in Figure 9, the keywords with strongest citation bursts were “expression” (2002–2003), “culture” (2002–2003), and “progenitor cell” (2008–2012). The most recent burst keyword included “knee” (2014–2021), “platelet rich plasma” (2015–2021), “osteoarthritis” (2015–2021), and “scaf-fold” (2018–2021).

Discussion

This study provided a bibliometric analysis of MSCs in orthopedics over the last 2 decades (2002 to 2021). As far as we know, this is the first bibliometric and visual analysis of MSCs in the field of orthopedics, which comprehensively reveals the research status and development trend in the field, and helps scholars analyze landmark research results and latest research hotspots in this field. We found that the research in this field reached a small peak in 2002, and then after a period of steady development, the number of publications in this field gradually climbed, and the average annual publications had been significantly increased compared with 20 years ago, up to 136. With the resumption of production after the COVID-19 pandemic and increasing fund investment, the amount of research in this field was still on the rise. This showed that scholars all over the world paid attention to the application

of MSCs in orthopedic diseases, indicating that there is still a large potential for exploration in the future. The number of publications increased suddenly in 2002, which was considered to be the breakthrough of basic research on MSCs (18, 19). For example, in 2002, Bartholomew et al. (20) found that MSCs did not generate proliferation of allogeneic lymphocytes, and *in vivo* administration of MSCs could prolong the survival time of transplants. These immunomodulatory functions demonstrated in this study provided a strong theoretical basis for tissue regeneration and stem cell engineering in the future. Jiang et al. (21) showed that cells with the characteristics of multipotent adult progenitor cells could be separated not only from bone marrow but also from brain and muscle tissue. This study demonstrated that MSCs exist in multiple tissues, and their sources are extensive and convenient.

According to the visualization analysis of Citespace software, it can be seen that USA, China and Japan were the top three productive countries in research field of MSCs in orthopedic diseases. It was worth noting that USA published 553 articles from 2002 to 2021, accounting for 36.4% of the total number of publications, indicating that the country’s scientific research strength was very strong. USA had more research institutes comparing with other countries. Among the top ten institutions with the number of publications, 5 of them belong to USA, indicating that USA is still the primary research area in this field. But at the same time, the number of publications in other countries was gradually increasing, and there were many high-quality articles. For example, Bourin et al. (22), from France, proved in 2013 that MSCs from fatty tissue could be distinguished from bone marrow by their positive for surface antigen CD36 and negative for CD106, which provided guidance for the scientific community to utilize MSCs derived from fatty tissue and was widely recognized by scholars. In 2011, Davatchi et al. (23) from Iran injected MSCs extracted from bone marrow into knee joints with osteoarthritis at the first time, and the pain symptoms improved significantly.

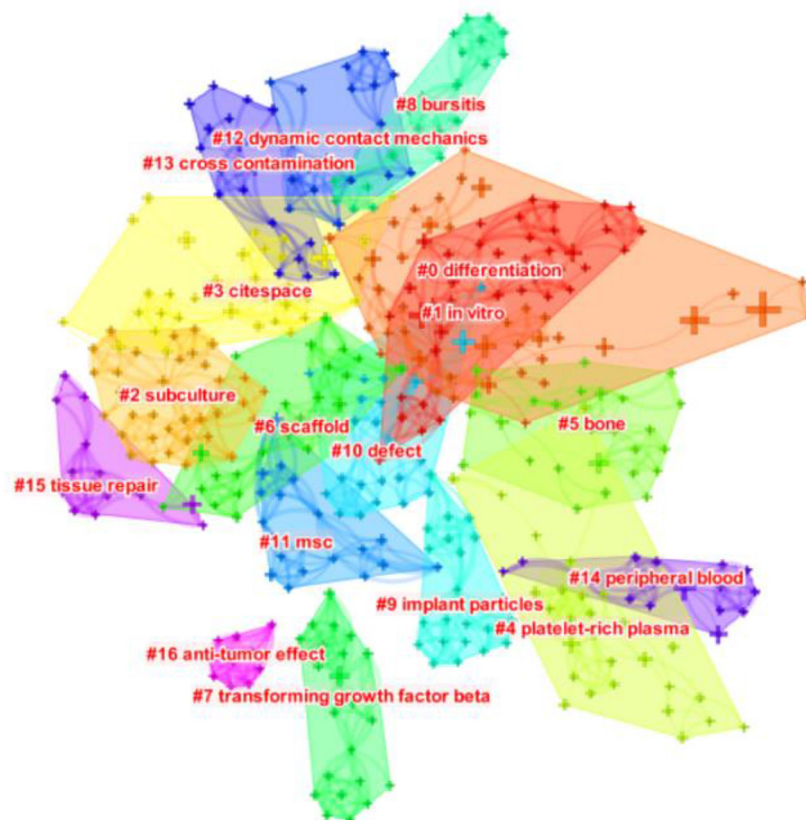


FIGURE 7

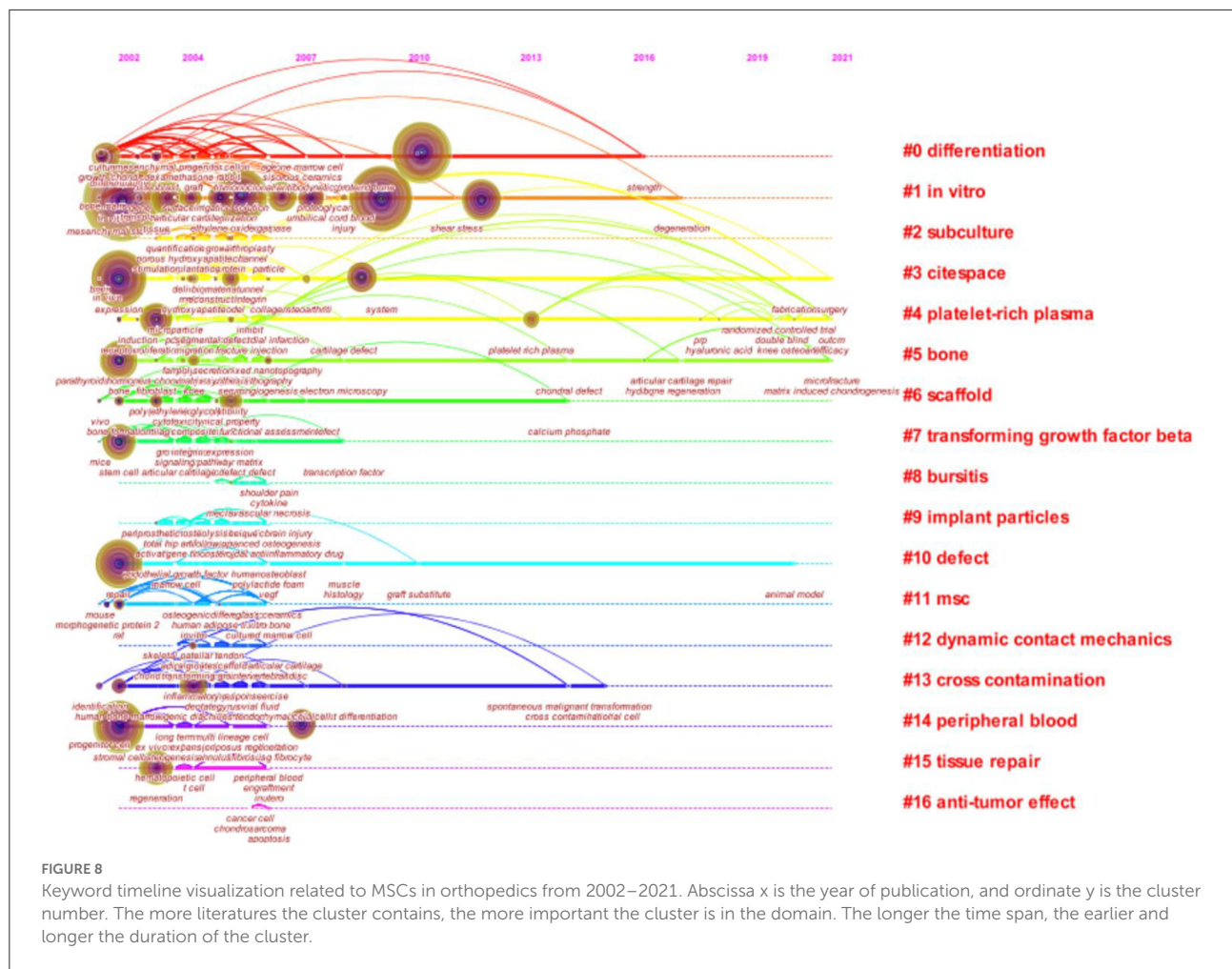
The clustering map of keywords related to MSCs in orthopedics from 2002–2021. The different colored squares in the figure represent different clusters.

The highly cited literatures reflected some important research achievements and indirectly proved that these fruits are the research basis of this field. Although the number of publications in China ranked the second (230), the total number of citations only ranked the fifth, indicating that there were still few basic studies published in this field in China, and efforts are still needed to improve high-quality articles. The articles with high centrality represent the key literatures in this field. Although the Netherlands was not in the top 5 countries in publication quantity and total citation times, the average citation time was the highest (73.15). Rombouts et al. (24) found in 2003 that the *in vitro* proliferation of bone marrow-derived MSCs significantly reduced their homing in femur and spleen, which provided a strong basis for the application of MSCs in the precision treatment of injured sites.

At the same time, this study found that many institutions began to invest in the exploration of MSCs in orthopedic diseases, and the publications number (196) of top 10 institutions only accounted for 12.9% of the total number of publications. Shanghai Jiao Tong University (33) was the institution that had published the most papers, which reflected

its great influence on MSCs in orthopedics. Its frequent cooperation institutions included University of Bologna and Columbia University. Of the top 10 institutions in number of publications, five belonged to American. This reflected the high level of American medical and scientific capabilities. However, as shown in the cooperation network map of institutions (Figure 4), cooperation between institutions was relatively rare and not closely connected. For the long-term development of MSCs in the field of orthopedics, it is recommended to strengthen cooperation among institutions in the future.

Among the top 10 journals by number of publications, *Journal of Orthopedic Research* (IF: 3.493) had the most publications (402), reflecting the international influence of this journal in the field of MSCs application in orthopedics. There were 4 journals with IF > 4, and *Biomaterials* (IF: 12.497) had the highest IF. *Biomaterials*, as the top journal of materials science, ranked the second in terms of the number of publications, indicating that MSCs in orthopedic disease has a promising application in the field of biomaterials and tissue engineering (25, 26).



Rochy S. Tuan (National Institutes of Health, USA) was the most productive author in this field, with 13 publications and an average of 74.38 citations. He also had a high centrality and was one of the authors who cooperated most closely with others. Tuan et al. found that cells derived from bone trabecular fragments of adult have the potential to differentiate into a variety of mesenchymal lineage cells *in vitro* (27). At the same time, Tuan et al. demonstrated that traumatic muscle-derived MSCs exhibited similar phenotypes as bone marrow-derived MSCs and also had differentiation potential (28). It can differentiate into osteoblasts, adipocytes and chondrocytes (29). Therefore, MSCs extracted from the injured muscle tissue of orthopedic trauma patients who need debridement treatment can be considered for regenerative medicine (30). Rochy S. Tuan was an early participant in this field and had an important influence on later researches. As MSCs had become a hot topic in the treatment of diseases, both positive and negative reports have aroused great interest of orthopedic surgeons. As the author with the highest average citation frequency, Scott A. Rodeo (100.9) had made outstanding contributions to

the basic scientific research and clinical application of MSCs. He highlighted the lack of consensus on optimal preparation, source, delivery method, and dosage of MSCs as a biologic therapy, and the need to pay attention to their safety and efficacy in clinical use (31, 32). Further clinical prospective randomized controlled trials are needed to better determine how, when, and where MSCs are used for optimal efficacy. In addition, a number of high-impact authors, such as Zhen et al. (33) (Johns Hopkins University, USA) demonstrated in 2013 that transforming growth factor β 1 in subchondral MSCs is key to initiating osteoarthritis, providing a potential therapeutic option to treat this disease.

In this study, the top three keywords with the high frequency were “Mesenchymal stem cell” (649), “*in vitro*” (304) and “Differentiation” (295). As for the keyword “Mesenchymal stem cell” (MSC), it was necessary to explore its original source. It was first proposed in 1999 that MSC could differentiate into mesenchymal tissue lineage, that is, single stem cells could still retain their multilineage potential when expanded into colonies. With the development of research, the huge

Top 15 Keywords with the Strongest Citation Bursts

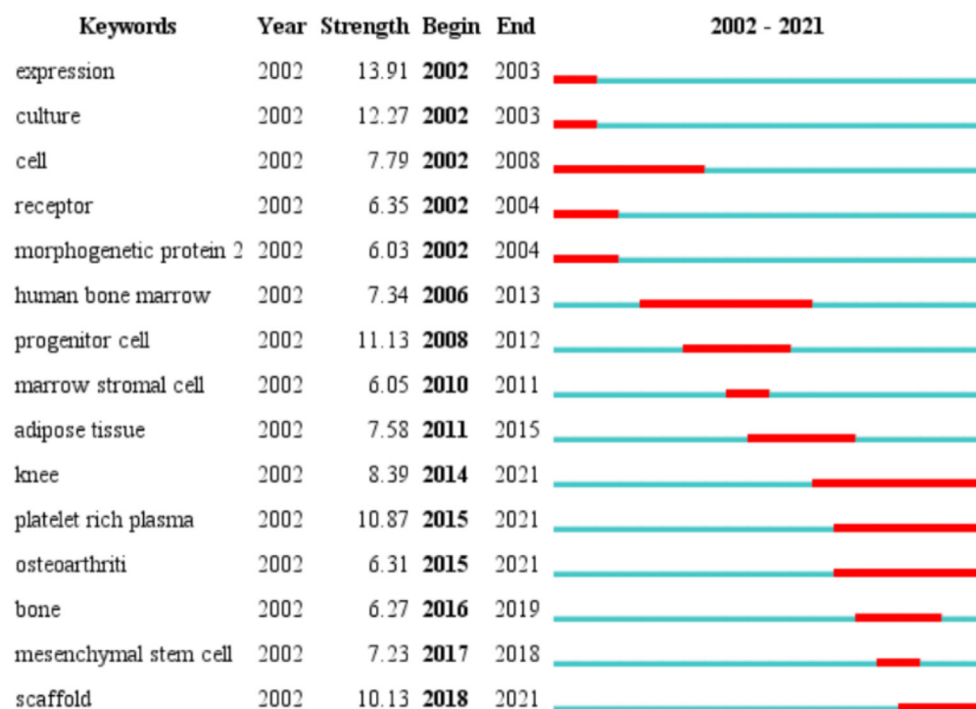


FIGURE 9

The top 15 keywords with the strongest citation bursts.

therapeutic potential of MSCs has attracted the intense attention of biomedical scholars. At the same time, the Mesenchymal and Tissue Stem Cell Committee of the International Society for Cellular Therapy proposed minimal criteria for defining human MSC (34). Firstly, MSC must be plastic-adherent under standard culture conditions. Secondly, MSC must express CD105, CD73 and CD90 markers and lack expression of CD45, CD34, CD14 or CD11b, CD79 α or CD19 and HLA-DR surface molecules. Thirdly, MSC must differentiate into osteoblasts, adipocytes and chondroblasts *in vitro*. The above criteria make it possible to compare the results of different studies on MSCs on the basis of different isolation and expansion methods and cell characterization. At the same time, with the study on MSCs derived from peripheral blood, fat and cord blood, it was found that they not only have similar phenotype and differentiation potential with bone marrow-derived MSCs, but also have a wide range of sources and convenient sampling, and have fewer complications compared with bone marrow cell extraction (35, 36). The keyword “*in vitro*” ranked second in citation times. As an important bridge between basic theories and clinical trials, cell experiment has always been the most direct and necessary method to study the mechanism and efficacy of MSCs. However, due to different sources of MSCs, different

preparation methods, individual differences and other factors, many conclusions about *in vitro* have been controversial. There are still few clinical researches on MSCs, so *in vitro* is still the primary method of current research. As the third most cited keyword, “differentiation” is an important part in inducing the transformation of MSCs to osteocyte and chondrocytes. Studies have shown that Wnt/ β -catenin (37), BMP/Smad (38), MAPK (39), PI3K/AKT (40), TGF- β , Notch, NF- κ B and other signaling pathways play important regulatory roles in the differentiation of MSCs into bone or cartilage (41). Its positive or negative regulatory effects alone or in combination have also aroused active exploration by scholars. It was believed that with the sustainable development of molecular biology and the continuous advancement of basic research, the cognition of the differentiation regulatory network of MSCs will be gradually clear, and then the process of precise intervention will be achieved.

Morphogenetic protein 2, as a functional protein, can stimulate DNA synthesis and cell replication and promote the directional differentiation of MSCs into osteoblasts (42). “Knee” was one of the keywords with a long bursts time. For cartilage injury, meniscus injury, cruciate ligament rupture and other knee diseases, when the condition is serious, can not

heal by itself, and at the same time, the operation is more difficult. Therefore, MSCs, as the most promising seed cells in the field of regenerative medicine, have gradually been applied to diseases of knee joint (9). Saw et al. (43) conducted an *in vivo* experiment, which injected MSCs or hyaluronic acid into the articular cavity once a week for 5 weeks in patients with knee cartilage defects, and the results showed that the hyaline cartilage regenerated in the MSCs group, but not in the hyaluronic acid group. At the same time, MSCs can also differentiate into ligament fibroblasts, contributing to the regeneration of cruciate ligament, and the differentiation process can be regulated (44). In addition, it can also promote the repair of meniscus injury (45). Platelet-rich plasma (PRP) is a product of platelet concentration obtained from peripheral blood after repeated centrifugation, which has been used in clinical treatment since the 1980s (46). The application of PRP combined with MSCs in orthopedic diseases is another research hotspot, which has attracted the attention of many scholars. Ito et al. (47) demonstrated that tissue-engineered bone containing MSCs and PRP had better histological and mechanical properties than PRP-only graft material or autologous bone, so the combined protocol could be applied to early bone regeneration. In addition, studies on PRP also showed that the combined application of MSCs and PRP could significantly promote the maturation and repair of allogeneic tendon and ligament tissues (48). And “Scaf-fold”, as an emerging bursts keyword, is another research frontier now. Because of the rapid development of tissue engineering technology in recent years, the experimental research on the combination of seed cells and various scaf-folds has become a hot spot and is becoming increasingly mature. These biological scaf-folds have good biocompatibility and biodegradability, which are composed of inorganic materials (such as hydroxyapatite, tricalcium phosphate, bioactive glass), natural scaf-fold materials (such as collagen, fibrin, elastin, gelatin, hyaluronic acid, chitosan), synthetic polymers (such as polylactic acid, polycaprolactone, polyethylene glycol, polylactic acid-glycolic acid), titanium and other scaf-fold materials. These scaf-folds need to have sufficient mechanical strength and plasticity (49). The ideal scaffold can promote the osteogenic or chondrogenic differentiation of MSCs, facilitate the arrangement of tension fibers, cell expansion and differentiation, and also play a crucial role in regulating the adhesion and proliferation of MSCs (50). For example, Wang et al. (51) prepared a double-layer bionic cartilage scaf-fold by simulating the structure, chemical and mechanical properties of mature articular cartilage. The surface layer of the scaf-fold was made of collagen, chitosan and sodium hyaluronate, and the transition layer with microtubule array structure was prepared with collagen, chitosan and silk fibroin. Then, the MSCs-loaded scaf-fold was implanted into a rabbit model of knee osteoarthritis cartilage defect. The results showed that the bionic cartilage scaf-fold could induce the proliferation and differentiation of MSCs and effectively repair the cartilage

defect. It is worth noting that the lack of vascularization in addition to osteogenic induction is the next problem for stem cells to be solved by biological scaf-folds (52). Growth factors play an irreplaceable role in the regulation of angiogenesis and osteogenic differentiation. Therefore, future bone tissue engineering will focus on the composite of biological scaf-folds through different manufacturing technologies and the addition of growth factors and other chemotactic peptides to maximize the function of MSCs. However, many studies were still in the stage of *in vitro* or animal experiments. The author believes that with the in-depth research, the application of MSCs in orthopedic diseases will make further breakthrough progress.

This is the first time in the orthopedic field to perform bibliometric and visual analysis on mesenchymal stem cells. Despite the fact that rigorous and standard bibliometric analysis have been performed, there are still some unavoidable limitations. Firstly, we only retrieved publication from the WoS database, which may have missed relevant publications reported in other databases, such as Scopus and PubMed (53). In addition, we only recruit publications in the English language, which may cause some important non-English research in this area to be overlooked. Finally, we did not include the most recent publications in 2022 because they lacked sufficient time to accumulate a large number of citations, which may influence our conclusions about the research frontier to some extent.

Conclusion

In general, this study summarized the valuable information and research trends in the field of MSCs in orthopedics by bibliometric analysis. The USA, China, Japan and the United Kingdom were the primary contributors in this field. Shanghai Jiao Tong University was the most productive institution. *Journal of Orthopedic Research* was the journal that published the most Research results. *Experimental Hematology* was the journal with the highest average citation frequency. Rochy S. Tuan was the most productive author. Scott A. Rodeo was the most cited author on average. While there was not much collaborations among the authors in this field, showing that increased collaboration is needed to boost the development of MSCs research in orthopedics. The main research hotspots of MSCs in orthopedics are the source of MSCs, *in vitro* experiments, and the differentiation of MSCs into bone and chondrocytes. The frontiers of this field are the combination of MSCs and PRP, the treatment of knee diseases, osteogenic differentiation, and the application of biological scaf-folds combined with MSCs. Meantime, it can be seen that the research focus of MSCs has gradually changed from the basic research level of cell culture to clinical application. However, clinical transformation of MSCs requires

clinical trials with larger sample size and longer follow-up period. All in all, we believe that this bibliometric study can provides a new perspective for researchers to quickly acquire the background knowledge and research hotspots in this field. It also helps exploring new research directions, such as the combined application of MSCs with other biological agents, or endophytic plants, the potential of MSCs in tissue engineering, and the innovation of special MSCs dosage forms for different orthopedics diseases.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

All named authors have substantially contributed to conducting this research and drafting this manuscript. ZD and FL designed the experiments and wrote this manuscript. YL and JL searched articles and extracted data. DK and CS made the visualized analysis. JX examined the original study data, provided technical guidance, and approved the final manuscript. All authors read and approved the final manuscript.

References

- Oh EJ, Lee HW, Kalimuthu S, Kim TJ, Kim HM, Baek SH, et al. *In vivo* migration of mesenchymal stem cells to burn injury sites and their therapeutic effects in a living mouse model. *J Control Release*. (2018) 279:79–88. doi: 10.1016/j.jconrel.2018.04.020
- Berebichez-Fridman R, Montero-Olvera PR. Sources and clinical applications of mesenchymal stem cells: state-of-the-art review. *Sultan Qaboos Univ Med J*. (2018) 18:e264–e77. doi: 10.18295/squmj.2018.18.03.002
- Yu H, Adesida AB, Jomha NM. Meniscus repair using mesenchymal stem cells - a comprehensive review. *Stem Cell Res Ther*. (2015) 6:86. doi: 10.1186/s13287-015-0077-2
- Niu W, Guo W, Han S, Zhu Y, Liu S, Guo Q. Cell-based strategies for meniscus tissue engineering. *Stem Cells Int*. (2016) 2016:4717184. doi: 10.1155/2016/4717184
- Wang G, Cao K, Liu K, Xue Y, Roberts AI, Li F, et al. Kynurenic acid, an IDO metabolite, controls TSG-6-mediated immunosuppression of human mesenchymal stem cells. *Cell Death Differ*. (2018) 25:1209–23. doi: 10.1038/s41418-017-0006-2
- Shi Y, Zhang X, Wan Z, Liu X, Chen F, Zhang J, et al. Mesenchymal stem cells against intestinal ischemia-reperfusion injury: a systematic review and meta-analysis of preclinical studies. *Stem Cell Res Ther*. (2022) 13:216. doi: 10.1186/s13287-022-02896-y
- Lv J, Yang S, Lv M, Lv J, Sui Y, Guo S. Protective roles of mesenchymal stem cells on skin photoaging: a narrative review. *Tissue Cell*. (2022) 76:101746. doi: 10.1016/j.tice.2022.101746
- Longhini ALF, Salazar TE, Vieira C, Trinh T, Duan Y, Pay LM, et al. Peripheral blood-derived mesenchymal stem cells demonstrate

Funding

This work was supported by the Joint key projects of Fujian Province in 2019 (2019-WJ-01), the Medical Innovation Project of Fujian Provincial Health Department (2019-CX-1), the Firestone Research Project of Fujian Provincial Hospital (2020029HSJJ), the Fujian Provincial Natural Science Foundation Projects (2020J05270), the Medical Innovation Project of Fujian Provincial Health Department (2020QNA009), the Major Scientific Research Project of Fujian Province (2021ZD01003), and the Fujian Provincial Natural Science Foundation Projects (2021J01376).

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.

immunomodulatory potential for therapeutic use in horses. *PLoS ONE*. (2019) 14:e0212642. doi: 10.1371/journal.pone.0212642

9. Pers YM, Ruiz M, Noël D, Jorgensen C. Mesenchymal stem cells for the management of inflammation in osteoarthritis: state of the art and perspectives. *Osteoarthritis Cartil*. (2015) 23:2027–35. doi: 10.1016/j.joca.2015.07.004

10. Guo S, Wang L, Xie Y, Luo X, Zhang S, Xiong L, et al. Bibliometric and visualized analysis of stem cells therapy for spinal cord injury based on web of science and citespace in the last 20 years. *World Neurosurg*. (2019) 132:e246–e58. doi: 10.1016/j.wneu.2019.08.191

11. Xia D, Wu J, Zhou F, Wang S, Zhang Z, Zhou P, et al. Mapping thematic trends and analysing hotspots concerning the use of stem cells for cartilage regeneration: a bibliometric analysis from 2010 to 2020. *Front Pharmacol*. (2021) 12:737939. doi: 10.3389/fphar.2021.737939

12. Ozsoy Z, Demir E. Which bariatric procedure is the most popular in the world? A bibliometric comparison. *Obes Surg*. (2018) 28:2339–52. doi: 10.1007/s11695-018-3163-6

13. Synnvestedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. *AMIA Annu Symp Proc*. (2005) 2005:724–8.

14. Giannoudis PV, Chloros GD, Ho YS. A historical review and bibliometric analysis of research on fracture nonunion in the last three decades. *Int Orthop*. (2021) 45:1663–76. doi: 10.1007/s00264-021-05020-6

15. Wu H, Cheng K, Guo Q, Yang W, Tong L, Wang Y, et al. Mapping knowledge structure and themes trends of osteoporosis in rheumatoid arthritis: a bibliometric analysis. *Front Med*. (2021) 8:787228. doi: 10.3389/fmed.2021.787228

16. Wu H, Cheng K, Tong L, Wang Y, Yang W, Sun Z. Knowledge structure and emerging trends on osteonecrosis of the femoral head: a bibliometric and visualized study. *J Orthop Surg Res.* (2022) 17:194. doi: 10.1186/s13018-022-03068-7
17. Yeung AWK, Atanasov AG, Sheridan H, Klager E, Eibensteiner F, Völkl-Kernsöck S, et al. Open innovation in medical and pharmaceutical research: a literature landscape analysis. *Front Pharmacol.* (2020) 11:587526. doi: 10.3389/fphar.2020.587526
18. Zhao LR, Duan WM, Reyes M, Keene CD, Verfaillie CM, Low WC. Human bone marrow stem cells exhibit neural phenotypes and ameliorate neurological deficits after grafting into the ischemic brain of rats. *Exp Neurol.* (2002) 174:11–20. doi: 10.1006/exnr.2001.7853
19. Noort WA, Kruisselbrink AB, in't Anker PS, Kruger M, van Bezooijen RL, de Paus RA, et al. Mesenchymal stem cells promote engraftment of human umbilical cord blood-derived CD34(+) cells in NOD/SCID mice. *Exp Hematol.* (2002) 30:870–8. doi: 10.1016/S0301-472X(02)00820-2
20. Bartholomew A, Sturgeon C, Siatskas M, Ferrer K, McIntosh K, Patil S, et al. Mesenchymal stem cells suppress lymphocyte proliferation *in vitro* and prolong skin graft survival *in vivo*. *Exp Hematol.* (2002) 30:42–8. doi: 10.1016/S0301-472X(01)00769-X
21. Jiang Y, Vaessen B, Lenvik T, Blackstad M, Reyes M, Verfaillie CM. Multipotent progenitor cells can be isolated from postnatal murine bone marrow, muscle, and brain. *Exp Hematol.* (2002) 30:896–904. doi: 10.1016/S0301-472X(02)00869-X
22. Bourin P, Bunnell BA, Casteilla L, Dominici M, Katz AJ, March KL, et al. Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells: a joint statement of the International Federation for Adipose Therapeutics and Science (IFATS) and the International Society for Cellular Therapy (ISCT). *Cytotherapy.* (2013) 15:641–8. doi: 10.1016/j.jcyt.2013.02.006
23. Davatchi F, Abdollahi BS, Mohyeddin M, Shahram F, Nikbin B. Mesenchymal stem cell therapy for knee osteoarthritis. Preliminary report of four patients. *Int J Rheum Dis.* (2011) 14:211–5. doi: 10.1111/j.1756-185X.2011.01599.x
24. Rombouts WJ, Ploemacher RE. Primary murine MSC show highly efficient homing to the bone marrow but lose homing ability following culture. *Leukemia.* (2003) 17:160–70. doi: 10.1038/sj.leu.2402763
25. Damiati LA, Tsimbouri MP, Hernandez VI, Jayawarna V, Ginty M, Childs P, et al. Materials-driven fibronectin assembly on nanoscale topography enhances mesenchymal stem cell adhesion, protecting cells from bacterial virulence factors and preventing biofilm formation. *Biomaterials.* (2022) 280:121263. doi: 10.1016/j.biomaterials.2021.121263
26. Park H, Nazhat SN, Rosenzweig DH. Mechanical activation drives tenogenic differentiation of human mesenchymal stem cells in aligned dense collagen hydrogels. *Biomaterials.* (2022) 286:121606. doi: 10.1016/j.biomaterials.2022.121606
27. Nöth U, Osyczka AM, Tuli R, Hickok NJ, Danielson KG, Tuan RS. Multilineage mesenchymal differentiation potential of human trabecular bone-derived cells. *J Orthop Res.* (2002) 20:1060–9. doi: 10.1016/S0736-0266(02)00018-9
28. Nesti LJ, Jackson WM, Shanti RM, Koehler SM, Aragon AB, Bailey JR, et al. Differentiation potential of multipotent progenitor cells derived from war-traumatized muscle tissue. *J Bone Joint Surg Am.* (2008) 90:2390–8. doi: 10.2106/JBJS.H.00049
29. Jackson WM, Lozito TP, Djouad F, Kuhn NZ, Nesti LJ, Tuan RS. Differentiation and regeneration potential of mesenchymal progenitor cells derived from traumatized muscle tissue. *J Cell Mol Med.* (2011) 15:2377–88. doi: 10.1111/j.1582-4934.2010.01225.x
30. Jackson WM, Aragon AB, Djouad F, Song Y, Koehler SM, Nesti LJ, et al. Mesenchymal progenitor cells derived from traumatized human muscle. *J Tissue Eng Regen Med.* (2009) 3:129–38. doi: 10.1002/term.149
31. Murray IR, Chahla J, Safran MR, Krych AJ, Saris DBF, Caplan AI, et al. International expert consensus on a cell therapy communication tool: DOSES. *J Bone Joint Surg Am.* (2019) 101:904–11. doi: 10.2106/JBJS.18.00915
32. Lamplot JD, Rodeo SA, Brophy RH. A practical guide for the current use of biologic therapies in sports medicine. *Am J Sports Med.* (2020) 48:488–503. doi: 10.1177/0363546519836090
33. Zhen G, Wen C, Jia X, Li Y, Crane JL, Mears SC, et al. Inhibition of TGF- β signaling in mesenchymal stem cells of subchondral bone attenuates osteoarthritis. *Nat Med.* (2013) 19:704–12. doi: 10.1038/nm.3143
34. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The international society for cellular therapy position statement. *Cytotherapy.* (2006) 8:315–7. doi: 10.1080/14653240600855905
35. Hopper N, Henson F, Brooks R, Ali E, Rushton N, Wardale J. Peripheral blood derived mononuclear cells enhance osteoarthritic human chondrocyte migration. *Arthritis Res Ther.* (2015) 17:199. doi: 10.1186/s13075-015-0709-z
36. Hoang DH, Nguyen TD, Nguyen HP, Nguyen XH, Do PTX, Dang VD, et al. Differential wound healing capacity of mesenchymal stem cell-derived exosomes originated from bone marrow, adipose tissue and umbilical cord under serum- and xeno-free condition. *Front Mol Biosci.* (2020) 7:119. doi: 10.3389/fmolb.2020.00119
37. Fu HD, Wang HR, Li DH. BMP-7 accelerates the differentiation of rabbit mesenchymal stem cells into cartilage through the Wnt/ β -catenin pathway. *Exp Ther Med.* (2017) 14:5424–8. doi: 10.3892/etm.2017.5210
38. Zhou Q, Zhang JH, Yuan S, Shao JH, Cai ZY, Chen S, et al. A new insight of kartogenin induced the Mesenchymal Stem Cells (MSCs) selectively differentiate into chondrocytes by activating the Bone Morphogenetic Protein 7 (BMP-7)/Smad5 pathway. *Med Sci Monit.* (2019) 25:4960–7. doi: 10.12659/MSM.916696
39. Qiong J, Xia Z, Jing L, Haibin W. Synovial mesenchymal stem cells effectively alleviate osteoarthritis through promoting the proliferation and differentiation of meniscus chondrocytes. *Eur Rev Med Pharmacol Sci.* (2020) 24:1645–55. doi: 10.26355/eurrev_202002_20338
40. Yang A, Lu Y, Xing J, Li Z, Yin X, Dou C, et al. IL-8 enhances therapeutic effects of BMSCs on bone regeneration via CXCR2-Mediated PI3k/Akt signaling pathway. *Cell Physiol Biochem.* (2018) 48:361–70. doi: 10.1159/000491742
41. Endo I, Mastumoto T. [Bone and stem cells. Regulatory mechanism of mesenchymal stem cell differentiation to osteoblasts]. *Clin Calcium.* (2014) 24:555–64.
42. Cheng SL, Lou J, Wright NM, Lai CF, Avioli LV, Riew KD. *In vitro* and *in vivo* induction of bone formation using a recombinant adenoviral vector carrying the human BMP-2 gene. *Calcif Tissue Int.* (2001) 68:87–94. doi: 10.1007/BF02678146
43. Saw KY, Anz A, Merican S, Tay YG, Ragavanaidu K, Jee CS, et al. Articular cartilage regeneration with autologous peripheral blood progenitor cells and hyaluronic acid after arthroscopic subchondral drilling: a report of 5 cases with histology. *Arthroscopy.* (2011) 27:493–506. doi: 10.1016/j.arthro.2010.11.054
44. Ogata Y, Mabuchi Y, Shinoda K, Horiike Y, Mizuno M, Otabe K, et al. Anterior cruciate ligament-derived mesenchymal stromal cells have a propensity to differentiate into the ligament lineage. *Regen Ther.* (2018) 8:20–8. doi: 10.1016/j.reth.2017.12.001
45. Kawata K, Koga H, Tsuji K, Miyatake K, Nakagawa Y, Yokota T, et al. Extracellular vesicles derived from mesenchymal stromal cells mediate endogenous cell growth and migration via the CXCL5 and CXCL6/CXCR2 axes and repair menisci. *Stem Cell Res Ther.* (2021) 12:414. doi: 10.1186/s13287-021-02481-9
46. Ornetti P, Nourissat G, Berenbaum F, Sellam J, Richette P, Chevalier X. Does platelet-rich plasma have a role in the treatment of osteoarthritis? *Joint Bone Spine.* (2016) 83:31–6. doi: 10.1016/j.jbspin.2015.05.002
47. Ito K, Yamada Y, Nagasaka T, Baba S, Ueda M. Osteogenic potential of injectable tissue-engineered bone: a comparison among autogenous bone, bone substitute (Bio-oss), platelet-rich plasma, and tissue-engineered bone with respect to their mechanical properties and histological findings. *J Biomed Mater Res A.* (2005) 73:63–72. doi: 10.1002/jbm.a.30248
48. Hexter AT, Sanghani-Kerai A, Heidari N, Kalaskar DM, Boyd A, Pendegrass C, et al. Mesenchymal stromal cells and platelet-rich plasma promote tendon allograft healing in ovine anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* (2021) 29:3678–88. doi: 10.1007/s00167-020-06392-9
49. Polymeri A, Giannobile WV, Kaigler D. Bone marrow stromal stem cells in tissue engineering and regenerative medicine. *Horm Metab Res.* (2016) 48:700–13. doi: 10.1055/s-0042-118458
50. Sun M, Chi G, Xu J, Tan Y, Xu J, Lv S, et al. Extracellular matrix stiffness controls osteogenic differentiation of mesenchymal stem cells mediated by integrin $\alpha 5$. *Stem Cell Res Ther.* (2018) 9:52. doi: 10.1186/s13287-018-0798-0
51. Wang J, Wang Y, Sun X, Liu D, Huang C, Wu J, et al. Biomimetic cartilage scaffold with orientated porous structure of two factors for cartilage repair of knee osteoarthritis. *Artif Cells Nanomed Biotechnol.* (2019) 47:1710–21. doi: 10.1080/21691401.2019.1607866
52. Weng Y, Wang Z, Sun J, Han L, Li X, Wu B, et al. Engineering of axially vascularized bone tissue using natural coral scaffold and osteogenic bone marrow mesenchymal stem cell sheets. *J Stomatol Oral Maxillofac Surg.* (2021) 122:397–404. doi: 10.1016/j.jormas.2021.01.013
53. Wu H, Sun Z, Tong L, Wang Y, Yan H, Sun Z. Bibliometric analysis of global research trends on male osteoporosis: a neglected field deserves more attention. *Arch Osteoporos.* (2021) 16:154. doi: 10.1007/s11657-021-01016-2



OPEN ACCESS

EDITED BY

Shazia Qasim Jamshed,
Sultan Zainal Abidin
University, Malaysia

REVIEWED BY

Rosemary M. Caron,
University of New Hampshire,
United States
Krzysztof Goniewicz,
Polish Air Force University, Poland
Doaa Galal,
Soliman Fakeeh Hospital, Saudi Arabia
Nauman Khalid,
University of Management and
Technology Lahore, Pakistan

*CORRESPONDENCE

Duaa Aljabri
daljabri@iau.edu.sa

SPECIALTY SECTION

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 05 May 2022

ACCEPTED 23 August 2022

PUBLISHED 03 October 2022

CITATION

Aljabri D and Albinali H (2022) Public
awareness and use of 997 emergency
medical service phone number during
the COVID-19 pandemic.
Front. Public Health 10:937202.
doi: 10.3389/fpubh.2022.937202

COPYRIGHT

© 2022 Aljabri and Albinali. 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.

