frontiers | Research Topics

Children's health and safety: What we learned from the COVID-19 pandemic and future policy's perspective

Edited by
Biagio Solarino, Nicola Laforgia and Antonio Oliva

Published in
Frontiers in Public Health
Frontiers in Pediatrics

ISSN 1664-8714
ISBN 978-2-8325-2750-4
DOI 10.3389/978-2-8325-2750-4

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

Children's health and safety: What we learned from the covid-19 pandemic and future policy's perspective

Topic editors

Biagio Solarino — University of Bari Aldo Moro, Italy
Nicola Laforgia — UOC NEONATOLOGY UTIN AOUC POLICLINICO
Antonio Oliva — Catholic University of the Sacred Heart, Rome, Italy

Citation

Solarino, B., Laforgia, N., Oliva, A., eds. (2023). *Children's health and safety: What we learned from the COVID-19 pandemic and future policy's perspective*.
Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-2750-4

Table of contents

frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 06 June 2023
DOI 10.3389/fpubh.2023.1220977

OPEN ACCESS

EDITED AND REVIEWED BY
Michelle Plusquin,
University of Hasselt, Belgium

*CORRESPONDENCE
Simona Nicoli
✉ simona.nicoli@uniba.it

RECEIVED 11 May 2023
ACCEPTED 24 May 2023
PUBLISHED 06 June 2023

CITATION
Solarino B, Nicoli S, Benevento M, Zedda M and Oliva A (2023) Editorial: Children's health and safety: what we learned from the COVID-19 pandemic and future policy's perspective. *Front. Public Health* 11:1220977. doi: 10.3389/fpubh.2023.1220977

Editorial: Children's health and safety: what we learned from the COVID-19 pandemic and future policy's perspective

Biagio Solarino[1], Simona Nicoli[1]*, Marcello Benevento[1], Massimo Zedda[2] and Antonio Oliva[2]

[1]Section of Legal Medicine, Department of Interdisciplinary Medicine, University of Bari, Bari, Italy, [2]Department of Health Surveillance and Bioethics, Section of Legal Medicine, Fondazione Policlinico A. Gemelli Istituto di Ricovero e Cura a Carattere Scientifico, Università Cattolica del Sacro Cuore, Rome, Italy

KEYWORDS

children safety, bioethics in pediatrics, risk management, public health, SARS-Cov2, children

Editorial on the Research Topic
Children's health and safety: what we learned from the COVID-19 pandemic and future policy's perspective

The wellbeing of minors and older adults has always been a public health target. The health and wellbeing of children, enshrined in the Convention on the Rights of the Child (CRC) in 1989, refer to multiple physical, psychological, social, and economic aspects (1). The main factors reventing these rights from being secured are poverty, social isolation, and persistent discrimination.

It is well-known that the health system assumes primary importance in investigating and ensuring the wellbeing of little patients.

The extreme care that has always characterized everything concerning children can also be found in pediatric health issues influencing the sector's workers to deal with thorny implications like patient safety, bioethics, and risk management in a generally multidisciplinary setting.

The scientific literature concerning risk management, patient safety, and bioethics in the pediatric environment requires continuous and updated study by healthcare professionals, in an effort that encounters obstacles not always easy to overcome and in most cases connected with the complexity of the children's health.

We aimed to collect contributions about risk management in pediatric settings concerning bioethical topics and patient safety. Furthermore, in this setting, we also suggest considering the challenges faced by the recent COVID-19 pandemic.

Among the main problems that emerged during the global health emergency, mental disorders in the adolescent population have been addressed by several authors. Kim et al. investigated a possible association between families' economic hardship and mental disorders in Korean adolescents. Anxiety, depressive symptoms, and suicidal ideation seem to be related to the family's economic features, suggesting how economic policies may have a pivotal role in mental health and how it would be helpful to intervene in the health sector by employing online screening and counseling. This last consideration entails consistent ethical and medico-legal challenges to be considered since a complex trade-off between ethical and legal principles must be met to pursue the principle of the best interests of the child (2).

Moreover, Yang et al. investigated a similar issue in the Chinese pediatric population, looking for the risk factors for the increase of the obesity rate. The study identified "grandchild care" as a risk factor for poor pediatric hygiene, i.e., child care provided by older family members, inadequate health insurance policies, and inequalities in socioeconomic factors. This study also offered new prospects for an early intervention involving families, schools, health facilities, and the government, in a multi-level intervention system, with new protections and new social policies. The lockdown imposed by governments has uncovered significant problems relating to hygiene and care of children, highlighting the inadequacy of some parental behaviors and habits and highlighting how the domestic environment often hides many pitfalls and unhealthy behaviors for children.

In this regard, it should be noted that domestic abuse represented a public health concern even before the pandemic, being mainly represented by neglect. However, the risk of interpersonal abuse has globally been increased by the pandemic-related restrictions and thus a frontier in research was to verify if the frequency of minors witnessing interpersonal violence had been increased by the lockdown.

In particular, Focardi et al., an Italian research group analyzed the access in the last 4 years to the Emergency Department of an Italian tertiary hospital due to witnessed violence in the pediatric population. The results highlighted a stationary incidence of the phenomenon compared to previous years. The results are consistent with most studies covering the same period, although in some cases an increase in domestic abuse of minors has been reported (3). This discrepancy could be explained by the protective role played by schools closed during the lockdown, in which educators are generally the first to notice mistreatment. At the same time, promoting education may enhance secondary prevention interventions.

From a clinical perspective, Juul et al. addresses a further challenging issue about surgical waiting lists, which also have implications for pediatric units. This study found that the pandemic has significantly affected the waiting times for elective urological procedures and showed a decrease in the number of those performed. The paper highlights the need for healthcare providers to develop strategies to shorten wait times by ensuring delay-free healthcare.

The access to care of the patients and the safety of the health operators is a critical balance since both clinical and forensic practice hospital environment has different sources of infections, that represent critical hazards if the relatively long persistence of SARS-CoV-2 even on inanimate surfaces is considered. Safety protocols and screening tests of various kinds proved their effectiveness in different hospital contexts (4, 5). Regarding the microbiological risk during the pandemic era, Song et al. found that the transmission of SARS-CoV-2, and thus the infectivity of the virus, varied among different age groups of patients. Furthermore, gastrointestinal symptoms may be the initial presentation of COVID-19 or the only manifestation of the disease in children, and therefore symptoms such as vomiting, diarrhea, and abdominal pain should be considered as part of the screening in pediatric patients.

In this Research Topic, Vetrugno et al. and Bilotta et al. addressed different aspects of the COVID-19 pandemic, highlighting the importance of early screening for SARS-CoV-2 in hospitalized patients and of the vaccination in the pediatric population.

While the first article focuses on preventing the spread of the virus within hospitals, the second study emphasizes the need to protect the health of children and prevent the spread of the virus in the broader community, both providing essential insights into the challenges posed by the pandemic and the need for proactive measures to address these challenges. Bilotta examines the ethical principles of autonomy, beneficence, and non-maleficence in the context of COVID-19 vaccination in children, emphasizing the importance of informed consent and the need for healthcare providers to provide parents with accurate and comprehensive information about the vaccine.

Therefore, the collection of articles on children's health and safety in this Frontiers Research Topic highlights the need for new intervention perspectives and proactive actions for better management of clinical, social, and economic pediatric issues, not forgetting the training gaps of healthcare personnel already operational or still in training. Although the issue of safety in the care of pediatric patients has multiple facets, bioethical issues are still little treated. In conclusion, ensuring a multidisciplinary approach in terms of health care, social interventions, and policy is necessary for the overall wellbeing of children.