Public awareness and use of 997 emergency medical service phone number during the COVID-19 pandemic

Duaa Aljabri* and Hissah Albinali

Health Information Management and Technology Department, College of Public Health, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

Background: Emergency medical services (EMSs) are an important element of the healthcare system as it provides an opportunity to respond to critical medical conditions and save people's lives. In Saudi Arabia, EMS is offered via the EMS phone number "997" and mobile application "Asefny".

Methods: This was an observational cross-sectional survey study exploring public awareness and use of the EMS phone number during the COVID-19 pandemic in Saudi Arabia. A bivariate analysis was performed to investigate factors affecting awareness and use of the EMS phone number and to compare the EMS acceptance to transport and timelines of ambulance arrival between requests made via the "997" EMS phone number and the "Asefny" mobile application during the country's emergency lockdown.

Results: A total of 805 participants were included in the analysis, where 66% reported awareness of the EMS phone number and 75% of them accurately identified the nature of the service provided by dialing the number. The men who participated, those with a bachelor's degree, with children, and with chronic conditions were more aware of the EMS phone number compared to the other participants. Of the total sample, 46.7% used EMS phone numbers at least one time (ever users). During the COVID-19 lockdown, the EMS accepted to transport 87% of the calls made by 997 phone number and 56.2% of the mobile application requests ($P < 0.00$). The ambulance arrived in ≤ 8 min in 53.6% of the 997 phone calls and 35.5% of the Asefny mobile requests ($P < 0.00$).

Conclusions: Findings showed commendable levels of awareness and the use of EMS phone numbers. However, the results suggest room for improvement by developing promotional and educational campaigns inspired by the factors identified as influential on both awareness and use. Mobile applications in EMS are promising to improve prehospital emergency service accessibility, which needs to be further investigated to assess its impact on the public health informatics experience.

KEYWORDS

997 phone number, awareness, COVID-19, emergency medical service (EMS), healthcare management, public health, Saudi Arabia

Introduction

Emergency medical services (EMSs) are an important element of the healthcare system as it provides an opportunity to respond to critical medical conditions and save people's lives. Those conditions need rapid assessment and timely transportation to the nearest health facility to enhance survival and prevent disability (1).

Many countries in the world are working on improving EMS using phone services and mobile applications. For example, India primarily uses two EMS models to support service delivery; the 108 emergency service works as a response system for accident and trauma victims by providing critical care (2), and the 102 ambulance service offers basic patient transport to referral and home facilities (3). In the United States, EMS has steadily grown and reached a level where the federal government is working to ensure that all adults are aware of the services they can receive (4). Many Americans use mobile health applications rather than the phone services because they allow them to access their medical history, consult their doctors, receive prescriptions, and recommendations for nearby facilities in case of emergencies. In Saudi Arabia, the Saudi Red Crescent Authority (SRCA) is the national entity responsible to operate the EMS *via* a dedicated call number 997 and "Asefny", i.e., "Save me" mobile application. The mobile application service was introduced in 2017 as part of the Saudi National Transformation Program and the Saudi Vision 2030 plan and provided *via* two-way communication between the SRCA dispatch center and the reporter using the short message service (5). This communication aids the dispatcher in triage and requests medical history that support decision-making for medical transport. The application also includes features to precisely locate the reporter, which saves time for the emergency team. It also provides locations of the closest health facilities to the user and other emergency numbers and the ability to build a profile of the user's medical history.

Markedly, the primary role of emergency services is to address public care needs within a short time possible. The International Standards Organization has adopted response time as a crucial indicator of the level of emergency services being delivered in local, national, and international settings (3). Many nations globally, including Saudi Arabia, use the 8 min interval between call receipt and arrival at the scene to determine the emergency medical services' effectiveness (6). However, while most people know the availability of EMS, only a handful understands this care's innate attributes (7). In addition, as the prehospital associated death rates have increased over recent years, that has raised several concerns regarding the awareness and utilization of ambulance services (8).

There is a gap in the literature in terms of examining the public awareness of the EMS phone number in Saudi Arabia. Only two studies were conducted to examine awareness; one

in the western region (9), where 33% were unaware of the free-of-charge EMS number 997, and another recent study in Riyadh (7), where 73.2% claimed to know the EMS phone number and 38.5% recalled the number correctly. As Saudi Arabia is experiencing a series of pandemics in the past few decades such as MERS, EBOLA, and COVID-19, the demand for EMS has significantly increased (10). Thus, it is highly important that people's awareness of emergency numbers must be assessed at regular intervals. Furthermore, previous studies (8, 11–13) suggest that the mobile health applications can significantly improve emergency medical services, which can facilitate improved healthcare service accessibility. The previous studies focused mostly on the programs' content, nature, and formulation, thereby ignoring the community's awareness of the ambulance number and the proper use of the ambulance service in emergency cases. That being said, the literature gaps between the initiative formulation, people's awareness about it, and their use still exist. Therefore, the purpose of this study is to evaluate the public awareness and the use of the EMS phone number and to identify the factors affecting awareness and use. In addition, the study compares EMS response and timelines between requests made *via* the 997-phone number and "Asefny" mobile application during the COVID-19 lockdown in Saudi Arabia.

Methods

The study is an observational cross-sectional study that targeted all people living in Saudi Arabia. A bilingual (Arabic and English) survey was developed and validated to measure the public awareness and use of the EMS phone number and "Asefny" mobile application. In the validation stage, the survey was sent to four academic experts for content validity. It was then pilot-tested by nine randomly selected individuals from the public to ensure clarity. An online survey link was created for the survey using Google surveys. Due to the COVID-19 pandemic, physical interaction with the participants would have posed considerable health risks. Thus, social media platforms such as WhatsApp and Twitter were used in the dissemination process. The survey had two sections: the questions in the first section were marked for one point, asking about participants' demographics, such as gender, age, nationality, geographic location, and education status. The questions in the second section collected information about participants' awareness and use of 997 EMS phone number, which were visible one by one with no chance to move between questions. This logic was built in the electronic survey to limit the introduction of bias in the results. Awareness was assessed by asking two questions: "Are you aware of the EMS phone number?" (Yes/No). Only if the respondent answers with yes does the second question appear, "Which of the following do you think 997 service provide?", to assess true awareness (where responding to medical and trauma

TABLE 1 Study sample characteristics ($N = 805$).

Variable	N	%
Gender		
Female	382	47.5
Male	423	52.5
Age		
15–19	26	3.2
20–29	267	33.2
30–39	303	37.6
40–49	142	17.6
50–59	50	6.2
60+	17	2.1
Nationality		
Residents (Non-Saudi)	57	7.1
Citizens (Saudi)	748	92.9
Geographic location		
Middle region	172	21.4
Eastern region	370	46.0
Northern region	88	10.9
Southern region	92	11.4
Western region	83	10.3
Education		
High school	178	22.1
Diploma	113	14.0
Bachelor degree	442	54.9
Graduate studies	72	8.9
Having children (Yes)	446	55.4
Having chronic disease (Yes)	88	10.9

emergencies was the correct answer). Incorrect responses to the second question were considered false awareness about the EMS number.

The use was assessed by answering positively to “Have you ever called EMS for an ambulance?” (Yes/No). The survey was distributed in 2 months (October and November 2020), using the snowball sampling technique, where participants were requested to forward the survey link to their colleagues, friends, and families in order to increase the sample size. The total responses received were 936, out of which 131 were incomplete. After excluding incomplete responses, the valid responses for analysis were 805 responses.

Data analysis was carried out using the IBM® SPSS® software platform. The data analysis mainly involved the use of descriptive techniques such as percentages and frequencies. A bivariate analysis using the chi-square test was used to compare percentages and identify factors that may influence awareness and use. A p -value of < 0.05 was considered significant.

Results

The total number of respondents of the survey was 805. Table 1 presents the demographic characteristics of the sample. Most participants in the sample speak Arabic as their primary language (94.9%, $n = 764$). The sample was balanced from a gender perspective, with men and women participants contributing to 52.5% ($n = 423$) and 47.5% ($n = 382$) of the sample, respectively. A review of the age distribution in the sample shows that it mirrors the national trends, with persons aged over 60 y only representing 2.1% ($n = 17$) of the sample. The age groups 20–29 (33.2%, $n = 267$) and 30–39 (37.6%, $n = 303$) had the highest representation in the sample. All of the responses were from Saudi citizens (92.2%, $n = 748$), while 7.1% ($n = 57$) were residents. Responses from all five geographic regions were included in the sample. However, the Eastern region appears to be overrepresented, being 46% ($n = 370$) of all the participants. Only 10.9% ($n = 88$) of the respondents reported having at least one chronic disease.

The results (Table 2) revealed that 66% ($n = 531$) of the participants were aware of the 997 EMS phone number. Of those, 24.6% ($n = 131$) had false awareness, as they were unaware of the nature of the service provided by 997. In addition, 26.8% ($n = 216$) of the participants reported that they had called the wrong emergency number for help. About half of the participants (46.7%, $n = 367$) requested emergency services at least one time (ever-users). During the COVID-19 lockdown, 60.9% ($n = 229$) of ever-users have requested an ambulance; 41% ($n = 94$) by dialing 997, and 59% ($n = 135$) by requesting services from Asefny mobile application.

Table 3 shows separate bivariate analyses using the chi-squared test, between the awareness and use of the EMS phone number, separately, and the study of independent variables. The awareness was significantly associated with gender, geographic location, nationality, education, having children, and having a chronic illness ($p < 0.05$). The use was significantly associated with gender, age, geographic location, and having children ($p < 0.001$).

Table 4 presents a comparison of the use of 997 and the Asefny mobile application during the COVID-19 lockdown. Differences were found, where the type of emergency, responding with an ambulance, and response time (≤ 8 min) were significantly different between the two EMS modes of request.

Discussion

The study aimed to assess the awareness and use of the 997-EMS number during the COVID-19 pandemic in Saudi Arabia. The study also investigated factors that may affect the awareness and use of the 997-EMS number and compared the type of emergencies and response to requests made by phone

TABLE 2 Public awareness and use of EMS phone number (N = 805).

Questions	N	%
Awareness 1: Are you aware of the EMS phone number?		
No	274	34.0
Yes	531	66.0
Awareness 2: Which of the following do you think the 997 phone number provides? (N = 531)		
Medical appointments	23	4.3
Respond to medical & trauma emergency (correct answer)	400	75.3
Medical consultations	52	9.7
Road assistance service	30	5.6
I do not know	26	4.8
Have you ever had an emergency and called the wrong number for help?		
No	589	73.2
Yes	216	26.8
Use: Have you ever called EMS for an ambulance?		
No	429	53.3
Yes	376	46.7
Have you requested EMS for an ambulance during COVID-19 lockdown? (N = 376)		
Yes	229	60.9
Mode of request (N = 229)		
Calling 997	94	41.0
Asefny mobile application	135	59.0

vs. the mobile application during the lockdown. The findings revealed that 66% reported awareness about the 997, while only 24% were not able to recall the service provided by 997 number correctly. Regardless of false awareness, public awareness in this study is considered the highest among awareness trends studied previously in the country; 33% in 2015 and 38.5% in 2021 (2, 3). In addition, the percentage of 997 ever-users was 46.7%, where 61% of them requested an ambulance during the lockdown. This rate is considerably higher than those reported in the United Kingdom, where the NHS 911 service utilization rate was 9% (14).

Such an increase in the rate of awareness and use is subject to the COVID-19 pandemic and lockdown. The first case of COVID-19 in Saudi Arabia was confirmed on 2 March 2020. On 23 March 2020, an order was issued by the government that restricted movement from 1900 hrs to 0600 hrs. These restrictions lasted until 28 June 2020, when the government began implementing its return to normal policy plan.

It is important to note that almost 27% reported calling the wrong emergency number for help. As several three-digit numbers for public service agencies in Saudi Arabia exist; for example, medical consultations and appointments is 937, the police is 999, and the civil defense is 998; this may create confusion among the people, especially among those who had false awareness in this study.

The study showed that awareness could be influenced by gender, geographic location, nationality, education, having children, and having a chronic illness. Having chronic illness

and children is likely to lead to increased interest in and awareness of health information, including emergency services (15). Education can affect awareness of the emergency number *via* health literacy and information-seeking behavior (16). Individuals in urban areas are usually more aware of the service compared to those in remote regions due to the high accessibility to healthcare services (17). The Eastern region, which is predominantly urban, had the highest rates of both awareness and the use of the emergency service number, which is in line with this expectation. Gender differences in health literacy within Saudi Arabia could explain the role of gender in both awareness and its use (18).

The study shows that there are differences in the modes of requesting EMS: dialing 997 or sending a message *via* Asefny mobile application. First, the use of Asefny mobile application was higher than the use of the 997 number. Second, there was also a higher preference to use the Asefny application over calling 997 during the lockdown and curfew. There was also a noticeable difference in the type of emergency requested in the two modes: Asefny was preferred in cases of medical illness and when seeking a permit. A permit from EMS can be used to transport the patient to the nearest hospital by the service requester, whereas calls to 997 were mainly observed in case of emergency situations such as violence, trauma, burn, and suicide attempts.

There were significant differences in both the response to the calls or requests and the timeliness of the responses. The ambulance service responded more to the 997-emergency

TABLE 3 Bivariate analysis of awareness and use of 997 EMS phone number.

	Aware ^a N = 400 (%)	Not aware N = 274 (%)	P	Users N = 376 (%)	Non-users N = 429 (%)	P
Gender			<0.001			<0.001
Female	164 (41.0%)	195 (52.7%)		146 (38.8%)	236 (55.0%)	
Male	236 (59.0%)	175 (47.3%)		230 (61.2%)	193 (45.0%)	
Age			0.17			<0.001
15–19	12 (2.8%)	14 (3.8%)		1 (0.3%)	25 (5.8%)	
20–29	144 (36.0%)	106 (28.6%)		102 (27.1%)	165 (38.5%)	
30–39	140 (35.0%)	152 (41.1%)		155 (41.2%)	148 (34.5%)	
40–49	69 (17.3%)	69 (18.6%)		77 (20.5%)	65 (15.2%)	
50–59	28 (7.0%)	21 (5.7%)		36 (9.6%)	14 (3.3%)	
60+	7 (1.8%)	8 (2.2%)		5 (1.3%)	12 (2.8%)	
Geographic location			<0.001			<0.001
Middle region	91 (22.8%)	69 (18.6%)		69 (18.4%)	103 (24.0%)	
Eastern region	217 (54.3%)	141 (38.1%)		157 (41.8%)	213 (49.7%)	
Northern region	29 (7.3%)	53 (14.3%)		53 (14.1%)	35 (8.2%)	
Southern region	34 (8.5%)	57 (15.4%)		55 (14.6%)	37 (8.6%)	
Western region	29 (7.3%)	50 (13.5)		42 (11.2%)	41 (9.6%)	
Nationality			0.01			0.31
Residents (Non-Saudi)	19 (4.8%)	35 (9.5%)		23 (6.1%)	34 (7.9%)	
Citizens (Saudi)	381 (95.3%)	335 (90.5%)		353 (93.9%)	395 (92.1%)	
Education			<0.001			0.22
High school	68 (17.0%)	105 (28.4%)		81 (21.5%)	97 (22.6%)	
Diploma	45 (11.3%)	64 (17.3%)		63 (16.8%)	50 (11.7%)	
Bachelor degree	239 (59.8%)	179 (48.4%)		200 (53.2%)	242 (56.4%)	
Graduate studies	48 (12.0%)	22 (5.9%)		32 (8.5%)	40 (9.3%)	
Having children (Yes)	238 (59.5%)	191 (51.6%)	0.04	231 (61.4%)	215 (50.1%)	<0.001
Having chronic disease (Yes)	61 (15.3%)	24 (6.5%)	<0.001	46 (12.2%)	42 (9.8%)	0.26

^a Awareness is based on knowing the service provided by 997 accurately. Participants unable to recall the correct service (i.e. respond to medical and trauma emergency) were excluded from this group ($n = 131$).

The bold values indicate the significant association.

service than they did for requests made *via* the mobile application because the requests over the phone may be more critical to analyze as the caller may be under stress. Second, the ambulances were more likely to respond in less than 8 min for those requests made *via* the 997-emergency line when compared to the requests made *via* the mobile application. However, in a similar study comparing responses through 997 and Asefny, no differences in the response times were identified (10). The differences in both the response to the calls or requests and the timeliness of the responses may be due to the extensive infrastructure behind the 997-emergency service. The interval between scene arrival and call receipt is the commonly accepted and used parameter in Saudi Arabia to discern the quality of emergency services being offered (8, 10). Many countries globally deploy necessary efforts to achieve the response time of 8 min, set by the International Standards Organization (3). The findings suggest that the 997-emergency

service is outperforming the mobile application in terms of the proportion of responses to requests and the timeliness of the responses.

Strengths and limitations

The study used a large sample size that enhanced its reliability and replication among different groups of participants. The 805 participants selected using the recruitment procedure and ethical consideration would eliminate bias from the researcher's end and encourage the provision of accurate data by participants. The use of an online survey improved the confidence of the participants who would feel intimidated to respond in face-to-face interviews. Despite these strengths, the study has some limitations. First, the most significant limitation is recall bias since we did not

TABLE 4 Comparison of the purpose and response time of EMS service requested by phone number vs. mobile application during the COVID-19 lockdown.

	Total (<i>N</i> = 229) <i>n</i> (%)	997 phone number (<i>N</i> = 94) <i>n</i> (%)	Asefny mobile application (<i>N</i> = 135) <i>n</i> (%)	<i>P</i>
Type of emergency				<0.001
Medical illness	79 (34.4)	21 (22.3)	58 (42.9)	
Violence	26 (11.3)	17 (18.0)	9 (6.6)	
Trauma	38 (16.5)	27 (28.7)	11 (8.1)	
Burn	13 (5.6)	10 (10.6)	3 (2.2)	
Suicide attempt	2 (0.8)	2 (2.1)	0 (0)	
Unconsciousness	15 (6.5)	12 (12.7)	3 (2.2)	
Request permit to travel during curfew	56 (24.4)	5 (5.6)	51 (37.7)	
Responded with an ambulance (Yes)	158 (68.9)	82 (87.2)	76 (56.2)	<0.001
Ambulance arrived in ≤8 min (Yes)	71 (31.0)	44 (53.6)	27 (35.5)	<0.001

The bold values indicate the significant association.

collect data during the pandemic lockdown period and have asked for data retrospectively. Second, half of the participants in the study were from the eastern region. Thus, there is the risk that the views of participants from this region can pass for the views of Saudi residents. Third, the cross-sectional survey design of this study does not allow for cause-and-effect inferences. From the study, it cannot be concluded that having a chronic illness causes one to be more aware of the 997-emergency service. Thus, future scientific studies should seek to determine whether the observed association between the use or awareness rates and gender, education, geographical region, having a child, and having a chronic condition constitute a cause-and-effect relationship. Furthermore, future studies should endeavor to use geographically balanced samples by employing stratified sampling. Also, further investigations on the barriers to using the mobile application are recommended.

Study implications

This study has both theoretical and practical implications, which emphasize the importance of findings in this study. First, this study contributes to the current health emergency literature related to public awareness of health emergency numbers, the use of health emergency applications, and the response times from both approaches. Second, the changes observed in this study with respect to awareness levels compared to the previous studies can enable practitioners and decision-makers to taking appropriate decisions. For instance, assessing the issues for higher response times for requests made through Asefny highlights the need to re-engineer and redesign the existing processes to improve the response times. In addition, the study has implications for policymakers to promote public awareness

and usage rates to maximize the value of this service. As most public agencies in the country have a free-of-charge 3-digit number, the EMS number can be easily confused with other services and cause a delay in reaching the needed service (19). The media can contribute to awareness by education campaigns or short films and scenarios that are well-perceived by the community of different age, educational backgrounds, geographic regions, and medical illnesses. For instance, the media can endeavor to popularize the emergency service in predominantly rural regions, among persons with chronic conditions, and with lower levels of education. The findings of this study can support targeting the groups that have displayed lower levels of EMS awareness or use by eliminating barriers to the service while enhancing the awareness and usage statistics.

Conclusion

The main aim of the study was to investigate public awareness and use of the EMS phone number in Saudi Arabia and identify factors affecting awareness and use during the pandemic. We found that 66% reported awareness about the 997 phone number and 46.7% were ever-users. Being male and having children were significant factors associated with both awareness and use of the 997 phone number. During the COVID-19 pandemic, we observed that Asefny emergency requests were more common than those made *via* 997, suggesting the usefulness of mobile applications as a supplementary EMS service. Yet, 87% of the calls made by 997 were accepted for medical transport while only 56.2% of the Asefny requests were accepted. More medical-related emergencies were made *via* 997 while the Asefny was more commonly used for travel permits. To our knowledge, this is the only study to date that explored the acceptance of medical

transport and timeliness of ambulance arrival between requests made through the EMS phone number vs. mobile application during the pandemic lockdown at a national level. The study provides insights for policymakers in planning strategies for the effective use of mobile applications in emergencies to support prehospital care.

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 ethical approval was obtained from the Institutional Review Board of Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia (IRB-PGS-2021-03-049). Participants provided their written informed consent to participate in this study.

Author contributions

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

References

1. Kobusingye OC, Hyder AA, Bishai D, Joshipura M, Hicks ER, Mock C. Emergency medical services. In: Jamison DT, Breman JG, Measham AR, et al., editors. *Disease Control Priorities in Developing Countries*. 2nd edition. Washington (DC): The International Bank for Reconstruction and Development/The World Bank. (2006).
2. Modi PD, Solanki R, Nagdev TS, Yadav PD, Bharucha NK, Desai A, et al. Public awareness of the emergency medical services in Maharashtra, India: A questionnaire-based survey. *Cureus*. (2018) 10:e3309. doi: 10.7759/cureus.3309
3. Sharma M, Brandler ES. Emergency medical services in India: the present and future. *Prehosp Disaster Med*. (2014) 29:307–10. doi: 10.1017/S1049023X14000296
4. Pearce AP. Emergency medical services at the crossroads. *Emerg Med J*. (2009) 26:685. doi: 10.1136/emj.2009.072025
5. Saudi Vision 2030. National Transformation Program. Vision 2030. (2021). Available online at: <https://www.vision2030.gov.sa/v2030/vrps/ntp/> (accessed December 18, 2021).
6. Cabral E, Castro W, Florentino D, Viana D, Costa Junior J, Souza R, et al. Response time in the emergency services. *Acta Cirurgica Brasileira*. (2018) 33:1110–21. doi: 10.1590/s0102-865020180120000009
7. Alabdali A, Alfraidi A, Almuhanha A, Alhamdan A, Alharbi A, Alshaqha A, et al. Public awareness of emergency medical services phone number. *Saudi J Emerg Med*. (2021) 2:147–52. doi: 10.24911/SJEMed/72-1595710177
8. Alnemer K, Al-Qumaizi KI, Alnemer A, Alsayegh A, Alqahtani A, Alrefaie Y, et al. Ambulance response time to cardiac emergencies in Riyadh. *Imam J Appl Sci*. (2016) 1:33–8.
9. Hamam AF, Bagis MH, AlJohani K, Tashkandi AH. Public awareness of the EMS system in Western Saudi Arabia: identifying the weakest link. *Int J Emerg Med*. (2015) 8:70. doi: 10.1186/s12245-015-0070-7
10. Althumairi A, Alnasser Z, Alsadeq S, Al-Kahtani N, Aljaffary A. Mobile ambulatory application asafny and traditional phone request 997: A

Acknowledgments

We would acknowledge the College of Public Health, Imam Abdulrahman Bin Faisal University for their administrative support and thank the study sample who participated in the survey.

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.

- comparative cross-sectional study. *Open Access Emerg Med*. (2021) 12:471–80. doi: 10.2147/OAEM.S279969
11. Al-Ghamdi AS. Emergency medical service rescue times in Riyadh. *Accid Anal Prev*. (2002) 34:499–505. doi: 10.1016/S0001-4575(01)00047-1
12. Hassounah M, Raheel H, Alhefzi M. Digital response during the COVID-19 pandemic in Saudi Arabia. *J Med Internet Res*. (2020) 22:e19338. doi: 10.2196/19338
13. Al-Wathinani A, Hertelendy AJ, Alhurishi S, Mobrad A, Alhazmi R, Altuwajri M, et al. Increased emergency calls during the COVID-19 pandemic in Saudi Arabia: A national retrospective study. *Healthcare (Basel)*. (2020) 9:14. doi: 10.3390/healthcare9010014
14. Knowles E, O'Cathain A, Turner J, Nicholl J. Awareness and use of a new urgent care telephone service, NHS 111: cross-sectional population survey. *J Health Serv Res Policy*. (2014) 19:224–30. doi: 10.1177/1355819614535571
15. Gille S, Griesse L, Schaeffer D. Preferences and experiences of people with chronic illness in using different sources of health information: results of a mixed-methods study. *Int J Environ Res Public Health*. (2021) 18:13185. doi: 10.3390/ijerph182413185
16. Almubark R, Basyouni M, Alghanem A, et al. Health literacy in Saudi Arabia: Implications for public health and healthcare access. *Pharmacol Res Perspect*. (2019) 7:e00514. doi: 10.1002/prp2.514
17. Chen X, Orom H, Hay JL, et al. Differences in rural and urban health information access and use. *J Rural Health*. (2019) 35:405–17. doi: 10.1111/jrh.12335
18. Abdel-Latif MMM, Saad SY. Health literacy among Saudi population: a cross-sectional study. *Health Promot Int*. (2019) 34:60–70. doi: 10.1093/heapro/dax043
19. Al-Rayes SA, Alumran A, Aljabri D, Aljaffary A, Aldoukhi E, Alahmedalyousif Z, et al. Public awareness and utilization of 937-telephone health services in the kingdom of Saudi Arabia before and during the COVID-19 pandemic: longitudinal study. *J Med Internet Res*. (2021) 23:e27618. doi: 10.2196/27618



OPEN ACCESS

EDITED BY

Rosemary M. Caron,
University of New Hampshire,
United States

REVIEWED BY

Jiaoling Huang,
Shanghai Jiao Tong University, China
Fuyong Jiao,
Xi'an Jiaotong University, China

*CORRESPONDENCE

Yanfeng Yang
ymm810301@163.com

[†]These authors have contributed
equally to this work

SPECIALTY SECTION

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 03 June 2022

ACCEPTED 03 October 2022

PUBLISHED 17 October 2022

CITATION

Zhang Y, Wang X, Cai J, Yang Y, Liu Y,
Liao Y, Zhou Y, He B, Wen W,
Zhuang Q and Lin Y (2022) Status and
influencing factors of medication
literacy among Chinese caregivers of
discharged children with Kawasaki
disease.
Front. Public Health 10:960913.
doi: 10.3389/fpubh.2022.960913

COPYRIGHT

© 2022 Zhang, Wang, Cai, Yang, Liu,
Liao, Zhou, He, Wen, Zhuang and Lin.
This is an open-access article
distributed under the terms of the
[Creative Commons Attribution License
\(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

Status and influencing factors of medication literacy among Chinese caregivers of discharged children with Kawasaki disease

Yingzi Zhang^{1†}, Xiuqiong Wang^{1†}, Jianghui Cai^{2†},
Yanfeng Yang^{1*}, Yiling Liu¹, Yeling Liao¹, Yanhong Zhou¹,
Baoqin He¹, Wen Wen¹, Qian Zhuang¹ and Yonghong Lin³

¹Department of Pediatric Cardiology, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China, ²Department of Pharmacy, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China, ³Department of Obstetrics and Gynecology, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China

Background: The information on medication literacy among Chinese caregivers of discharged children with Kawasaki disease (KD) is unknown. We aimed to investigate the status of medication literacy among caregivers of discharged children with KD and evaluate the influencing factors of medication literacy.

Methods: From March 2020 to February 2021, 106 caregivers with a KD child were recruited for the present study. We collected the sociodemographic characteristics of the KD caregivers using structured interviews. The medication literacy of the KD caregivers was assessed by the Chinese version of Medication Literacy Assessment. KD patients' demographic and clinical data were obtained from the medical records. The multiple logistic regression was performed to identify factors associated with medication literacy.

Results: (1) The average medication literacy score was 4.91 ± 1.51 . (2) Most of the Chinese KD caregivers had insufficient medication literacy (≤ 5 scores), and only 39.2% of the caregivers had adequate medication literacy (> 5 scores). (3) The multiple logistic regression shows that education level, monthly income, and duration of hospitalization are the independent influencing factors on the medication literacy of KD caregivers.

Conclusion: There is preliminary evidence that medication literacy among KD caregivers is low and needs improvement. A higher level of education, higher income, and longer duration of hospitalization were influencing factors of adequate medication literacy.

KEYWORDS

Kawasaki disease, caregivers, medication literacy, Medication Literacy Assessment, influencing factors

Introduction

Medication literacy (ML) was first mentioned in 2005 in a government document to provide medication information to individuals with low health literacy (1). The international perspective on the definition of medication literacy is the degree to which individuals can obtain, comprehend, communicate, calculate, and process patient-specific information about their medication to make informed medication and health decisions to safely and effectively use their medications regardless of the mode by which the content is delivered (e.g., written, oral, and visual) (2). ML can be a critical predictor of rational medication use and significantly impacts medication safety in clinical practice (3, 4). Patients with a higher level of ML usually had better medication compliance (5, 6). On the contrary, patients with limited ML may have problems understanding medication information and undergo more frequent re-hospitalization, emergency department visits, and serious adverse drug events (5, 7–9). In addition, previous studies have found that most medication-related adverse events would be preventable with better medication literacy (10, 11). Thus, ML determines how well patients can manage their medication regimens correctly and plays an important role in reducing and avoiding adverse drug events (12, 13).

Kawasaki disease (KD) is an acute, self-limited febrile illness of unknown cause that predominantly affects children <5 years of age (14). KD is now recognized as a leading cause of acquired heart disease in children in developed countries. KD has been reported in more than 60 countries since first described in Japan (15–25). Patients with KD require long-term medication after discharge. It is critical for patients with KD to use medicine regularly and correctly over the long term to reduce the occurrence of coronary artery lesions.

There is an urgent need to investigate the status of medication literacy among caregivers of discharged children with KD, as most KD kids cannot take care of themselves and use medicine appropriately. However, the medication literacy among Chinese caregivers of discharged children with KD remains unknown. There is an urgent need in clinical practice to appraise available evidence and evaluate where gaps exist. A survey showed that about 70% of preventable adverse drug events in pediatric outpatients were due to parents' lack of knowledge about medication administration (26). Considering that China is one of the most populous countries and the increasing incidence of KD (22, 27, 28), it is imperative to understand the medication literacy status among Chinese caregivers of discharged children with KD. To the best of our knowledge, no study has explored medication literacy among Chinese caregivers of discharged children with KD. Therefore, we aimed to preliminarily investigate medication literacy among Chinese KD caregivers and examine the influencing factors of medication literacy.

Methods

Ethics and informed consent

This study received approval from the Research Ethics Committee of Chengdu Women's and Children's Central Hospital (NO. 202013). All participants gave their written informed consent for inclusion before the study.

Study setting

Caregivers of discharged KD patients were recruited from the pediatric cardiology department of Chengdu Women's and Children's Central Hospital from March 2020 to February 2021. The caregiver was defined as the person responsible for attending to the needs of a child with KD. Detailed information on the proportion of the relationship between KD patients and caregivers can be seen in [Appendix S1](#).

Participants

Discharged children with KD and caregivers were eligible if they met the following inclusion criteria:

- Patients < 18 years old; AND
- The diagnosis of complete or incomplete KD was established according to the American Heart Association guideline in 2017 (14); AND
- Patients of initial onset of KD; AND
- KD patients without any major medical conditions; AND
- Currently taking at least one medication; AND
- Informed consent was obtained from all participants; AND
- Caregivers have normal cognitive function and competent communication ability.

Exclusion criteria were as follows:

- The patient was previously diagnosed with KD and had a recurrence; OR
- Caregivers were diagnosed with any psychiatric disorders; OR
- Caregivers had medical work experience; OR
- Unwilling to participate in the survey.

All KD kids received the standard therapy, which included high doses of IVIG (2 g/kg) as a single infusion and aspirin (30–50 mg/kg/d during the acute phase of illness) immediately after the diagnosis. The dose of aspirin was lowered to 3–5 mg/kg/d after the child had been afebrile for 48–72 h. The 2nd IVIG of the same dosage was administrated for KD patients with

initial IVIG-resistant. If fever persists 36 h after the 2nd IVIG infusion, intravenous methylprednisolone (30 mg/kg/dose) was performed for 3 consecutive days. No other therapies, including infliximab, plasma exchange, and cytotoxic agents, were used in the treatment protocol. Initial IVIG resistance was defined as recurrent or persistent fever for at least 36 h but not longer than 7 days after initial IVIG treatment (14). CAL was defined as a coronary artery internal diameter with a z score of ≥ 2.5 in at least one of the following coronary arteries: left, right anterior descending, and left-main (29).

Data collection tools and survey procedures

Sociodemographic characteristics of KD caregivers

On the day of discharge, KD patients' demographic and clinical data, such as age, male/female, and length of hospitalization, were retrieved from the electronic medical records. The attending doctor provided instructions for the drugs to the KD caregivers, including the names, therapeutic effects, dosage, frequency of use, and main side effects at discharge. There were no teaching sessions related to medicine for KD caregivers during the hospital stay.

Eligible KD caregivers were invited to participate in the study and provided with information on the study objectives, study content, and investigation procedures. The survey was carried out through face-to-face interviews using the paper-and-pencil method. A self-developed and structured questionnaire designed by a researcher (BH) was used to obtain information on the sociodemographic variable of the KD caregivers. The questionnaires were required to be filled out on the spot. Caregivers of discharged children with KD completed questionnaires anonymously after giving signed informed consent. For illiterate participants, the interviewers read the question items word by word exactly, and participants' responses were recorded on the questionnaires. The questionnaires were collected immediately after completion, checked for missing information, and followed up with the participants.

The Chinese version of the Medication Literacy Assessment

Due to the COVID-19 pandemic, stringent rules for pandemic protection measures were diligently applied. We assess the medication literacy of KD caregivers by telephone. Twenty days after discharge, the interviewers made telephone calls to the KD caregivers to assess their medication literacy based on an outlined structured interview. All patients had at least one follow-up in the outpatient department from hospital discharge before ML assessment. Medication literacy was measured by the Chinese version of the Medication

Literacy Assessment for Discharged Patients (MedLitRxSE-Chinese). Maniaci and colleagues first proposed the Medication Literacy Assessment in English (MedLitRxSE-English) (30). The MedLitRxSE-English was used to measure the ability of patients to read, comprehend, calculate, and cope with medication-related problems in the medical information environment to assess their level of medication literacy (31). The MedLitRxSE-Chinese is a self-administered scale. It was introduced by Zheng et al. (32) according to the principles of Brislin and culture adjustment (33). The questionnaire assessed the patient's ability to understand, calculate, and process drug information.

The MedLitRxSE-Chinese includes nine items with a dichotomy scoring system (1 for correct answers and 0 for errors). Item 7 has only a "Yes" or "No" answer, and item 9 has specific names. Therefore, items 7 and 9 do not contribute to the total score. As a result, the maximum scale score is 7. The total score ranges from 0 to 7, and a higher score reflects a higher level of medication literacy. The scores were divided into three groups: adequate literacy (≥ 6), marginal literacy (4–5), and inadequate literacy (< 4). The MedLitRxSE-Chinese has good reliability and validity in Chinese populations (Cronbach's α coefficient = 0.850, content validity index of the questionnaire = 0.812, and retesting reliability coefficient = 0.94) (32, 34). Specifically, in item 3, the original question was: "Did you know the generic names of the medicines that your kids are taking". Considering the name of drugs may be difficult to know by all KD caregivers as it is medical jargon. The brand names of medicines seem to be easier to bear in mind. So we changed the question to: "Did you know the generic or brand names of the medicines your kids are taking".

Before conducting the Medication Literacy Assessment, the researchers obtained oral informed consent. Each KD caregiver was required to answer the MedLitRxSE-Chinese. The investigators checked the nine scales through an electronic medical record system to determine whether the answer was correct. The flow chart of the survey process can be seen in [Appendix S2](#).

Data analysis

Continuous variables were directly expressed as a range. Categorical variables were expressed by presenting the frequency and proportion in each category. Demographic information was analyzed by descriptive statistical analysis. We used *t*-tests, analysis of variance, and the Kruskal–Wallis H test for the univariate analysis. Logistic regression analysis was used to analyze the independent influencing factors of medication literacy. All *P*-values were from 2-sided tests, and the results were considered statistically significant at $P < 0.05$. Statistical analysis was performed with SPSS (version 22.0, Chicago, U.S.).

Results

General characteristics of caregivers

From March 2020 to February 2021, 106 caregivers of discharged children with KD who met the inclusion criteria were included in the present study. Nine were further excluded in the data cleaning stage because of missing variables. A total of 97 completed questionnaires were received, with a valid response rate of 91.5%. There were no significant differences in gender of KD caregivers, education level, income, employment status and follow-up intervals. Meanwhile, there were significant differences in the age of KD caregivers, type of KD patients (complete VS. incomplete), the complication of KD patients (CAL VS. non-CAL), and duration of hospitalization ($P < 0.05$). The general characteristics of KD caregivers and patients are presented in Table 1.

Medication literacy of caregivers of discharged children with KD

In brief, the mean score of medication literacy was 4.91 (1.51). Caregivers who obtained a score \geq of 6 were 39.2% (38) and considered adequate medication literacy. Those who obtained a score of 4-5 were 39.2% (38) and were considered marginal medication literacy, whereas 21.6% (21) obtained a score <4 and were considered inadequate medication literacy. Although all caregivers knew their kids had to take medicine after discharge, only 86.6% knew how many kinds of drugs their kid should take daily, and 76.3% could name the medications their kid was taking. 78.4% knew the frequency of taking medications every day, only 38.1% knew the effects, and 32.9% had been informed of the side effects of drugs. Furthermore, only 19.6% knew the side effects of each kind of medicine their kid was taking (Table 2).

Influencing factors of medication literacy

Table 3 shows the results of the univariate analysis. Five factors were significantly associated with medication literacy, with higher scores observed in highly educated, a higher income, unemployed, shorter follow-up intervals, and longer duration of hospitalization.

The multiple logistic regression shows that education level, monthly income, and duration of hospitalization are the independent influencing factors on medication literacy of KD caregivers. Medication literacy scores increased with the educational level, monthly income, and length of hospitalization (Table 4).

TABLE 1 General characteristic of KD caregivers and KD patients.

Characteristics	Items	No. of participants (N = 97)	Percentage (%)
Age of KD caregivers (years)			
	≤ 35	65	67.01
	> 35	32	32.99
Gender of KD caregivers			
	Male	50	51.55
	Female	47	48.45
Education level			
	Middle school and below	20	20.62
	High school	30	30.93
	College	29	29.90
	Master/Doctoral	18	18.55
Income (monthly)			
	$< 2,000$ Yuan	30	30.93
	2,001–5,000 Yuan	23	23.71
	5,001–9,000 Yuan	23	23.71
	$> 9,000$ Yuan	21	21.65
Employment status			
	Full-time/Part-time	52	53.61
	Unemployed	45	46.39
Follow-up intervals (days)			
	≤ 7 days	54	55.67
	> 7 days	43	44.33
Duration of hospitalization (days)			
	≤ 5 days	37	38.14
	> 5 days	60	61.86
Age of KD patients (years)			
	< 5	40	41.24
	≥ 5	57	58.76
Number of medicines the KD patients currently taken			
	1	1	1.03
	2-3	83	85.57
	≥ 4	13	13.40
Type of KD patients (n)			
	Complete KD	68	70.10
	Incomplete KD	29	29.90
Complication of KD patients			
	CAL	19	19.59
	Non-CAL	78	80.41

CAL, Coronary artery lesions; Non-CAL, Non-coronary artery lesions.

TABLE 2 Medication literacy for caregivers of discharged children with KD.

Items	Number of correct answers no. (%) (n = 97)
1. Did your kids take medicines after discharge from hospital?	97 (100%)
2. How many kinds of medicines did your kids need to take every day?	84 (86.6%)
3. Did you know the generic or brand names of the medicines that your kids are taking?	74 (76.3%)
4. Did you know the dosage of each kinds of medicine that your kids are taking?	92 (94.8%)
5. Did you know how many times a day for each kind of medicine?	76 (78.4%)
6. Do you know the purpose (effect) of each kind of drug?	37 (38.1%)
7. Have you ever been warned of side effects of the medicines that your kids are taking?	32 (32.9%)
8. Did you know the common side effects of each kinds of medicine your child is taking?	19 (19.6%)
9. Did you know whom you should consult with in case of questions related to the medicines you are taking?	
A. Physician	6 (6.2%)
B. Pharmacist	63 (64.9%)
C. Nurse	23 (23.7%)
D. I have no idea	3 (3.1%)
E. Others	2 (2.1%)

Discussion

Our study described the status of medication literacy among Chinese caregivers of discharged children with KD and explored possible influencing factors of medication literacy. Our findings showed that most of the Chinese KD caregivers had insufficient medication literacy (≤ 5 scores), and only 39.2% of the caregivers had adequate medication literacy (> 5 scores). Meanwhile, our study also found that educational level, monthly income, and length of hospitalization were independently associated with medication literacy.

To properly use their medications, patients must read the related medical information, including medication labels and instructions, and take the accurate dose. Our study is of obvious importance, considering that KD predominantly affects children < 5 years of age. Most KD patients lack medication adherence and do not know how to self-medication properly. Thus, knowing the status and exploring the influencing factors of medication literacy among KD is essential.

Our study showed that medication literacy among KD caregivers needs improvement as the overall medication literacy scores are low, consistent with previous reports of Chinese populations (10, 35). Thus, it is critical to improve the medication literacy of the KD caregivers as inappropriate medication use was identified to be significantly associated with low medication literacy (6, 8, 10).

Several factors were associated with higher medication literacy. Our findings are consistent with the results of other studies that showed higher education levels and higher income were significantly associated with a higher medication literacy score (13, 31, 36, 37). Highly educated obtain higher medication literacy scores indicating that general knowledge may contribute to understanding medication information. The higher the educational level of caregivers, the stronger their ability to obtain medication information, the wider the channels for obtaining information, and the stronger the ability to make correct medication decisions (38). It was worth noting that most caregivers in this population had a low education level and limited knowledge of medication regimes, indicating that they are prone to trusting physicians about their treatment. Higher monthly income is another influencing factor, suggesting that caregivers with higher incomes might have more access to medication knowledge and were more likely to pay more attention to promoting health levels. Therefore, caregivers who are less educated and earned less should be targeted for medication literacy improvement.

Duration of hospitalization was another independent factor affecting medication literacy. We found that those with a longer duration of hospitalization were more likely to have a higher level of medication literacy, which is consistent with an early study (39). It indicated that medical staff should focus on caregivers with shorter duration. A possible explanation was the longer the patients stayed in the hospital, the more health information their caregivers received from doctors and other nurses. Meanwhile, these caregivers may pay more attention to their kids' conditions while in the hospital, thus improving their medication literacy.

Based on the results of this study, we provide several suggestions to improve medication literacy among KD caregivers. First, effective communication between caregivers and health care providers is needed. Second, high-quality and comprehensible education materials (e.g., booklets, online medical information) should be designed as caregivers sometimes cannot remember detailed medication information and guidance verbally communicated by physicians. Third, provide a training education to improve the nursing knowledge and level of Kawasaki disease among medical staff. Besides, regular follow-ups are important methods to gain medication knowledge and improve medication literacy.

TABLE 3 Univariate analysis of determinants of medication literacy for KD caregivers.

Variables	No.	The score of ML			t/H/ χ^2	P
		0–3	4–5	6–7		
Age of KD caregivers (years)					4.619	0.099
≤35	65	10	28	27		
>35	32	11	10	11		
Gender of KD caregivers					0.317	0.853
Male	46	11	17	18		
Female	51	10	21	20		
Education level					52.555	<0.001
Middle school and below	20	16	3	1		
High school	30	2	16	12		
College	29	2	12	15		
Master/Doctoral	18	1	7	10		
Income (monthly)					46.240	<0.001
<2,000 Yuan	30	15	8	7		
2,001–5,000 Yuan	23	6	11	6		
5,001–9,000 Yuan	23	0	16	7		
>9,000 Yuan	21	0	3	18		
Employment status					12.646	0.002
Full-time/Part-time	52	13	27	12		
Unemployed	45	8	11	26		
Follow-up intervals					−3.792	<0.001
≤7 days	54	4	22	28		
>7 days	43	17	16	10		
Duration of hospitalization					18.161	<0.001
≤5 days	37	15	16	6		
>5 days	60	6	22	32		
Age of KD patients (years)					0.083	0.959
<5	40	9	15	16		
≥5	57	12	23	22		
Number of medicines the KD patients currently taken					4.957	0.292
1	1	/	/	1		
2–3	83	17	31	35		
≥4	13	4	7	2		
Type of KD patients					1.592	0.451
Complete KD	68	15	24	29		
Incomplete KD	29	6	14	9		
Complication of KD patients					4.074	0.13
CAL at the acute phase	19	1	10	8		
Non-CAL at the acute phase	78	20	28	30		

t, two-sample t-test; H, Kruskal–Wallis test; CAL, Coronary artery lesions; Non-CAL, Non-coronary artery lesions.

Limitations

This study has potential limitations. First, our study had a small sample size. Second, all the caregivers came from Sichuan, southwest of China, which limited the generalization of the findings. Future studies should focus on caregivers from other

districts and larger sample sizes. Third, we didn't collect data on where the caregivers learned information about the medication or their preferred way of receiving it. This could help medical care institutions improve their future services and the medical literacy level of their patients' caregivers. Four, the telephone call-based assessment may introduce bias.

TABLE 4 Multiple logistic regression of influencing factors among KD caregivers.

Determinants	B	S.E.	Wald	P	OR	95%C.I. of OR	
						Lower	Upper
Education level	1.461	0.544	7.21	<0.001	4.311	1.484	12.524
Income (monthly)	2.249	0.622	13.071	<0.001	9.474	2.8	32.058
Employment status (Employed)	−2.563	1.333	3.694	0.055	0.077	0.006	1.052
Follow-up intervals	−0.237	0.156	2.326	0.127	0.789	0.582	1.07
Duration of hospitalization	0.399	0.169	5.545	0.019	1.49	1.069	2.076

B, Partial regression coefficient; SE, Standard error; CI, Confidence intervals.

Conclusion

The overall level of medication literacy among KD caregivers is low and needs to be improved. A higher level of education, higher income, and longer duration of hospitalization were influencing factors of adequate medication literacy. However, further multiple-center research with bigger sample size is needed to find effective measures to improve medication literacy among caregivers.

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 the Research Ethics Committee of Chengdu Women's and Children's Central Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

YY had full access to all of the data in the study and takes responsibility for the integrity of the data. YZha, XW, and JC

drafted the manuscript. JC contributed to the design of the search strategy. YLia, YZho, WW, and QZ collected the data. BH designed the self-developed and structured questionnaire. YLia and YLin did the statistical analysis. All authors read, provided feedback, and approved the final 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/fpubh.2022.960913/full#supplementary-material>

References

1. Raynor DK. Medication literacy is a 2-way street. *Mayo Clin Proc.* (2008) 83:520–2. doi: 10.4065/83.5.520
2. Pouliot A, Vaillancourt R, Stacey D, Suter P. Defining and identifying concepts of medication literacy: an international perspective. *Res Social Adm Pharm.* (2018) 14:797–804. doi: 10.1016/j.sapharm.2017.11.005
3. Cordina M, Hämeen-Anttila K, Lauri J, Tabone S, Enlund H. Health and medication literacy and the desire to participate in pharmacotherapy decision making - comparison of two countries. *Res Social Adm Pharm.* (2018) 14:817–23. doi: 10.1016/j.sapharm.2018.06.009
4. Raynor DK. Addressing medication literacy: a pharmacy practice priority. *Int J Pharm Pract.* (2009) 17:257–9. doi: 10.1211/ijpp.17.05.0001
5. Zhong Z, Zheng F, Guo Y, Luo A. Medication literacy in a cohort of Chinese patients discharged with Acute Coronary Syndrome. *Int J Environ Res Public Health.* (2016) 13:720. doi: 10.3390/ijerph13070720

6. Lee CH, Chang FC, Hsu SD, Chi HY, Huang LJ, Yeh MK. Inappropriate self-medication among adolescents and its association with lower medication literacy and substance use. *PLoS ONE*. (2017) 12:e0189199. doi: 10.1371/journal.pone.0189199
7. Zhang J, Gilmour S, Liu Y, Ota E. Effect of health literacy on quality of life among patients with chronic heart failure in China. *Qual Life Res*. (2020) 29:453–61. doi: 10.1007/s11136-019-02332-4
8. Kripalani S, Henderson LE, Jacobson TA, Vaccarino V. Medication use among inner-city patients after hospital discharge: patient-reported barriers and solutions. *Mayo Clin Proc*. (2008) 83:529–35. doi: 10.4065/83.5.529
9. Neiva Pantuzza LL, Nascimento ED, Crepalde-Ribeiro K, Botelho SF, Parreiras Martins MA, Camila de Souza Groia Veloso R, et al. Medication literacy: a conceptual model. *Res Social Adm Pharm*. (2022) 18:2675–82. doi: 10.1016/j.sapharm.2021.06.003
10. Zheng F, Ding S, Luo A, Zhong Z, Duan Y, Shen Z. Medication literacy status of outpatients in ambulatory care settings in Changsha, China. *J Int Med Res*. (2017) 45:303–9. doi: 10.1177/0300060516676726
11. Pouliot A, Vaillancourt R. Medication literacy: why pharmacists should pay attention. *Can J Hosp Pharm*. (2016) 69:335–6. doi: 10.4212/cjhp.v69i4.1576
12. Mosher HJ, Lund BC, Kripalani S, Kaboli PJ. Association of health literacy with medication knowledge, adherence, and adverse drug events among elderly veterans. *J Health Commun*. (2012) 17 Suppl 3:241–51. doi: 10.1080/10810730.2012.712611
13. Shen Z, Shi S, Ding S, Zhong Z. Mediating effect of self-efficacy on the relationship between medication literacy and medication adherence among patients with hypertension. *Front Pharmacol*. (2020) 11:569092. doi: 10.3389/fphar.2020.569092
14. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. (2017) 135:e927–99. doi: 10.1161/CIR.0000000000000484
15. Al-Ammouri I, Al-Wahsh S, Khuri-Bulos N. Kawasaki disease in Jordan: demographics, presentation, and outcome. *Cardiol Young*. (2012) 22:390–5. doi: 10.1017/S1047951111001818
16. Alexopoulos A, Vekiou A, Lycopoulou L, Tavena A, Lagona E, Kakourou T. Kawasaki disease in Greek children: a retrospective study. *J Eur Acad Dermatol Venereol*. (2013) 27:580–8. doi: 10.1111/j.1468-3083.2012.04488.x
17. Arkachaisri T. Pediatric rheumatology in Southeast Asia: insights from the Singapore experience. *Curr Rheumatol Rep*. (2011) 13:117–22. doi: 10.1007/s11926-010-0159-1
18. Bar-Meir M, Haklai Z, Dor M. Kawasaki disease in Israel. *Pediatr Infect Dis J*. (2011) 30:589–92. doi: 10.1097/INF.0b013e31820e3849
19. Davaalkham D, Nakamura Y, Baigalmaa D, Davaa G, Chimedsuren O, Sumberzul N, et al. Kawasaki disease in Mongolia: results from 2 nationwide retrospective surveys, 1996–2008. *J Epidemiol*. (2011) 21:293–8. doi: 10.2188/jea.JE20100144
20. Huang SK, Lin MT, Chen HC, Huang SC, Wu MH. Epidemiology of Kawasaki disease: prevalence from national database and future trends projection by system dynamics modeling. *J Pediatr*. (2013) 163:126–31.e121. doi: 10.1016/j.jpeds.2012.12.011
21. Singh S, Aulakh R, Bhalla AK, Suri D, Manojkumar R, Narula N, et al. Is Kawasaki disease incidence rising in Chandigarh, North India? *Arch Dis Child*. (2011) 96:137–40. doi: 10.1136/adc.2010.194001
22. Uehara R, Belay ED. Epidemiology of Kawasaki disease in Asia, Europe, and the United States. *J Epidemiol*. (2012) 22:79–85. doi: 10.2188/jea.JE20110131
23. Salo E, Griffiths EP, Farstad T, Schiller B, Nakamura Y, Yashiro M, et al. Incidence of Kawasaki disease in northern European countries. *Pediatr Int*. (2012) 54:770–2. doi: 10.1111/j.1442-200X.2012.03692.x
24. Masuda H, Ae R, Koshimizu TA, Matsumura M, Kosami K, Hayashida K, et al. Epidemiology and risk factors for giant coronary artery aneurysms identified after acute Kawasaki disease. *Pediatr Cardiol*. (2021) 42:969–77. doi: 10.1007/s00246-021-02571-8
25. Matsubara Y, Matsubara D, Ae R, Kosami K, Aoyama Y, Yashiro M, et al. Cumulative incidence of Kawasaki disease with cardiac sequelae in Japan. *Pediatr Int*. (2020) 62:444–50. doi: 10.1111/ped.14164
26. Kaushal R, Goldmann DA, Keohane CA, Christino M, Honour M, Hale AS, et al. Adverse drug events in pediatric outpatients. *Ambul Pediatr*. (2007) 7:383–9. doi: 10.1016/j.ambp.2007.05.005
27. Du ZD, Zhang T, Liang L, Meng X, Li T, Kawasaki T, et al. Epidemiologic picture of Kawasaki disease in Beijing from 1995 through 1999. *Pediatr Infect Dis J*. (2002) 21:103–7. doi: 10.1097/00006454-200202000-00004
28. Singh S, Vignesh P, Burgner D. The epidemiology of Kawasaki disease: a global update. *Arch Dis Child*. (2015) 100:1084–8. doi: 10.1136/archdischild-2014-307536
29. McCrindle BW, Li JS, Minich LL, Colan SD, Atz AM, Takahashi M, et al. Coronary artery involvement in children with Kawasaki disease: risk factors from analysis of serial normalized measurements. *Circulation*. (2007) 116:174–9. doi: 10.1161/CIRCULATIONAHA.107.690875
30. Maniaci MJ, Heckman MG, Dawson NL. Functional health literacy and understanding of medications at discharge. *Mayo Clin Proc*. (2008) 83:554–8. doi: 10.1016/S0025-6196(11)60728-3
31. Qiao L, Ding S, Zhong Z, Liu X, Lai L, Zheng F. Association between social support and medication literacy in Chinese patients with coronary heart disease. *Front Cardiovasc Med*. (2021) 8:705783. doi: 10.3389/fcvm.2021.705783
32. Zheng F, Zhong Z, Ding S, Luo A, Liu Z. [Modification and evaluation of assessment of medication literacy]. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. (2016) 41:1226–31. doi: 10.11817/j.issn.1672-7347.2016.11.01
33. Jones PS, Lee JW, Phillips LR, Zhang XE, Jaceldo KB. An adaptation of Brislin's translation model for cross-cultural research. *Nurs Res*. (2001) 50:300–4. doi: 10.1097/00006199-200109000-00008
34. Zheng F, Ding S, Zhong Z, Pan C, Xie J, Qin C. Investigation on status of discharged patients' medication literacy after coronary artery stent implantation. *Chin Nurs Res*. (2015) 29:1732–4. doi: 10.3969/j.issn.10096493.2015.14.024
35. Zheng F, Ding S, Lai L, Liu X, Duan Y, Shi S, et al. Relationship between medication literacy and medication adherence in inpatients with coronary heart disease in Changsha, China. *Front Pharmacol*. (2019) 10:1537. doi: 10.3389/fphar.2019.01537
36. Ma G, Luo A, Shen Z, Duan Y, Shi S, Zhong Z. The status of medication literacy and associated factors of hypertensive patients in China: a cross-sectional study. *Intern Emerg Med*. (2020) 15:409–19. doi: 10.1007/s11739-019-02187-0
37. Shi S, Shen Z, Duan Y, Ding S, Zhong Z. Association between medication literacy and medication adherence among patients with hypertension. *Front Pharmacol*. (2019) 10:822. doi: 10.3389/fphar.2019.00822
38. Qu J, Zhou T, Xue M, Sun H, Shen Y, Liu Y. Relationship between medication literacy and frailty in elderly inpatients with coronary heart disease: a cross-sectional study in China. *Front Pharmacol*. (2021) 12:691983. doi: 10.3389/fphar.2021.691983
39. Zhong Z, Ma G, Zheng F, Duan Y, Ding S, Luo A. Medication literacy in a cohort of Chinese patients discharged with essential hypertension. *Front Public Health*. (2019) 7:385. doi: 10.3389/fpubh.2019.00385



OPEN ACCESS

EDITED BY

Melody Goodman,
New York University, United States

REVIEWED BY

Lei Shi,
Southern Medical University, China
Feiying He,
Southern Medical University, China

*CORRESPONDENCE

Xue-Zheng Jin
yaya22nd@hotmail.com
Yi-Bo Wu
bjmuwuyibo@outlook.com

SPECIALTY SECTION

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 05 July 2022

ACCEPTED 15 September 2022

PUBLISHED 18 October 2022

CITATION

Liu J, Hao Y-Y, Mao H-J, Sun X-J,
Huang X-L, Quan C-X, Cao M-L,
Wei S-T, Jin X-Z and Wu Y-B (2022)
Evidence-based core information for
health communication of tobacco
control: The effect of smoking on risks
of female disease.
Front. Public Health 10:986430.
doi: 10.3389/fpubh.2022.986430

COPYRIGHT

© 2022 Liu, Hao, Mao, Sun, Huang,
Quan, Cao, Wei, Jin and Wu. This is an
open-access article distributed under
the terms of the [Creative Commons
Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

Evidence-based core information for health communication of tobacco control: The effect of smoking on risks of female disease

Jin Liu¹, Yun-Yi Hao², Hui-Jia Mao³, Xiang-Ju Sun⁴,
Xiao-Lu Huang⁵, Chen-Xin Quan⁶, Mei-Ling Cao⁷,
Shu-Ting Wei⁸, Xue-Zheng Jin^{9*} and Yi-Bo Wu^{10*}

¹The Second Affiliated Hospital, China Medical University, Shenyang, China, ²School of Public Health, Shandong University, Jinan, China, ³School of Pharmaceutical Sciences, Jiangxi University of Traditional Chinese Medicine, Nanchang, China, ⁴The Fourth Affiliated Hospital, Harbin Medical University, Harbin, China, ⁵The Third Clinical Department, China Medical University, Shenyang, China, ⁶School for Policy Studies, University of Bristol, Bristol, United Kingdom, ⁷Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Traditional Chinese Medicine, Nanjing, China, ⁸School of Basic Medical Sciences, Shandong University, Jinan, China, ⁹Department of Health Communication, Chinese Center for Health Education, Beijing, China, ¹⁰School of Public Health, Peking University, Beijing, China

Objective: Cigarettes have become the the biggest killer of contemporary female's health and beauty. What kind of health information is suitable for the general public is an important issue to be discussed globally. The purpose of this study is to generate systematic, rigorous, public-demand-oriented and appropriate core information relevant to tobacco control based on the best available evidence, combined with audience preferences and pre-dissemination content review from multidisciplinary expertise in order to improve the effectiveness of health communication of tobacco control.

Methods: Relevant systematic reviews meta-analysis that reported smoking on risks of female disease were identified by searching PubMed, Embase, the Cochrane Library, Web of Science, Clinical Trials.gov, and the International Clinical Trial Registry Platform. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) process was applied to assess the evidence in order to make rigorous core information. The audience prevalence survey was conducted to ensure that core information was targeted and tailored. Finally, the expert assessment was used for a pre-dissemination content review and to evaluate whether the core information was appropriate or not.

Results: The final core information consisted of eight parts concerning the effects of smoking and female cardiovascular disease, diabetes, rheumatoid arthritis, respiratory disease, digestive system disease, mental disease, non-pregnant female reproductive system disease, as well as pregnant women and their fetuses. A total of 35 items of core information suitable for dissemination was included and the quality of evidence, the degree of public demand and the outcome of pre-dissemination content review were reported.

Conclusion: The core information related to female cardiovascular system diseases, as well as liver cancer and upper gastrointestinal cancer is the preferred content for health communication of tobacco control. The quality of evidence for core information related to pregnant women and their infants, as well as diseases of reproductive system, respiratory system, and diabetes needs to be improved to meet high public demand. The core information related to mental disease is more suitable for dissemination to patients with mental illness than to the general public. Besides, dissemination of core information should be individualized. Evidence-based Core Information for Health Communication of Tobacco Control would be helpful to provide evidence support for health communication related to tobacco control and enhance public health literacy for international communities that have high smoking prevalence and related disease burden.

KEYWORDS

tobacco control, smoking, smoking cessation, female diseases, health communication, core information

Introduction

The sheer number of diseases and deaths caused by tobacco underscores the importance of tobacco control as an urgent global health priority (1–5), especially for women, with their special physiological conditions which are different from males, the harm of smoking to them deserves more attention (6–14). The nicotine in tobacco can reduce the production of estrogen in women, which can lead to disorders in the body and the development of tumors (10, 11). And smoking can significantly reduce activated immune cells and lymphocytes, thereby reducing the immunity of the reproductive tract, increasing the risk of female gynecological diseases, and adversely affecting reproduction (12). The magnitude of change in trends in female smoking prevalence over the past 20 years signifies that female prevalence has not changed significantly since 2000 in most countries, or declined by < 10 percentage points (6, 7). Recently, a global smoking epidemic data shows that female smoking prevalence was 34–40% in Pacific Island countries (Nauru, Micronesia, Kiribati), 10–19% in several OECD (the Organization for Economic Co-operation and Development) countries (Canada, the USA, the UK, Australia and New Zealand) as well as many countries in Western Europe, and < 2–3% in several countries in Africa, as well as Tajikistan and Sri Lanka (6, 7).

Substantial global effort was devoted to curtailing the tobacco epidemic over the past two decades (15), including health communication for tobacco control which is an important part of tobacco control measures (e.g., tobacco pictorial health warnings, point-of-sale health communication campaigns, tobacco prevention education campaigns in university, media campaigns for tobacco control, interpersonal

communication in tobacco control campaigns) (16–20), the pace of progress in reducing smoking prevalence has been with little success due to heterogeneous across development status, public literacy and age (21) as well as complicated evidence (7).

As demonstrated by GBD 2015 Tobacco Collaborators (21), countries with higher SDI (Socio-demographic Index) have higher prevalence of daily smoking and age patterns varied more by SDI. Female smoking prevalence typically peaked around age 25 years for high and high-middle SDI countries, while prevalence generally increased until age 60 years in low to middle SDI countries (21). This reminds us that tailored tobacco control health communication strategies (22–24) need to be adopted for different development status, public literacy and age pattern. Furthermore, health communication of tobacco control requires systematic, rigorous, targeted and appropriate evidence on smoking level. To meet this demand in the context of health communication, we propose “core information,” an unprecedented concept. Core information is condensed and suitable health information to be provided to health workers for dissemination to the public. Its development refers to the methods of evidence formation from WHO handbook, based not only on the best available evidence, but also on audience preferences and pre-dissemination content review from multidisciplinary expertise.

Therefore, the Evidence-based Core Information for Health Communication of Tobacco Control is formed in order to improve the effectiveness of health communication of tobacco control and subsequently reduced smoking prevalence, risks of related disease. It will also be helpful to enhance public health literacy for international communities that have high smoking prevalence and related disease burden.

Methods

Preliminary research basis for core information

This study was supposed to develop according to the methods of evidence formation from WHO handbook (25). The study followed the latest definition of evidence formation of Institute of Medicine(IOM) (26, 27) and conformed to the requirements for evidence in Reporting Items 2.0 for Practice Guidelines in Healthcare(RIGHT) (28), the RIGHT statement (29) and Appraisal Of Guidelines For Research & EvaluationII(AGREE II) (30). The technical route for development of Evidence-based Core Information for Health Communication of Tobacco Control is shown in Figure 1.

This study was initiated by the Health Communication Working Committee of the Chinese Medical Doctor Association, with methodological support provided by the Drug Evaluation Center of Peking University School of Medicine, and academic support provided by China Smoking Control Association, Beijing Smoking Control Association and other units. And this project was registered on the International Practice Guidelines Registry Platform (<http://www.guidelines-registry.org/>). The registration number was IPGRP-2020CN072.

Guideline evidence

Literature search and screening

PICOs (participants, female; interventions (equivalent to exposure), smoking; comparisons, smokers vs. non-smokers; outcomes, incidence and mortality of various diseases; study types, systematic reviews) questions (10) followed literature pre-retrieving, International guideline reference and consulting with clinicians, clinical pharmacists, nurses, behavioral epidemiologists and health communication workers. Then the search strategy was determined through the final PICOs questions. To ensure the comprehensiveness of the evidence, we searched PubMed, Embase, and Web of Science, which are recognized as authoritative medical databases worldwide. The Cochrane Library was searched for evidence-based medical literature. Considering unpublished studies and their study details, we also searched Clinical Trials.gov and the International Clinical Trial Registry Platform. The retrieval time was from database construction to February 2021. The search formula consisted of keywords related to smoking and related diseases. Taking smoking and cardiovascular disease in women as an example, the search terms included: (cigarette OR cigarettes OR tobacco OR smoking OR smoking) AND (hypertension OR blood pressure) OR cancer OR (CVD OR cardiovascular disease OR coronary cardiovascular disease OR coronary heart disease). The language of the

publication was Chinese or English and systematic reviews and meta-analysis were included. References and gray literature information (i.e., non-published literature, e.g., non-published government literature, dissertations, etc.) of the included literature were also manually searched and screened. The literature screening process was completed independently by two trained researchers. If there was a disagreement, a third researcher would join the discussion to reach a consensus.

GRADE assessment

The GRADE (Grade Recommendations Assessment, Development, and Evaluation) tool (31) was used to evaluate the quality of evidence in order to make rigorous core information (For specific implementation content, see Supplementary material 1). The evidence quality was divided into four levels: high, medium, low and very low (Table 1), considering five downward factors (study limitations, imprecision, inconsistency of results, indirectness of evidence and publication bias likely) and three upward factors (large magnitude of effect, dose effect and confounders likely minimize the effect) (Figure 1 and Supplementary material 1).

Audience preference and value survey

The core information development group conducted an audience preference and value survey on the content of the core information (For specific implementation content, see Supplementary material 2). 670 participants was recruited, taking into account the distribution of age, gender, education level, occupation, smoking situation and chronic diseases in line with socio-demographic characteristics. Researchers of the development group explained the background and necessity of core information and discussed them with participants (32). Participants rated the core information using the Likert Level 5 scale: 5 for very necessary, 4 for necessary, 3 for equivocal, 2 for unnecessary, and 1 for very unnecessary. the mean \pm standard deviation of each core information and the overall were calculate. The mean \pm standard deviation of the overall was 3.10 ± 0.10 , based on which, the degree of public demand was divided into four levels: low, medium, high and very high (Table 2). Finally, the results were formed and summarized and analyzed to provide reference for expert assessment group.

Expert assessment of core information

Expert assessment process: An expert assessment survey (For specific implementation content, see Supplementary material 3) was used for the pre-dissemination content review and to evaluate whether the core information

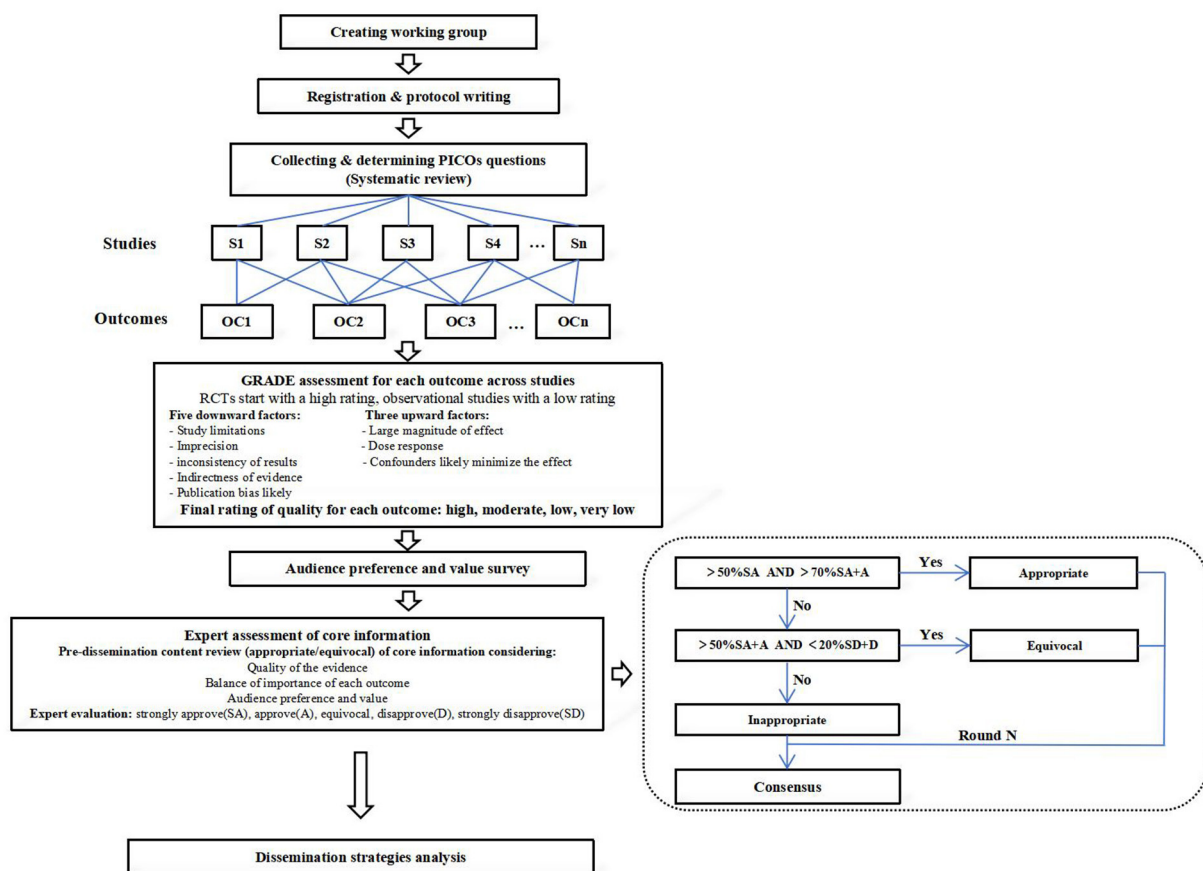


FIGURE 1
The technical route for development of Evidence-based Core Information for Health Communication of Tobacco Control.

TABLE 1 Grade Recommendations Assessment, Development, and Evaluation (GRADE) system.

Score	Grade	Definition
2	High	Further research is very unlikely to change confidence in the estimate of effect.
1	Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
−1	Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
−2	Very low	Any estimate of effect is very uncertain

was appropriate or not based on quality of evidence, audience preferences and values, balance of importance of each outcome, equity, feasibility, acceptability etc. After two rounds of evaluation and modification of

TABLE 2 The description of public demand for core information.

Public demand	Description
High	Mean value of core information $\geq 3.10 + 0.10$
Relatively high	$3.10 \leq \text{Mean value of core information} < 3.10 + 0.10$
Moderate	$3.10 - 0.10 \leq \text{Mean value of core information} < 3.10$
Low	Mean value of core information was $< 3.10 - 0.10$

core information, the final version of core information suitable for dissemination was reached (see Table 5 in Supplementary material 3) (33).

The experts participating in this survey were distributed across the country, including 32 multidisciplinary experts whose professional level was high (see Table 2 in Supplementary material 3). They voted anonymously through the Chinese online ‘Questionnaire Star’ platform. This process was monitored by the guideline development group. If the voting ratio of “5” was more than 50% and the voting ratio

of “5” + “4” was more than 70%, the item was appropriate; if the voting ratio of “5” + “4” was more than 50% and the voting ratio of “2” + “1” was < 20%, the item was equivocal (Figure 1) (29). In the remaining cases, it was deemed inappropriate.

Results

Summary of core information

The correlation between smoking and risks of non-pregnant female reproductive system disease

Female reproductive system diseases mainly include gynecological inflammation, gynecological tumors, menstrual disorders and infertility, which bring both physical and mental effects to women and seriously reduce their quality of life. According to WHO global report on trends in prevalence of tobacco use 2000-2025, there were as many as 244 million women using tobacco in 2018 (30). It has been shown that cigarette smoke contains a variety of toxins that affect reproductive function to varying degrees (10), and smoking is therefore considered to be an important factor in the increased prevalence and mortality of female reproductive disorders (31–38)(For summary of evidence, see [Supplementary material 1](#)). Our study found that the degree of public was concentrated in “Moderate” and “Relatively High,” but the quality of evidence needed to be improved to meet the general public demand (Table 3). The core information in this field can be used as the content of tobacco control health communication. The specific summary of core information of female reproductive system disease is shown in Table 3.

Effects of smoking on pregnant women and their fetuses

Considering that pregnancy is a special period for women, pregnant women and fetuses are more susceptible to external influences during this period. Studies have shown that prenatal exposure to maternal smoking during pregnancy is harmful to mothers and fetuses (10, 39–44), including congenital heart disease, schizophrenia, attention deficit and hyperactivity disorder in the fetus as well as postpartum depression, coronary heart disease, abnormal pregnancy and all stages of reproduction in pregnant women. Our study revealed that the public had the greatest demand for core information in this field, but the quality of evidence needed to be improved (Table 4). The core information in this field can be used as the content of tobacco control health communication.

TABLE 3 The correlation between smoking and risks of female reproductive system disease.