Author contributions

BS and AO contributed to the conception and design of the editorial. SN, MB, and MZ wrote the first draft of the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

Publisher's note

References

1. Simon J, Luetzow A, Conte JR. Thirty years of the convention on the rights of the child: developments in child sexual abuse and exploitation. *Child Abuse Negl.* (2020) 110(Pt 1):104399. doi: 10.1016/j.chiabu.2020.104399

2. Ferorelli D, Mandarelli G, Solarino B. Ethical challenges in health care policy during COVID-19 pandemic in Italy. *Medicina.* (2020) 56:691. doi: 10.3390/medicina56120691

3. Kourti A, Stavridou A, Panagouli E, Psaltopoulou T, Spiliopoulou C, Tsolia M, et al. Domestic violence during the COVID-19 pandemic: a systematic review. *Trauma Violence Abuse.* (2023) 24:719–45. doi: 10.1177/15248380211038690

4. Lv Y, Ma Y, Si Y, Zhu X, Zhang L, Feng H, et al. Rapid SARS-CoV-2 antigen detection potentiates early diagnosis of COVID-19 disease. *Biosci Trends.* (2021) 15:93–9. doi: 10.5582/bst.2021.01090

5. Filograna L, Manenti G, Grassi S, Zedda M, Cazzato F, Ryan CP, et al. Virtual autopsy in SARS-CoV-2 breakthrough infection: a case report. *Forensic Imaging.* (2022) 30:200520. doi: 10.1016/j.fri.2022.200520

frontiers in Public Health

ORIGINAL RESEARCH
published: 15 March 2022
doi: 10.3389/fpubh.2022.850206

Age-Specific Transmissibility Change of COVID-19 and Associations With Breathing Air Volume, Preexisting Immunity, and Government Response

Qifa Song[1†], *Chao Cao*[2†], *Yi Xiang*[3†], *Liemin Ruan*[4*] *and Guoqing Qian*[4*]

[1] Medical Data Center, Ningbo First Hospital, Ningbo University, Ningbo, China, [2] Department of Respiratory and Critical Medicine, Ningbo First Hospital, Ningbo University, Ningbo, China, [3] Ningbo Women and Children's Hospital, Ningbo, China, [4] Department of Infectious Diseases, Ningbo First Hospital, Ningbo University, Ningbo, China

Background: The comprehensive impacts of diverse breathing air volumes and preexisting immunity on the host susceptibility to and transmission of COVID-19 at various pandemic stages have not been investigated.

Methods: We classified the US weekly COVID-19 data into 0–4, 5–11, 12–17, 18–64, and 65+ age groups and applied the odds ratio (OR) of incidence between one age group and the 18–64 age group to delineate the transmissibility change.

Results: The changes of incidence ORs between May, 2020 and November, 2021 were 0.22–0.66 (0–4 years), 0.20–1.34 (5–11 years), 0.39–1.04 (12–17 years), and 0.82–0.73 (65+ years). The changes could be explained by age-specific preexisting immunity including previous infection and vaccination, as well as volumes of breathing air. At the early pandemic, the ratio that 0–4-year children exhaled one-fifth of air and discharge a similar ratio of viruses was closely associated with incidence OR between two age groups. While, after a rollout of pandemic and vaccination, the much less increased preexisting immunity in children resulted in rapidly increased OR of incidence. The ARIMA model predicted the largest increase of relative transmissibility in 6 coming months in 5–11-year children.

Conclusions: The volume of breathing air may be a notable factor contributing to the infectivity of COVID-19 among different age groups of patients. This factor and the varied preexisting greatly shape the transmission of COVID-19 at different periods of pandemic among different age groups of people.

Keywords: coronavirus disease 2019 (COVID-19), host susceptibility, volume of breathed air, age-specific transmissibility, preexisting immunity

OPEN ACCESS

Edited by:
Nicola Laforgia,
University of Bari Aldo Moro, Italy

Reviewed by:
Antonio Di Mauro,
Azienda Sanitaria Localedella Provincia di Barletta Andri Trani (ASL BT), Italy
Raffaella Panza,
Mater Dei Hospital, Italy

***Correspondence:**
Guoqing Qian
bill.qian@outlook.com
Liemin Ruan
lmruan@tom.com

[†]These authors have contributed equally to this work

Specialty section:
This article was submitted to Children and Health, a section of the journal Frontiers in Public Health

Received: *07 January 2022*
Accepted: *16 February 2022*
Published: *15 March 2022*

Citation:
Song Q, Cao C, Xiang Y, Ruan L and Qian G (2022) Age-Specific Transmissibility Change of COVID-19 and Associations With Breathing Air Volume, Preexisting Immunity, and Government Response. Front. Public Health 10:850206. doi: 10.3389/fpubh.2022.850206

INTRODUCTION

As of November 2021, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused more than 250 million cases of coronavirus disease 2019 (COVID-19) and 5.0 million deaths (1). The COVID-19 pandemic demonstrates distinctive age-specific infection rates (2), showing significantly lower infection rates in young children aged under 10 years at the early pandemic (3), as proved by the report of the first 149,082 US cases, consisting of only 2,572 (∼1.7%)

infants, children, and adolescents <18 years despite children <18 years making up 22% of the US population (4). This feature is contrasting with influenza, as reported that the odds ratio (OR) of influenza-like illness among children vs. adults was 3.1 (5), although both diseases are caused by respiratory RNA viruses alike.

Whether a virus can successfully invade individuals and causes symptoms depends on three determinant factors, including viral load reaching the host, environmental factors, and host susceptibility to the virus (6). Host susceptibility and viral load often demonstrate age-specific features (7). Previous studies have found similar distinctive age-specific infection rates of COVID-19 in many transmission scenarios (8, 9), suggesting that the distinctive host susceptibility between children and adults markedly accounts for lower transmissibility among children. Host susceptibility to infectious diseases usually depends on preexisting immunity and viral load entering individuals. Preexisting immunity to COVID-19 was determined by preceding infection and vaccination (10), both of which were more prominent in adults than in children because adults were prioritized for vaccination and had a higher incidence of COVID-19 in most countries.

As to the entrance of SARS-CoV-2 into the host, substantial evidence proved that airborne transmission through the respiratory route was the main mode of COVID-19 transmission (11). Airborne SARS-CoV-2 mainly comes from exhaled air of patients and previous studies have proved no difference in viral load in the breathing air between children and adults (12), hence, a higher volume of breathing air of patients results in a higher airborne viral load that greatly increases the transmissibility of COVID-19 (13). In human beings, the volume of breathing air is determined by breath rate and tidal volume. Tidal volume is the volume of air moving in or out of the lungs in one breathing cycle and is correlated with body weight, about 7 mL of breathing air per 1 kg body weight in one breath (14). A 70-kg adult breathes ∼500 mL of air per breath or 10 L per min when he/she breathes 20 times per min at the rest state. Generally, children have a faster rate of breath, i.e., 30–40, 25–30, and 20–25 breaths/min for children under 1, 1–3, and 4–14 years, respectively. A child weighing 10 kg (1 year old, 30 breaths/min) approximately has a tidal volume of 70 mL and breathes 2.1 L of air per min (15).

To date, the comprehensive impacts of diverse breathing air volumes and preexisting immunity on the transmission of COVID-19 at different pandemic stages have not been investigated. Especially, the diverse breathing air volumes among different age people have been overlooked in previous studies. We hypothesized that at the early stages of the COVID-19 pandemic, when the whole population have very low immunity to SARS-CoV-2, the difference in breathing air volume was a determinant factor that characterizes the relative transmissibility of COVID-19 in terms of ORs of incidence between children and adults. While after a duration of pandemic and vaccination, the increased preexisting immunity would discretely affect the transmission in different age groups.

In this study, we used the age-stratified incidence of the US COVID-19 data to describe the change of relative host susceptibility and transmissibility among different age groups. Risk factors including different volumes of breathing air, preexisting immunity, and government responses were analyzed for host susceptibility and transmissibility during various stages of the pandemic. We also made a prediction of relative transmissibility among different age groups by the autoregressive integrated moving average (ARIMA) model.