Number	Core information	Evidence quality	Expert assessment	Public demand
7 The correlation between smoking and risks of non-pregnant female reproductive system disease				
7.1	Smoking decreases the risk of non-pregnant female endometrial cancer	Moderate	Equivocal	Moderate
7.2	Smoking increases the risk of non-pregnant female cervical cancer	Very low	Equivocal	Moderate
7.3	Smoking increases the risk of non-pregnant female breast cancer	Low	Equivocal	Moderate
7.4	Smoking increases the risk of non-pregnant female serous or/and mucinous tumors of ovary	Very low	Equivocal	Moderate

The correlation between smoking and risks of female respiratory disease

Of all risk factors, Smoking is the leading risk factor for chronic respiratory diseases, For women, the leading cause of smoking-attributable DALYs is COPD (21). Evidences found that female current smokers had with increasing age (especially beyond age 45 to 50 years in the pre and post menopausal periods) a significantly faster annual decline in FEV1% (a golden indicator of COPD) predicted than male current smokers (linear regression analysis, $R^2 = 0.56$; $p = 0.008$), and this trend was evident even in female smokers who smoked only a modest amount of cigarettes (<15 g/day) (45). (For summary of evidence, see [Supplementary material 1](#)). Besides, smoking may also have a greater negative impact on lung growth in female than male during childhood and adolescence (46, 47). This suggests that the relationship between gender, age and changes in FEV1% may be U-shaped. The mechanisms responsible for the increased susceptibility of women than men to cigarette smoke can be summarized as: (1) smoking-inflammation pathway in the pre and post-menopausal periods (48, 49); (2) bronchial hyperresponsiveness in women compared to men (50–52); (3) hormonal status (53); (4) differences in lung development between females and males (54–56). Our study showed that the public demand for core information in this area was high, but the quality of evidence was low (Table 5). The dangers of smoking on the respiratory system are obvious, but evidence for women is still lacking. This is because women smoke less than men, so most surveys focus on male groups.

TABLE 4 Effects of smoking on pregnant women and their fetuses.

Number	Core information	Evidence quality	Expert assessment	Public demand
8 Effects of smoking on pregnant women and their fetuses				
8.1	Smoking can adversely affect the various stages of pregnancy in female reproduction (reproductive function, follicular development, steroid development, embryo transfer, endometrial receptivity, endometrial angiogenesis, uterine blood flow and myometrium)	Very low	Equivocal	High
8.2	Smoking increases the chance of abnormal pregnancy in pregnant women	Very low	Equivocal	High
8.3	Smoking increases the risk of postpartum depression in pregnant women	Low	Equivocal	Relatively high
8.4	Smoking increases the risk of fetal schizophrenia in pregnant women	Very low	Equivocal	High
8.5	Smoking increases the risk of fetal attention deficit and hyperactivity disorder in pregnant women	Moderate	Equivocal	High
8.6	Smoking increases the risk of fetal coronary heart disease in pregnant women	Very low	Appropriate	High

Therefore, it is of great urgency to explore high-quality and sufficient evidence in this area to meet public health needs, and pay more attention to health education for adolescent and menopausal female. The specific summary of core information of female respiratory disease is shown in [Table 5](#).

The correlation between smoking and risks of female cardiovascular disease

Several studies have shown that smoking is recognized as independent risk factors for cardiovascular diseases (21), which

TABLE 5 The correlation between smoking and risks of female diabetes, rheumatoid arthritis and respiratory disease.

Number	Core information	Evidence quality	Expert assessment	Public demand
2 The correlation between smoking and risks of female diabetes				
2.1	Smoking increases the risk of female type 2 diabetes	Very low	Equivocal	Moderate
3 The correlation between smoking and risks of female rheumatoid arthritis				
3.1	Increased smoking increases the risk of female rheumatoid arthritis	Very low	Equivocal	Low
4 The correlation between smoking and risks of female respiratory disease				
4.1	Smoking increases the risk of female chronic obstructive pulmonary disease	Low	Appropriate	High

not only increases the oxidative stress, causing the oxidation of low-density lipoproteins (LDL), but also increases inflammation (57). It affects all stages of atherosclerosis, and eventually leads to cardiovascular diseases. In postmenopausal women, the estrogen, regarded as the guardian of blood vessels, is greatly reduced, which results in increased LDL and decreased high-density lipoproteins (HDL), thereby accelerating hardening of the arteries and leads to an increased risk of coronary heart disease, heart failure, sudden cardiac death, stroke and overall cardiovascular diseases (58–62) (For summary of evidence, see [Supplementary material 1](#)). Our research found that the quality of evidence, the degree of public demand and the results of expert assessments were relatively consistent and high in this area ([Table 3](#)). This is because cardiovascular diseases are closely related to people's lives and carry a high risk of death. Researches have found that the global mortality of cardiovascular diseases has increased by 12.5% over the past decade, and cardiovascular diseases currently account for about one-third of global deaths (63), so preventing cardiovascular diseases will greatly improve global health. This means that the core information in this field is the preferred content for health communication of tobacco control. Furthermore, It is worth noting that lifestyle and other factors are important control variables and should be considered in the health communication of tobacco control when discussing the impact of smoking on female cardiovascular disease. Smokers are more likely to have poor lifestyles like high-fat diet (increases triglyceride and cholesterol levels in the blood, causing hyperlipidemia and atherosclerosis), lack of exercise (leads to obesity and metabolic syndrome) and being sedentary (results in thrombosis), which jointly contribute to

TABLE 6 The correlation between smoking and risks of female cardiovascular disease.

Number	Core information	Evidence quality	Expert assessment	Public demand
1 The correlation between smoking and risks of female cardiovascular disease				
1.1	Smoking increases the risk of female coronary heart disease	Moderate	Appropriate	High
1.2	Smoking increases the mortality of female coronary heart disease	Low	Appropriate	High
1.3	Smoking increases the mortality of female heart failure	Low	Appropriate	Relatively high
1.4	Smoking increases the risk of female sudden cardiac death	Moderate	Appropriate	High
1.5	Smoking increases the risk of female stroke	Moderate	Appropriate	Relatively high
1.6	Smoking increases the mortality of female stroke	Low	Appropriate	Relatively high
1.7	Smoking increases the risk of female overall cardiovascular disease	Moderate	Appropriate	High
1.8	Smoking increases the mortality of female overall cardiovascular disease	Moderate	Appropriate	High

the development of cardiovascular diseases (64, 65). The specific summary of core information is shown in Table 6.

The correlation between smoking and risks of female mental disease

Mental illness have a huge burden on health in the world today. According to statistics, the global burden of mental illness accounts for 32.4% of years lived with disability (YLDs) and 13.0% of disability-adjusted life-years (DALYs) (66). Smoking rate was high in patients with mental illness, and it was estimated that more than 200,000 of 520,000 people suffer from mental illness who died mainly from chronic diseases caused by smoking in the United States (67). Especially for women, changes in their sex hormone levels (for example, the “recession” of sex hormones in menopausal women aged 45–55 years old, causing a series of physiological changes, imbalances in Nervous system activity and reduced adaptability

TABLE 7 The correlation between smoking and risks of female mental disease.

Number	Core information	Evidence quality	Expert assessment	Public demand
6 The correlation between smoking and risks of female mental disease				
6.1	Smoking increases the risk of female Alzheimer's disease	Very low	Equivocal	Moderate
6.2	Smoking increases the risk of female all-cause dementia	Very low	Equivocal	Moderate

to the outside world), as well as social stereotypes and low inclusion of women, lead to a higher prevalence of depression in this group, resulting in high smoking rates. Besides, female smoking groups are more likely to be discriminated against and stigmatized in social life (68), and they themselves are more sensitive and vulnerable to social impact (such as more passive to be exposed to smoking, more susceptible to negative emotions with smoking addiction) (69), causing further damage to their mental health. Our study found that the quality of evidence, the degree of public demand and the results of expert assessments are relatively consistent and low in this area (Table 7). This is because the effects of smoking on psychiatric disorders are mainly indirect (66–68) and unclear (70, 71) (For summary of evidence, see Supplementary material 1). In most cases, it is the mental illness itself that leads to the action of smoking. Therefore, this result suggests to health communicators that core information in this field is less appropriate for dissemination to the general public compared with other core information, but is more suitable for patients with mental illnesses. The specific summary of core information of female mental disease is shown in Table 7.

The correlation between smoking and risks of female digestive system disease

The chemicals in cigarette smoke including tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons and aromatic amines play a major role in the development of digestive diseases by causing genetic mutations (72). Additionally, unhealthy diet like low fruit and vegetables intake (64), high fat eating (64), high salt consumption (73) and excessive alcohol ingestion (74, 75) (which itself has the effect of disease-promoting) and inappropriate daily habits like smoking after meals (which is harmful not only to the respiratory system, but also the digestive system) could be crucial reasons for an increased risk of digestive diseases, as these factors had synergistic effects with smoking. A total of 14 articles reported the effect of smoking on morbidity and mortality of female digestive diseases (76–89),

TABLE 8 The correlation between smoking and risks of female digestive system disease.

Number	Core information	Evidence quality	Expert assessment	Public demand
5 The correlation between smoking and risks of female digestive system disease				
5.1	Smoking increases the risk of female pancreatitis	Moderate	Equivocal	Moderate
5.2	Smoking increases the risk of female chronic pancreatitis	Moderate	Equivocal	Moderate
5.3	Smoking increases the risk of female pancreatic cancer	Low	Equivocal	Moderate
5.4	Smoking increases the mortality of female pancreatic cancer	Low	Equivocal	Moderate
5.5	Smoking increases the risk of female liver cancer	Low	Equivocal	Relatively high
5.6	Smoking increases the mortality of female liver cancer	Low	Equivocal	Relatively high
5.7	Smoking increases the risk of female gastric cancer	Low	Equivocal	Moderate
5.8	Smoking increases the risk of female upper gastrointestinal cancer	Moderate	Equivocal	Relatively high
5.9	Smoking increases the risk of female colon cancer	Low	Equivocal	Moderate
5.10	Smoking increases the risk of female rectal cancer	Low	Equivocal	Moderate
5.11	Smoking increases the risk of female diverticular disease	Low	Equivocal	Moderate
5.12	Smoking increases the risk of female colitis	Low	Equivocal	Moderate

including pancreatitis, pancreatic cancer, liver cancer, stomach cancer, upper gastrointestinal cancer, colon cancer, rectal cancer, diverticular disease, colitis (For summary of evidence, see [Supplementary material 1](#)). In this field, The quality of evidence and public demand for liver and upper gastrointestinal cancers

were high, which might be related to the higher incidence of these cancers. For such diseases that are closely related to people's lives, these core information can be used as the first choice in the health communication of tobacco control, and the factors about the unhealthy diet and inappropriate daily habits mentioned above need to be paid enough attention to. The specific summary of core information of female digestive disease is shown in [Table 8](#).

The correlation between smoking and risks of female diabetes

Two studies have shown that smoking increases the risk of diabetes in women, with results of 1.42 (95%: 1.19, 1.69) and 1.33 (95%: 1.26–1.41) relative risks of diabetes for current smokers respectively ([90, 91](#)) (For summary of evidence, see [Supplementary material 1](#)). The prevalence of type 2 diabetes (T2D) has gradually increased over the past three decades and has become a major global public health challenge. Given the high prevalence of smoking in many countries and the increasing burden of diabetes worldwide, reducing tobacco use should be prioritized as an important public health strategy that may contribute to the prevention and control of diabetes ([90](#)). This was also in line with a moderate public demand for core information in this area, but the quality and quantity of evidence was low ([Table 4](#)). This suggests that high-quality and sufficient evidence is urgently needed in this field to meet public health needs. The specific summary of core information of female diabetes is shown in [Table 5](#).

The correlation between smoking and risks of female rheumatoid arthritis

Rheumatoid arthritis (RA) is a major autoimmune disease and is typically characterized by chronic inflammation of the articulations and bone destruction ([92](#)). As the most common form of inflammatory arthritis, its worldwide prevalence is approximately 1%, with women at two to three times the risk of developing rheumatoid arthritis compared to men due to the effect of estrogen on the immune system. The cumulative adult prevalence is 3.6% for women and 1.7% for men ([93](#)). Two systematic reviews have shown that smoking increases the risks of rheumatoid arthritis in women ([94, 95](#)), and male smokers are at greater risk than female smoker ([95–97](#)) (For summary of evidence, see [Supplementary material 1](#)). But the results of different original articles were inconsistent. Whether smoking habits caused RA was not clear. Our study found that the quality of evidence, the degree of public demand and the results of expert assessments were relatively consistent and low in this area ([Table 5](#)). This result suggests to health communicators that core information in this field is less suitable for tobacco control health communication. The specific

summary of core information of female rheumatoid arthritis is shown in [Table 5](#).

Dissemination analysis of core information

Dissemination of core information should be individualized. Based on audience preferences survey, we conducted a dissemination analysis of core information to guide health communicators how to spread the core information to audiences.

Different levels of education, gender and age had an effect on the degree of need for core information ([Table 1](#) in [Supplementary material 2](#)). Among them, college students and undergraduates, women, and groups aged 26–45 were in greater demand. Most smokers were not only well educated but also aware of the dangers of smoking, however, they rarely received advice or help to quit ([98](#)). We suggest that middle-aged non-smoking women with higher education can be regarded as the main target for health communication workers to spread tobacco control core information. Because they can not only obtain more information about tobacco control for themselves and their families, but also play the role of supervision and persuasion.

Different occupations had different degrees of demand for core information, and the demand of medical workers was higher than that of non-medical workers, indicating that medical workers paid more attention to the impact of smoking on diseases ([Table 1](#) in [Supplementary material 2](#)). Because of the particularity of their occupations, medical staff paid more attention to health-related information than other occupations, especially for the information needs of smoking hazards. Studies have shown that health education and health promotion can effectively improve medical staff's awareness of the dangers of smoking and their support for comprehensive smoking bans in medical and health institutions. This suggests that it is necessary to increase tobacco control education for medical personnel, and at the same time encourage and drive more medical personnel to contribute to medical education, scientific research, and international cooperation related to tobacco harm.

The public with chronic diseases had a higher demand for core information than the public without chronic diseases ([Table 1](#) in [Supplementary material 2](#)). A large number of studies have shown that smoking is an important risk factor for the occurrence and death of various chronic non-communicable diseases, so people with these chronic diseases also paid more attention to the information on whether smoking control affected their health. In chronic disease management, the importance of smoking cessation-related health education was particularly important. It is recommended to increase the intensity of tobacco control health education among elderly

patients with chronic diseases, which is of great significance for the effective management of chronic diseases, curbing the progress and adverse outcomes of the disease, and improving the quality of life of patients.

Compared with smokers, non-smokers had a higher degree of demand, indicating that non-smokers were more concerned about the information that smoking was harmful to health ([Table 3](#) in [Supplementary material 2](#)). Our research also showed that the reason for the willingness to quit smoking among smokers was mainly "fear of getting sick." Therefore, strengthening publicity and education about the harm of smoking can help smokers generate their willingness to quit ([99](#)).

Additionally, core information can be explained in a simple, science-based way that is more appropriate to the general public. This coincides with the importance of using visuals, telling real stories and using familiar language, as highlighted by the WHO Strategic Communication Framework for Effective Communications ([100](#)). Furthermore, attention should be paid to multi-culture group differences in health communication and tailored and targeted health communication strategies ([22–24](#)) are adopted for different groups. And different population groups based on the characteristics of the recipients (education, age and occupation) in the same culture context also need diversified communications to ensure effectiveness ([101–103](#)). A WHO scoping review noted that arts-based approaches are particularly useful in programming for multicultural groups and for building trust around sensitive health topics ([104](#)).

Discussion

This study focused on women's health, with rigorous, public-demand-oriented and appropriate core information covering eight parts and proposing 35 core information to maximize coverage of the dangers of smoking on all systems in females and to provide guidance on the health communication for tobacco control. Of all the core information, the core information related to female cardiovascular system diseases, as well as liver cancer and upper gastrointestinal cancer is the preferred content for health communication of tobacco control. The quality of evidence for core information related to pregnant women and their infants, as well as diseases of reproductive system, respiratory system, and diabetes needs to be improved to meet high public demand. The core information related to mental disease is more suitable for dissemination to patients with mental illness than to the general public. Besides, dissemination of core information should be individualized.

Advantages of this study are as follows. Initially, it is the first systematic and comprehensive evidence-based core information for health communication in the field of tobacco control, which will be of great significance to improve the reliability of evidence. In the past, tobacco control in health communication was primarily composed of the media communication channels

(105, 106), whose reliability was often influenced by some large stakeholders, which led to frequent rumors in this field (7). Secondly, the formation of core information took into account the needs of the public with a reasonable distribution of age, gender, education level, occupation, smoking status and chronic disease status according to sociodemographic characteristics during the survey. This can ensure that the core information keeps “the common touch.” Thirdly, the expert assessment pre-dissemination content expert review from multidisciplinary expertise (29) was used and factors such as the quality of evidence, the degree of public demand, balance of importance of each evidence, equity, feasibility, acceptability were considered comprehensively so that core information is not only scientifically correct, but also suitable for dissemination.

However, this study has certain limitations. First, available evidences supporting this core information were actually weak due to ethical concerns (smoking is a detrimental factor and not suitable as an intervention), which contributed to a lack of large-scale randomized controlled trials (RCTs) and then led to scarcity of high quality evidence. Secondly, the public prevalence survey and expert assessment were mainly confined to the national conditions of China, which resulted in limitations in the scope of application. Thirdly, given that the overall number of smoking women was still less than that of men, related to specific diseases like rheumatoid arthritis, might be deviated from the objective reality.

For future perspectives, there are several important areas that need to be improved:

First, smoking and passive smoking are recognized as one of the main causes of cardiovascular diseases, and they are also independent risk factors for such diseases (21). Evidences show that the relationship between smoking and cardiovascular disease has received widespread attention and is of relatively high quality, recommendation and public need. Future investigations still require high-quality researches in this area.

Second, the relationship between smoking and respiratory disease is well known (21), as the respiratory system is the first system to be exposed to smoke and is susceptible to oxidative damage, resulting in chronic inflammatory responses and airway remodeling and, in severe cases, cancerous lesions. However, the available research lacks separate data on women and extensive empirical epidemiological evidence. Future development in this areas is of great value to assist tobacco control in women.

Third, future investigations on effects of smoking on pregnant women and their fetuses are of great importance to assist tobacco control in women due to greater susceptibility to tobacco among pregnant women and fetuses during pregnancy. At the same time, researches on the harm of second-hand smoke (in a passive way) to pregnant women and their fetuses are also worthy of attention. It suggests that future researches can form core information about

the effects of passive smoking on pregnant women and their fetuses.

Fourth, the current study focuses less attention on the effect of smoking on female mental diseases which is a huge burden on health in the world today (66, 67). As large-scale, prospective studies are actually lacking in this areas, further studies are required for more convincing evidence.

Fifth, core information concerning smoking on female rheumatoid arthritis was controversial and with low evidence and public need and weak recommendation. Future investigation in this field need to be more comprehensive, accurate and rigorous.

Sixth, tobacco control health communication strategies of core information of this guideline are also needed for more tailored and targeted for different development status, public literacy and age pattern.

Finally, future development of evidence-based core information of tobacco control for health communication can focus on the effectiveness of positive interventions on tobacco control, such as mobile health interventions; and include more high-quality and large-scale RCTs.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary material](#), further inquiries can be directed to the corresponding authors.

Author contributions

Draft writing: JL, Y-YH, X-LH, Y-BW, and X-ZJ. Draft revising and reviewing: Y-BW and X-ZJ. Conception and design: Y-BW, X-ZJ, JL, and C-XQ. Guideline registration and protocol writing: JL, C-XQ, and S-TW. Collecting and determining PICO questions: JL, Y-YH, H-JM, M-LC, and S-TW. GRADE assessment: JL and Y-YH. Audience value survey: X-JS and JL. Delphi expert consensus survey: JL, H-JM, Y-YH, Y-BW, and X-ZJ. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the Bloomberg Initiative to Reduce Tobacco Use(CHINA-25-07).

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/fpubh.2022.986430/full#supplementary-material>

References

1. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. (2020) 396:1223–49. doi: 10.1016/S0140-6736(20)30752-2
2. GBD 2019 Tobacco Collaborators. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019 [published correction appears in *Lancet*. *Lancet*. (2021) 397:2337–60. doi: 10.1016/S0140-6736(21)01169-7
3. Ezzati M, Lopez AD. Estimates of global mortality attributable to smoking in 2000. *Lancet*. (2003) 362:847–52. doi: 10.1016/S0140-6736(03)14338-3
4. Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr, Doll R. Mortality from smoking worldwide. *Br Med Bull*. (1996) 52:12–21. doi: 10.1093/oxfordjournals.bmb.a011519
5. Peto R, Lopez AD, Boreham J. Health effects of tobacco use: global estimates and projections. In: Slama K, editors. *Tobacco and Health*. Boston, MA: Springer. (1995). p. 109–20.
6. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. (2020) 396:1204–22. doi: 10.1016/S0140-6736(20)30925-9
7. Dai X, Gakidou E, Lopez AD. Evolution of the global smoking epidemic over the past half century: strengthening the evidence base for policy action. *Tob Control*. (2022) 31:129–37. doi: 10.1136/tobaccocontrol-2021-056535
8. Bolego C, Poli A, Paoletti R. Smoking and gender. *Cardiovasc Res*. (2002) 53:568–76. doi: 10.1016/S0008-6363(01)00520-X
9. Marom-Haham L, Shulman A. Cigarette smoking and hormones. *Curr Opin Obstet Gynecol*. (2016) 28:230–5. doi: 10.1097/GCO.0000000000000283
10. Hughes EG, Brennan BG. Does cigarette smoking impair natural or assisted fecundity? *Fertil Steril*. (1996) 66:679–89. doi: 10.1016/S0015-0282(16)58618-X
11. Mattison DR. The effects of smoking on fertility from gametogenesis to implantation. *Environ Res*. (1982) 28:410–33. doi: 10.1016/0013-9351(82)90139-6
12. Practice Committee of the American Society for Reproductive Medicine. Practice Committee of the American Society for Reproductive Medicine. Smoking and infertility: a committee opinion. *Fertil Steril*. (2018) 110:611–18. doi: 10.1016/j.fertnstert.2018.06.016
13. Malik A, Jeyaraj PA, Shankar A, Rath GK, Mukhopadhyay S, Kamal VK. Passive smoking and breast cancer—a suspicious link. *Asian Pac J Cancer Prev*. (2015) 16:5715–9. doi: 10.7314/APJCP.2015.16.14.5715
14. Tanaka K, Miyake Y, Hanioka T, Arakawa M. Active and passive smoking and prevalence of periodontal disease in young Japanese women. *J Periodontol Res*. (2013) 48:600–5. doi: 10.1111/jre.12044
15. Flor LS, Reitsma MB, Gupta V, Ng M, Gakidou E. The effects of tobacco control policies on global smoking prevalence. *Nat Med*. (2021) 27:239–43. doi: 10.1038/s41591-020-01210-8
16. van Mourik DA, Nagelhout GE, de Vries H, van den Putte B, Cummings KM, Borland R, et al. Quasi-experimentally examining the impact of introducing tobacco pictorial health warnings: Findings from the International Tobacco Control (ITC) 4C and Netherlands surveys in the Netherlands, Australia, Canada, United Kingdom, and the United States. *Drug Alcohol Depend*. (2020) 207:107818. doi: 10.1016/j.drugalcdep.2019.107818
17. Sutfin EL, Lazard AJ, Wagoner KG, King JL, Cornacchione Ross J, Wiseman KD, et al. Point-of-Sale health communication campaigns for cigarillos and waterpipe tobacco: effects and lessons learned from two cluster randomized trials. *Health Commun*. (2021) 15:1–12. doi: 10.1080/10410236.2021.1996910
18. Mackert M, Case K, Lazard A, Oh J, Hughes Wagner J, Hawk E, et al. Building a health communication brand for University of Texas System tobacco control. *J Am Coll Health*. (2019) 67:291–8. doi: 10.1080/07448481.2018.1469504
19. Duella CS. Communication is a determinant of public health: a media campaign for tobacco control in India. *BMJ*. (2013) 347:f6275. doi: 10.1136/bmj.f6275
20. Karletsos D, Hutchinson P, Leyton A, Meekers D. The effect of interpersonal communication in tobacco control campaigns: a longitudinal mediation analysis of a Ghanaian adolescent population. *Prev Med*. (2021) 142:106373. doi: 10.1016/j.ypmed.2020.106373
21. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet*. (2017) 389:1885–906. doi: 10.1016/S0140-6736(17)30819-X
22. Agrawal PK, Aruldas K, Khan ME. *Training Manual on Basic Monitoring and Evaluation of Social and Behavior Change Communication Health Programs*. New Delhi: Population Council. (2014).
23. Kreuter MW, Wray RJ. Tailored and targeted health communication: strategies for enhancing information relevance. *Am J Health Behav*. (2003) 27 (Suppl. 3):S227–32. doi: 10.5993/AJHB.27.1.s3.6
24. Noar S, Harrington N, Van Stee SK, Aldrich RS. Tailored health communication to change lifestyle behaviors. *Am J Lifestyle Med*. (2010) 5:112–22. doi: 10.1177/1559827610387255
25. World Health Organization. *WHO Handbook for Guideline Development*. World Health Organization. (2014).
26. Institute of Medicine (US) Committee to Advise the Public Health Service on Clinical Practice Guidelines. In: Field MJ, Lohr KN, editors. *Clinical Practice Guidelines: Directions for a New Program*. Washington (DC): National Academies Press (US). (1990).
27. Institute of Medicine. *Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Institute of Medicine. Clinical Practice Guidelines We Can Trust*. (2011).
28. Schünemann HJ, Wiercioch W, Etzeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 20: systematic development of a comprehensive checklist for a successful guideline enterprise. *CMAJ*. (2014) 186:E123–42. doi: 10.1503/cmaj.131237
29. Chen Y, Yang K, Marušić A, Qaseem A, Meerpohl JJ, Flottorp S, et al. RIGHT (Reporting Items for Practice Guidelines in Healthcare) Working Group. A reporting tool for practice guidelines in health care: the RIGHT statement. *Ann Intern Med*. (2017) 166:128–32. doi: 10.7326/M16-1565

30. WHO Global Report on Trends in Prevalence of Tobacco Use 2000-2025. Fourth Edition. Geneva: World Health Organization. (2021).
31. Sugawara Y, Tsuji I, Mizoue T, Inoue M, Sawada N, Matsuo K, et al. Research group for the development and evaluation of cancer prevention strategies in Japan. Cigarette smoking and cervical cancer risk: an evaluation based on a systematic review and meta-analysis among Japanese women. *Jpn J Clin Oncol.* (2019) 49:77–86. doi: 10.1093/jjco/hyy158
32. Kaderli R, Schnüriger B, Brügger LE. The impact of smoking on HPV infection and the development of anogenital warts. *Int J Colorectal Dis.* (2014) 29:899–908. doi: 10.1007/s00384-014-1922-y
33. Han YD, Wang XB, Cui NH, Zhang S, Wang C, Zheng F. Associations of P16INK4a promoter hypermethylation with squamous intra-epithelial lesion, cervical cancer and their clinicopathological features: a meta-analysis. *Oncotarget.* (2017) 8:1871–83. doi: 10.18632/oncotarget.12202
34. Macacu A, Autier P, Boniol M, Boyle P. Active and passive smoking and risk of breast cancer: a meta-analysis. *Breast Cancer Res Treat.* (2015) 154:213–24. doi: 10.1007/s10549-015-3628-4
35. Sollie M, Bille C. Smoking and mortality in women diagnosed with breast cancer: a systematic review with meta-analysis based on 400,944 breast cancer cases. *Gland Surg.* (2017) 6:385–93. doi: 10.21037/gs.2017.04.06
36. Jordan SJ, Whiteman DC, Purdie DM, Green AC, Webb PM. Does smoking increase risk of ovarian cancer? A systematic review. *Gynecol Oncol.* (2006) 103:1122–9. doi: 10.1016/j.ygyno.2006.08.012
37. Santucci C, Bosetti C, Peveri G, Liu X, Bagnardi V, Specchia C, et al. Dose-risk relationships between cigarette smoking and ovarian cancer histotypes: a comprehensive meta-analysis. *Cancer Causes Control.* (2019) 30:1023–32. doi: 10.1007/s10552-019-01198-8
38. Faber MT, Kjær SK, Dehlendorff C, Chang-Claude J, Andersen KK, Høgdall E, et al. Ovarian cancer association consortium. Cigarette smoking and risk of ovarian cancer: a pooled analysis of 21 case-control studies. *Cancer Causes Control.* (2013) 24:989–1004. doi: 10.1007/s10552-013-0174-4
39. Chen HL, Cai JY, Zha ML, Shen WQ. Prenatal smoking and postpartum depression: a meta-analysis. *J Psychosom Obstet Gynaecol.* (2019) 40:97–105. doi: 10.1080/0167482X.2017.1415881
40. Hunter A, Murray R, Asher L, Leonardi-Bee J. The effects of tobacco smoking, and prenatal tobacco smoke exposure, on risk of schizophrenia: a systematic review and meta-analysis. *Nicotine Tob Res.* (2020) 22:3–10. doi: 10.1093/ntr/nty160
41. Dong T, Hu W, Zhou X, Lin H, Lan L, Hang B, et al. Prenatal exposure to maternal smoking during pregnancy and attention-deficit/hyperactivity disorder in offspring: A meta-analysis. *Reprod Toxicol.* (2018) 76:63–70. doi: 10.1016/j.reprotox.2017.12.010
42. Lee LJ, Lupo PJ. Maternal smoking during pregnancy and the risk of congenital heart defects in offspring: a systematic review and metaanalysis. *Pediatr Cardiol.* (2013) 34:398–407. doi: 10.1007/s00246-012-0470-x
43. Dechanet C, Anahory T, Mathieu Daude JC, Quantin X, Reyftmann L, Hamamah S, et al. Effects of cigarette smoking on reproduction. *Hum Reprod Update.* (2011) 17:76–95. doi: 10.1093/humupd/dmq033
44. Shulman A, Ellenbogen A, Maymon R, Bahary C. Smoking out the oestrogens. *Hum Reprod.* (1990) 5:231–3. doi: 10.1093/oxfordjournals.humrep.a137077
45. Gan WQ, Man SF, Postma DS, Camp P, Sin DD. Female smokers beyond the perimenopausal period are at increased risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respir Res.* (2006) 7:52. doi: 10.1186/1465-9921-7-52
46. Patel BD, Luben RN, Welch AA, Bingham SA, Khaw KT, Day NE, et al. Childhood smoking is an independent risk factor for obstructive airways disease in women. *Thorax.* (2004) 59:682–6. doi: 10.1136/thx.2003.010215
47. Gold DR, Wang X, Wypij D, Speizer FE, Ware JH, Dockery DW. Effects of cigarette smoking on lung function in adolescent boys and girls. *N Engl J Med.* (1996) 335:931–7. doi: 10.1056/NEJM199609263351304
48. Hutchinson WL, Koenig W, Fröhlich M, Sund M, Lowe GD, Pepys MB. Immunoradiometric assay of circulating C-reactive protein: age-related values in the adult general population. *Clin Chem.* (2000) 46:934–8. doi: 10.1093/clinchem/46.7.934
49. Gan WQ, Man SF, Sin DD. The interactions between cigarette smoking and reduced lung function on systemic inflammation. *Chest.* (2005) 127:558–64. doi: 10.1378/chest.127.2.558
50. Tashkin DP, Altose MD, Blecker ER, Connett JE, Kanner RE, Lee WW, et al. The lung health study: airway responsiveness to inhaled methacholine in smokers with mild to moderate airflow limitation. The Lung Health Study Research Group. *Am Rev Respir Dis.* (1992) 145:301–10. doi: 10.1164/ajrccm/145.2_Pt_1.301
51. Leynaert B, Bousquet J, Henry C, Liard R, Neukirch F. Is bronchial hyperresponsiveness more frequent in women than in men? A population-based study. *Am J Respir Crit Care Med.* (1997) 156:1413–20. doi: 10.1164/ajrccm.156.5.9701060
52. Paoletti P, Carrozzi L, Viegi G, Modena P, Ballerin L, Di Pede F, et al. Distribution of bronchial responsiveness in a general population: effect of sex, age, smoking, and level of pulmonary function. *Am J Respir Crit Care Med.* (1995) 151:1770–7. doi: 10.1164/ajrccm.151.6.7767519
53. Baron JA, La Vecchia C, Levi F. The antiestrogenic effect of cigarette smoking in women. *Am J Obstet Gynecol.* (1990) 162:502–14. doi: 10.1016/0002-9378(90)90420-C
54. Skobeloff EM, Spivey WH, St Clair SS, Schoffstall JM. The influence of age and sex on asthma admissions. *JAMA.* (1992) 268:3437–40. doi: 10.1001/jama.1992.03490240045034
55. Hibbert ME, Couriel JM, Landau LI. Changes in lung, airway, and chest wall function in boys and girls between 8 and 12 yr. *J Appl Physiol Respir Environ Exerc Physiol.* (1984) 57:304–8. doi: 10.1152/jappl.1984.57.2.304
56. Merkus PJ, Borsboom GJ, Van Pelt W, Schrader PC, Van Houwelingen HC, Kerrebijn KE, et al. Growth of airways and air spaces in teenagers is related to sex but not to symptoms. *J Appl Physiol.* (1985). (1993) 75:2045–53. doi: 10.1152/jappl.1993.75.5.2045
57. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. *J Am Coll Cardiol.* (2004) 43:1731–7. doi: 10.1016/j.jacc.2003.12.047
58. Woodward M, Lam TH, Barzi F, Patel A, Gu D, Rodgers A, et al. Asia Pacific Cohort Studies Collaboration. Smoking, quitting, and the risk of cardiovascular disease among women and men in the Asia-Pacific region. *Int J Epidemiol.* (2005) 34:1036–45. doi: 10.1093/ije/dyi104
59. Hackshaw A, Morris JK, Boniface S, Tang JL, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. *BMJ.* (2018) 360:j5855. doi: 10.1136/bmj.j5855
60. Huxley RR, Woodward M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. *Lancet.* (2011) 378:1297–305. doi: 10.1016/S0140-6736(11)60781-2
61. Aune D, Schlesinger S, Norat T, Riboli E. Tobacco smoking and the risk of sudden cardiac death: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol.* (2018) 33:509–21. doi: 10.1007/s10654-017-0351-y
62. Peters SA, Huxley RR, Woodward M. Smoking as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 81 cohorts, including 3,980,359 individuals and 42,401 strokes. *Stroke.* (2013) 44:2821–8. doi: 10.1161/STROKEAHA.113.002342
63. Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, et al. Reducing the global burden of cardiovascular disease, part 1: the epidemiology and risk factors. *Circ Res.* (2017) 121:677–94. doi: 10.1161/CIRCRESAHA.117.308903
64. Thompson, Dewi H, Warburton DM. Lifestyle differences between smokers, ex-smokers and non-smokers, and implications for their health. *Psychol Health.* (1992) 7:311–21. doi: 10.1080/08870449208403160
65. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol.* (2012) 2:1143–211. doi: 10.1002/cphy.c110025
66. Vigo D, Thornicroft G, Atun R. Estimating the true global burden of mental illness. *Lancet Psychiatry.* (2016) 3:171–8. doi: 10.1016/S2215-0366(15)00505-2
67. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Prev Chronic Dis.* (2006) 3:A42.
68. Brown-Johnson CG, Cataldo JK, Orozco N, Lisha NE, Hickman NJ, 3rd, Prochaska JJ. Validity and reliability of the internalized stigma of smoking inventory: an exploration of shame, isolation, and discrimination in smokers with mental health diagnoses. *Am J Addict.* (2015) 24:410–8. doi: 10.1111/ajad.12215
69. Helman TJ, Headrick JP, Vider J, Peart JN, Stapelberg NJC. Sex-specific behavioral, neurobiological, and cardiovascular responses to chronic social stress in mice. *J Neurosci Res.* (2022) 100:2004–27. doi: 10.1002/jnr.25115
70. Durazzo TC, Mattsson N, Weiner MW. Alzheimer's disease neuroimaging initiative. smoking and increased Alzheimer's disease risk: a review of potential mechanisms. *Alzheimers Dement.* (2014) 10:S122–45. doi: 10.1016/j.jalz.2014.04.009
71. Zhong G, Wang Y, Zhang Y, Guo JJ, Zhao Y. Smoking is associated with an increased risk of dementia: a meta-analysis of prospective cohort studies with investigation of potential effect modifiers. *PLoS ONE.* (2015) 10:e0118333. doi: 10.1371/journal.pone.0118333

72. Hecht SS. Tobacco carcinogens, their biomarkers and tobacco-induced cancer. *Nat Rev Cancer*. (2003) 3:733–44. doi: 10.1038/nrc1190
73. Gherasim A, Arhire LI, Niță O, Popa AD, Graur M, Mihalache L. The relationship between lifestyle components and dietary patterns. *Proc Nutr Soc*. (2020) 79:311–23. doi: 10.1017/S0029665120006898
74. Zeka A, Gore R, Kriebel D. Effects of alcohol and tobacco on aerodigestive cancer risks: a meta-regression analysis. *Cancer Causes Control*. (2003) 14:897–906. doi: 10.1023/B:CACO.0000003854.34221.a8
75. Bagnardi V, Blangiardo M, La Vecchia C, Corrao G. Alcohol consumption and the risk of cancer: a meta-analysis. *Alcohol Res Health*. (2001) 25:263–70.
76. Andriulli A, Botteri E, Almasio PL, Vantini I, Uomo G, Maisonneuve P. Ad Hoc Committee of the Italian Association for the Study of the Pancreas. Smoking as a cofactor for causation of chronic pancreatitis: a meta-analysis. *Pancreas*. (2010) 39:1205–10. doi: 10.1097/MPA.0b013e3181df27c0
77. Ye X, Lu G, Huai J, Ding J. Impact of smoking on the risk of pancreatitis: a systematic review and meta-analysis. *PLoS ONE*. (2015) 10:e0124075. doi: 10.1371/journal.pone.0124075
78. Iodice S, Gandini S, Maisonneuve P, Lowenfels AB. Tobacco and the risk of pancreatic cancer: a review and meta-analysis. *Langenbecks Arch Surg*. (2008) 393:535–45. doi: 10.1007/s00423-007-0266-2
79. Lugo A, Peveri G, Bosetti C, Bagnardi V, Crippa A, Orsini N, et al. Strong excess risk of pancreatic cancer for low frequency and duration of cigarette smoking: a comprehensive review and meta-analysis. *Eur J Cancer*. (2018) 104:117–26. doi: 10.1016/j.ejca.2018.09.007
80. Ben QW, Liu J, Sun YW, Wang LF, Zou DW, Yuan YZ. Cigarette smoking and mortality in patients with pancreatic cancer: a systematic review and meta-analysis. *Pancreas*. (2019) 48:985–95. doi: 10.1097/MPA.0000000000001383
81. Lee YC, Cohet C, Yang YC, Stayner L, Hashibe M, Straif K. Meta-analysis of epidemiologic studies on cigarette smoking and liver cancer. *Int J Epidemiol*. (2009) 38:1497–511. doi: 10.1093/ije/dyp280
82. Pang Q, Qu K, Zhang J, Xu X, Liu S, Song S, et al. Cigarette smoking increases the risk of mortality from liver cancer: a clinical-based cohort and meta-analysis. *J Gastroenterol Hepatol*. (2015) 30:1450–60. doi: 10.1111/jgh.12990
83. Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P. Smoking and colorectal cancer: a meta-analysis. *JAMA*. (2008) 300:2765–78. doi: 10.1001/jama.2008.839
84. Tsoi KK, Pau CY, Wu WK, Chan FK, Griffiths S, Sung JJ. Cigarette smoking and the risk of colorectal cancer: a meta-analysis of prospective cohort studies. *Clin Gastroenterol Hepatol*. (2009) 7:682–88.e6885. doi: 10.1016/j.cgh.2009.02.016
85. Cheng J, Chen Y, Wang X, Wang J, Yan Z, Gong G, et al. Meta-analysis of prospective cohort studies of cigarette smoking and the incidence of colon and rectal cancers. *Eur J Cancer Prev*. (2015) 24:6–15. doi: 10.1097/CEJ.0000000000000011
86. Aune D, Sen A, Leitzmann MF, Tonstad S, Norat T, Vatten LJ. Tobacco smoking and the risk of diverticular disease - a systematic review and meta-analysis of prospective studies. *Colorectal Dis*. (2017) 19:621–33. doi: 10.1111/codi.13748
87. Ladeiras-Lopes R, Pereira AK, Nogueira A, Pinheiro-Torres T, Pinto I, Santos-Pereira R, et al. Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. *Cancer Causes Control*. (2008) 19:689–701. doi: 10.1007/s10552-008-9132-y
88. Ansary-Moghaddam A, Huxley RR, Lam TH, Woodward M. The risk of upper aero digestive tract cancer associated with smoking, with and without concurrent alcohol consumption. *Mt Sinai J Med*. (2009) 76:392–403. doi: 10.1002/msj.20125
89. Al Momani L, Balagani H, Alomari M, Gaddam S, Boonpherg B, Aasen T, et al. The association between smoking and both types of microscopic colitis: a systematic review and meta-analysis. *Arab J Gastroenterol*. (2020) 21:9–18. doi: 10.1016/j.ajg.2020.01.004
90. Pan A, Wang Y, Talaei M, Hu FB, Wu T. Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. (2015) 3:958–67. doi: 10.1016/S2213-8587(15)00316-2
91. Akter S, Goto A, Mizoue T. Smoking and the risk of type 2 diabetes in Japan: a systematic review and meta-analysis. *J Epidemiol*. (2017) 27:553–61. doi: 10.1016/j.je.2016.12.017
92. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet*. (2010) 376:1094–108. doi: 10.1016/S0140-6736(10)60826-4
93. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. *Nat Rev Dis Primers*. (2018) 4:18001. doi: 10.1038/nrdp.2018.1
94. Sugiyama D, Nishimura K, Tamaki K, Tsuji G, Nakazawa T, Morinobu A, et al. Impact of smoking as a risk factor for developing rheumatoid arthritis: a meta-analysis of observational studies. *Ann Rheum Dis*. (2010) 69:70–81. doi: 10.1136/ard.2008.096487
95. Stolt P, Källberg H, Lundberg I, Sjögren B, Klareskog L, Alfredsson L. EIRA study group. Silica exposure is associated with increased risk of developing rheumatoid arthritis: results from the Swedish EIRA study. *Ann Rheum Dis*. (2005) 62:582–6. doi: 10.1136/ard.2004.022053
96. Rayman M, Callaghan A. *Nutrition and Arthritis*. Oxford, UK: Blackwell Publishing. (2006). doi: 10.1002/9780470775011
97. Lee EH, Shin SH, Jeong GC. Smoking awareness and intention to quit smoking in smoking female workers: secondary data analysis. *Int J Environ Res Public Health*. (2022) 19:2841. doi: 10.3390/ijerph19052841
98. Eccles M, Mason J, Freemantle N. Developing valid cost effectiveness guidelines: a methodological report from the north of England evidence based guideline development project. *Qual Health Care*. (2000) 9:127–32. doi: 10.1136/qhc.9.2.127
99. World Health Organization. *The Strategic Communications Framework for Effective Communications*. (2019). <https://www.who.int/mediacentre/communication-framework.pdf> Website (accessed January 13, 2020).
100. Institute of Medicine (US) Committee on Communication for Behavior Change in the 21st Century: improving the health of diverse populations. *Speaking of Health: Assessing Health Communication Strategies for Diverse Populations*. Washington (DC): National Academies Press (US). (2002).
101. Parker RM, Gazmararian JA. Health literacy: essential for health communication. *J Health Commun*. (2003) 8 (Suppl 1):116–8. doi: 10.1080/713851963
102. Maibach EW, Maxfield A, Ladin K, Slater M. Translating health psychology into effective health communication: the American Healthstyles audience segmentation project. *J Health Psychol*. (1996) 1:261–77. doi: 10.1177/135910539600100302
103. Fancourt D, Finn S. *What is the Evidence on the Role of the Arts in Improving Health and Well-Being? A Scoping Review*. Copenhagen: WHO Regional Office for Europe. (2019).
104. Davis RM. *The Role of the Media in Promoting and Reducing Tobacco Use: Executive Summary*. US Department of Health and Human Services, National Institutes of Health, National Cancer Institute. (2008).
105. Li L, Fenghua T, Qin T, Yubo L, Yan C. Application of new media on health communication. *Chin J Health Educat*. (2013) 29:94–5.



OPEN ACCESS

EDITED BY
Sunjoo Kang,
Yonsei University, South Korea

REVIEWED BY
Deborah L. Billings,
University of South Carolina,
United States
Salvatore Giovanni Vitale,
University of Messina, Italy

*CORRESPONDENCE
Natnael Atnafu Gebeyehu
jossyatnafu2020@gmail.com

SPECIALTY SECTION
This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 27 June 2022
ACCEPTED 21 November 2022
PUBLISHED 06 December 2022

CITATION
Gebeyehu NA, Tegegne KD, Biset G,
Sewuyew DA, Alemu BW and
Yitayew AM (2022) Discontinuation of
long acting reversible contraceptive
use and its determinants among
women in Ethiopia: Systematic review
and meta-analysis.
Front. Public Health 10:979231.
doi: 10.3389/fpubh.2022.979231

COPYRIGHT
© 2022 Gebeyehu, Tegegne, Biset,
Sewuyew, Alemu and Yitayew. 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.

Discontinuation of long acting reversible contraceptive use and its determinants among women in Ethiopia: Systematic review and meta-analysis

Natnael Atnafu Gebeyehu^{1*}, Kirubel Dagnaw Tegegne²,
Gebyaw Biset³, Dagne Addisu Sewuyew⁴,
Biresaw Wassihun Alemu⁵ and Alemker Mola Yitayew⁶

¹Department of Midwifery, College of Medicine and Health Science, Wolaita Sodo University, Sodo, Ethiopia, ²Department of Comprehensive Nursing, College of Medicine and Health Science, Wollo University, Dessie, Ethiopia, ³Department of Pediatrics and Child Health Nursing, College of Medicine and Health Science, Wollo University, Dessie, Ethiopia, ⁴Department of Midwifery, College of Medicine and Health Science, Debre Tabor University, Debre Tabor, Ethiopia, ⁵Department of Midwifery, College of Medicine and Health Science, Injbara University, Injbara, Ethiopia, ⁶School of Medicine, College of Medicine and Health Science, Wolaita Sodo University, Wolaita, Ethiopia

Introduction: Contraception discontinuation is a major public health issue that leads to unwanted pregnancies and unsafe abortions. Therefore, this systematic review and meta-analysis aimed to estimate discontinuation of contraceptives and its determinants in Ethiopia.

Methods: PubMed, Google Scholar, Scopus, Science Direct, and Addis Ababa University online library were searched. Data were extracted using Microsoft Excel and analyzed using STATA statistical software (v. 14). Publication bias was checked by forest plot, Begg's rank test, and Egger's regression test. To look for heterogeneity, I^2 was computed, and an overall estimated analysis was carried out. Subgroup analysis was done by region, study setting, and publication. The pooled odds ratio for associated factors was also computed.

Results: Out of 654 studies assessed, 20 met our criteria and were included in the study. The total number of study participants was 8,780. The pooled prevalence of discontinuation of long acting reversible contraceptive use was 36.94% (95% CI: 28.547–45.326). According to sub-group analysis, Amhara region (45%) and institution-based studies (47.9%) had the highest prevalence. The most common reason for contraceptive discontinuation was negative side effect (42.3%).

Women experienced side effects (AOR = 2.833; 95% CI: 2.005–4.003), didn't receive counseling on side effects (AOR = 2.417; 95% CI: 1.591–3.672), didn't appoint follow up (AOR = 2.820; 95% CI: 2.048–3.881), dissatisfied with the given service (AOR = 5.156; 95% CI: 3.644–7.296), and a desire to be pregnant (AOR = 2.366; 95% CI: 1.760–3.182) were predictors of discontinuation of contraceptives.

Conclusion: In Ethiopia, the pooled prevalence of long acting contraceptive discontinuation was high. Side effects, not being informed about side effects, dissatisfaction with the provided service, no insertion follow-up, and a desire to become pregnant were all associated factors. Healthcare professionals should

focus on the client's reproductive goals, proper management of side effects, counseling, and post-insertion visits.

Systematic review registration: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022347860, identifier CRD42022347860.

KEYWORDS

contraceptive device, contraceptive agents, birth control, long acting, family planning, discontinuation, long acting contraceptive, Ethiopia

Introduction

Reduced maternal mortality and universal access to reproductive health care are both improved by family planning (1, 2). As a result, it contributes to a 44% reduction in maternal mortality and a 21% reduction in deaths among children under the age of five (3). Long-acting reversible contraceptives include copper intrauterine devices and hormonal implants (4). In the world, 15% of women use long-acting reversible contraception (5). However, just 3% of women in Sub-Saharan Africa use long acting reversible contraception on a regular basis (6).

Even though the use of long-acting reversible contraception is improving, discontinuation is becoming to be a serious issue. Within a year of insertion, 20% of women in low-income countries discontinue using long acting reversible contraceptive methods (7). When women who “begin a contraceptive technique and cease it for any reason while still at risk of becoming pregnant,” this is known as contraceptive discontinuation (8). Contraception use, fertility, unexpected pregnancies, induced abortions, and miscarriages are all affected (9–11).

There has been a noticeable shift from an emphasis on “adopters” to a concern over “discontinuers” in the predictors of contraceptive ever-use across strategies, as per earlier studies (8, 12). Family planning programs would therefore be better off focusing on maintaining current users than on attracting new ones in order to avoid contraceptive discontinuation. Discontinuation can occur for a number of reasons, but the most common one is side effects that arise while in an emergency (8).

In Ethiopia, providing a long-acting form of family planning is a free but highly effective method of preventing unintended pregnancies (13). Cramping and changes in bleeding patterns are commonly reported as reasons for removal of the intrauterine device and implant, with 6–17% of long-acting reversible contraceptive discontinuation occurring between 6 and 12 months (14).

Long-acting contraceptives are discontinued, which leads to unintended pregnancy, unwanted births, and abortion, all of which are detrimental to women's health. Every year, one-third

of the 182 million pregnancies worldwide are unplanned, resulting in larger families, higher fertility, and social, economic, and physical problems (15). Evidence showed that after 3 months of use, 40% of women in Egypt, 51% in Kenya, 73% in Malawi, 56% in United Republic of Tanzania, and 47% in Zimbabwe were at risk of conception (10). By 3 years of use, 45% of intrauterine devices and 61% of implants had been discontinued in Ethiopia (16).

The primary goal of contraception is to avoid unwanted or untimely pregnancies (17). As a result, effective contraception might save 54 million unintended pregnancies, 79,000 maternal deaths, and one million baby deaths per year (18). In contrast, Ethiopia has one of the world's highest maternal death rates, with 412 per 100,000 live births (19). To address this, Ethiopia's Minister of Health outsourced long-acting family planning services to Health Extension Workers at the health post level (20).

Despite the fact that various primary studies have documented the proportion of long-acting contraceptive discontinuation in Ethiopia, there is no data at the country level. Therefore, the purpose of this systematic review and meta-analysis was to estimate the proportion of discontinued of long acting contraceptives and associated factors in Ethiopia. The results of this study will give family planning providers and other stakeholders the fundamental information they need to assist and manage women's discontinuation of long acting reversible contraception.

Methods

Reporting

This systematic review and meta-analysis study was conducted to determine cause, magnitude and its determinant of discontinuation of long acting reversible contraceptives in Ethiopia using the standard PRISMA checklist guideline (21) (Additional file 1). The review protocol was registered with the international prospective register of systematic review (PROSPERO) as number CRD42022347860.

Search strategy

International online databases (Pub Med, Science Direct, Scopus, and Google Scholar) were used to search articles on the prevalence of discontinuation of long acting reversible contraceptives and determinant's. We also retrieved gray literature from Addis Ababa University's online research institutional repository. The search string was established using "AND" and "OR" Boolean operators. The following core search terms and phrases with Boolean operators were used to search related articles: (((Discontinuation) OR ("Discontinuation" OR "Early removal")) AND Long acting contraception) OR ("Long acting contraception" OR "Implants" OR "Implanon" OR "Jadelle" OR "Intrauterine contraceptive device" OR "Contraceptive" OR "Family planning" OR "Contraceptive device" OR "Contraceptive agent" OR "Birth control device")) AND Ethiopia. Search terms were based on PICO principles to retrieve relevant articles through the databases mentioned above. The search period covered studies conducted from 2010 to 2021 and published from 2015 to 2022 from April 1, 2022, to May 10, 2022.

Outcome measurement

Long acting reversible contraceptive methods

Contraceptive methods which serve as 3–10 years but can be removed at any time; only implants and IUCD (22).

Discontinuation of long-acting reversible contraceptives

Initiating and stopping long-acting reversible contraceptives before the end of the prescribed period due to a method difficulty (23).

Inclusion and exclusion criteria

Only English language papers, including published and unpublished studies with full text available for search, and studies that took place in Ethiopia were included in this meta-analysis. This systematic review and meta-analysis excluded research that used duplicated sources, qualitative studies from developed nations, and articles without full text.

Quality assessment

Two authors (NAG and KDT) independently appraised the standard of the studies using the Joanna Briggs Institute (JBI) standardized quality appraisal checklist (24). The disagreement raised during the quality assessment was resolved through

a discussion led by the third author (BWA). Finally, the argument was solved and reached with an agreement. The critical analysis checklist has eight parameters with yes, no, unclear, and not applicable options. The parameters involve the following questions:

- (1) Where were the criteria for inclusion in the sample clearly defined?
- (2) Were the study subjects and, therefore, the setting described in detail?
- (3) Was the exposure measured result validly and reliably?
- (4) Were the main objective and standard criteria used to measure the event?
- (5) Were confounding factors identified?
- (6) Were strategies to affect confounding factors stated?
- (7) Were the results measured indeed and dependably? and
- (8) Was the statistical analysis suitable?. Studies were considered low risk when they scored 50% and above on the quality assessment indicators, as reported in [Additional File 2](#).

Risk of bias assessment

Two authors (NAG and BWA) independently assessed included studies for risk of bias through the bias assessment tool developed by Hoy et al. (25), consisting of ten items that assess four domains of bias and internal and external validity. Any disagreement raised during the risk of bias assessment was resolved through a discussion led by DS. Finally, the argument was solved and reached with an agreement. The first four items (items 1–4) evaluate the presence of selection bias, non-response bias, and external validity. The other six items (items 5–10) assess the presence of measuring the bias, analysis-related bias, and internal validity. Therefore, studies that received "yes" for eight or more of the ten questions were classified as "low risk of bias." If studies that received "yes" for six to seven of the ten questions were classified as "moderate risk" whereas studies that received "yes" for five or fewer of the ten questions were classified as 'high risk' as reported in a [Additional File 3](#).

Data extraction

Microsoft Excel spreadsheet (2016) and STATA version 14 software were utilized for data extraction and analysis. Two authors (NAG and KDT) independently extracted all relevant data using a standardized Joanna Briggs Institute data extraction format. The disagreement raised during data extraction was resolved through a discussion led by the BA. Finally, the argument was solved and reached with an agreement. The data automation tool was not used due to this study's absence of the paper form (manual data). The name of the first author,

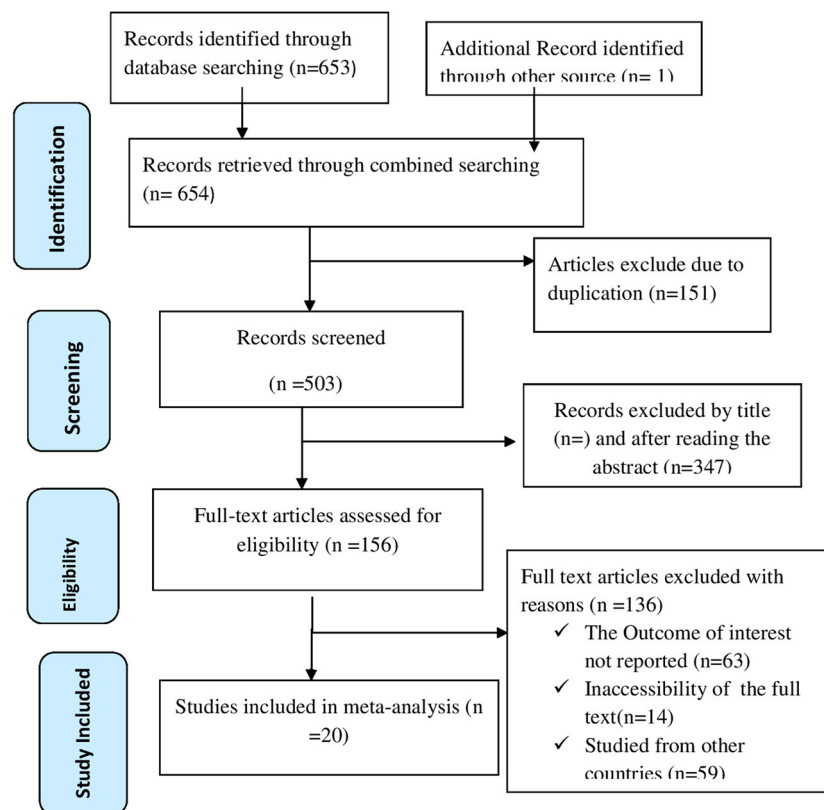


FIGURE 1
PRISMA flow chart displays the article selection process for discontinuation of long acting reversible contraceptives in Ethiopia.

year of publication, study region, study setting, study design, the prevalence of knowledge, attitude, practice, sample size, and quality of each paper was extracted.

Data analysis

After extracting all relevant findings in a micro-soft excel spreadsheet, the data were exported to STATA software version 14 for analysis. The pooled prevalence of unintended pregnancy was computed using a 95% confidence interval. Publication bias was checked by funnel plot and more objectively through Begg and Egger's regression tests, with $P < 0.05$ indicating potential publication bias. The presence of between-study heterogeneity was checked by using the Cochrane Q statistic. This heterogeneity between studies was quantified using I^2 , in which a value of 0, 25, 50, and 75% represented no, low, medium, and high heterogeneity, respectively. A forest plot was used to visually assess the presence of heterogeneity, which presented at a high-level random-effect model was used for analysis to estimate the overall prevalence of knowledge, attitude, and practice of exclusive breastfeeding. Subgroup analysis was done

by study setting, study design, study region, year of insertion and cause of discontinuation. Sensitivity analysis was executed to see the effect of a single study on the overall prevalence of the meta-analysis estimate. The findings of the study were presented in the form of text, tables, and figures.

Results

Search findings and study characteristics

Through online search engines such as PubMed, Scopus, Google Scholar, Science direct, and online research repository home, 654 articles were found using a search strategy on discontinuation of long acting reversible contraceptive methods in Ethiopia. There were 503 studies left after duplicates were deleted. After then, the remaining 503 studies were evaluated based on their entire titles and abstracts. As a result, 156 full-text articles were assessed for eligibility criteria, with 136 studies being excluded due to various factors. Finally, for this systematic review and meta-analysis study, 20 publications (23, 26–44) were used as presented by PRISMA diagram (Figure 1).

TABLE 1 Characteristics of the included studies in the systematic review and meta-analysis for the prevalence of discontinuation long acting reversible contraception in Ethiopia 2022.

References	Region	Study setting	Study design	Sample size	Cause	Prevalence	quality
Dagnew et al. (26)	Amhara	Institutional	cross-sectional	527	NR	37	Low-risk
Nageso and Gebretsadik (27)	SNNPR	Community	Cross-sectional	683	Side effect	23.4	Low-risk
Siyoun et al. (27)	Amhara	Community	Cross-sectional	314	Menstrual problem	40.5	Low-risk
Wondie et al. (29)	Amhara	Community	Cross-sectional	312	Side effect	16.7	Low-risk
Melkamu et al. (30)	Amhara	Institutional	Cross-sectional	499	Side effect	65	Low-risk
Weldekidan et al. (31)	SNNPR	Community	Cross-sectional	222	Menstrual problem	22.5	Low-risk
Gaenamo (32)	SNNPR	Institutional	Cohort	473	Desire of pregnancy	38.4	Low-risk
Abebe et al. (23)	SNNPR	Institutional	Cross-sectional	442	Menstrual problem	56.6	Low-risk
Obsu et al. (33)	Oromia	Community	Cross-sectional	360	Side effect	42	Low-risk
Mesha et al. (34)	SNNPR	Community	Cross-sectional	430	NR	34	Low-risk
Habte et al. (35)	SNNPR	Institutional	Cohort	502	Side effect	40.5	Low-risk
Amare and Reda (36)	SNNPR	institutional	Cross-sectional	351	Menstrual problem	49.3	Low-risk
Nega et al. (37)	SNNPR	Community	Cross-sectional	475	Side effect	23.2	Low-risk
Tesfaye et al. (38)	Oromia	Community	Cross-sectional	430	NR	19.3	Low-risk
Geja et al. (39)	SNNPR	Community	Cross-sectional	429	Desire of pregnancy	22.4	Low-risk
Tolesa et al. (44)	SNNPR	Institution	Cross-sectional	1,050	Side effect	69.8	Low-risk
Abraha et al. (40)	Tigray	Institutional	Cohort	413	Side effect	18.2	Low-risk
Gebrekidan et al. (42)	Tigray	Institutional	Cross-sectional	229	Desire of pregnancy	38	Low-risk
Birhane (43)	Tigray	Community	Cross-sectional	224	Health concern	16	Low-risk
Yilkal (41)	Amhara	Institutional	Cross-sectional	415	Side effect	66	Low-risk

The cross-sectional study type was used in seventeen studies, whereas the retrospective cohort study approach was used in three. Both community and institutional studies were equally represented (10 studies in each). Nine studies conducted in Southern Nations Nationalists and Peoples Region (23, 27, 31, 32, 34–37, 39), five in Amhara (26, 28–30, 41), three in Tigray (40, 42, 43), and three in Oromia (33, 38, 44). The sample sizes ranged from 222 to 1050. The prevalence of discontinued of long acting contraceptive method ranged from 16 to 69.8. All of the studies were evaluated using the Joanna Briggs Institute (JBI) quality appraisal checklist, and all of them were found to be low risk (Table 1).

Meta-analysis

Prevalence of discontinuation of long acting contraceptive methods in Ethiopia

The overall burden of discontinuation of long acting contraceptives method is presented with a forest plot (Figure 2). Therefore, the national pooled estimate of discontinuation of long acting contraceptive methods in Ethiopia was 36.94% (95% CI: 28.547–45.326; $I^2 = 98.7\%$, $P < 0.001$).

Sub-group analysis

The sub-group analysis was done based on study region, setting, cause of discontinuation, year of insertion and study design. The Amhara region had the highest rate of discontinuation of long-acting contraceptive methods (45%), whereas Oromia region had the lowest rate (30.6%). Institutional studies (47.9%) found a greater rate of long-acting contraceptive methods discontinuation than community-based research (25.9%). In terms of study design, cross-sectional studies (37.7%) revealed a higher rate of long-acting family planning method discontinuation than cohort studies (32.3%). On the other hand, side effects were cited as a main reason for the discontinuation of long-acting family planning methods (42.3%). Within three years, the highest rate of discontinuation of long-acting contraceptive methods (48.9%) was found (Table 2).

Leave-one-out-sensitivity analysis

A leave-one-out sensitivity analysis was carried out to detect the effect of each study on the overall prevalence of discontinuation of long acting contraceptive methods by

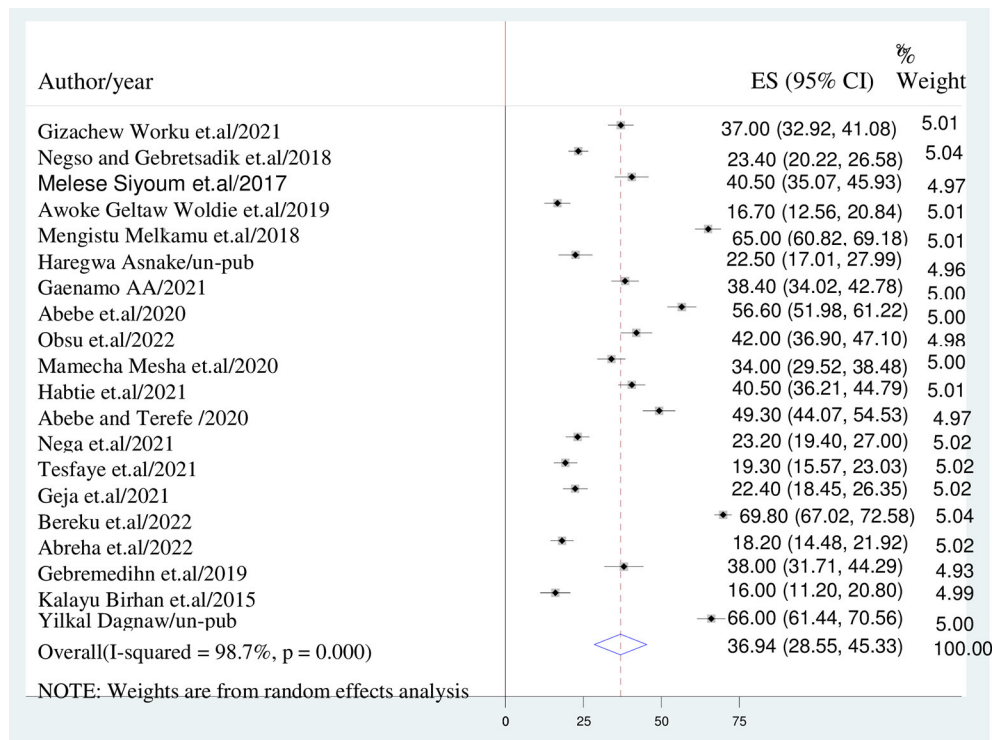


FIGURE 2
Forest plot displaying of discontinuation of long acting reversible contraceptives.

TABLE 2 The overall estimated of discontinuation of long acting reversible contraceptive in Ethiopia, 95% CI, and heterogeneity estimate with a *p*-value for sub-group analysis.

Variables	Characteristics	Pooled estimate of LARCs 95% CI	I ² (P-value)
Region	SNNPR	38.020% (25.995–50.045)	98.9% (0.000)
	Amhara	45.036% (26.098–63.975)	98.8% (0.000)
	Tigray	36.937% (28.547–45.326)	94.2% (0.000)
	Oromia	30.581% (28.336–52.826)	98% (0.007)
Study setting	Institutional	47.897% (36.365–59.429)	98.7% (0.000)
	Community	25.891% (20.739–31.043)	93.2% (0.000)
Study design	Cross-sectional	37.748% (28.153–47.343)	98.9% (0.000)
	Cohort	32.330(17.731– 46.929)	97.3% (0.000)
Cause	Side effect	42.269% (27.869–56.669)	99.3% (0.000)
	Menstrual problem	40.529% (25.345–55.713)	6.8% (0.000)
	Desire for pregnancy	32.812% (21.491–44.132)	94.1% (0.000)
	Health concern	16% (28.547–45.326)	0.000(0.000)
Year of use	Within 1 year	29.518% (21.744–37.292)	97.6% (0.000)
	within 2 year	47.642% (28.547–45.326)	89.9% (0.000)
	Within 3 year	48.885% (39.691–58.079)	99.1% (0.000)

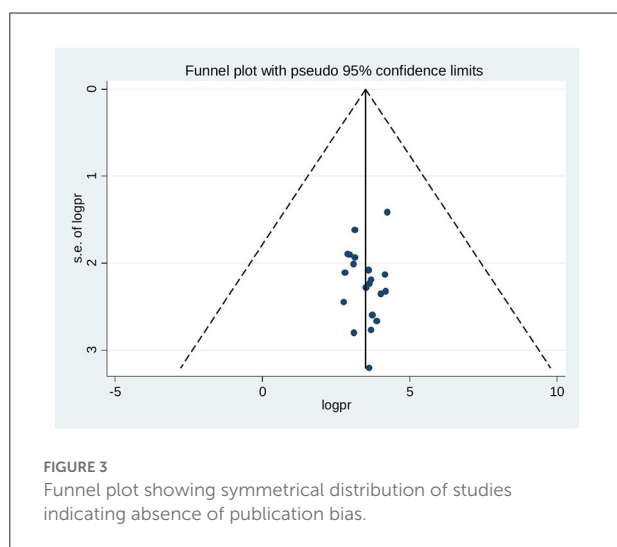
excluding one study at a time. As a result, studies omitted at a time did not show a significant change on the overall prevalence of a discontinuation of long acting contraceptive method (Table 3).

Publication bias

The funnel plot was assessed for asymmetry distribution of discontinuation of long acting reversible contraceptives by

TABLE 3 The pooled prevalence of discontinuation of long acting reversible contraceptives in Ethiopia when one study omitted from the analysis a step at a time 2022.

Study omitted	Pooled estimate	95% CI
Dagnew et al. (26)	36.934	28.075–45.793
Nageso and Gebretsadik (27)	37.655	28.888–46.421
Siyoun et al. (27)	36.751	28.004–45.497
Wondie et al. (29)	38.004	29.456–46.552
Melkamu et al. (30)	35.457	27.133–43.780
Weldekidan et al. (31)	37.691	29.030–46.352
Gaenamo (32)	36.860	28.034–45.686
Abebe et al. (23)	35.903	27.299–44.507
Obsu et al. (33)	36.671	7.911–45.432
Mesha et al. (34)	37.091	28.282–45.902
Habte et al. (35)	36.7492	27.919–45.579
Amare and Reda (36)	36.290	27.587–44.993
Nega et al. (37)	37.663	28.938–46.388
Tesfaye et al. (38)	37.869	29.254–46.485
Geja et al. (39)	37.705	29.005–46.404
Tolesa et al. (44)	35.182	28.022–42.342
Abraha et al. (40)	37.928	29.350–46.506
Gebrekidan et al. (42)	36.882	28.169–45.594
Birhane (43)	38.036	29.482–46.590
Yilkal (41)	35.408	27.065–43.751



visual inspection (Figure 3). The presence of publication bias was also assessed by Egger's regression test p -value of 0.875 and Begg's rank correlation test of p -value 0.230 with no evidence of publication bias.

Factors associated with discontinuation of long acting reversible contraceptive methods in Ethiopia

In this study, women experienced side effect of long acting contraceptive methods had higher odds of family planning than their counter parts (AOR = 2.833; 95% CI: 2.005–4.003), I^2 : 67.1%, P = 0.000 (Figure 4). In addition, the odds of having discontinuation of long acting contraceptives among mothers who didn't receive counseling on side effects was 2.4 times than their counter parts (AOR = 2.417; 95% CI: 1.591–3.672), I^2 : 69.1%, P = 0.000 (Figure 5).

Women who had no follow up visit after post-insertion of long acting contraception were 2.8 (AOR = 2.820; 95% CI: 2.048–3.881), I^2 = 0.0%, P = 0.000) times more likely to discontinue the method than mothers attending follow up visit (Figure 6).

The chance of discontinuation of long acting contraceptive method was 5 times (AOR = 5.156; 95% CI :3.644–7.296), I^2 = 0.0%, P = 0.000) among mothers didn't satisfy with services provided than those satisfied by service provision (Figure 7).

Women who had a desire of pregnancy were 2.4 (AOR = 2.366; 95% CI: 1.760–3.182), I^2 = 0.0%, P = 0.000) times more likely to discontinue the method than women who had no desire of pregnancy (Figure 8).

Discussion

The purpose of this systematic review and meta-analysis was to determine the magnitude of long-acting contraceptive discontinuation and its determinants among Ethiopian women. As a result, the overall prevalence of long-acting contraceptive discontinuation in this study was 36.94 % (95% CI: 28.547–45.326). The current study's findings are higher than those of studies conducted in Malaysia (22.86 %) (45), Nigeria (26.1%) (46), Egypt (26%) (47), a multicenter investigation in nine other countries (20%) (48), and meta-analysis study by Adal (7) (20 %). The possible explanation might be due to the difference in the composition of respondents as most of these studies are done by focusing on the rural population and time gap between studies. For example, the above mentioned meta-analysis done by Girum T. includes articles published from 1997 to 2017.

In contrast, the current study's findings are lower than those of research conducted in the Netherlands (47%) (49) and Australia (60%) (50). The time gap between the study and the attention given to the provision of long-acting contraception could be the cause of this discrepancy. This has been supported by the Ethiopian government's adoption of a health extension program to raise awareness and facilitate long-acting contraceptive availability at health post level in the community, which has a favorable impact on discontinuation rates (20, 51).

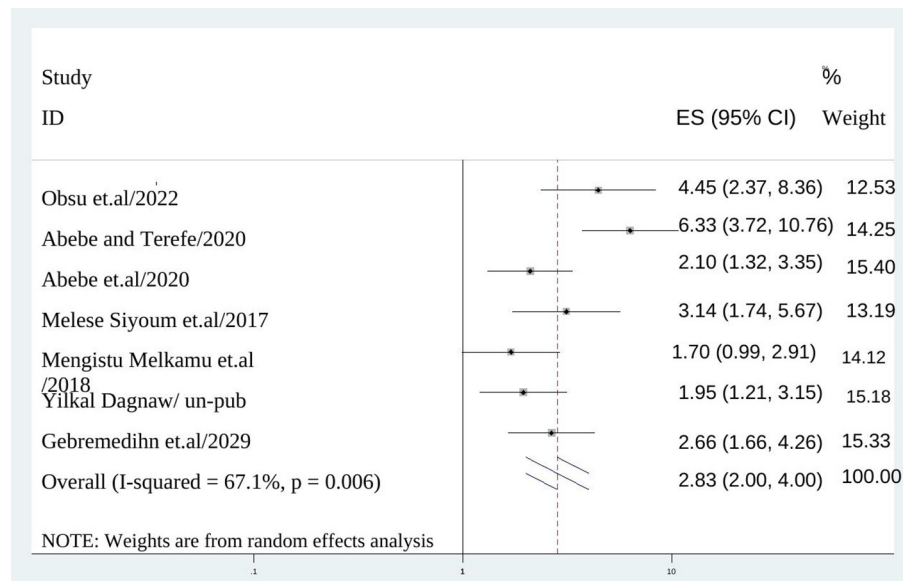


FIGURE 4

The association between experiencing side effects and discontinuation of long acting reversible contraception.

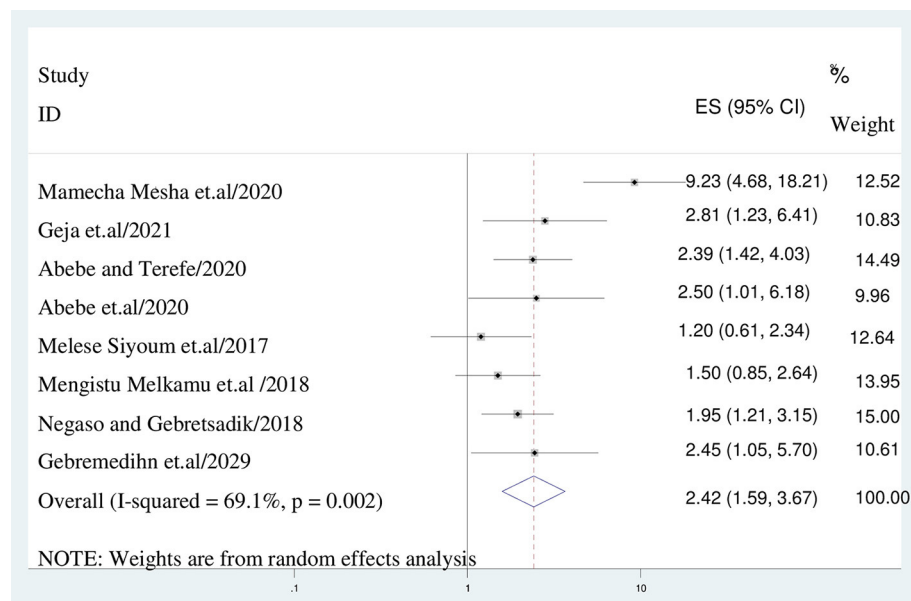


FIGURE 5

The association between lack of counseling on side effects and discontinuation of long acting reversible contraception.

Sub-group analysis was done based on study region, setting, design, year of insertion and reason of discontinuation of long acting contraceptive methods. As a result, the Amhara region had a higher rate of contraceptive discontinuation (45%) than the Oromia region (35.6%). This could be due to regional socio-cultural and awareness differences.