METHODS

Study Data

The COVID-19 weekly incidence of cases (number of cases/100,000 persons) and full vaccination rate (percentage) stratified by age were obtained from the US CDC (https://covid.cdc.gov/covid-data-tracker/#demographicsovertime). The data covered from May, 2020 to November, 2021. OR of incidence between an age group and 18–64 years group was calculated. Mean body weights of 0–4, 5–11, and 12–17 years were designated as 12, 25, and 48 kg that were the median body weight using the WHO children's standard weight. People of 18–64 and 65+ years were all adults and were designated a mean body weight of 70 kg. Their tidal volumes were calculated according to the equation of 7 mL × kg of body weight. The volume of breathing air per minute was calculated by tidal volume × breathing rate (**Table 1**). Ratio of volume of breathing air per minute between an age group and 18–64 years was calculated. Preexisting immunity in each age group was represented by the sum of infection percentage and full vaccination percentage.

Association Between Volume of Breathing Air and Incidence Among Different Age Populations

As airborne transmission through the respiratory route is the main mode of COVID-19 transmission, the transmissibility of COVID-19 is correlated with the viral load inhaled from the contaminated air. This viral load largely depends on the volume of exhaled or inhaled air by the patient. When children and adults were exposed to the same environment, such as in the household, they inhaled and exhaled age-specific viral loads because of different volumes of breathing air.

We used the breathing air volume calculated from body weight to represent the relative viral load transmitted *via* breathing air, which was referred to as the relative transmissibility in terms of OR. We designated the transmissibility of 70-kg adults to be 1. The ORs representing transmissibility and relative host susceptibility between one age group and 18–64-year adults were calculated.

ARIMA Models

Time series analysis aims to reveal reliable and meaningful statistics and use this knowledge to predict future values of a series of data. The ARIMA model is one of the most used time series models and was applied in the analysis of COVID-19 transmission (16). The current study applied the automatic time series forecasting package in R to conduct ARIMA analysis (17). The weekly ORs between an age group and 18–64 age group were accompanied by time information and were typical time series data. We used these data to construct an ARIMA model to predict

TABLE 1 | Body weight and volume of breathing air in different age individuals.

Age group (year)	Weight (kg)	Tidal volume (mL)	Breathing rate (times/m)	Exhaled air/m (mL)	Ratio of volume of breathing air[a]
0– 4	12	84	30	2,520	0·26
5–11	25	175	25	4,375	0·45
12–17	48	336	20	6,720	0·69
18–64	70	490	20	9,800	1
65–	70	490	20	9,800	1

[a]*Ratio of volume of breathing air is calculated by comparing volume of exhaled air per min of an age group to that of the 18–64-year group.*

the change of OR in the following 26 weeks. The model that minimized the Akaike information criterion (AIC) amongst all appropriate models with different time period was selected as the best model for prediction.

RESULTS

Up to November, 2021, 49 million cases were reported by the US CDC. Based on body weight, similar exposure chances in households, schools, and workplaces, we defined five age groups of 0–4, 5–11, 12–17, 18–64, and 65+ years by averaging the incidence of the component age groups. In May, 2020, 0–11-year children had the lowest risk of infection, while as the pandemic developed, the infection rate in school children (5–17 years) gradually increased to the high infection rates in November, 2021. The 65+ elders and 0–4 young children had low risk in the late pandemic (**Figure 1**). Compared with the 18–64 age group, the ORs of weekly incidence for 0–4, 5–11, and 12–17 age groups climbed from 0.22, 0.2, and 0.39 in May, 2020 to 0.66, 1.34, and 1.04 in November, 2021, respectively (**Figure 2**). This drastic raise of ORs indicated the relative increasing transmissibility of COVID-19 among the 0–17 years population. In contrast, the OR of the 65+ age group declined from 0.82 to 0.73 during the same period, suggesting a reduced relative susceptibility to COVID-19 in the 65+ years. Moreover, the 12–17 age group had two peaks of susceptibility increase around May and August, 2021.

In 2021, the vaccination was rolled out rapidly among the 12–17, 18–64, and 65+ age groups (**Figure 3**). As of November 2021, the full vaccination rates were 0, 1, 51.4, 66.2, and 85.9% among five age groups, respectively, indicating massively lower preexisting immunity rates among the 0–11-year children than the >12-year population.

As proposed above, when preexisting immunity has not been established at the early epidemic of an emerging respiratory virus like SARS-CoV-2, the airborne viral load inhaled and exhaled by patients was the key contributor to infection. Such a postulation was strongly proved by the evident relationship between OR of breathing air volume and OR of incidence at the early period of COVID-19 pandemic (**Table 1**). Compared with the volume of breathing air of 18–64-year adults, the ratios of breathing air volume for the 0–4, 5–11, 12–17, and 65+ age groups were 0.25, 0.45, 0.69, and 1, respectively. At the early pandemic period of May, 2020, the ORs of incidence of these age groups were 0.22, 0.20, 0.39, and 0.82, which was highly associated with the ORs of breathing air volume. For the 0–4-year children, the OR of incidence was very similar to the ratio of volume of breathing air, implicating the marked contribution of the volume of breathing air to host susceptibility. However, at the late pandemic period of November, 2021, the corresponding ORs of incidence in the 0–4, 5–11, 12–17 age groups were 0.66, 1.34, and 1.04. The increased OR of incidence in young children (0–4 and 5–11 years) suggested less contribution of breathing air volume to infection rate.

Finally, to investigate the OR trend denoting the relative host susceptibility of COVID-19 infection among different age groups, ARIMA model of weekly OR values of each age group was employed to make a 26-week prediction, i.e., from November, 2021 to May, 2022 (**Figure 4**). The model demonstrated that the 0–4 and 5–11 age groups would increase from 0.63 to 0.78, and from 1.14 to 1.4, respectively, while the 12–17 and 65+ age groups would remain a steady level. The results suggested that 0–11- year-young children would continuously experience an increased host susceptibility to COVID-19, an average increase by 26% as compared with adults.

DISCUSSION

We used the US weekly COVID-19 data to highlight the age-specific transmissibility change of COVID-19 resulting from host susceptibility during the COVID-19 pandemic. We demonstrated associations between host susceptibility and two risk factors of volume of breathing air and preexisting immunity. We conclude that at the early COVID-19 pandemic, varied volumes of breathing air are a notable positive determinant factor of host susceptibility and transmissibility of COVID-19, while at the late pandemic, preexisting immunity develops to be an increasing age-specific impact. The ARIMA model predicts a probable long-term increase of transmissibility in 0–11-year children.

By now, the age-specific transmissibility of SARS-CoV-2 requires further study. Previous research reported that children were less susceptible to COVID-19 infection than adults. Data from the first few months of the pandemic revealed that individuals aged under 20 years had approximately half of the infection rate of adults aged 20 years and older (18). However, these conclusions failed to describe the distinctive change of susceptibility among different age groups at different stages of the pandemic. This phenomenon also seemed puzzling when we considered that SARS-CoV-2 was RNA virus and had a similar respiratory transmission mode like influenza virus to