The discontinuation rates of institutional-based studies (47.9%) are greater than those of community-based studies (25.9%). It could be because mothers in institutional based research are sufficiently informed of their right to discontinue a method if they get pregnant or unsatisfied with a service.

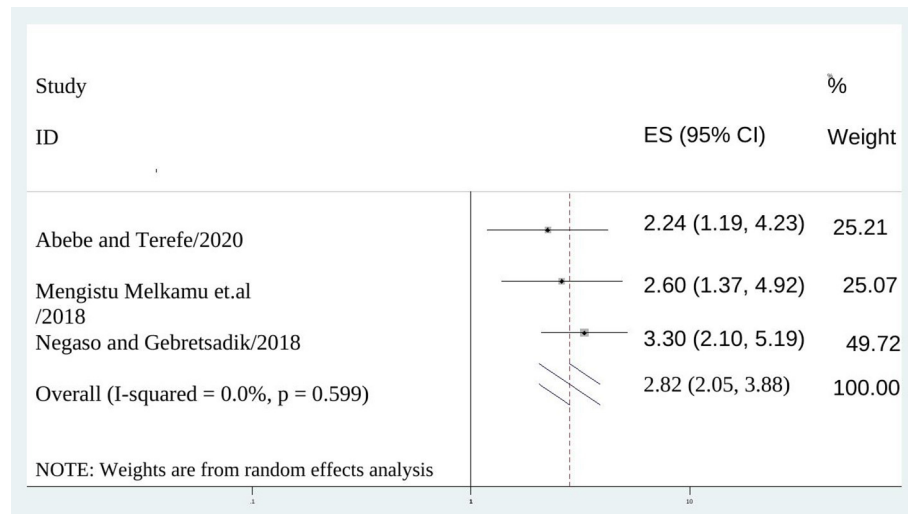


FIGURE 6

The association between not scheduled for follow up and discontinuation of long acting reversible contraception.

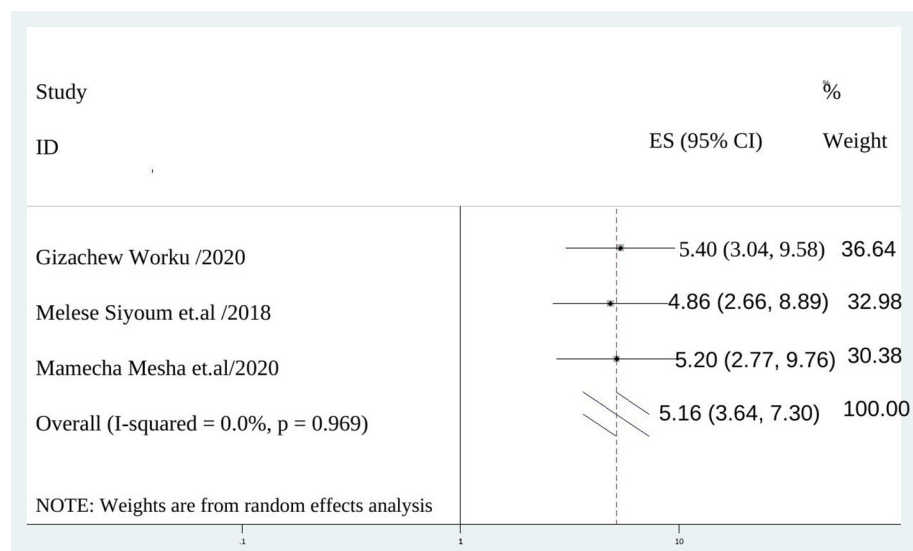


FIGURE 7

The association between not satisfied with provided service and discontinuation of long acting reversible contraception.

The pooled prevalence of long-acting contraceptive discontinuation based on study design also showed significant difference, with 37.7% for cross-sectional studies and 32.3% for cohort studies, respectively. Indeed, cross-sectional studies determine prevalence rather than cohort studies, which identify and quantify risks. More evidence is needed, to the best of the researcher's knowledge, to justify this statistical discrepancy.

Side effects were indicated as a significant cause for discontinuing reversible long-acting contraceptives in the current study, which was supported by previous studies

in Port Harcourt (7, 52). This could be due to women's intolerance of modest side effects from reversible long-acting contraceptive methods.

In this study, the proportion of discontinuation rate within the first year of insertion was 29.5 percent, which is higher than studies conducted in 20% of women in Adal (7), Nigeria (8%) (53), Spain (9%) (54), 14 developing countries (13.2%) (55), and Senegal (6.3%) (56). However, this result is lower than that of a research conducted in South Africa (96.3%) (57). The above discrepancy could be attributed to a lack of

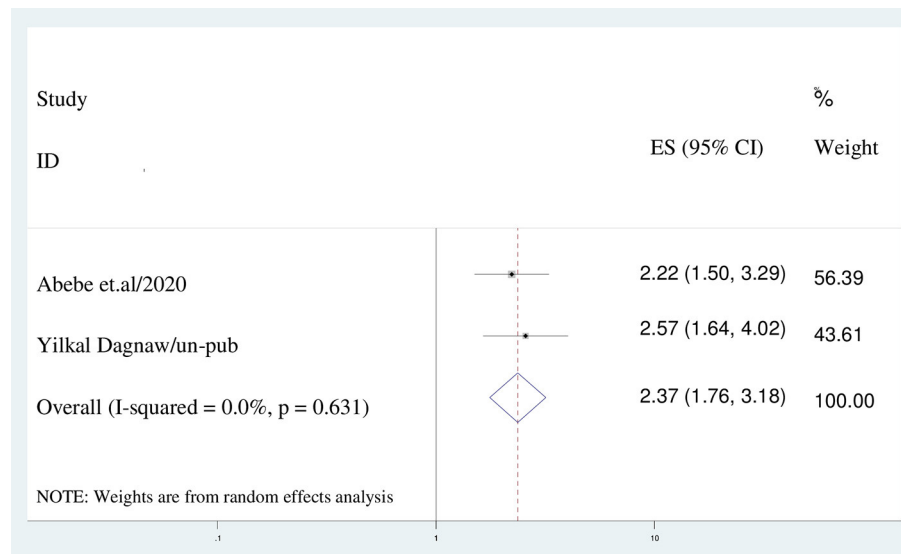


FIGURE 8

The association between a desire to be pregnant and discontinuation of long acting reversible contraception.

effective pre-insertion counseling about predicted side effects, sample size, socio-cultural differences, or the study's time gap. Another explanation could be that most health professionals in our country are reluctant to accept complaints of removal. The findings also revealed that there is no significant change in discontinuation rates between the second (47.6%) and third (48.8%) years of insertion, which is consistent with Bangladesh's (48%) (58).

In our study, women who had long-acting contraceptive side effects were 2.8 times more likely to stop using the method than those who did not (AOR = 2.833; 95% CI: 2.005–4.003). This conclusion is supported by research from Kenya (59), Nigeria (60, 61), and Nepal (62). Women's intolerance of minor side effects and vaginal bleeding, which interferes with their sexual experience, could be a viable rationale. Another explanation could be that family planning professionals' lack of ability and experience in dealing with side effects leads to mothers' need to stop using the methods.

Women who were dissatisfied with the services they received were 5 times more likely to discontinue long-acting reversible contraceptives than mothers who were satisfied (AOR = 5.15; 95% CI: 3.644–7.296). This could be attributed to women who were uninterested in method selection, privacy, secrecy, communication competency, and explanation from service providers, all of which have an impact on service continuity.

Women who were not counseled about side effects of long acting reversible contraceptives were 2.4 times more likely to discontinue the method than their counterparts (AOR = 2.417; 95% CI: 1.591–3.672). This is in line with research from Nigeria (53) and Jordan (63). This is due to the fact that mothers who do not receive adequate side effect counseling may develop a

negative attitude toward the method when they experience a side effect.

Women who did not schedule a follow-up appointment were 2.8 times more likely to discontinue than those who did (AOR = 2.820; 95% CI: 2.048–3.881). This is congruent with a study conducted in Port Harcourt (52). This means that during follow-up, women may receive more counseling time from care providers regarding managing side effects and receiving supportive treatment information.

Those who wanted to get pregnant were 2.4 times more likely to stop using long-acting contraceptives than women who didn't (AOR = 2.366; 95% CI: 1.760–3.182). This is consistent with a study done in Nigeria (61). Long-acting contraceptives must be discontinued when clients want to get pregnant (64).

To handle a large variance that occurred in between-study heterogeneity, a random-effect model was used in this research. We conducted leave-one-out sensitivity, and the results reveal that no single study had a substantial effect on the overall prevalence of contraception discontinuation.

We assessed the possible variability source *via* subgroup analysis using the study settings, regions, study design, cause of discontinuation, and year of insertion. The high heterogeneity might be due to differences in the sample populations, paper qualities, or socio-cultural, ethnic, and regional differences.

Conclusion

In conclusion, the overall prevalence of long-acting contraceptive discontinuation in Ethiopia was high (36.9%).

Furthermore, the pooled discontinuation rate differed by research region, setting, reason, design, and insertion year. Experienced side effects, not being advised about side effects, dissatisfaction with the provided service, no follow-up after insertion, and a desire to become pregnant were all variables that contributed to the discontinuation of long-acting reversible contraceptives, as per this study. The Amhara region of Ethiopia had the highest percentage of discontinuation. It is advisable to address discontinuation by recognizing the significance of side effects in counseling sessions, pregnancy intention, considering the sustainability of currently used contraceptives in view of Ethiopian women's philosophy, and effectively managing and counseling of side effects.

Strength and limitation

This study has some limitations. First, there was no adequate similar study to compare the findings of the study. Second, articles were restricted to only being published in the English language and placed in Ethiopia. Third, some of the included studies were cross-sectional, which might affect the outcome variable because of other confounding factors. This research has also some strength. First, compressive electronic online international searching engines were used. Second, our review incorporated gray literature as part of the primary studies.

Third, discontinued long acting contraceptive predictors were discovered.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary material](#), further inquiries can be directed to the corresponding author/s.

References

1. Crespi S, Hanisch M. *Implanon (etonogestrel implant) application for WHO EML*. Geneva: WHO (2014).
2. Rowlands S, Searle S. Contraceptive implants: current perspectives. *Open Access J Contr.* (2014) 5:73–84. doi: 10.2147/OAJC.S55968
3. Starbird E, Norton M, Marcus R. Investing in family planning: key to achieving the sustainable development goals. *Global Health Sci Prac.* (2016) 4:191–210. doi: 10.9745/GHSP-D-15-00374
4. Caetano C, Blikendaal S, Engler Y, Lombardo M. From awareness to usage of long-acting reversible contraceptives: Results of a large European survey. *Int J Gynecol Obst.* (2020) 151:366–76. doi: 10.1002/ijgo.13363
5. Secura G. Long-acting reversible contraception: a practical solution to reduce unintended pregnancy. *Minerva Ginecol.* (2013) 65:271–7.
6. Adedini SA, Omisakin OA, Somefun OD. Trends, patterns and determinants of long-acting reversible methods of contraception among women in sub-Saharan Africa. *PLoS ONE.* (2019) 14:e0217574. doi: 10.1371/journal.pone.0217574
7. Adal TG. Early discontinuation of long-acting reversible contraceptives among married and in union women: a systematic review and meta-analysis. *Ann Med Health Sci Res.* (2017) 7:6.
8. Castle S, Askew I. *Contraceptive discontinuation: reasons, challenges, and solutions. solutions.* (2015). Available online at: <http://www.familyplanning2020.org/resources/12011> (accessed December 8, 2015).
9. Curtis S, Evens E, Sambisa W. Contraceptive Discontinuation and Unintended Pregnancy: An Imperfect Relationship. (2017). Available online at: <http://citeseerxist.psu.edu/viewdoc/download?> (accessed September 15, 2017).
10. Ali MM, Cleland JG, Shah IH. Causes and consequences of contraceptive discontinuation: evidence from 60 demographic and health surveys. *World Health Organ.* (2012) 978:4.
11. Jain AK, Winfrey W. Contribution of contraceptive discontinuation to unintended births in 36 developing countries. *Stud Fam Plann.* (2017) 48:269–78. doi: 10.1111/sifp.12023

Author contributions

NG conceptualized the study. NG, KT, and BA contributed during data extraction and analysis. NG, GB, and AY wrote result interpretation. NG and KT prepared the first draft. NG, KT, DS, and BA contributed during the conceptualization, interpretation of results, and substantial revision. NG, KT, DS, GB, BA, and AY revised and finalized the final draft manuscript. All the authors read and approved the final version of the manuscript.

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/fpubh.2022.979231/full#supplementary-material>

12. Jain A. *The leaking bucket phenomenon in family planning. Champions for Choice*, 1–7. (2014). Available online at: <http://champions4choice.org/2014/09/the-leaking-bucket-phenomenon-in-family-planning/#more-1429> (accessed September 9, 2014).
13. Kesetebirhan A. *National Guideline for Family Planning Services in Ethiopia*. Ethiopia: Federal Democratic Republic. (2011).
14. Garbers S, Haines-Stephan J, Lipton Y, Meserve A, Spieler L, Chiasson MA. Continuation of copper-containing intrauterine devices at 6 months. *Contraception*. (2013) 87:101–6. doi: 10.1016/j.contraception.2012.09.013
15. Staveteig S, Mallick L, Winter R. Uptake and discontinuation of long-acting reversible contraceptives (LARCs) in low-income countries. *DHS Anal Stud*. (2015) 54:61.
16. Fekadu GA, Omigbodun AO, Roberts OA, Yalew AW. Factors associated with early long-acting reversible contraceptives discontinuation in Ethiopia: evidence from the 2016 Ethiopian demographic and health survey. *Archives Pub Health*. (2020) 78:1–10. doi: 10.1186/s13690-020-00419-w
17. Sedgh G, Singh S, Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plan*. (2014) 45:301–14 doi: 10.1111/j.1728-4465.2014.00393.x
18. Bongaarts J, Cleland JC, Townsend J, Bertrand JT, Gupta MD. *Family Planning Programs for the 21st Century: Rationale and Design*. New York, NY: Population Council (2012).
19. Central Statistical Authority (CSA) and ORC Macro. *Ethiopia Demographic and Health Survey 2015*. Calverton, MD, USA: CSA and ORC Macro. (2016).
20. Tilahun Y, Asnake M, Ayalew D. *Task Shifting in the Delivery of Long Acting Family Planning Services at Community Level in Ethiopia*. Addis Ababa: Pathfinder International Ethiopia (2011).
21. Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. (2009) 6:e1000097. doi: 10.1371/journal.pmed.1000097
22. Seninde J. *Factors Associated with Contraceptive Discontinuation among Women (15-49 Years) In Uganda*. (Doctoral dissertation, Makerere University) (2019)
23. Abebe BA, Assefa N, Mengistie B. Discontinuation of reversible long-acting contraceptive and associated factors among female users in health facilities of Hawassa City, Southern Ethiopia: cross-sectional study. *Open Access J Contr*. (2020) 11:113. doi: 10.2147/OAJC.S259978
24. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. *Checklist for Analytical Cross-Sectional Studies*. Adelaide: Joanna Briggs Institute Reviewer's Manual (2017).
25. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of inter-rater agreement. *J Clin Epidemiol*. (2012) 65:934–9 doi: 10.1016/j.jclinepi.2011.11.014
26. Dagnew GW, Gelaw YM, Asresie MB, Anteneh ZA. Level and timing of implanon discontinuation and associated factors among women who used implanon in Andabet district, public health facilities, north-west Ethiopia. *Biomed Res Int*. (2021) 7:6647660. doi: 10.21203/rs.2.12467/v2
27. Nageso A, Gebretsadik A. Discontinuation rate of Implanon and its associated factors among women who ever used Implanon in Dale District, Southern Ethiopia. *BMC Women's Health*. (2018) 18:189. doi: 10.1186/s12905-018-0678-x
28. Siyoum M, Mulaw Z, Abuhay M, Kebebe H. Implanon Discontinuation Rate and Associated Factors among Women who ever Used Implanon in the Last Three Years in Debre Markos Town, Northwest Ethiopia, 2016, Cross Sectional Study. *ARC J Pub Health Commun Med*. (2017) 2:8–16. doi: 10.20431/2456-0596.0201003
29. Wondie AG. Implanon discontinuation rate and its associated factors in Debre Tabor Town, North Central Ethiopia. *Sci J Clin Med*. (2019) 8:6–12. doi: 10.11648/j.sjcm.20190802.11
30. Melkamu Asaye M, Siyoum Nigussie T, Mequannt Ambaw W. Early implanon discontinuation and associated factors among implanon user women in Debre Tabor Town, public health facilities, Northwest Ethiopia, 2016. *Int J Rep Med*. (2018) 10:3597487. doi: 10.1155/2018/3597487
31. Weldekidan HA, Lemlem SB, Sinishaw Abebe W, Sori SA. Discontinuation rate of long acting Reversible contraceptives and factors Associated among reproductive age women in Butajira town, southern Ethiopia, 2020. *Women Health*. (2020) 18:17455057221104656. doi: 10.1177/17455057221104656
32. Gaenamo AA, Abebe DN. Time to discontinuation of long acting reversible contraceptive methods among married reproductive age women in Hadiya Zone. *J Public Health Policy Plann*. (2022) 6:101. doi: 10.35841/aaphpp-6.1.101
33. Obsu M, Hundessa B, Garoma S, Aman H, Merga H. Magnitude and associated factors of early Implanon discontinuation among rural women in public health facilities of central Ethiopia: a community-based cross-sectional study. *BMC Women's Health*. (2022) 22:72. doi: 10.1186/s12905-022-01651-y
34. Mesha M, Alemayehu A, Daka D. Prevalence and factors associated with early discontinuation rate of Implanon utilization among women who ever used Implanon in Kucha District Gamo Gofa Zone, Southern Ethiopia. *BMC Women's Health*. (2020) 20:239. doi: 10.1186/s12905-020-01096-1
35. Habte A, Wondimu M, Abdulkadir H. Survival time to Implanon discontinuation and its predictors among a cohort of Implanon users who enrolled in public hospitals of southern Ethiopia, 2021: a retrospective cohort study. *Arch Pub Health*. (2022) 80:89. doi: 10.1186/s13690-022-00859-6
36. Amare A, Reda T. Discontinuation of implants use and associated factors among women attending health facility clinics in Hawassa City, Southern Ethiopia, 2019; cross-sectional study. *Contr Rep Med*. (2020) 5:29. doi: 10.1186/s40834-020-00128-343
37. Nega G, Abera M, Tadele A. Discontinuation rate and associated factors among contraceptive implant users in Kersa district, southwestern Ethiopia. *Arch Pub Health*. (2021) 79:75. doi: 10.1186/s13690-021-00603-6
38. Tesfaye H, Negara E, Bayisa K. Early implanon discontinuation and associated factors among women ever used implanon in Mettu district, Oromia regional state, southwest Ethiopia, 2021. *Reprod Health*. (2021) 18:176. doi: 10.1186/s12978-021-01222-8
39. Geja E, Belayneh F, Legesse D, Tsegaw D, Abuka T, Gebremariam A. Prevalence of early removal of long-acting contraceptive methods and its associated factors in Sidama regional state, Ethiopia. *Open Access J Cont*. (2021) 12:35–44. doi: 10.2147/OAJC.S280405
40. Abraha HE, Gezae KE, Kahsay AB, Tequare MH. Incidence and predictors of first-year unplanned discontinuation of Implanon at Ayder comprehensive specialized hospital, northern Ethiopia: a retrospective follow-up study. *PLoS ONE*. (2022) 17:e0259234. doi: 10.1371/journal.pone.0259234
41. Melesse YD, Zegeye AM, Kebede GD, Tarik YD, Fenta SL, Getu AA, et al. Discontinuation of Long-Acting Reversible Contraceptive methods and associated factors among women in health facilities of Bahir Dar city, Northwest Ethiopia: A Cross-sectional study. doi: 10.21203/rs.3.rs-1212900/v1
42. Gebrekidan KG, Nerea MK, Gerezgiher H, Haftu M. Early Implanon discontinuation rate and its associated factors in health institutions of Mekelle City, Tigray, Ethiopia 2016/17. *BMC Res Notes*. (2019) 12:8. doi: 10.1186/s13104-018-3992-3
43. Birhane KA, Hagos SE, Fantahun M. Early discontinuation of implanon and its associated factors among women who ever used implanon in Ofra District, Tigray, Northern Ethiopia. *IJPSR*. (2015) 6:554–1.
44. Tolesa B, Alem G, Papelon T. Factors associated with contraceptive discontinuation in Agarfa district, Bale Zone, south east Ethiopia. *Epidemiology*. (2015) 5:1. doi: 10.4172/2161-1165.1000179
45. Mastor A, Khaing SL, Omar SZ. Users' perspectives on Implanon in Malaysia, a multicultural Asian country. *Open Access J Cont*. (2011) 2:79–84. doi: 10.2147/OAJC.S9674
46. Balogun O, Olaomo N, Adeniran A, Fawole A. Implanon sub-dermal implant: an emerging method of contraception in Ilorin, Nigeria. *J Med Biomed Sci*. (2014) 3:1–5. doi: 10.4314/jmbs.v3i1.1
47. Said MA-RM, Cairo U. *Implanon Use Pattern Among Ministry of Health and Population Clients 2008–2012*. Cairo: Faculty of Medicine (2012).
48. Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, et al. Continuation and satisfaction of reversible contraception. *Obstet Gynecol*. (2011) 117:1105–1113. doi: 10.1097/AOG.0b013e31821188ad
49. Teunissen AM, Grimm B, Roumen FJ. Continuation rates of the subdermal contraceptive Implanon® and associated influencing factors. *Eur J Contracept Reprod Health Care*. (2014) 19:15–21. doi: 10.3109/13625187.2013.862231
50. Harvey C, Seib C, Lucke J. Continuation rates and reasons for removal among Implanon® users accessing two family planning clinics in Queensland, Australia. *Contraception*. (2009) 80:527–32. doi: 10.1016/j.contraception.2009.05.132
51. Hubacher D, Dorfinger L. Avoiding controversy in international provision of subdermal contraceptive implants. *Contraception*. (2012) 85:432–3. doi: 10.1016/j.contraception.2011.11.018
52. Ojule JD. Implanon implant contraception at the university of Port Harcourt teaching hospital. *Asian J Med Health*. (2018) 11:1–6 doi: 10.9734/AJMAH/2018/40017
53. Ezegwui H, Ikeako L, Ishiekwene C, Oguanua T. The discontinuation rate and reasons for discontinuation of implanon at the family planning clinic of University of Nigeria Teaching Hospital (UNTH) Enugu, Nigeria. *Niger J Med*. (2011) 20:448–50.

54. Arribas-Mir L, Rueda-Lozano D, Agrela-Cardona M. Insertion and 3-year follow-up experience of 372 etonogestrel subdermal contraceptive implants by family physicians in Granada, Spain. *Contraception*. (2009) 80:457–62. doi: 10.1016/j.contraception.2009.04.003
55. Ali, Mohamed M, Sadler Rachael K, Cleland John, Ngo Thoai D, Shah Iqbal H. *Long Term Contraceptive Protection, Discontinuation and Switching Behaviour: Intrauterine Device (IUD) Use Dynamics in 14 Developing Countries*. London: World Health Organization and Marie Stopes International (2011).
56. Barden-O'Fallon J, Speizer IS, Calhoun LM, Corroon M. Women's Contraceptive discontinuation and switching behavior in urban Senegal, 2010–2015. *BioMed Central*. (2018) 18:1–5. doi: 10.1186/s12905-018-0529-9
57. Mrwebi KP, Goon DT, Owolabi EO, Adeniyi OV, Seekoe E, Ajayi AI. Reasons for discontinuation of Implanon among users in buffalo city metropolitan municipality, South Africa: a cross-sectional study. *Afr J Reprod Health*. (2018) 22:113–9. doi: 10.29063/ajrh2018/v22i1.1159
58. Mahboob El-Alam, Searing H, Bradley J, Shabnam F. *IUD Use and Discontinuation in Bangladesh*. New York, NY: The Acquire Project (2010).
59. Maina SW, Sanjo GO, Dwigah SN. Determinants of discontinuation of contraceptive methods among women at Kenyatta National Hospital, Kenya. *Afr J Pharmacol Ther*. (2016) 5:283
60. Igwe N. Intrauterine contraceptive device use in Abakaliki, Southeast Nigeria: a 5-year review. *Trop J Med Res*. (2016) 19:138. doi: 10.4103/1119-0388.185441
61. Muthir J, Nyango D. Indications for removal of Etonogestrel implant within two years of use in Jos, Nigeria. *East Afr Med J*. (2010) 87:11.
62. Thapa S. Early discontinuation of intrauterine device in Nepal—a retrospective study. *WHO South-East Asia J Public Health*. (2012) 1:309–19. doi: 10.4103/2224-3151.207027
63. Kanhawi C, Underwood H, Jabre B. Clientcentered counseling improves client satisfaction with family planning visits: evidence from Irbid, Jordan. *Global Health: Sci Prac J*. (2013) 1:180–92. doi: 10.9745/GHSP-D-12-00051
64. Weldemariam KT, Gezae KE, Abebe HT. Reasons and multilevel factors associated with unscheduled contraceptive use discontinuation in Ethiopia: evidence from Ethiopian demographic and health survey 2016. *BMC Public Health*. (2019) 19:1–15. doi: 10.1186/s12889-019-8088-z



OPEN ACCESS

EDITED BY

Shazia Qasim Jamshed,
Sultan Zainal Abidin
University, Malaysia

REVIEWED BY

Maryam Farooqui,
Qassim University, Saudi Arabia
Ihsane Hmamouchi,
Mohammed V University at
Souissi, Morocco

*CORRESPONDENCE

Madeeha Malik
madeehamalik19@gmail.com

SPECIALTY SECTION

This article was submitted to
Public Health Education and
Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 29 June 2022

ACCEPTED 22 November 2022

PUBLISHED 04 January 2023

CITATION

Malik M, Hussain A, Hashmi A,
Saeed H, Azhar H and Abbasi AS (2023)
Barriers to gender equity for female
healthcare academicians and
researchers in Pakistan: Is it still an
issue? *Front. Public Health* 10:981178.
doi: 10.3389/fpubh.2022.981178

COPYRIGHT

© 2023 Malik, Hussain, Hashmi, Saeed,
Azhar and Abbasi. This is an
open-access article distributed under
the terms of the [Creative Commons
Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

Barriers to gender equity for female healthcare academicians and researchers in Pakistan: Is it still an issue?

Madeeha Malik^{1,2*}, Azhar Hussain³, Ayisha Hashmi²,
Hamza Saeed², Hafsa Azhar¹ and Aqsa Sajjid Abbasi¹

¹Department of Pharmacy Practice, Hamdard Institute of Pharmaceutical Sciences, Hamdard University Islamabad, Islamabad, Pakistan, ²Cyntax Health Projects, Pvt., Ltd., Contract Research Organization and Corporate Firm, Islamabad, Pakistan, ³Institute of Applied Sciences and Technology, Haripur, Pakistan

Introduction: Gender inequity in healthcare academia is rising. Female healthcare professionals are struggling to balance their work and family leading to reduced productivity and disparity in three main areas of academic evaluation including teaching, service and research.

Objective: The objective of the current study was to explore perceptions of healthcare academicians regarding gender equity and its associated barriers in healthcare academia in Pakistan.

Methodology: A qualitative study design was used. Study site for this research included medical colleges, pharmacy schools and healthcare educational institutes. Study respondents included healthcare professionals including doctors and pharmacists working as faculty members. Snow ball sampling was used and interviews were conducted till saturation point was achieved. All interviews recorded were transcribed verbatim. Transcribed interviews were then subject to thematic analysis and were analyzed for relevant content.

Results: Thematic analysis of the study yielded many themes and sub themes. The main themes include: Gender equity an issue for healthcare academicians; Barriers toward promoting gender equity among healthcare academicians; Perceived teaching effectiveness among female healthcare academicians; Professional relationship of female healthcare academicians; Representation of female healthcare academicians at leadership positions; Research opportunities for female healthcare academicians; impact of academia as profession on married life and Strategies for improving gender equity disparities in academia of healthcare profession. The results showed that almost all the females as well as male healthcare academicians were of the view that female academicians are competent, hardworking and committed with their jobs. Mixed responses were observed regarding teaching effectiveness of female academicians. Half of the females as well male healthcare academicians thought that female were more effective teachers while other half was of the view that teaching effectiveness is based on individual trait irrespective of gender.

Conclusion: The results of the present study concluded that majority of the male as well as female healthcare professionals perceived gender equity as

an issue in academia in Pakistan, especially in underprivileged areas. Non-conducive work environment, harassment at workplace and cultural issues were the main barriers identified toward gender equity in healthcare academia in Pakistan.

KEYWORDS

academician, gender equity, Pakistan, female, healthcare professionals

Introduction

Equity is defined as “distribution of variable number and types of resources within a group to achieve results in equal magnitude”. However, in contrast, the phenomenon of equality follows “one size fits all” approach which promotes distribution of equal resources among individuals (1). Gender disparities in the field of healthcare has been subject of interest from many years and increasing trends of gender inequity in healthcare academia has been witnessed over the last decade (2). Despite rigorous efforts, the disparity lies in availability of growth opportunities and resources as well as rewards for both genders. It has been observed that women are subjected to both inequity and inequality in the field of academia by assigning them greater work load in terms of teaching and advisory duties which further decreases their participation in research as compared to their male colleagues (3, 4). Throughout the field of healthcare academia, managerial positions are mostly led by males allowing them to take decisions as well as have more opportunities for social networking. The recent global pandemic has further increased the gender gap (5). Female healthcare professionals are striving hard to balance their work and family commitments leading to reduced productivity and disparity in three main parameters of academic evaluation including teaching, professional service and research. In the recent years, the focus on improving women’s representation in the fields of science, technology, engineering, and mathematics (STEM) has increased; however, interventions focused on increasing gender equity in these fields still has long way to go (6). These gender disparities are more prominent within the field of academia. The proportion of women faculty in STEM remains low despite of the increased women acquiring their post graduate degrees in the past few years (7). Numerous factors contribute toward under representation and disparity including workplace stereotypes, low social support from colleagues and uncomfortable work environments. Harassment and discrimination are also common factors contributing to the rising gender inequity. Inadequate opportunities for mentoring, networking and professional growth also increases the gender gap in academia (8, 9).

Among all the countries, gender disparity is common in South Asia including Pakistan (10). According to World Economic Forum, Pakistan is on number 56th among the 58 countries that have progressed toward improving status of gender equity in the country despite of the fact that gender equality has already been a part of the country legislation since 1973 (11). In Pakistan, women are expected to be responsible for taking care of households while decision making is considered to be the responsibility of male counterparts (12). Literature review has highlighted that female faculty members teaching in universities in Pakistan had experienced gender discrimination and had low levels of job satisfaction. Female academicians are usually not part of committees involved in decision making and only few females have access to leadership positions in academia. The chances for professional growth in academia is low for female academicians in the country as well as they have to face more discriminatory barriers in the field (13, 14). There is also lack of equal access to professional development opportunities. Limited research has been conducted to identify barriers linked to gender equity in healthcare academia. Therefore, the present study was designed to explore the perceptions of healthcare professionals regarding gender equity in healthcare academia in Pakistan.

Methodology

Study design

A qualitative study design was used to explore perceptions of healthcare professionals toward gender equity in healthcare academia in Pakistan.

Study site and respondents

Study site for this research included medical colleges, pharmacy schools and healthcare educational institutes. Study respondents included healthcare professionals including doctors and pharmacists working as faculty members.

Ethical approval

Ethical approval was obtained for this study by the Ethical Review Board of Hamdard University, Islamabad, Pakistan (ERB/HUIC/295). A comprehensive description of the study was introduced to the participants at the first of the interview; they were allowed to reject answering or withdrawing at any time thereafter. The participants were assured that their answers would be kept confidential and that their names would not be disclosed during the study and in the final report.

Sampling technique and sample size

Non probability sampling technique was used i.e., Snow ball sampling was adopted as it is the best way of identifying the respondents having common characteristics, experience and job profile which were difficult to contact. Any pharmacist and doctor of both genders teaching in any public or private university/medical college with at least 1 year experience willing to participate was included in the study. Interviews were conducted till saturation point was achieved. The sample size at saturation point for different respondents was: Female Pharmacists ($n = 9$), Female Doctors ($n = 10$), Male Pharmacists ($n = 10$) and Male Doctors ($n = 11$).

Study tool

After extensive and critical literature review a semi structured interview guide was developed and used as a study tool (3, 4, 9, 13, 15). To get detailed views of respondents, the focus was to design questions as open as possible. The tool comprised of 3 major sections with a total of 15 questions. First section included questions regarding gender equity as an issue and related barriers toward promoting gender equity for healthcare academicians. The second section was comprised of questions about perceived traits, competency, skill set, teaching effectiveness and professional relationship with male colleagues. The third section consisted of questions regarding representation at leadership positions, research opportunities, impact of academia as profession on eligibility for marriage and suggestions for promoting gender equity in Pakistan. Face and content validation of interview guide was done by panel of experts.

Interview conduction

The selected respondents were contacted either personally or through phone for getting interview appointment date and time. Written consent was obtained from the study respondents before conducting interview. When necessary, probing

questions were used. Each interview lasted approximately 20–30 min. Every respondent was given chance to express his/her views at the end of interview session. All interviews were conducted in the local language i.e., Urdu. Interviews were conducted till point of saturation was achieved. All interviews were recorded after getting permission from the respondents.

Thematic analysis

All interviews recorded were transcribed verbatim. The interviews were transcribed verbatim and were then subject to thematic analysis and were drawn using bottom up approach.

Results

Demographic characteristics of the respondents

Majority of the respondents from both groups i.e., male and female pharmacists as well as doctors were in the age group of 36–45 years. Most of the respondents (72.5%; $n = 29$) from both groups were having postgraduate degree. Most of them (32.5%; $n = 13$), were having experience of 6–10 years (Table 1).

Theme 1: Gender equity an issue for healthcare academicians

Most of the female healthcare professionals were of the view that gender equity is not an issue for female healthcare professionals in academia in Pakistan. However, most of them stated that it could be seen as a major barrier for females working in other fields and underprivileged areas. On the other hand, it was interesting to notice that majority male healthcare professionals perceived gender equity as an issue in Pakistan.

“Gender equity is not an issue of Pakistan especially for female pharmacists working in academia. In every province female faculty is present beyond the equity issue. However, in public sector universities, females might be uncomfortable with their environment and not working but vacancies are available for them”. (F.Pharm.01)

“According to me gender equity is not a big issue for female doctors. As females have progressed over the years and are giving tough competition to the male doctors in academia, research as well as practice in Pakistan. I think it all depends on one’s personal will and skills”. (F.Doc.03)

“Yes, I think gender equity is not only an issue for academicians but is a major challenge seen for overall employment opportunities. I think in Pakistan, in recruitment or selection process for almost every employment opportunity,

TABLE 1 Demographic characteristics of the respondents.

		Pharmacists		Doctors	
		Females (N = 09) n (%)	Males (N = 10) n (%)	Females (N = 10) n (%)	Males (N = 11) n (%)
Sector	Public	4 (44.5 %)	5 (50 %)	6 (60 %)	5 (45.5 %)
	Private	5 (55.5 %)	5 (50 %)	4 (40 %)	6 (54.5 %)
Qualification	Bachelors	2 (22.2 %)	3 (30 %)	4 (40 %)	2 (18.2 %)
	Postgraduate	7 (77.8 %)	7 (70 %)	6 (60 %)	9 (81.8 %)
Age	25–35 years	2 (22.2 %)	3 (30 %)	2 (20 %)	2 (18.2 %)
	36–45 years	4 (44.5 %)	5 (50 %)	3 (30 %)	5 (45.5 %)
	Greater than 45 years	3 (33.3 %)	2 (20 %)	5 (50 %)	4 (36.3 %)
Teaching experience	1–2 years	2 (22.2 %)	3 (30 %)	2 (20 %)	2 (18.2 %)
	3–5 years	2 (22.2 %)	2 (20 %)	3 (30 %)	3 (27.3 %)
	6–10 years	3 (33.4 %)	3 (30 %)	3 (30 %)	4 (36.3 %)
	Greater than 10 years	2 (22.2 %)	2 (20 %)	2 (20 %)	2 (18.2 %)

male dominance and preference exists and I think male candidates are preferred till date over female candidates. In my opinion, this practice equally exists in both public and private sector". (M.Pharm.03)

"Yes, gender equity is an issue in Pakistan. Although, a good number of female doctors are working as faculty in various medical colleges but usually they are not offered administrative positions at times due to their family commitments irrespective of their professionalism". (M.Doc.01)

"Obviously not, because if you look at the population ratio, more than 50% of the population is female but if you look at the employment opportunities, or if you conduct a general survey in academics, you will find an overwhelming majority of males working in universities as compared to female employs. Therefore, I think population ratio is not justified at all and the requirement of female academician is not fulfilled at all". (M.Pharm.07)

"I think there are more females working in academia than males. I think this trend is similar in both sectors but more evident in private sector at present, due to less working hours and shifts". (M.Pharm.02)

"I believe appropriate number of females doctors are working as academicians. This is due to less job stress and work load in teaching as compared to practice". (M.Doc.03)

Theme 2: Employment to population ratio with respect to female academician in healthcare profession

Mix responses were seen among the respondents. Female pharmacists were of the view that employment to population ratio of female academician was low while female doctors thought that their employment ratio was sufficient. On the other hand, nearly half of the male pharmacists thought that employment ratio was low while the other half were of the view that it was appropriate. In contrary, majority of the male doctors were of the view that employment to population ratio with respect to female doctors was good.

"I think there are more female doctors working in academia as it is a much relaxing job and it is easy for the females to manage work and family life". (F.Doc.02)

"No, I think less females are employed with respect to population in academia due to different issues including transportation, work-life balance, and different family pressures". (F.Pharm.04)

Theme 3: Barriers toward promoting gender equity among healthcare academicians

Different barriers identified by both male and female healthcare professionals toward promoting gender equity among healthcare academicians included mainly as lack of support at workplace, workplace harassment and cultural issues.