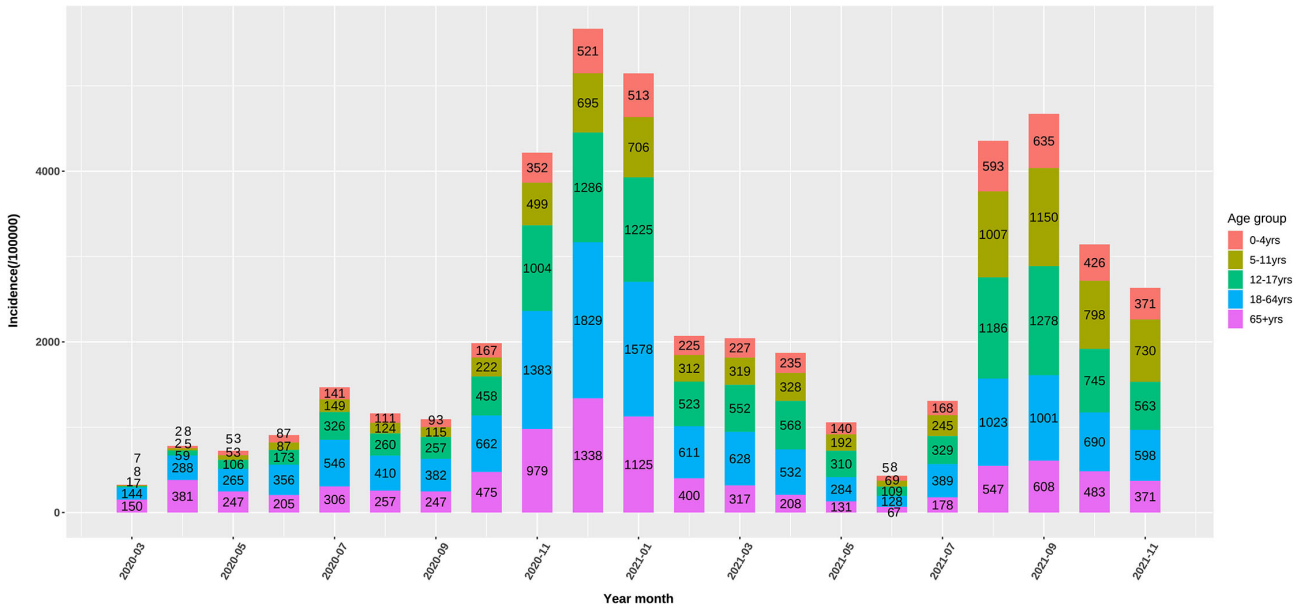


FIGURE 1 | Monthly incidence (/100000) of the US COVID-19 confirmed cases in 0–4, 5–11, 12–17, and 65+ age groups.

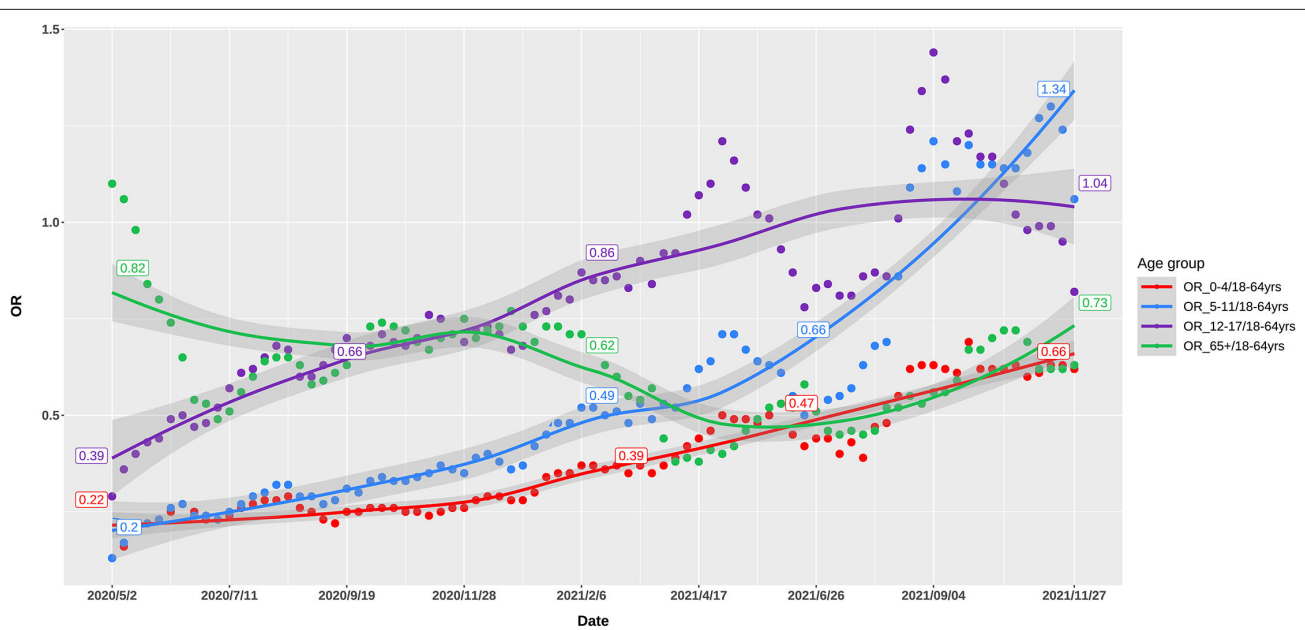


FIGURE 2 | Odds ratio of weekly incidence of the US COVID-19 cases in 0–4, 5–11, 12–17, and 65+ age groups, as compared with 18–64 age group.

which children are more susceptible. We undertook to figure out this discrepancy by investigating pivotal factors affecting host susceptibility. Besides the preexisting immunity, we included the volume of breathing air that varied dramatically between children and adults and determined the breathed viral load.

We applied OR of the incidence of COVID-19 between one age group and 18–64 age group to delineate the relative transmissibility among different age groups, as these OR values were more telling in demonstrating the changing incidence among various groups. These ORs changed differentially from the early to late COVID-19 pandemic, showing age-specific trajectories of host susceptibility change between age groups. As compared to 18–64 age group, the ORs of weekly incidence in 0–4, 5–11, and 12–17 age groups increased by 200, 570, and 266% from May, 2020 to November, 2021, respectively, while the OR for the 65+ age group

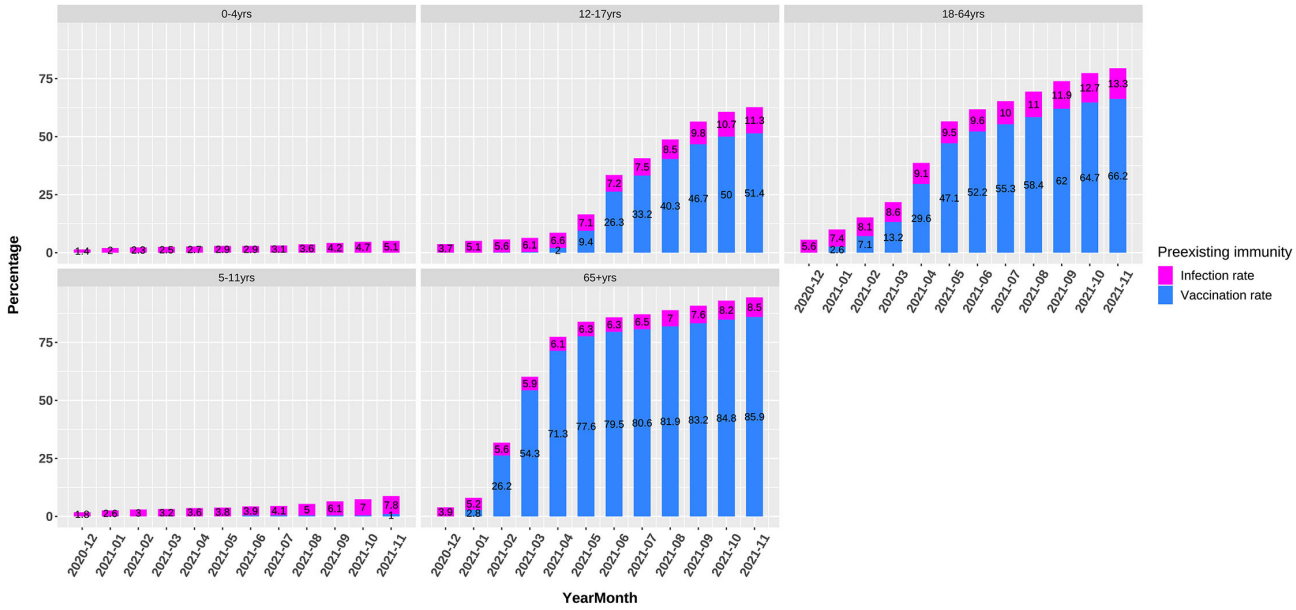


FIGURE 3 | Preexisting immunity including infection and vaccination rates in 0–4, 5–11, 12–17, 18–64, and 65+ age groups.

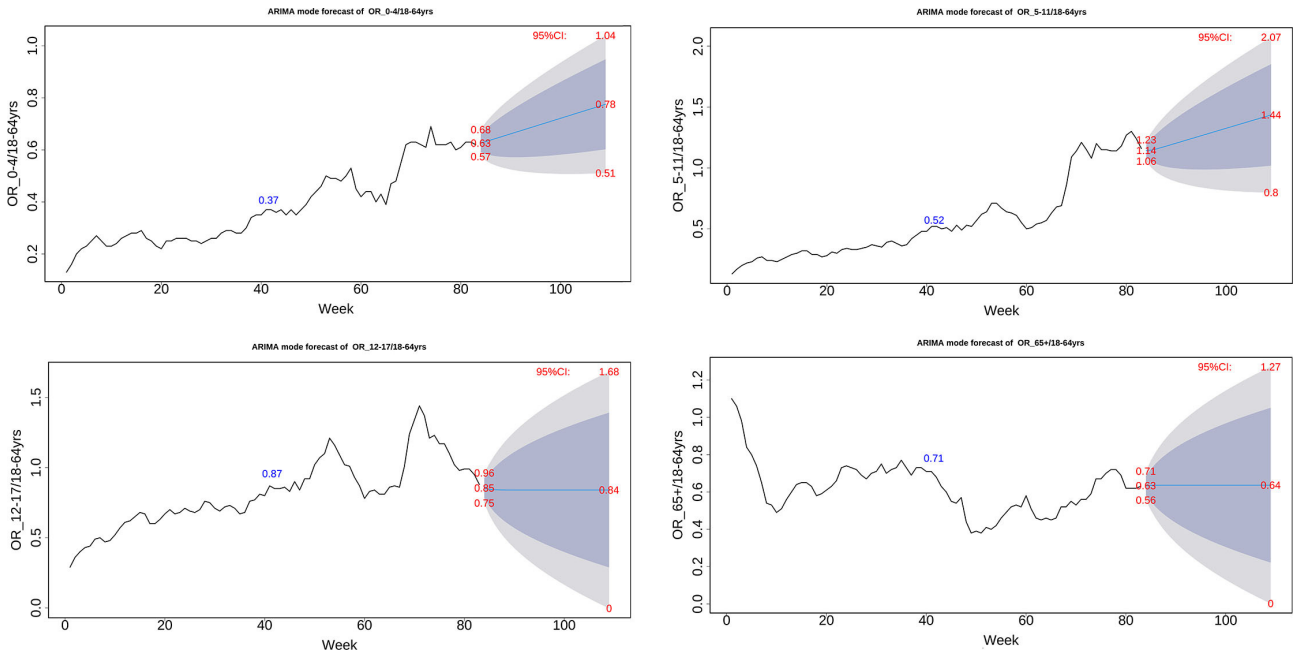


FIGURE 4 | ARIMA model of weekly odds ratio of the US COVID-19 incidence between one age group and 64+ age group.

declined by 11% (**Figure 1**). Notably, the 65+ age group had a rapid decrease in the OR around January–April, 2021, while 5–17 children had a rapid increase. Although mutated SARS-CoV-2 might partly account for the changes of transmissibility, the continuous age-specific OR changes implied persistently changing host susceptibility among different age groups.

As noted already, host susceptibility is chiefly affected by viruses successfully entering individuals and preexisting immunity. The magnitude of these two factors varied substantially among different age groups in a developing pandemic by an emerging pathogen. Our findings denoted that at the early stages of the COVID-19 pandemic when preexisting immunity was not established, the volume of breathing air played

a pivotal role in determining the viral load exhaling from and inhaling into a patient and thus the transmissibility, as proved by the highly similar ORs between the volume of breathing air and the incidence among different age groups in May, 2020 (**Table 1**, **Figure 2**). The association between transmissibility and volume of breathing air could be easily inferred because the titration of the viruses in the air exhaled by adults and children was similar, while adults breathed more air (19). The ratio that a 70-kg adult breathes five times of air per minute as a 0–4-year child was almost the same as the OR of incidence between these two age groups. At the late stages of the pandemic, adults established a higher level of preexisting immunity due to higher infection rates and prioritized vaccination (**Figure 3**).

To what extent preexisting immunity can influence the transmissibility of COVID-19 among different age people for a long time remains a challenging question. We can get a clue from the characteristics of influenza transmission that rages on human beings for more than 100 years. Influenza infects people in many similar aspects such as transmission mode, mutation, as well as viral biological features. After years of fighting against influenza virus, adults are much less susceptible compared to children, owing to a higher-level preexisting immunity gradually established with age, as illustrated by a cross-sectional study in England in 2008 investigating baseline antibody titration to influenza A H1N1 infection. The England study showed age-dependent positive rates of baseline antibody as follows: 4.9% (0–4 years), 12.3% (5–14 years), 29.1% (15–24 years), 44.6% (50–64 years), and 83.7% (>80 years) (20), revealing great difference in baseline antibody levels among different age groups. This excellently explained the order of attack rate for 2009 pandemic influenza A (H1N1) that was 5–18, 0–4, 19–64, and 65+ years (21).

Considering the more than 1-year pandemic of COVID-19, preexisting immunity differed greatly between 18–64-year adults and 0–11-year children because of the age-specific vaccination policy and infection levels (**Figure 3**). We can view 0–4-year children as a baseline of preexisting immunity before a respiratory pandemic like SARS-CoV-2 and influenza virus because they do not experience enough exposure. When and how people have a profile of preexisting influenza-like immunity to COVID-19 is a vital issue to investigate and monitor. The ORs of different age groups in our study in November, 2021 showed an order trend partly like influenza, i.e., 5–11, 12–17, 18–64, 65+, and 0–4 age groups (**Figures 1**, **2**). We found that the 65 + age group had preexisting immunity level of 94.4%, which was close to 2009 H1N1 (83.7%) in the preceding report. The current study suggests that preexisting immunity similar to influenza is developing in population in the COVID-19 pandemic.

Finally, ARIMA analysis made an age-specific prediction of the relative susceptibility. In the following 6 months, a steady increase in OR was predicted for the 0–4 and 5–11 age groups, whereas the 17–19 and 65+ age groups were predicted to remain an unchanged OR trend (**Figure 4**). We believe a longer time is required to reach transmission features like influenza that most age groups have a high level of preexisting immunity.

The present study had strengths and weak. The strength is that the American COVID-19 data have accurate information about age-specific incidence for the whole period. We used OR of incidence between age groups to vividly illustrate the relative transmissibility among different age groups. The weak aspect is that many confounding factors other than the three risk factors discussed above might affect the COVID-19 transmission. We managed to compensate other underlying factors using OR of incidence.

To summarize, our study highlights that varied preexisting immunity at the early and late stages of the COVID-19 pandemic wields distinctive impacts on people of different ages. The volume of breathing air may be a notable factor contributing to the infectivity of COVID-19 among different age groups of patients. Intensified monitor about the age-specific impacts of preexisting immunity on the transmissibility of the pandemic is imperative.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: CDC (https://covid.cdc.gov/covid-data-tracker/#demographicsovertime).

ETHICS STATEMENT

This methodological study was waived for ethical approval by the Ethics Committee of Ningbo First City Hospital as no patients were involved.

AUTHOR CONTRIBUTIONS

QS, CC, and YX designed the study and wrote the manuscript. LR and GQ provided the fund and reviewed the manuscript. QS analyzed the data and wrote the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by Natural Science Foundation of Ningbo (2021J270), Ningbo City COVID-19 Epidemic Prevention and Control Project (202002N7033), and Public Welfare Fund of Zhejiang Province, China (No. LGF22G030010).