Support at workplace

Majority of the female as well as male healthcare professionals were of the view that lack of support at work place is one of the biggest challenges faced by the female healthcare academicians due to which they are not able to balance between work and family.

"I think lack of support at workplace in terms of provision of transport & day care facilities and struggle to prove oneself in a highly male dominance society are one of the important reasons towards lack of gender equity opportunities in this society" (F.Pharm.03)

"Family commitments are a problem for a female as her job is usually considered as a secondary thing. Most of the employers do not provide transportation and child daycare facilities which is one of the biggest issues for the females to manage their job with family life". (F. Doc.06)

"I think lack of supportive work and family environment is one of the barriers which is most commonly faced by the female academicians" (M.Pharm.02)

"In my opinion, most of the organizations do not provide transport and daycare facilities due to which most of the females fail to manage their work life balance and often quit" (M.Doc.04)

Workplace harassment

Most of the female as well male healthcare professionals considered workplace harassment as a barrier toward gender equity in Pakistan.

"Yes, unfortunately female academicians have to face this issue. This happens relatively more in public sector. However, I have also seen some females taking undue advantage and when they don't get this they blame a male for harassment" (F.Pharm.01)

"Yes, I think workplace harassment is one of the major issues faced by female academicians. There is more harassment in public setup as people come from different backgrounds and possess different mindset, especially lower rank people don't know how to behave with females. However, in private setup this is less because departments are more interconnected due to which there are less harassments issues" (F.Doc.06)

"Well, in my opinions the topmost barrier is lack of suitable work environment and workplace harassment" (M.Pharm.02)

"I think workplace harassment is one of the issues faced by female academicians especially more commonly in universities located in underprivileged areas of Pakistan" (M.Doc.07)

Salary disparity

Low salary was identified as one of the issues faced by both genders. Majority of the female as well as male respondents stated that usually the salary in academia is set with respect to qualification, research publication and experience and the market trends follow this for both genders.

"I do not see any disparity in salary of female academicians versus males as the salary bracket is set according to qualification, research profile and experience. However, overall we are underpaid in academia" (F.Pharm.05)

"Salary in academia is according to qualification and experience and does not depend upon gender. However, I think academicians are low paid in the country" (F.Doc.02)

"I think salary in academics follow market trends set as per qualification and experience equally for both genders" (M.Pharm.01)

"I do not find any disparity in the salary of female or male academicians as it is defined by a criterion irrespective of gender. But I must admit that academicians are paid quite less" (M.Doc.02)

Emotional intelligence

Emotional Intelligence was identified as one of the issues faced by females. Almost all the female as well as male respondents stated that emotional instability is one of the challenges faced by female academicians.

"Yes, it is one of the major issue faced by females as if you can't understand your emotions you will stick to them missing rationality" (F.Pharm.01)

"Yes this is an issue for the females as most of them don't come relaxed from home so all the stress is reflected at workplace as they can't manage their emotions" (F.Doc.07)

"Yes, emotional instability is an issue faced by female academicians. Main reason are lack of decision power and at times getting influenced by environment" (M.Pharm.08)

"Yes, definitely, females have this issue, they lack patience and easily get influenced by whatever they see or listen. Females rely a lot on others and quickly build their perceptions without getting into depth of scenario" (M.Doc.02)

Cultural issues

All the male and female academicians agreed that culture was an important barrier toward gender equity especially in case of remote areas including KPK and Baluchistan.

"Yes, definitely cultural values don't change. In cities, like Mardan and Swat females have limited social life so they have literally no communication with males due to which they struggle to cope up with them if they have to work with males in future" (F.Pharm.07)

"Yes, one of the biggest cultural barrier is the language. Some males lack appropriate accent for communicating with females and are considered rude. Moreover, cultural favoritism during appointments is quite common, especially

in KPK and Baluchistan and usually females are not preferred while hiring” (F.Doc.01)

“Yes it counts a lot as culture of one province vary from other. Mindset of people is dominated by their culture, however, it seems to be improved at higher posts. Unfortunately, in KPK still few families don’t prefer working women and do not allow them to work” (M.Pharm.03)

“Yes, definitely it has an impact. We have examples of KPK and Baluchistan where it is very difficult for females to teach in universities. Although, situation is improving, but still there is long way to go” (M.Doc.04)

Wearing a veil

Mixed responses were received on considering veil as a barrier toward promoting gender equity by female academicians. However, all the male academicians did not see veil as barrier toward gender equity.

“No, it is not a big issue in academia. I think females covering their faces are seen with more respect in our country. It may varies according to the profession but I think mostly it is not an issue in academia” (F.Pharm.05)

“Yes, students are less comfortable with female teachers covering their faces as they can’t see their expressions and may not pay proper attention towards them. Few male coworkers also hesitate to talk to such females” (F.Doc.02)

“No I don’t think it is an issue in Pakistan and has anything to do with number of opportunities for females. It might be an issue in Europe or Western countries but not in Pakistan” (M.Pharm.07)

“I don’t think there is any place in Pakistan where a female is rejected just because of her veil” (M.Doc.03)

Theme 4: Perceived traits, competency and commitment skill set among female healthcare academicians

Almost all the females as well as male healthcare academicians were of the view that female academicians are competent, hardworking and committed with their jobs.

“I think both male and female academicians are equally competent but female academicians possess more assertiveness, better decision making, commitment and communication skillset” (F.Pharm.02)

“I think female academicians are more productive as they are more focused towards producing results in shorter duration. On the other hand, males are not so serious towards meeting tasks deadlines” (F.Doc.06)

“I feel females are more competent working in all fields including academia as compared

to males as they are more committed, convincing and dedicated” (M.Pharm.07)

“I think that female academicians are more punctual and committed. However, males are generally casual as they know the tactics to get the work done in short time span” (M.Doc.02)

Theme 5: Perceived teaching effectiveness among female healthcare academicians

Mixed responses were observed regarding teaching effectiveness of female academicians. Half of the females as well male healthcare academicians thought that female were more effective teachers while other half was of the view that teaching effectiveness is based on individual trait irrespective of gender.

“I think female teachers possess the skills to make a hard subject easy for her students as they are more innovative than males” (F.Pharm.02)

“I think females are more hardworking than males and are far better teachers than them” (F.Doc.01)

“I believe it depends on an individual’s personality and his/her ability to involve all the class. I think both genders can be equally effective” (F.Pharm.03)

“I think it is an individual trait and has nothing to do with gender. It all depends on competency of academicians as teaching is an art and only knowledge cannot improve it. It requires skills and competency for delivery” (M.Pharm.05)

“I had experience of being taught by both male and female teachers during my student life and based on my experience, I think that female teachers are more convincing and have better teaching effectiveness as compared to male teachers. I think reason for this is the element of softness in attitude, more commitment, better preparation of lectures and way of delivering the concept in the lecture” (M.Pharm.08)

“I believe females are very effective as far as teaching is concerned as they have better conceptual knowledge and delivery skills than males” (M.Doc.07)

Theme 6: Professional relationship of female healthcare academicians

Mixed responses were received by both male and female healthcare professionals toward professional relationship of female academicians with their counterparts and male colleagues.

"Yes, I think female academicians support their female colleagues especially in private sector. I have seen such female role models academicians in private sector universities who support and train their female colleagues. It varies individual to individual as I have seen many males being mentors of their female colleagues and few giving them tough time" (F.Pharm.06)

"I think females are usually jealous and very keen observers. They never like other females to cross them. They don't generally work in harmony with each other. However, I have seen most of the male in a supporting role for their female coworkers. But it is difficult for them to except females as their boss" (F.Doc.07)

"I do not think that females support each other. However, I have witnessed many males supporting their female colleagues" (M.Pharm.02)

"Well, I think in my opinion jealousy factor exists among females, so in certain cases female academicians do not play supportive role for their colleagues, unless there is a strong friendship. But most of the males support their female colleagues" (M.Doc.01)

Theme 7: Representation of female healthcare academicians at leadership positions

Almost all the females as well as male healthcare academicians were of the view that female academicians are better administrators and possess leadership qualities but have less representation at leadership positions.

"I believe females are very good administrators, if given the opportunity but they are usually not given fair chance to represent themselves at leadership positions" (F.Pharm.03)

"To be honest they do not have appropriate representation at leadership positions. However, they have the potential to lead the show more effectively" (F.Doc.02)

"I think although, trend is changing these days as more females are working at leadership positions and are playing their roles very well but still it has long way to go" (M.Pharm.01)

"I do not think females are given ample representation at leadership positions worldwide, especially in Pakistan" (M.Doc.02)

Theme 8: Research opportunities for female healthcare academicians

Almost all the females as well as male healthcare academicians were of the view that equal opportunities

are available for both genders but still it seems difficult for female academicians to avail them due to their personal issues.

"I think equal research opportunities are available for both genders but at times females could not avail them due to personal issues like field work or travelling" (F.Pharm.02)

"Equal opportunities exist for both genders but at times it gets difficult for females to avail them" (F.Doc.06)

"I think both have equal opportunities but at times it is difficult for females to do research along with their household duties" (M.Pharm.04)

"Both have equal opportunities but at times research is not a priority for them due to work life balance" (M.Doc.05)

Theme 9: Impact of academia as profession on married life

Almost all the females as well as male healthcare academicians were of the view that females being academicians has an impact on married life.

Improved eligibility for marriage

Almost all the females as well as male healthcare academicians were of the view that being female academicians improve eligibility for marriage.

"I feel that it is an added advantage for marriage as most families prefer academicians as daughter in law due to the fixed job timing" (F.Pharm.06)

"Yes, I think most of the families prefer working women as academicians for marriage" (F.Doc.02)

"Yes, it has an added advantage for marriage as worldwide teaching is considered respectable job" (M.Pharm.08)

"Yes, it has benefit as working women are now preferred for marriage in Pakistan. Teaching is still recognized as a respectable profession and female academicians are obviously preferred" (M.Doc.08)

Impact of higher salary than partner

Almost all the females as well as male healthcare academicians were of the view that having higher salary than the husband effect the marital life.

"Yes, I think it is always difficult for the males to accept their partners being paid more than them and it effects the quality of their marital relationship" (F.Pharm.01)

"Yes it effects the marital life as the males in our society can't accept this fact and feel inferiority complex which leads

to fights. Husbands always want to have that upper hand over their spouse in terms of financial literacy" (F.Doc.05)

"Yes, quality of marriage is effected by this as males suffer from inferiority complex" (M.Pharm.06)

"Yes it has an impact on the marriage. The impact might be positive as well as negative. Positive impact includes the addition of financial resources and sharing of burden. However, negative impact include jealousy and inferiority complex" (M.Doc.01)

"I think a conducive working environment along with daycare and transport facilities can help to improve the situation. Moreover, family members especially males must encourage and empower them as working women" (M.Pharm.06)

"I think there should not be any discrimination in salaries of males and females having same position and qualification. Male academicians in private sector are usually paid more than females. Moreover, transport facilities, flexible working hours, conducive work environment and most importantly open mindedness and supportive role of family members can help to promote gender equity" (M.Doc.01)

Theme 10: Job turnover ratio among female healthcare academicians

Mixed responses were received from females as well as male healthcare academicians. Half of them were of the view that females switch more and the other half felt vice versa.

"I think males switch jobs more than females as they have to support their families in terms of finances" (F.Pharm.02)

"In my view, females switch jobs more due to multiple reasons including out of station marriage, family restrictions, gender disparity and job workplace culture" (F.Doc.03)

"I think females generally prefer to work at the same place as they usually they get emotionally attached to workplace relatively more than males" (M.Pharm.05)

"I think males switch jobs more often than females to avail better opportunities in terms of finances to support their families" (M.Doc.02)

Theme 11: Strategies for improving gender equity disparities in academia of healthcare profession

All females as well as male healthcare academicians were of the view that by providing conducive environment, family & peer support, flexible working hours, transport and day care facilities can help to improve gender equity disparities for the female workforce.

"I think the gender equity policies need to be devised and implemented to counter negative attitude of males as boss towards their competent female colleagues. However, I feel that only 10% of the females possess strong leadership qualities, therefore, we as females need to work on our leadership traits to address gender disparities at workplace" (F.Pharm.01)

"We have to provide the female workforce with favorable working environment. Day care facility should be provided for child bearing mothers. Transport issues must be resolved and females should get this facility for free" (F.Doc.06)

Discussion

Gender equity is still a challenge across various labor markets including health market. Physicians, nurses and pharmacists among many other professionals are no exception to the global trends of gender inequity at workplace. Gender equity is vital in healthcare profession in order to ensure effective, long term and sustainable career advancement for women. The results of the present study highlighted that majority of the female healthcare professionals were of the view that gender equity is not an issue in academia in Pakistan with the exception of females working in other fields and from underprivileged areas. However, majority of the male healthcare professionals perceived gender equity as an issue in Pakistan. Similar results were observed in a study conducted in Canada where gender inequity was observed in academia especially at leadership positions (16). As reported by Global Gender Gap Report 2014, Pakistan rank at 141 amongst the 142 countries in gender gap. The labor force participation was reported as 86 males and 25 females with female to male ratio as 0.30 (17). Despite the increased influx of women as healthcare professionals over the last decade, still horizontal and vertical occupational gender inequities exist. The results of the present study highlighted that majority of the female as well as male pharmacists were of the view that employment to population ratio of female academicians was low. On the other hand, male and female doctors were of the view that that employment to population ratio with respect to female doctors in academia was adequate. The findings are consistent with a study conducted in USA which concluded that male healthcare professionals were present in a higher employment ratio as compared to female healthcare professionals in academic healthcare centers (18). Women in healthcare fields face challenges related to poor work environments including limited opportunities for career advancement, work-related stress, unsatisfactory working conditions and unfavorable policies to promote leadership and salary disparities. In addition, women in the US earned less than their male colleagues despite sharing equal amount of work, qualifications, experience and output. The current study

revealed that non-conducive work environment, harassment at workplace and cultural issues were the main barriers identified toward gender equity in healthcare academia in Pakistan. Similar findings were reported in a study conducted in USA where cultural and workplace factors were highlighted as major barriers toward achieving gender equity (15).

Gender equity and women's empowerment have been set as prime goals by the United Nations for the 2030 global agenda for sustainable development. Although, progress has been made toward achieving these goals and women participation in the workforce has been growing rapidly over the course of time but still women occupy less than one third leadership and management positions. The current study reported that generally female academicians are perceived competent, hardworking and committed with their jobs. They are considered more effective teachers but have limited access to opportunities for leadership positions as compared to males. Similar results were reported by a study conducted in Germany where majority of the women doctors were of the view that they have less access to administrative positions as compared to their male counterparts (19). Gender inequity has been a major issue in developing countries. Pakistan has been facing this issue from generations where women are mostly deprived of their equal rights as compared to men. Most of the time they are not allowed to work or chose partner for marriage. The notion of working women are not well perceived in few provinces of Pakistan, especially the remote and tribal areas. The results of the study revealed that female academicians are generally more accepted in the society for marriage than any other profession. Generally, less support is provided by the male partners and usually most of them are dissatisfied with higher salary and career progression of their better halves. Similar results were reported from a study which showed that young professionals had poor marital relationships due to wage differences among partners (20).

Gender disparity is a worldwide phenomenon. This disparity is not only with respect to opportunities and resources but also in rewards, and exists in all regions and classes. Managerial positions are usually held by males, who not only have more decision making power but also have more opportunities of social networking. Women have to achieve a successful career at the cost of their family life. The results of the current study showed that equal research opportunities exist for both genders but female academicians are unable to access them due to their personal issues and family commitments. Almost, <30% of the world's researchers are women (21). Inadequate support for women at the workplace result in work-life imbalance and affect family responsibilities, while stereotyping and inequity lead to stress, low life satisfaction and less productivity. Low life satisfaction affects overall performance of an individual both personally and professionally. Hence,

implementing strategies like flexible timing and part-time work from home might improve motivation at the workplace, which in turn could strengthen and support gender equity across healthcare organizations. There is a critical need to develop organizational policies for promotion of gender equity through healthcare academia. The results of the current study highlighted that organizational policies should be introduced to promote work-life balance for women academicians. Conducive work environment, childcare support, transport facility, equal salary packages and family support could help to address the barriers linked to achieving gender equity in the country. These findings are in line with the results obtained from a study conducted in Canada where organizational support strategies helped in reducing gender disparity among academicians (5).

Study limitation

The present study was conducted in twin cities of Pakistan and results may not be generalized to rest of the country. Responses of respondents may not depict their true feelings. Few of the respondents were reluctant for audio recording of the interview.

Conclusion

The results of the present study concluded that majority of the male as well as female healthcare professionals perceived gender equity as an issue in academia in Pakistan, especially in underprivileged areas. Non-conducive work environment, harassment at workplace and cultural issues were the main barriers identified toward gender equity in healthcare academia in Pakistan. Equal research opportunities exist for both genders but female academicians are unable to access them due to their personal issues and family commitments. Generally, female academicians are perceived competent, hardworking, committed and more effective teachers but still have limited access to opportunities for leadership positions as compared to the males. Although, female academicians are generally more accepted in the society for marriage than any other profession but still less support is provided by the male partner. Appropriate organizational policies must be introduced to address recruitment and advancement processes to ensure quality between women and men; equal pay for equal work; recognition and rewards that are unbiased and based on contribution and performance; non-discriminatory approaches to care and family responsibilities; and genuine access to various positions and levels of leadership by removing gender-based barriers in order to improve status of gender equity and economic development in Pakistan.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Hamdard University Islamabad Ethical Committee. 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

MM and AHu conceptualized the project and contributed equally to data analysis and interpretation. HS, HA, AHa, and AA contributed with data collection. MM, AHu, and AHa

contributed with manuscript writing and revision. All authors read and approved the final manuscript.

Conflict of interest

Authors MM, AHa, and HS were employed by Cyntax Health Projects, Pvt., Ltd.

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.

References

1. Van Doorslaer E, Koolman X, Puffer F. *Equity in the Use of Physician Visits in OECD Countries: Has Equal Treatment for Equal Need Been Achieved. Measuring Up: Improving Health System Performance in OECD Countries*. Paris: OECD Publishing (2003).
2. Monroe K, Ozyurt S, Wrigley T, Alexander A. Gender equality in academia: Bad news from the trenches, and some possible solutions. *Perspect Pol.* (2008) 6:215–33. doi: 10.1017/S1537592708080572
3. Kjeldal SE, Rindfleish J, Sheridan A. Deal-making and rule-breaking: Behind the façade of equity in academia. *Gender Educ.* (2005) 17:431–47. doi: 10.1080/09540250500145130
4. Xu YJ. Gender disparity in STEM disciplines: a study of faculty attrition and turnover intentions. *Res High Educ.* (2008) 49:607–24. doi: 10.1007/s11162-008-9097-4
5. Oleschuk M. Gender Equity Considerations for Tenure and Promotion during COVID-19. *Can Rev Sociol.* (2020) 57:502–15. doi: 10.1111/cars.12295
6. Sattari N, Sandefur RL. Gender in academic STEM: A focus on men faculty. *Gender Work Org.* (2019) 26:158–79. doi: 10.1111/gwao.12249
7. Ragins BR, Townsend B, Mattis M. Gender gap in the executive suite: CEOs and female executives report on breaking the glass ceiling. *Acad Manag Perspect.* (1998) 12:28–42. doi: 10.5465/ame.1998.254976
8. Zhuge Y, Kaufman J, Simeone DM, Chen H, Velazquez OC. Is there still a glass ceiling for women in academic surgery? *Annals Surg.* (2011) 253:637–43. doi: 10.1097/SLA.0b013e3182111120
9. Casad BJ, Franks JE, Garasky CE, Kittleman MM, Roesler AC, Hall DY, et al. Gender inequality in academia: Problems and solutions for women faculty in STEM. *J Neurosci Res.* (2021) 99:13–23. doi: 10.1002/jnr.24631
10. Strachan G, Adikaram A, Kailasapathy P. Gender (in) Equality in South Asia: Problems, Prospects and Pathways. New Delhi: SAGE Publications Sage India (2015). p. 1–11.
11. Ashraf I, Ali A. Socio-economic well-being and women status in Pakistan: an empirical analysis. *Bull Bus Econ.* (2018) 7:46–58.
12. Goheer NA. *Women Entrepreneurs in Pakistan: How to Improve Their Bargaining Power*. 2003. Geneva: International Labour Organization Geneva, International Labour Office (2003).
13. Shaukat S, Siddiquah A, Pell AW. Gender discrimination in higher education in Pakistan: a survey of university faculty. *Eurasian J Educ Res.* (2014) 56:1–17. doi: 10.14689/ejer.2014.56.2
14. Ashraf Y, Gardezi SMJH, Saeed F. A comparative analysis of gender and educational leadership in Pakistan and the United Kingdom. *Pakistan Social Sciences Review.* (2021) 5:484–98. doi: 10.35484/pssr.2021(5-IV)37
15. Carr PL, Szalacha L, Barnett R, Caswell C, Inui T. A "ton of feathers": gender discrimination in academic medical careers and how to manage it. *J Women's Health.* (2003) 12:1009–18. doi: 10.1089/154099903322643938
16. Tricco AC, Bourgeault I, Moore A, Grunfeld E, Peer N, Straus SE. Advancing gender equity in medicine. *CMAJ.* (2021) 193:E244–50. doi: 10.1503/cmaj.200951
17. Hausmann R, Tyson LD, Bekhouche Y, Zahidi S. *Gender Gap Report 2014*. In World Economic Forum 2014 Nov (Vol. 4). Available online at: https://www3.weforum.org/docs/GGGR14/GGGR_CompleteReport_2014.pdf (accessed November 10, 2021).
18. Gambhir S, Daly SC, Elfenbein D, Sheehan B, Maithel S, Smith M, et al. The effect of transparency on the gender-based compensation gap in surgical disciplines within a large academic healthcare system. *Surg Endosc.* (2021) 35:2607–12. doi: 10.1007/s00464-020-07679-1
19. Dettmer S, Wenzel A, Trenkwalder T, Tiefenbacher C, Regitz-Zagrosek V. Gender and career in cardiology—a cross-sectional study. *Herz.* (2021) 46:150–7. doi: 10.1007/s00059-021-05027-0
20. Brennan RT, Barnett RC, Gareis KC. When she earns more than he does: a longitudinal study of dual-earner couples. *J Marriage Fam.* (2001) 63:168–82. doi: 10.1111/j.1741-3737.2001.00168.x
21. Annan K. *A Challenge to the World's Scientists*. Washington, DC: American Association for the Advancement of Science (2003). p. 1485.



OPEN ACCESS

EDITED BY

Sunjoo Kang,
Yonsei University, Republic of Korea

REVIEWED BY

Francesca Buttini,
University of Parma, Italy
Sidra Noor,
COMSATS University Islamabad, Abbottabad
Campus, Pakistan
Shefaat Ullah Shah,
Gomal University, Pakistan

*CORRESPONDENCE

Gul Shahnaz
✉ gshahnaz@qau.edu.pk

SPECIALTY SECTION

This article was submitted to
Public Health Education and Promotion,
a section of the journal
Frontiers in Public Health

RECEIVED 01 July 2022

ACCEPTED 30 January 2023

PUBLISHED 09 March 2023

CITATION

Balquis F, Sohail MF, Hamid H, Ullah W,
Khan AH and Shahnaz G (2023) Potential and
weak links in the management of tuberculosis
by Pakistani private pharmacy staff.
Front. Public Health 11:983997.
doi: 10.3389/fpubh.2023.983997

COPYRIGHT

© 2023 Balquis, Sohail, Hamid, Ullah, Khan and
Shahnaz. 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.

Potential and weak links in the management of tuberculosis by Pakistani private pharmacy staff

Fatima Balquis^{1,2}, Muhammad Farhan Sohail^{1,3}, Huma Hamid⁴,
Waseem Ullah^{1,2}, Amer Hayat Khan⁵ and Gul Shahnaz^{1*}

¹Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan, ²Department of Pharmacy Practice, Shifa College of Pharmaceutical Sciences, Shifa Tameer-e-Millat University, Islamabad, Pakistan, ³Riphah Institute of Pharmaceutical Sciences, Riphah International University–Lahore Campus, Lahore, Pakistan, ⁴Riphah Institute of Pharmaceutical Sciences, Riphah International University–Islamabad Campus, Islamabad, Pakistan, ⁵Discipline of Clinical Pharmacy, School of Pharmaceutical Science, University Sains Malaysia, Gelugor, Penang, Malaysia

Introduction: The emergence of MDR-TB is a global threat and an obstacle to the effective control of TB in Pakistan. A lack of proper TB knowledge among the staff in private pharmacies and the sale of compromised quality anti-TB drugs are the main instigators of multidrug-resistant tuberculosis (MDR-TB). Thus, this study was aimed at investigating the quality and storage conditions of fixed-dose combination (FDC) anti-TB drugs along with the awareness of staff working in private pharmacies regarding the identification of potential patients with TB and dispensing the inappropriate treatment regimens contributing to MDR-TB.

Methods: The study is completed in two phases. In phase I a cross-sectional study is performed using two quantitative research designs, i.e., exploratory and descriptive, to evaluate the knowledge of private pharmacy staff. The sample of 218 pharmacies was selected. While in phase II cross sectional survey is conducted in 10 facilities from where FDC anti TB drugs were sampled for analyzing their quality.

Result: Results revealed the presence of pharmacists only at 11.5% of pharmacies. Approximately 81% of staff at pharmacies had no awareness of MDR-TB, while 89% of pharmacies had no TB-related informative materials. The staff identified that most of the patients with TB (70%) were of poor socio-economic class, which restricted their purchase of four FDCs only up to 2–3 months. Only 23% were acquainted with the Pakistan National TB Program (NTP). Except for MDR-TB, the results showed a significant correlation between the experiences of staff with TB awareness. Findings from the quality evaluation of four FDC-TB drugs indicated that the dissolution and content assay of rifampicin were not according to the specifications, and overall, 30% of samples failed to comply with specifications. However, the other quality attributes were within the limits.

Conclusion: In light of the data, it can be concluded that private pharmacies could be crucial to the effective management of NTP through the timely identification of patients with TB, appropriate disease and therapy-related education and counseling, and proper storage and stock maintenance.

KEYWORDS

pharmacy practice, lower-middle-income countries, fixed dose combinations, community pharmacy, national TB control program, multi drug resistant tuberculosis, infectious disease

Introduction

Drug-resistant tuberculosis (DR-TB) continues to be a public health threat around the globe (1). DR-TB cases can be classified on the basis of different resistance patterns to anti-TB drugs: monoresistance (resistance to one first-line anti-TB drug only), polyresistance (resistance to two or more of these drugs, except for both rifampicin and isoniazid), multiresistance (resistance to at least both rifampicin and isoniazid), and extensive resistance (resistance to both rifampicin and isoniazid, a fluoroquinolone, and at least one of the three second-line injectable drugs). Although the TB incidence rate is annually declining by 2% and an estimated 54 million deaths have been averted during the last 17 years, the increasing incidence and spread of DR-TB are putting these achievements at stake (2). Presently, a median of 9.9% of *Mycobacterium tuberculosis* strains is now resistant to at least one drug in 35 countries or regions (3). Worldwide, in 2014, 5% of MDR-TB cases were reported to the WHO, including 35% of new cases, while 75% of relapse TB cases were reported in Central Asian and eastern European countries (4).

Pakistan ranks fifth among the list of 30 high-TB burden countries in the world, with an estimated number of 5,18,000 TB cases, including 15,000 MDR-TB cases (5). The Ministry of Health Pakistan, considering the WHO's global emergency declaration, launched a national TB program (NTP) in 1995 against TB and implemented directly observed treatment Directly Observed Therapy Shortcourse (DOTS) with fixed-dose combinations (FDCs) tablets [i.e., isoniazid, (H) rifampicin, (R) ethambutol, (E) and pyrazinamide (Z) (HRZE)] as the first-line therapy in 2001 (6). This policy was followed by launching a Programmatic Management of Drug-Resistant Tuberculosis (PMDT) model of care in 2010 (7) as well as engaging private TB stakeholders on a large scale in 2014, where presumptive patients with TB initially seek respiratory healthcare (8). After launching both PMDT and FDCs strategies, an important objective of NTP was also set to produce a quality product (FDC) locally, meeting the international quality attributes. Although the NTP DOTS program resulted in a high rate of detection (84%), later on, therapy failures owing to the emergence of multidrug resistance tuberculosis (MDR-TB) were reported (9). There is considerable agreement that inadequate treatment or improper use of anti-tuberculosis medications contributed significantly to these therapy failures. Many studies have highlighted that non-adherence to the treatment regimen is due to the lack of knowledge on practices regarding TB, socio-economic barriers, and the attitude of patients and prescribers (10). In terms of information on standard TB treatment protocols, poor/inadequate knowledge among pharmacy technicians and pharmacists working at privately owned pharmacies with regard to differences between simple cough and TB symptoms can be another factor that contributes toward the emergence of MDR-TB due to management fumble. These factors raised the importance of including these privately owned pharmacies in National Tuberculosis Control Programs (NTPs) and training their staff about the importance of the program, highlighting their vital role in the control and proper management of TB (11). The engagement of community pharmacies in detecting TB cases has been briefly adopted and launched across three districts, but the quality of anti-TB medication sold to patients undergoing self-medication has not been explored yet (12). Also,

a large network of private pharmacies exists who are working outside the umbrella of NTP and selling TB medications provided to them by medicine distribution/marketing teams without having any formal training and consultation in checking the quality of medicines procured by them (13).

Therefore, the present study was designed to investigate the quality and storage conditions of fixed-dose combination (FDC) anti-TB drugs sold at retail pharmacies and those under the supervision of National Tuberculosis Programs (NTPs). In addition, the knowledge of private pharmacy-associated staff was also monitored in terms of dispensing inappropriate treatment regimens without patients counseling, resulting in increased MDR-TB in the community of Pakistan.

Methodology

The study was completed in two different phases.

Phase I

A cross-sectional study was performed using two quantitative research designs, i.e., exploratory and descriptive, to evaluate the knowledge of private pharmacy staff. With an exploratory approach, the involvement of community pharmacies in "TB treatment outcome and control by NTP of Pakistan" was observed, while the descriptive study was designed to highlight the current practice and knowledge of community pharmacy staff and associated problems. Phase I was conducted in twin cities, i.e., Rawalpindi and Islamabad. The study period was 6 months.

Phase II

Phase II was aimed at mapping the quality of anti-TB drugs. A cross-sectional survey was conducted in purposively chosen 10 facilities from where FDC anti-TB drugs were sampled. These collected samples were analyzed for dissolution, disintegration, friability, weight variation, and assay and compared with the United State Pharmacopeia (USP) standards. Phase II was conducted in two cities, i.e., Multan and Islamabad. These two cities were chosen purposively due to climatic differences. The temperature of Multan is relatively high with less humidity as compared to Islamabad having humid and low temperatures. Dry, well-lit, ventilated places at a temperature of 15–30°C and relative humidity of 60% are normal storage requirements for medicines.

Study center

A total of 208 pharmacies were included in the Phase I survey from both Rawalpindi and Islamabad. A purposive sampling technique was used to ascertain the pharmacies having staff with relevant working experience and duration. In Phase II, a minimum of 50 tablets from each pharmacy were collected for quality control tests. A total of 3,248 tablets were collected and analyzed for different quality control parameters.

The pharmacies were included in the study based on the following inclusion and exclusion criteria.

Inclusion criteria

All pharmacies (category A), or community retail outlets, having staff with a work experience of more than 7 years and willing to participate in the study were included in the study.

For Phase II, all TB medicines, manufactured by local pharmaceutical companies, with intact packing and under proper storage conditions being consumed by the patients with TB visiting health facilities under the NTP and private community pharmacies and willing to provide the sample were included for random sampling of the medicines.

Exclusion criteria

All retail community pharmacies having staff with a work experience of fewer than 7 years and not willing to participate in the study were excluded from the study.

For Phase II, any anti-TB drug with broken seal packing, expired, or not protected from excessive light, and with no consent for sampling by the NTP or by local manufacturers were excluded from Phase II.

Data collection

For Phase I, the standardized questionnaire tool (pre-tested) was used to collect the data from community pharmacy staff, and pre-test participants were excluded from the main study. All the data were collected through face-to-face interviews conducted at each pharmacy during working hours.

For Phase II, the FDCs containing rifampicin 150 mg, pyrazinamide 400 mg, isoniazid 75 mg, and ethambutol 275 mg in single tablets were sampled from two different facilities, i.e., retail pharmacies and public health facilities of Islamabad. Tablets sampled from retail pharmacies in Islamabad are coded as I, II, and III and those from Multan are coded as IV, V, and VI. Tablets sampled from two public health facilities in Islamabad were coded as W and X and those from Multan were coded as Y and Z. A total of 3,248 tablets were sampled from 10 facilities as shown in [Table 1](#). The manufacturers of the sampled FDC tablets were coded as A, B, C, D, and E along with the percentage of tablets sampled.

Data collection and quality control methodology

For the Phase II study, an observation checklist was used to collect the details of the sample, its storage conditions, and the place of collection. The quality control test of sampled FDCs was conducted following the procedure mentioned in the respective USP monograph using a weighing balance (OHAUS corporation, PA 214C, USA) for the weight variation test, dissolution apparatus II (Erweka, DT-820, Heusenstamm, Germany) for dissolution, and disintegration apparatus (Pharma Test, Germany) for disintegration time. High performance liquid chromatography (HPLC) (Shimadzu SPD 20A, Japan) for drug quantification in various samples.

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences software version 22.0 (SPSS). The demographic profile

TABLE 1 Selected facilities and number of samples collected from each facility in different cities of Pakistan.

Selected facilities	Name of cities	Sample quantity	Number of tablets
Retail pharmacy I	Islamabad	5×20	100
Retail pharmacy II		10×8	80
Retail pharmacy III		10×10	100
Retail pharmacy IV	Multan	10×8	80
Retail pharmacy V		5×20	100
Retail pharmacy VI		10×10	100
Public health facility W*	Islamabad	24×28	672
Public health facility X*		24×28	672
Public health facility Y*	Multan	24×28	672
Public health facility Z*		24×28	672
Total number of tablets sampled from 10 facilities			3248

*FDC-TB drugs dispensed under the supervision of NTP.

of study contributors was entered as categorical variables. The knowledge and practice numbers of study contributors were added as continuous variables. According to bloom's cutoff points, the numbers were then categorized: 50% and below as poor, 60% and above as fair, and 70% and above as good ([11](#)).

In evaluating the potential of private pharmacies (Phase I), the frequency distributions of categorical variables, socio-demographic data, and practice, attitude, and knowledge of community pharmacy staff were estimated using a cross tab, while mean and median were estimated for continuous variables. The correlation between independent and outcome variables was determined using the Pearson chi-square test. However, *P*-value result was reported as statistically significant. While mapping the quality of the anti-TB drug (Phase II) study, data were entered into a Microsoft Excel sheet and then analyzed. A $p \leq 0.05$ was considered statistically significant.

Results

A total of 208 pharmacies were selected based on the willingness of pharmacy owners. The attributes of working staff and selected features of these pharmacies are shown in [Table 2](#).

Basic characteristics of pharmacies and their working staff

The basic characteristics of the working staff and the selected pharmacies are summarized in [Table 2](#). It was observed that among the working staff, most of the subjects were men (98.5%) aged between 21 and 40 years (79.5%) working as salesmen (63.5%) and had a working experience of ≤ 5 (76.5%) years ([Table 2](#)). As shown in [Table 2](#), most of the selected pharmacies

TABLE 2 Basic characteristics of working staff and selected pharmacies.

Characteristics	Number (n = 200)	Percentage
Gender		
Male	197	98.5
Female	3	1.5
Age (years)		
≤20	30	15.0
21–30	119	59.5
31–40	40	20.0
>40	11	5.5
Staff category		
Pharmacist	23	11.5
Pharmacy attendants	50	25.0
Salesman	127	63.5
Experience (years)		
≤5	153	76.5
6–15	21	10.5
>15	26	13.0
Years of establishment		
0–10	142	71.0
11–20	34	17.0
>20	24	12
Clients per day		
≤50	67	33.5
51–100	56	28.0
101–>200	77	38.5
Client documentation		
No documentation	132	66.0
Medicines sale register	64	32.0
Prescription filled	4	2.0
TB information		
No	178	89
Yes	22	11
Working staff		
1	23	11.5
2	63	31.5
3	39	19.5
4	17	8.5
5	15	7.5
>5	43	21.5

n, No of staff available at pharmacies.

had a working life between 0 and 10 years (71%), clientage per day between 50 and 200 (66.5%), with minimum client documentation (32%), and dissemination of TB information (11%), and almost >60% for pharmacies having a staff range of 1–3 (Table 2).