REFERENCES

1. WHO. *COVID-19 Weekly Epidemiological Update-Edition 59* (2021). Available online at: https://www.who.int/publications/m/item/weekly-operational-update-on-covid-19 (accessed November 03, 2021).

2. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis.* (2020) 20:689–96. doi: 10.1016/S1473-3099(20)30198-5

3. Goldstein E, Lipsitch M, Cevik M. On the effect of age on the transmission of SARS-CoV-2 in households, schools and the community. *J Infect Dis.* (2020) 223:362–9. doi: 10.1093/infdis/jiaa691
4. Team CC-R. Coronavirus disease 2019 in children - United States. *MMWR Morb Mortal Wkly Rep*. (2020) 69:422–6. doi: 10.15585/mmwr.mm6914e4
5. Sugimoto JD, Borse NN, Ta ML, Stockman LJ, Fischer GE, Yang Y, et al. The effect of age on transmission of 2009 pandemic influenza A (H1N1) in a camp and associated households. *Epidemiology*. (2011) 22:180–7. doi: 10.1097/EDE.0b013e3182060ca5
6. Leung NHL. Transmissibility and transmission of respiratory viruses. *Nat Rev Microbiol.* (2021) 19:528–45. doi: 10.1038/s41579-021-00535-6
7. Channappanavar R, Perlman S. Age-related susceptibility to coronavirus infections: role of impaired and dysregulated host immunity. *J Clin Invest.* (2020) 130:6204–13. doi: 10.1172/JCI144115
8. Zhang J, Litvinova M, Liang Y, Wang Y, Wang W, Zhao S, et al. Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China. *Science.* (2020) 368:1481–6. doi: 10.1126/science.abb8001
9. Dattner I, Goldberg Y, Katriel G, Yaari R, Gal N, Miron Y, et al. The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children. *PLoS Comput Biol*. (2021) 17:e1008559. doi: 10.1371/journal.pcbi.1008559
10. Sette A, Crotty S. Pre-existing immunity to SARS-CoV-2: the knowns and unknowns. *Nat Rev Immunol.* (2020) 20:457–8. doi: 10.1038/s41577-020-0389-z
11. Dyer O. Covid-19: airborne transmission is being underestimated, warn experts. *BMJ.* (2020) 370:m2720. doi: 10.1136/bmj.m2720
12. Yonker LM, Neilan AM, Bartsch Y, Patel AB, Regan J, Arya P, et al. Pediatric severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): clinical presentation, infectivity, and immune responses. *J Pediatr.* (2020) 227:45–52.e5. doi: 10.1016/j.jpeds.2020.08.037
13. Leung NHL, Chu DKW, Shiu EYC, Chan KH, McDevitt JJ, Hau BJP, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med.* (2020) 26:676–80. doi: 10.1038/s41591-020-0843-2
14. Simonis FD, Serpa Neto A, Schultz MJ. The tidal volume fix and more. *J Thorac Dis.* (2019) 11:E117–E22. doi: 10.21037/jtd.2019.08.39
15. WHO. *WHO Child Growth Standards* (2020). Available online at: https://www.who.int/childgrowth/standards/w_f_a_tables_z_boys/en/ (accessed July 08, 2020).
16. Ceylan Z. Estimation of COVID-19 prevalence in Italy, Spain, and France. *Sci Total Environ.* (2020) 729:138817. doi: 10.1016/j.scitotenv.2020.138817
17. Hyndman R, Athanasopoulos G, Bergmeir C, Caceres G, Chhay L, O'Hara-Wild M, et al. *Forecast: Forecasting Functions for Time Series and Linear Models*. R package version 8.15 (2021). Available online at: https://pkg.robjhyndman.com/forecast/
18. Davies NG, Klepac P, Liu Y, Prem K, Jit M, Group CC-w, Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nat Med.* (2020) 26:1205–11. doi: 10.1101/2020.03.24.20043018
19. Heald-Sargent T, Muller WJ, Zheng X, Rippe J, Patel AB, Kociolek LK. Age-related differences in nasopharyngeal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) levels in patients with mild to moderate coronavirus disease 2019 (COVID-19). *JAMA Pediatr.* (2020) 174:902–3. doi: 10.1001/jamapediatrics.2020.3651
20. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet.* (2010) 375:1100–8. doi: 10.1016/S0140-6736(09)62126-7
21. Yang Y, Sugimoto JD, Halloran ME, Basta NE, Chao DL, Matrajt L, et al. The transmissibility and control of pandemic influenza A (H1N1) virus. *Science.* (2009) 326:729–33. doi: 10.1126/science.1177373

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 | Frontiers in Public Health

ORIGINAL RESEARCH
published: 28 April 2022
doi: 10.3389/fpubh.2022.874758

How the First Year of COVID-19 Affected Elective Pediatric Urology Patients: A Longitudinal Study Based on Waiting Lists and Surveys From 10 European Centers

Nikolai Juul[1], Aurélie Cazals[2], Aybike Hofmann[3], Virginia Amesty[4], Gilvydas Verkauskas[5], Barbara Dobrowolska-Glazar[6], Gundela Holmdahl[7,8], Maria Escolino[9], Jacques Birraux[10], Tamas Kovacs[11], Nicolas Kalfa[2,12] and Magdalena Fossum[1,8]*

[1] Division of Pediatric Surgery, Department of Surgery and Transplantation, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark, [2] Service de Chirurgie Viscérale et Urologique Pédiatrique, Hôpital Lapeyronie, CHU de Montpellier, Montpellier, France, [3] Department of Pediatric Urology, KUNO Clinic St. Hedwig, University Medical Center, Regensburg, Germany, [4] Department of Pediatric Urology, Hospital Universitario La Paz, Madrid, Spain, [5] Children's Surgery, Orthopedics and Traumatology Center, Faculty of Medicine, Vilnius University, Vilnius, Lithuania, [6] Department of Pediatric Urology, Jagiellonian University Medical College, Krakow, Poland, [7] Department of Pediatric Surgery, Karolinska University Hospital, Stockholm, Sweden, [8] Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden, [9] Pediatric Surgery and Urology Unit, Federico II University Hospital, Naples, Italy, [10] Service de Chirurgie de l'Enfant et de l'Adolescent, Centre Universitaire romand de Chirurgie Pédiatrique, Hôpitaux Universitaire de Genève, Genève, Switzerland, [11] Division of Pediatric Surgery, Department of Pediatrics, Albert Szent-Gyorgyi Clinical Center, University of Szeged, Szeged, Hungary, [12] Université de Montpellier, Institut Debrest de Santé Publique IDESP, UMR INSERM, Montpellier, France*

OPEN ACCESS

Edited by:
Nicola Laforgia, Università degli Studi di Bari Aldo Moro, Italy

Reviewed by:
Mario Giordano, Giovanni XXIII Children's Hospital, Italy
Antonio Andrea Grosso, Careggi University Hospital, Italy

***Correspondence:**
Nikolai Juul
nikolai.juul.01@regionh.dk

Specialty section:
This article was submitted to Children and Health, a section of the journal Frontiers in Public Health

Received: *12 February 2022*
Accepted: *14 March 2022*
Published: *28 April 2022*

Citation:
Juul N, Cazals A, Hofmann A, Amesty V, Verkauskas G, Dobrowolska-Glazar B, Holmdahl G, Escolino M, Birraux J, Kovacs T, Kalfa N and Fossum M (2022) How the First Year of COVID-19 Affected Elective Pediatric Urology Patients: A Longitudinal Study Based on Waiting Lists and Surveys From 10 European Centers. Front. Public Health 10:874758. doi: 10.3389/fpubh.2022.874758

Introduction: COVID-19 impacted healthcare systems worldwide, and elective surgical activity was brought to a minimum. Although children were not primarily affected by the disease, pediatric urology was halted by clinical closedown and staff allocation. We aimed to document how these prioritizations affected waiting lists, and to investigate how European centers dealt with the challenge of these logistical and financial prioritizations.

Materials and methods: This was a 1-year prospective study, starting March 2020. Participants were surveyed at 3-month intervals about waiting lists for several common procedures as well as OR capacity and funding. Further, centers retrospectively reported on surgical and outpatient activity rates during 2019–2021. Waiting list tendencies were evaluated in relation to study baseline.

Results: A marked decrease in surgical and outpatient activity was seen in the spring of 2020. Some included pediatric urology centers were able to increase their budget (15%) and staff working hours (20%) during part of the study period. Still, at the end of the study, the centers had increased the total number of patients on waiting lists with 11%, whereas the average days on waiting lists had accumulated with 73%, yielding a total of 6,102 accumulated waiting days in the study population. Centers with decreased resources had markedly negative effects on waiting lists.

Conclusions: Correlations between COVID-19 derived burdening of healthcare systems and the availability of pediatric urology greatly depends on the prioritizations made at individual centers. Ongoing monitoring of these correlations is warranted to safely avoid unnecessary negative impact on the pediatric population.

Keywords: pediatrics, urology, waiting lists, COVID-19, multicenter study

INTRODUCTION

Coronavirus disease 2019 (COVID-19) deeply impacted the activity of pediatric urology cases in Europe and has had consequences during an extended period of time. Early on in the pandemic, statements and guidelines from European and North American pediatric urological societies recommended only to perform surgery in cases of organ- or life-threatening disease during lockdown, and further suggested to reduce all outpatient clinic consultations during the first wave of the COVID-19 pandemic (1–3). New protocols have been established to adopt minimally invasive surgery to treat pediatric surgical and urological pathologies during this pandemic, aiming at preserving both patient's and surgeon's safety (4, 5). While these guidelines were structured to prioritize cases in relation to urgency, clinics were also facing the challenge of complying with and taking in to account the varying degrees of less urgent, however already heavily surceased, elective procedures (6).

This initiative was undertaken in order to launch a collaborative European multicenter study on the COVID-19 pandemic and how this has affected pediatric urology cases and patients related to the ERN eUROGEN work stream 1 disease areas. The primary aim of the study was to evaluate how closure of elective interventions affected the pediatric urology population by increased time and patients on the waiting list for surgical interventions. The secondary aim was to evaluate how different centers dealt with the problem of an increased caseload before and after re-opening.

By prospectively gathering data from European centers, we intended to provide an overview of the current impacts which could be used as a tool for information and political decision-making at a local, regional, or European level. Since the COVID-19 pandemic is far from over, and since new pandemics may very well arise, this paper is meant to help in the future planning for dealing with pandemics or other major crises affecting societies and health care.

MATERIALS AND METHODS

This was a European multicenter study comprising 10 tertiary pediatric urological centers broadly representing most parts of western Europe (**Table 1**). Centers were recruited by asking representatives from all the health care providers that were part of the European reference network eUROGEN work stream 1 (rare congenital urogenital and rectal anomalies) or by direct contact with European centers fulfilling the European reference network inclusion criteria (7).

To be included in the study, the participating center would have to be a tertiary referral center performing advanced pediatric urology cases, although not by definition exclusively. Centers should have access to pediatric intensive care units, a minimum of 1 million population base for referrals of specialized pediatric urology and/or pediatric surgery cases, and in an area where COVID-19 closedown required cancellations of all elective surgery (only running emergency and imperative cases). Chief of department in all centers approved retrieval of information regarding waiting lists to surgery and data collection, and surveys were compiled and answered by the co-author representing each center. All reported data from waiting lists was anonymized on a patient level.

The study design was a longitudinal, prospective study based on pediatric urology cases waiting lists in different European centers. Centers participated over a 13-months study period (March 2020 to April 2021). At five timepoints (March, June, October, January, and April, respectively), centers were asked to count the waiting lists within a range of predetermined elective, non-emergent and non-oncologic urological procedures (**Table 2**). To differentiate our results further, centers were asked to report on both the number of patients waiting and

TABLE 1 | Participating centers with corresponding country codes and reference populations in million people.

Center	City (country)	Ref. population (mio.)
Clinic St. Hedwig University Medical Center	Regensburg (DE)	1.2
Federico II University Hospital	Naples (IT)	1.5
Vilnius University Hospital Santaros Klinikos	Vilnius (LI)	1.5
Albert Szent-Gyorgyi Clinical Center	Szeged (HU)	1.5
Hospital Universitario La Paz	Madrid (ES)	2
University Center of Pediatric Surgery of Western Switzerland	Geneva (CH)	2.4
Rigshospitalet University Hospital	Copenhagen (DK)	2.5
Hôpital Lapeyronie CHU de Montpellier	Montpellier (FR)	2.7
Karolinska University Hospital	Stockholm (SE)	3
Jagiellonian University Medical College	Krakow (PL)	3.3

Abbreviations: AUA, American Urology Association; ESPU, European Society of Pediatric Urology; ERN, European Reference Network; eUROGEN, ERN for rare urogenital diseases and complex conditions; OR, Operating room.

TABLE 2 | Total number of patients and mean days per person on waiting lists, for each procedure of interest and across all participating centers, presented in absolute numbers.

	March 2020 (T0)		June 2020 (T1)		October 2020 (T2)		January 2021 (T3)		April 2021 (T4)	
Intervention	**Patients**	**Days**	**Patients**	**Days**	**Patients**	**Days**	**Patients**	**Days**	**Patients**	**Days**
Hypospadias repair	298	142	298	185	311	167	317	176	272	193
Orchidopexy	257	75	228	109	275	104	314	95	274	110
Foreskinplasty (phimosis)	183	80	178	124	199	116	256	96	247	137
Cystoscopy (diagnostic or therapeutic)	85	79	92	114	76	96	91	118	89	127
Pyeloplasty (open or laparoscopic)	18	55	18	60	18	36	19	47	15	34
Heminephrectomy or nephrectomy (open)	10	90	13	96	8	104	15	65	13	51
Surgery of the kidney (laparoscopic or robotic)	4	36	2	119	4	38	5	66	6	7
Bladder surgery for ureteric pathologies (open)	49	76	30	124	26	118	30	102	32	79
Intervention for urolithiasis	3	20	4	66	7	122	9	48	8	78
Bladder exstrophy closure	1	30	3	77	3	148	5	50	1	49
Epispadias surgery	5	142	8	155	6	197	9	158	9	144
Surgery of the bladder (laparoscopic or robotic)	3	60	2	121	1	16	3	47	4	150
Bladder neck surgery for incontinence (open)	11	151	7	274	5	320	5	384	6	360
PSARP	9	32	8	55	8	65	6	93	5	78
Reversal of colostomy	8	56	7	80	7	101	3	242	3	313
Others	66	61	67	126	94	84	81	94	139	138
Total/mean	1,010	74	965	118	1,048	114	1,168	118	1,123	128

Procedures reported by centers in the category "Others" included: Hernias, JJ-stent removal, varicocele, hydrocele, urogenital sinus correction, urachal cyst correction, labia minora hypertrophy correction, various biopsies, vesicostomy, ureterostomy reconstruction, and buried penis correction.