Awareness among working staff

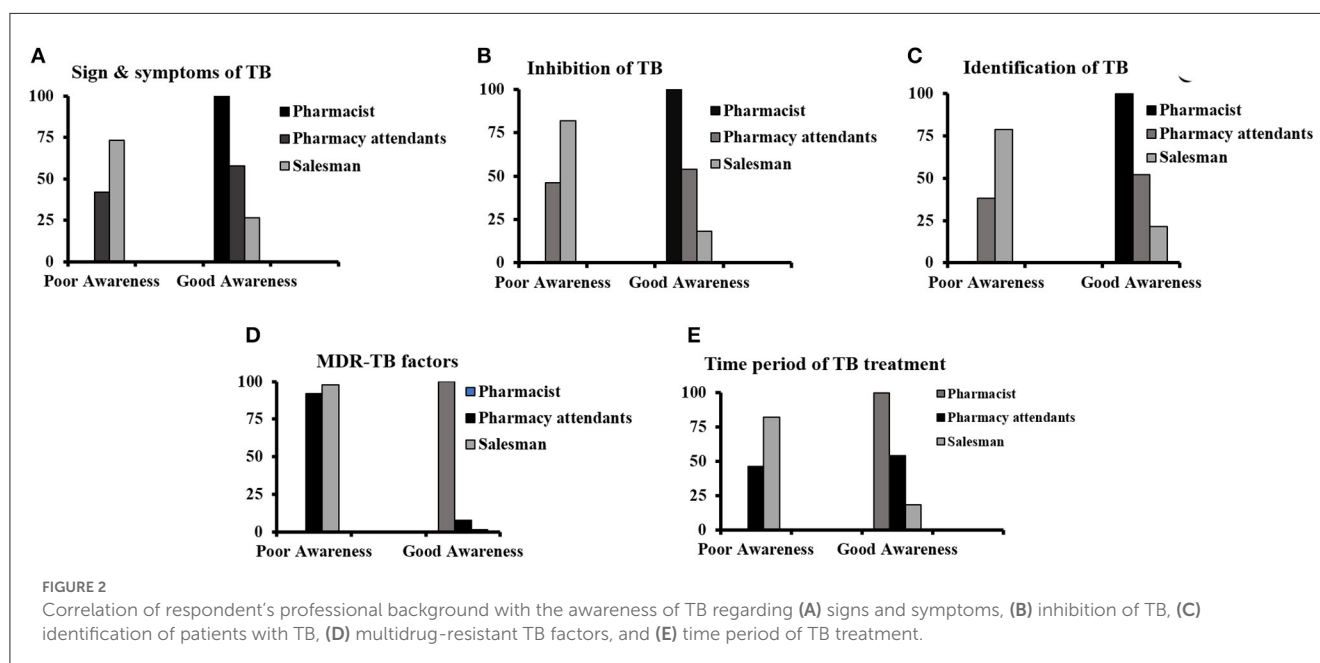
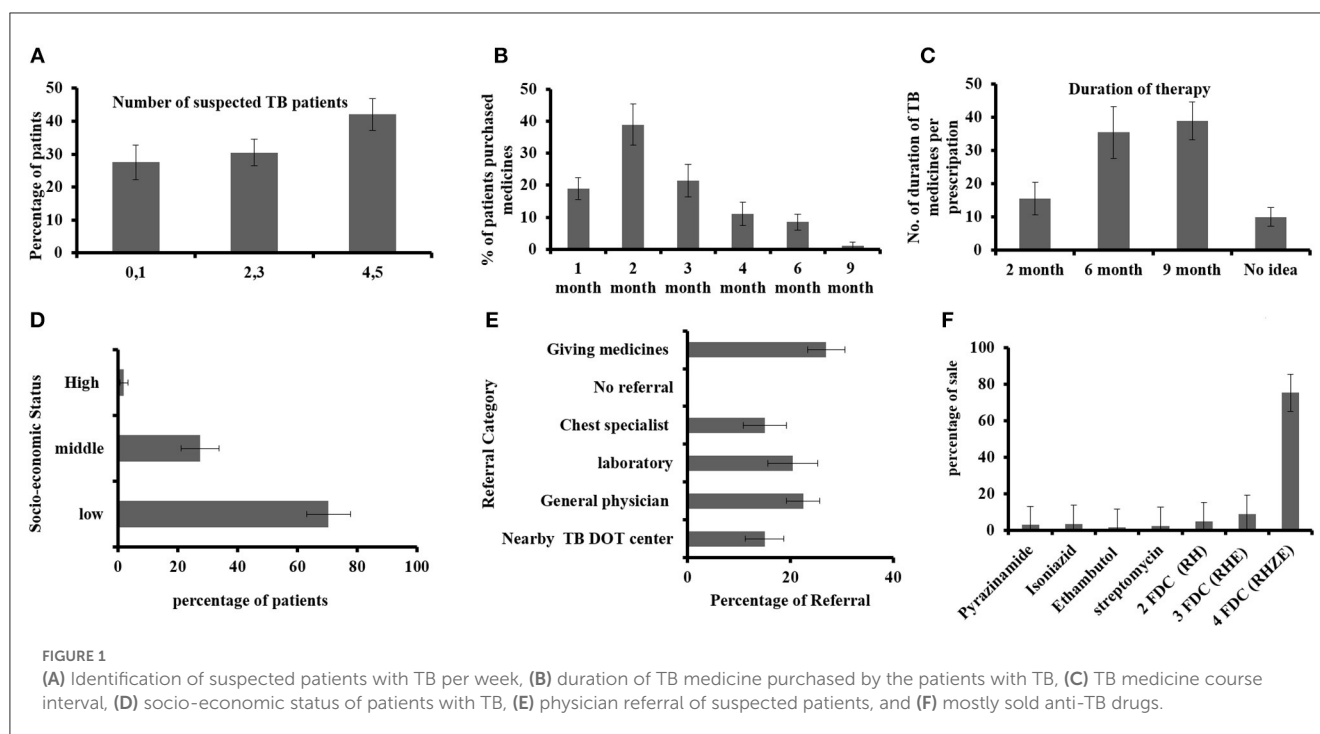
Tuberculosis awareness among the pharmacy staff was evaluated on five parameters. Only 23% of the participants knew about the ntp, while 77% of staff were unaware of the existence of ntp, which is an alarming situation. The (participants) knowledge about the signs and symptoms of TB showed that most patients mentioned cough (more than 2 weeks) and then a tightness in breathing and high temperature at night which is 29, 14, and 13%, respectively, as some of the major signs of positive TB case. About the proliferation of TB in a community, 26% of participants responded that TB proliferation in a community is *via* poverty, 24% reasoned the existence of patients with TB for proliferation, while 21% have no information. For TB identification, 29% of pharmacy staff answered that the most frequent test performed is the sputum smear test, which is followed by the chest X-ray indicated by 18% of staff, while 13% had no idea about the diagnostic tests for TB. Data of the participants views on the possible control of TB showed that the majority (42%) of the staff had an idea that using a mask can inhibit TB spread, whereas 20% said that treatment can inhibit the TB spread and the use of a mask, while 16% had no information. Regarding the emergence of MDR, out of 200 pharmacies, 81% had no knowledge or heard about MDR-TB. Furthermore, when asked about factors contributing to MDR-TB, only 2% of pharmacy staff knew that it was inappropriate treatment and 11% said that the incompleteness of recommended therapy is the reason behind that.

Sale of anti-TB medicines

The sale of anti-TB drugs was assessed through different parameters (as summarized in Figures 1A–F). Regarding the period of TB medicine purchase, almost 60% of interviewed staff answered that patients purchased TB medicines just up to 2 months (Figure 1B) only. When asked about the course of therapy, most of the participants (70%), as shown in Figure 1C, knew that TB therapy takes a 6-month time period, while 10% were unaware of that. The data showed that frequently sold anti-TB medicines were the four fixed-dose combination medicines, and to some extent, two (HZ: isoniazid, pyrazinamide) and three FDC (HZR: isoniazid, pyrazinamide, rifampicin) anti-TB drugs. Figure 1E shows the referral practice of suspected persons in which only 15% were referred to DOT centers, while 27% had no referral and they are giving medicines such as simple cough syrup and broad-spectrum antibiotics.

Correlation of respondent's professional background with the awareness of TB

The correlation between categories of working staff at private retail pharmacies and TB awareness is summarized in Figures 2A–E. In this study, TB awareness was significantly correlated with the professional background of participants and the *p*-value of 0.000 in all figures shows very strong evidence.



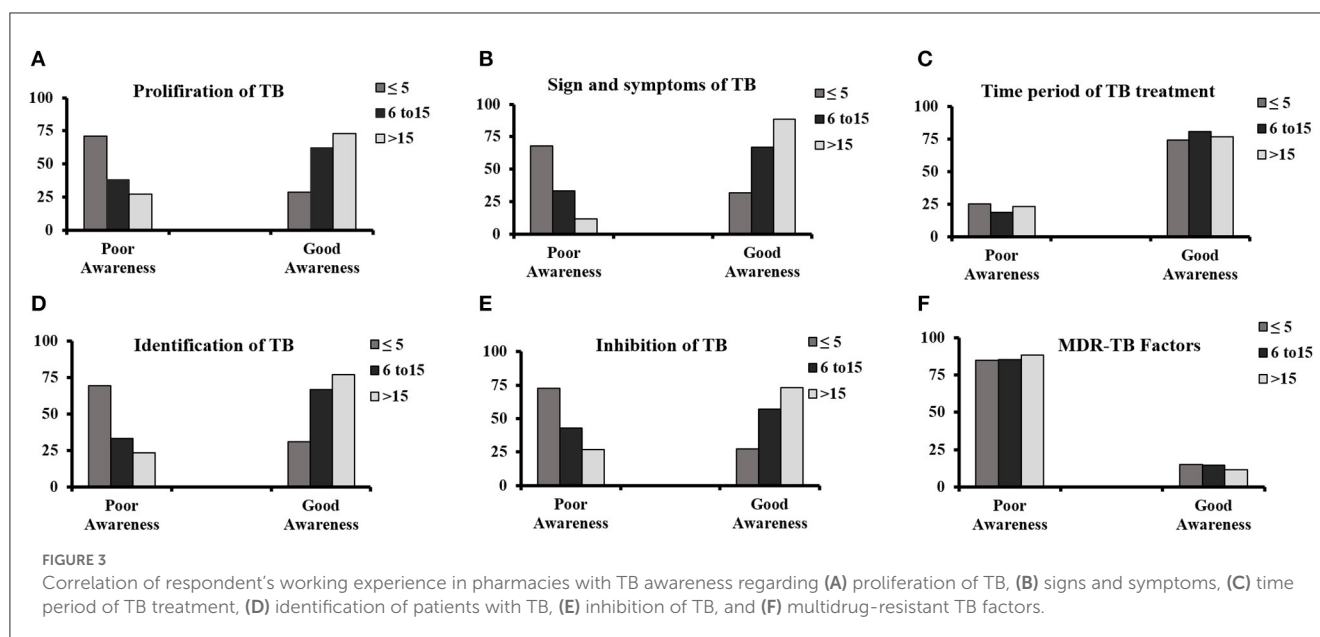
Correlation of respondent's working experience in pharmacies with TB awareness

The correlation between working experience of respondents with TB awareness is summarized in Figures 3A–F. The study showed a direct relationship between TB awareness and the experience of staff. The participants with <5 years' experience had poor knowledge in comparison with those with 6–15 and 15 years of experience. The awareness of TB was significant with a p -value of 0.000 and reveals a positive association with participants

having work experience except for the MDR-TB factors with a $p > 0.005$.

Correlation of respondents' work experience with the identification of patients with TB and the number of working staff with a load of clients

The results are summarized in Table 3. Pharmacies with a high number of working staff had a high number of clients' load,



and similarly, pharmacies with a high number of clients' load had a high number of suspected TB persons. With the exception of respondents' work experience to the customer load, all other variables show a significant result.

Qualitative evaluation of FDCs in different places

The quality of medicines is the prime factor for the efficient treatment and eradication of disease within the course of therapy. The provision of the substandard drug is also a contributor not only to treatment failure but also may result in the emergence of MDR against anti-TB drugs. The quality attributes of FDCs provided at private pharmacies and the NTP monitored at public healthcare facilities were evaluated on different parameters. The storage conditions and environment of the facilities were evaluated to determine the effect on these medicines.

Weight variation test

The results of weight variation studies conducted on various sampled FDCs are summarized in Table 4. The average weight of FDCs tablets was found within an acceptable range of USP (2007)¹ for weight variation, that is, for tablets weighing >324 mg, $\pm 5\%$ is the deviation limit.

Friability

Friability analysis of all the tablets sampled from different places showed that FDCs tablets were within an acceptable limit of USP, that is, <1% (USP, 2007)¹.

Disintegration time test

According to the standard procedure given in USP, the disintegration time for an uncoated tablet is <30 min. The results of the disintegration time studied for sampled FDC tablets are shown in Figure 4C. These results indicated that FDCs tablet samples from different facilities disintegrated within 30 min and, thus, passed the test.

Dissolution test

The result of the dissolution of isoniazid ranged from 91.6 for retail pharmacy I to 98% for public health facility Z. The dissolution of pyrazinamide indicated a minimum range of 92.2% at retail pharmacy IV to a maximum of 98.8% at public health facility Z. Drugs from all facilities complied with the dissolution of ethambutol and within limits, while in Figure 4B, the dissolution of rifampicin shows variation in one sample, which are 70% collected from retail pharmacy VI.

Assay of different FDCs tablets sampled from different facilities

The limit of drug assay is between 90 and 110% of the mentioned label claim. The assay of isoniazid, pyrazinamide, and ethambutol was found within the acceptable limit of specifications given in USP for the samples collected from different places. The assay of rifampicin in FDCs tablets taken from facilities (retail pharmacies II and V) did not meet the assay limits, while the FDC tablets taken from the rest of the facilities were found within the USP acceptable limit. The results of the assay of each drug sampled from different facilities are shown in Figure 4A.

¹ https://www.usp.org/sites/default/files/usp/document/harmonization/gen-chapter/g06_pf_ira_32_2_2006.pdf

TABLE 3 Number of patients with TB per week with regard to the number of staff and their working experience.

Number of patients with TB per week					
No. of customer/day	Identification of patients with TB			Total	p-value
	No. of patients with TB identified				
	0–1 (%)	2–3 (%)	4–5 (%)		
≤50	32 (42.7)	27 (36.0)	16 (21.3)	75	0.0001**
51–100	14 (27.5)	18 (35.3)	19 (37.3)	51	
101–>200	9 (12.2)	16 (21.6)	49 (66.2)	74	
Staff experience/year					
	≤5 (%)	6–15 (%)	> 15 (%)	Total	
≤50	58 (86.6)	6 (9.0)	3 (4.5)	67	0.114
51–100	40 (71.4)	7 (12.5)	9 (16.1)	56	
101–>200	55 (71.4)	8 (10.4)	14 (18.2)	77	
No. of pharmacy staff					
	1–2 (%)	3–4 (%)	≥5 (%)	Total	
≤50	14 (20.9)	30 (44.8)	23 (34.3)	67	0.002**
51–100	6 (10.7)	25 (44.6)	25 (44.6)	56	
101–>200	3 (3.9)	25 (32.5)	49 (63.6)	77	

TABLE 4 Uniformity of weight in FDCs tablets sampled from different facilities.

Selected facility	No of tablets	Deviation of weight	Conclusion
Retail pharmacy I	20	No variation	Within range
Retail pharmacy II	20	No variation	Within range
Retail pharmacy III	20	No variation	Within range
Retail pharmacy IV	20	No variation	Within range
Retail pharmacy V	20	No variation	Within range
Retail pharmacy VI	20	No variation	Within range
Public health facility W	20	No variation	Within range
Public health facility X	20	No variation	Within range
Public health facility Y	20	No variation	Within range
Public health facility Z	20	No variation	Within range

The quality control parameters evaluated for FDCs sampled from various places in both cities showed that overall 30% of the anti-TB FDCs sampled do not meet the specifications which might not produce the desired effects.

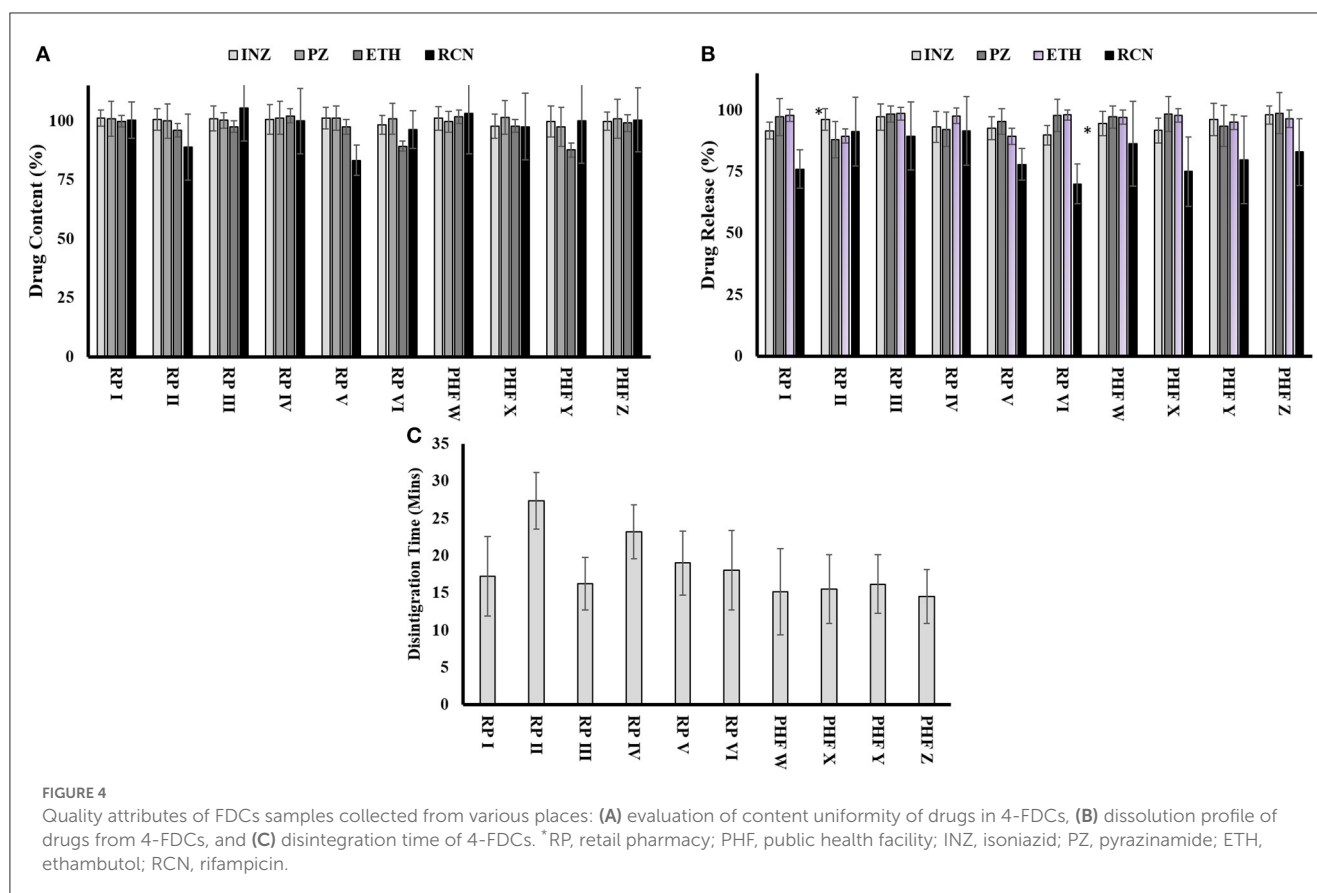
Quality association between retail and public health facilities

The paired comparison *t*-test was applied at a level of significance of 5% ($p = 0.05$) in order to check the association in the quality attributes of FDCs sampled from different facilities.

The results of FDC tablets in percent sampled from public health facilities (Islamabad and Multan) were taken as control as their results were within specifications, while the results of FDC tablets sampled from retail pharmacy facilities (Islamabad and Multan) were taken as test FDCs. Statistics showed that there is a significant association between control and test FDCs. The uniformity of weight, disintegration time, friability, dissolution, and the assay of pyrazinamide, isoniazid, and ethambutol from both retail and public health facilities were within specified limits; thus, for these tests, there was no quality difference between retail and public health facilities. However, in the case of dissolution studies of rifampicin between retail pharmacies and public health facilities, the *p*-value was 0.211, indicating non-significance. FDC tablets sampled from retail pharmacy facilities in the case of the content assay also showed non-significant association from the control as the *p*-values obtained for the assay was 0.0917. Overall, samples from three out of six retail pharmacies showed variations from reference parameters, while all the samples from public health facilities were within a specified range. However, the *p*-value is 0.0924, which is not a significant difference. This analysis suggests that *p*-values are greater than the level of significance (≤ 0.05) for the test parameters, indicating no significant association in the previously tested parameter when public health facilities in both regions were compared with test retail pharmacies.

The followed practice of storage conditions of anti-TB FDC among selected facilities

The storage conditions of drugs from selected facilities were recorded based on an observation checklist. Table 5 shows FDC tablet storage conditions in private retail pharmacies and public



health facilities. The packaging of all the samples was PVC-aluminum strip packs. Except for 1, all the premises were well-lighted and ventilated. The same situation was faced in shelving for drug storage. Among 10 facilities, eight used pallets at least 10 cm off the floor, while two used <10 cm off the floor plates. No expired, damaged, or defective seals or drugs in all facilities were found. In all the selected facilities, there was no monitoring of humidity and temperature. The policy of the first in and first out was followed. None of the facilities had thermometer/temperature control cards. The results in Table 5 showed that there was no proper monitoring of humidity and temperature with the absence of thermometer/temperature control cards in every chosen facility. The table also showed that there was no proper ventilation system. So the excessive temperature and humidity may have affected the quality and efficacy of FDC drugs.

Discussion

The failure in TB management and emergence of MDR or XDR TB is an outcome of various underlying factors such as timely diagnosis, the provision of quality medications along with proper counseling, and most importantly, the involvement and commitment of all stakeholders to decrease the TB burden. The current research was designed to explore two factors, i.e., the evaluation of the privately owned retail pharmacies as a neglecting link in TB control in terms of TB awareness/knowledge among

pharmacy staff. Second, the determination of the quality of four FDC anti-TB drugs available at retail pharmacies in comparison to public health centers provided by the NTP with their storage condition practice in the selected facilities.

One of the essential findings of our study was the lack of awareness about TB among private retail pharmacy-associated staff leading to unsatisfactory consultation and an inability to differentiate simple cough from TB symptoms. Among private retail pharmacies and staff, the same delusions and awareness gaps with respect to TB and its treatment were reported in several studies (12, 13). Pharmacy-associated staff with poor or no awareness about TB were unable to deal with and determine the patients with active TB. Proficient staff with TB knowledge elegantly establish a connection with patients with TB to expand TB knowledge in public and endorse adherence among patients, thus diminishing the rise of MDR-TB. The results highlighted a dire need for training the pharmacy staff with a healthcare framework and NTP regarding capacity building with directions on referral, signs and symptoms screening, and therapy support in TB control.

Another important finding of our study was the lack of qualified personnel in private retail pharmacies as depicted in Table 2 which is also supported by other similar research (14, 15). Qualified pharmacists in Pakistan do not prefer working at private pharmacies, and only 10% of pharmacists work in pharmacies (16). Low-income nations have a normal of 1.2% professional pharmacists for each 10,000 of the population in comparison with 4.4% in middle-income and 10.8 in high-income nations

TABLE 5 Storage conditions of FDC among selected facilities.

Factor	Response	Retail pharmacies (<i>n</i> = 6)	Public health centers (<i>n</i> = 4)	Public health center (<i>n</i> = 10)
		Facilities (%)	Facilities (%)	
Form of packaging	Strip pack	6 (100)	4 (100)	10 (100)
	Loosely packed	0 (0)	0 (0)	0 (0)
	Strongly closed bottle protected from light	0 (0)	0 (0)	0 (0)
Ventilation	Yes	6 (100)	3 (75)	9 (90)
	No	0 (0)	1 (25)	1 (10)
Shelving for drug storage	Yes	6 (100)	3 (75)	9 (90)
	No	0 (0)	1 (25)	1 (10)
Pallets used at least 10 cm off the floor	Yes	5 (83.33)	3 (75)	8 (80)
	No	1 (16.66)	1 (25)	2 (20)
Drugs with damage seals, defective packs, or expiry	Yes	0 (0)	0 (0)	0 (0)
	No	6 (100)	4 (100)	10 (100)
Inspect packages for expiry or defective medicines on receipt	Yes	6 (100)	4 (100)	10 (100)
	No	0 (0)	0 (0)	0 (0)
Drugs stored on floor	Yes	0 (0)	1 (25)	1 (10)
	No	6 (100)	3 (85)	9 (90)
Humidity and temperature monitored	Yes	0 (0)	0 (0)	0 (0)
	No	6 (100)	4 (100)	10 (100)
Adequate storage space	Yes	6 (100)	4 (100)	10 (100)
	No	0 (0)	0 (0)	0 (0)
First in first out practice	Yes	6 (100)	4 (100)	10 (100)
	No	0 (0)	0 (0)	0 (0)
Temperature control cards/thermometer present	Yes	0 (0)	0 (0)	0 (0)
	No	6 (100)	4 (100)	10 (100)
First expiry first out practice	Yes	6 (100)	4 (100)	10 (100)
	No	0 (0)	0 (0)	0 (0)

(17). The community sector of Pakistan can be helpful for TB control. Pharmacists and well-established community pharmacies can play a vital role in TB prevention and treatment. Most patients with TB do not follow their recommended course of therapy and directions associated with their disease leading to the emergence of drug resistance. Therefore, proper counseling for adherence to the prescribed therapy is essential for completing the course of therapy. Thus, for improving patient compliance and the rational use of medicines, there must be a qualified pharmacist in pharmacies at each level. Our research findings showed that most of the pharmacies dispensed simple cough and broad-spectrum antibiotics to patients with cough and fever symptoms, which lead to delayed TB diagnosis and resistance development (Figure 2E). The development of drug-resistant TB and TB diagnostic delays has been directly associated with the overuse of fluoroquinolones (18).

The patients buying anti-TB drugs from private retail pharmacies, with or without a prescription, showed less adherence

and were less likely to complete the recommended course of therapy. In this study, almost 75% of patients purchased anti-TB medicine only for a 2–3-month duration which clearly indicates poor adherence to the required treatment (Figure 2B). The lack of collaboration between pharmacies and public-sector TB control authorities may mean that TB medicines are unwittingly sold without knowledge about their rational use. The majority of patients with TB from the lower socioeconomic class visited private retail pharmacies and purchased TB medications for only a 7-day therapy at a time. Earlier studies also reported the same results (19, 20). Urbanization-associated factors such as poverty and other social forces made the patients with TB less adherent to complete the required course of treatment, thus, it might be a contributing factor to the emergence of drug resistance in the community of Pakistan. This study found that 89% of pharmacies had no informative stuff regarding TB (Table 2). The studies showed variations in

the identification of TB suspected persons, i.e., 1–3 persons per week.

In different studies in India, successful collaboration between Regional National TB Control Program (RNTCP) and private sectors has been accredited to improve the case detection rates of patients with TB (21). Our study indicated that the majority of dispensing drugs in private retail pharmacies were the four fixed-dose combination anti-tuberculosis drugs (Figure 3F). The use of poor-quality drugs is also one of the contributing factors to drug resistance in healthcare sectors. Thus, the second phase of the study aimed to evaluate the quality of anti-TB drugs, i.e., four FDCs (isoniazid, pyrazinamide, rifampicin, and ethambutol) provided to patients. The tablets were sampled from 10 different facilities (six retail pharmacies and four public health facilities) in two different climatic cities, i.e., Islamabad and Multan, Pakistan. Physical characteristics such as weight variation, friability, disintegration test, and content uniformity assay were performed in accordance with official procedures and specifications. All the physical characteristics tests for all facilities were found within the official limits and with no variations. But in case of chemical characteristics, rifampicin failed assay content test i.e., one from Multan and one from Islamabad. FDCs sampled from one retail pharmacy failed a dissolution test for rifampicin which was from Multan (Figure 4B). There was no significant variation among the different facilities, but overall, 30% variations were found. The variations might be due to defective manufacturing or due to the instability of rifampicin in combination with the other drugs present in the product due to the climatic effect. Different researchers have already reported variations in the physio-chemical properties of anti-TB FDCs products, and the results of present studies are a confirmation of what is reported earlier. Previously, the physicochemical stability of different FDCs (rifampicin, isoniazid, pyrazinamide, and ethambutol) available in India under ICH (48°C with RH of 75%) and WHO guidelines were conducted for a period of 3 months with/without packaging. The results showed the content of rifampicin, isoniazid, and pyrazinamide ranging from 90 to 110% initially, which after exposure to accelerated climatic conditions exhibited severe physicochemical instability for an unpackaged and packaged product. The possible reason behind instabilities might be the pyrazinamide with ethambutol that played a catalytic role in the isoniazid and rifampicin interaction (22).

The quality features of FDC and single drug preparations from different pharmacies and TB program centers manufactured by different countries (Estonia, Colombia, Latvia, India, and Vietnam) have already been evaluated, and results have described the effect of storage conditions on these medicines which somehow compromised the quality of FDCs (23).

This study revealed the presence of drugs with poor quality at private retail pharmacies, particularly in terms of dissolution and low content of rifampicin, one of the important antibiotics in TB treatment. Poor efficacy or low-quality drugs is an important factor in treatment failure and the emergence of resistance against anti-TB drugs. Thus, strict compliance with the storage conditions must be observed to protect the drug contents in anti-TB drugs in the market. Private pharmacies and

TB regulatory authorities' collaboration is important as a combined effort to offer better care to patients with TB and avoid drug resistance in Pakistan. Pharmacoeconomics is a significant factor that governs compliance with long-term therapy. It was noticed that due to financial problems, most patients discontinue their treatment which is one of the major factors in the emergence of drug resistance. Another important observation was the stigma associated with TB, which possibly leads to most of the patients buying medicine from private pharmacies rather than NTP, which provides free diagnostic and treatment services (24, 25). Significant improvements were seen in the notification of TB cases and therapy completion ratio after the contractual engagements of pharmacy owners in South Asia (26, 27), which indicates that the proper involvement of private pharmacies in the TB control program can make a significant difference in the disease burden and decrease the MDR. Thus, this study suggests that to implement the laws, there should be the presence of at least one certified pharmacist in each and every pharmacy. In addition, the recognition of community pharmacy-associated staff as a major and necessary healthcare provider for communicable and chronic diseases is important. The NTP should continue private pharmacy staff training and support to encourage them to take part in TB control. There is a need for public awareness to provide confidence to citizens that demand appropriate counseling regarding their disease and the medication use of TB from private pharmacy staff.

Conclusion

The study highlighted that the overall qualifications and training of technicians working at community pharmacies in Pakistan are inadequate regarding TB management. Patient adherence to TB medication is much higher for public health facilities as they provide free of cost treatment. The storage conditions were satisfactory to some extent in all selected private pharmacies and public health facilities, with an exception for temperature and humidity, which were not monitored in any of the selected facilities. The storage conditions showed some effects on the quality of the FDCs as 30% of samples showed variations from specifications for rifampicin content and dissolution profile as they failed to comply with the specifications. Moreover, the study also highlighted the implementation of the laws ensuring the presence of at least one certified pharmacist for proper supervision and ensuring the quality of medicine with proper storage conditions. The involvement of privately owned pharmacies and pharmacists in the TB control program can make a significant difference in terms of proper medication provision with patient counseling ensuring maximum adherence to the course of therapy.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval for conducting this project was obtained from the Advanced Studies and Research Board, Quaid-i-Azam University, Islamabad (REC-RIPS-2020/443).

Author contributions

FB conceived and designed the study, collected, interpreted, analyzed the data, drafted the first version of the manuscript, and revised the final manuscript. MS assisted in the data collection and reviewed the first draft. HH coordinated in data collection and revising of the manuscript. WU assisted in the analysis and writing. AK provided advice on data analysis and interpretation. GS assisted in the conceptual phase and study design, reviewed the first draft, and provided approval for the final manuscript. All authors contributed to the article and approved the submitted version.

References

1. WHO. *Global Tuberculosis Report 2020*. (2020). Available online at: <https://www.who.int/publications-detail-redirect/9789240013131> (accessed January 3, 2023).
2. Khan I, Ahmad N, Khan S, Muhammad S, Ahmad Khan S, Ahmad I, et al. Evaluation of treatment outcomes and factors associated with unsuccessful outcomes in multidrug resistant tuberculosis patients in Baluchistan province of Pakistan. *J Infect Public Health*. (2019) 12:809–15. doi: 10.1016/j.jiph.2019.04.009
3. Saeed W, Naseem A, Ahmed J. JPMA—journal of Pakistan medical association. *J Ayub Med Coll Abbottabad*. (2013) 63. Available online at: <https://jpma.org.pk/supplement-article-details/101>
4. Catho G, Couraud S, Grard S, Bouaziz A, Sénéchal A, Valour F, et al. Management of emerging multidrug-resistant tuberculosis in a low-prevalence setting. *Clin Microbiol Infect*. (2015) 21:472.e7–10. doi: 10.1016/j.cmi.2014.12.022
5. Ali S, Khan MT, Khan AS, Mohammad N, Khan MM, Ahmad S, et al. Prevalence of multi-drug resistant *Mycobacterium tuberculosis* in khyber Pakhtunkhwa—a high tuberculosis endemic area of Pakistan. *Pol J Microbiol*. (2020) 69:1–5. doi: 10.33073/pjm-2020-005
6. Waheed Y, Khan MA, Fatima R, Yaqoob A, Mirza A, Qadeer E, et al. Infection control in hospitals managing drug-resistant tuberculosis in Pakistan: how are we doing? *Public Health Action*. (2017) 7:26–31. doi: 10.5588/pha.16.0125
7. Abbas S, Kermod M, Kane S. Strengthening the response to drug-resistant TB in Pakistan: a practice theory-informed approach. *Public Health Action*. (2020) 10:147–56. doi: 10.5588/pha.20.0030
8. Ullah W, Wali A, Haq MU, Yaqoob A, Fatima R, Khan GM. Public-Private mix models of tuberculosis care in Pakistan: a high-burden country perspective. *Front Public Health*. (2021) 9:703631. doi: 10.3389/fpubh.2021.703631
9. Javaid A. Tuberculosis control in Pakistan. *Pak J Chest Med*. (2010) 16:07.
10. Yadav S, Damor R, Kantharia S, Tiwari M. Assessment of knowledge and treatment seeking behaviour among tuberculosis and multi-drug resistant tuberculosis patients—a case control study. *IOSR J Dent Med Sci*. (2015) 14:66–71. doi: 10.97900853-14726671
11. Rajeswari R, Balasubramanian R, Bose MSC, Sekar L, Rahman F. Private pharmacies in tuberculosis control—a neglected link. *Int J Tuberc Lung Dis*. (2002) 6:171–3.
12. Ullah W, Almansour H, Fatima R, Saini B, Khan GM. Engaging community pharmacies in early detection of missing tuberculosis patients through public-private mix intervention in Pakistan. *Am J Trop Med Hyg*. (2020) 103:221–30. doi: 10.4269/ajtmh.19-0939
13. Mustafa T, Shahzad Y, Kiani A. A survey of knowledge, attitude, and practices of private retail pharmacies staff in tuberculosis care: study from Dera Ismail Khan City, Pakistan. *J Pharm Policy Prac*. (2018) 11:7. doi: 10.1186/s40545-018-0134-1
14. Qidwai W, Krishanani M, Hashmi S, Afridi M, Ali R. Private drug sellers' education in improving prescribing practices. *J Coll Phys Surg Pak*. (2006) 16:743–6.
15. Butt ZA, Gilani AH, Nanan D, Sheikh AL, White F. Quality of pharmacies in Pakistan: a cross-sectional survey. *Int J Qual Health Care*. (2005) 17:307–13. doi: 10.1093/intqhc/mzi049
16. Azhar S, Hassali MA, Ibrahim MIM, Ahmad M, Masood I, Shafie AA. The role of pharmacists in developing countries: the current scenario in Pakistan. *Hum Resour Health*. (2009) 7:54. doi: 10.1186/1478-4491-7-54
17. FIP Pharmaceutique. *International Pharmaceutical Federation Reference Paper Collaborative Practice*. (2009). Available online at: https://www.fip.org/files/fip/PharmacyEducation/FIP_workforce_web.pdf (accessed June 30, 2022).
18. Chen T-C, Lu P-L, Lin C-Y, Lin W-R, Chen Y-H. Fluoroquinolones are associated with delayed treatment and resistance in tuberculosis: a systematic review and meta-analysis. *Int J Infect Dis*. (2011) 15:e211–6. doi: 10.1016/j.ijid.2010.11.008
19. Nair DM, George A, Chacko K. Tuberculosis in Bombay: new insights from poor urban patients. *Health Policy Plan*. (1997) 12:77–85. doi: 10.1093/heapol/12.1.77
20. Farmer P. Social scientists and the new tuberculosis. *Soci Sci Med*. (1997) 44:347–58. doi: 10.1016/S0277-9536(96)00143-8
21. Murthy K, Frieden T, Yazdani A, Hreshikesh P. Public-private partnership in tuberculosis control: experience in Hyderabad, India. *Int J Tuberc Lung Dis*. (2001) 5:354–9.
22. Bhutani H, Mariappan T, Singh S. The physical and chemical stability of anti-tuberculosis fixed-dose combination products under accelerated climatic conditions. *Int J Tuberc Lung Disease*. (2004) 8:1073–80.
23. Kenyon T, Kenyon A, Kgarebe B, Mothibedi D, Binkin N, Layloff T. Detection of substandard fixed-dose combination tuberculosis drugs using thin-layer chromatography. *Int J Tuberc Lung Dis*. (1999) 3:S347–50.
24. Lönnroth K, Uplekar M, Blanc L. Hard gains through soft contracts: productive engagement of private providers in tuberculosis control. *Bull World Health Organ*. (2006) 84:876–83. doi: 10.2471/BLT.06.029983
25. Uplekar M, Pathania V, Raviglione M. Private practitioners and public health: weak links in tuberculosis control. *Lancet*. (2001) 358:912–6. doi: 10.1016/S0140-6736(01)06076-7
26. Khan MS, Salve S, Porter JD. Engaging for-profit providers in TB control: lessons learnt from initiatives in South Asia. *Health Policy Plan*. (2015) 30:1289–95. doi: 10.1093/heapol/czu137
27. Lönnroth K, Karlsson M, Lan N, Buu T, Dieu T. Referring TB suspects from private pharmacies to the national tuberculosis programme: experiences from two districts in Ho Chi Minh City, Vietnam. *Int J Tuberc Lung Dis*. (2003) 7:1147–53.

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.

Frontiers in Public Health

Explores and addresses today's fast-moving healthcare challenges

One of the most cited journals in its field, which promotes discussion around inter-sectoral public health challenges spanning health promotion to climate change, transportation, environmental change and even species diversity.

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 Public Health