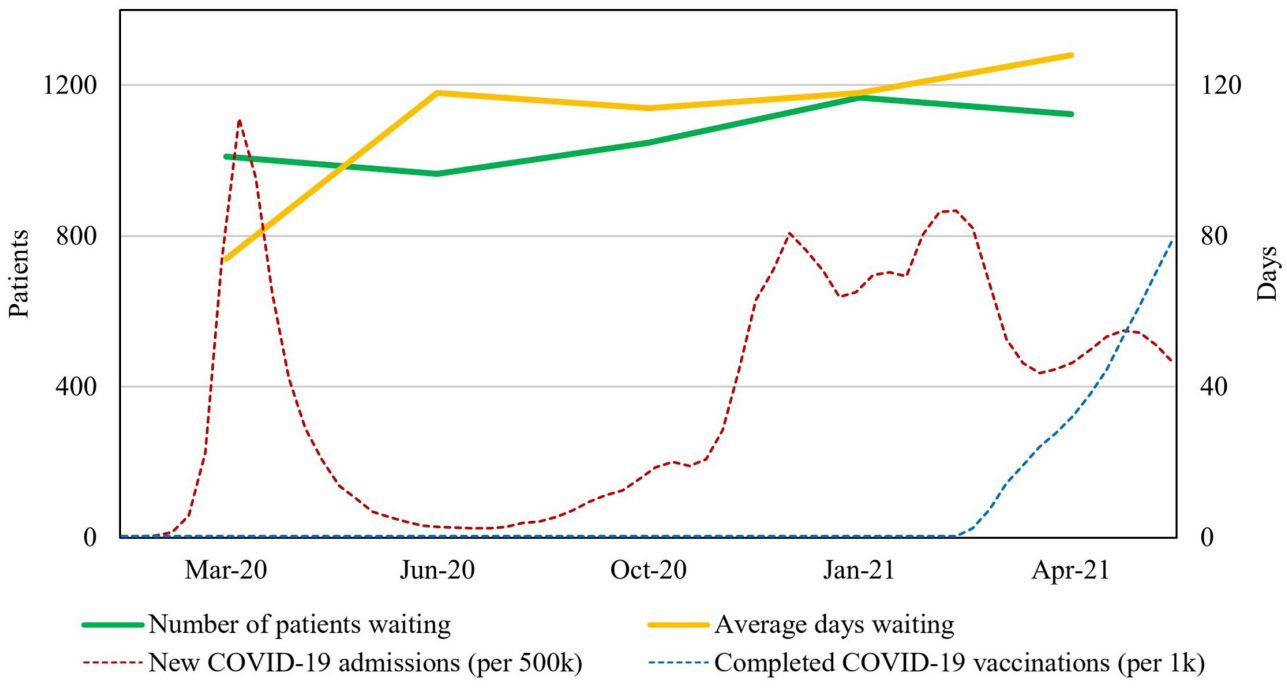


FIGURE 1 | Waiting list tendencies during the COVID-19 pandemic. Total number of patients and average days on waiting lists across all participating centers for all procedures of interests are presented in absolute numbers. Mean cross-European data on new COVID-19 admissions and completed vaccinations are shown in absolute numbers for intuitive comparison (note these should be read from secondary Y-axis).

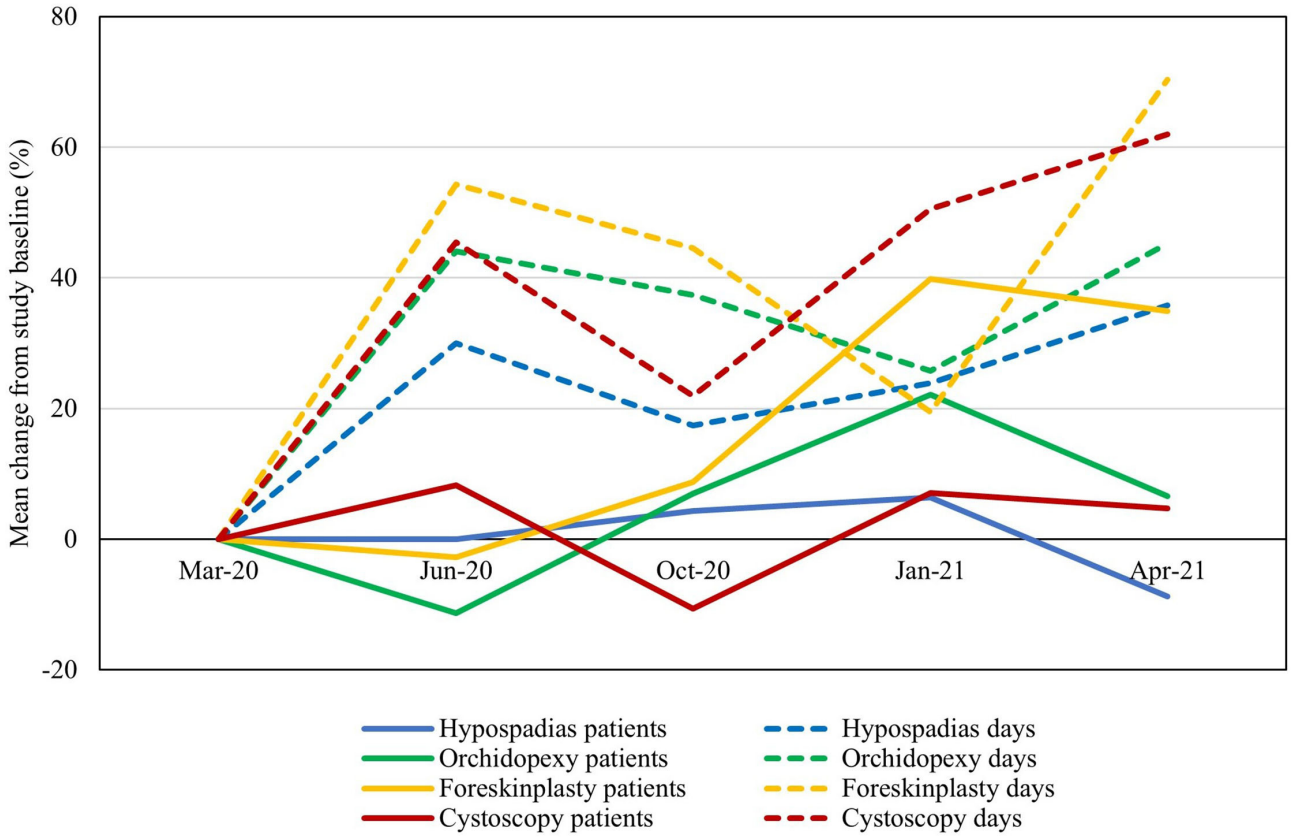


FIGURE 2 | Proportional changes in number of patients (straight lines) and mean days (dotted lines) on waiting lists for high-volume pediatric urological procedures during the total study period. The mean proportional changes (in percentage) across all centers are presented with reference to study baseline (March 2020).

the accumulated days waiting for each procedure. Averaged cross-country European COVID-19 numbers were included as an intuitive reference to the broadscale implications of the pandemic. Data on nationwide new weekly COVID-19 admissions and completed vaccinations were gathered from the publications of the European Center for Disease Prevention and Control (8).

To investigate whether the obtained waiting list data corresponded to the actual number of surgical procedures and outpatient consultations performed, before and during the study period, all centers were requested to further retrospectively report administrative data on these activities from January 2019 throughout September 2021. To compare with pre-COVID-19 capacities, as well as normal seasonal variation, this data was presented per annum. Moreover, to compare with the corresponding outpatient activities, data on external referrals for pediatric surgical evaluation during the same period was obtained from two participating centers.

Synchronously, qualitative online surveys regarding financial, logistic, and organizational changes were obtained using Redcap® (questions asked can be found in **Figure 6**). The participants were surveyed at four timepoints during the study period (June, October, January, and April, respectively).

Statistics

Descriptive statistics were based on absolute numbers from reported waiting list at the five study timepoints. Given the explorative nature of our data, further advanced hypothesis testing models were not considered appropriate. Centers that were not able to provide complete waiting list data on the respective procedures for all timepoints were not included in the quantitative results.

Since data from large-volume centers might dominate the statistical tendencies in the general results, we assessed the proportional waiting list changes, to level out possible skewing from varying center sizes and operative volumes. The mean of the percentual waiting list changes from each center were assessed with reference to the study baseline (March 2020). Due to low sample-sizes and high variance in rare procedures, this was only deemed suitable for a limited number of high-volume procedures, defined in this study as >10 patients per center waiting on average at each timepoint (i.e., hypospadias, phimosis, non-descended testes, cystoscopy).

Numeric survey data is presented separately in percentages in stacked bar charts. Data and figures were analyzed using Microsoft® Office Excel 2016 and IBM® SPSS Statistics version 25.

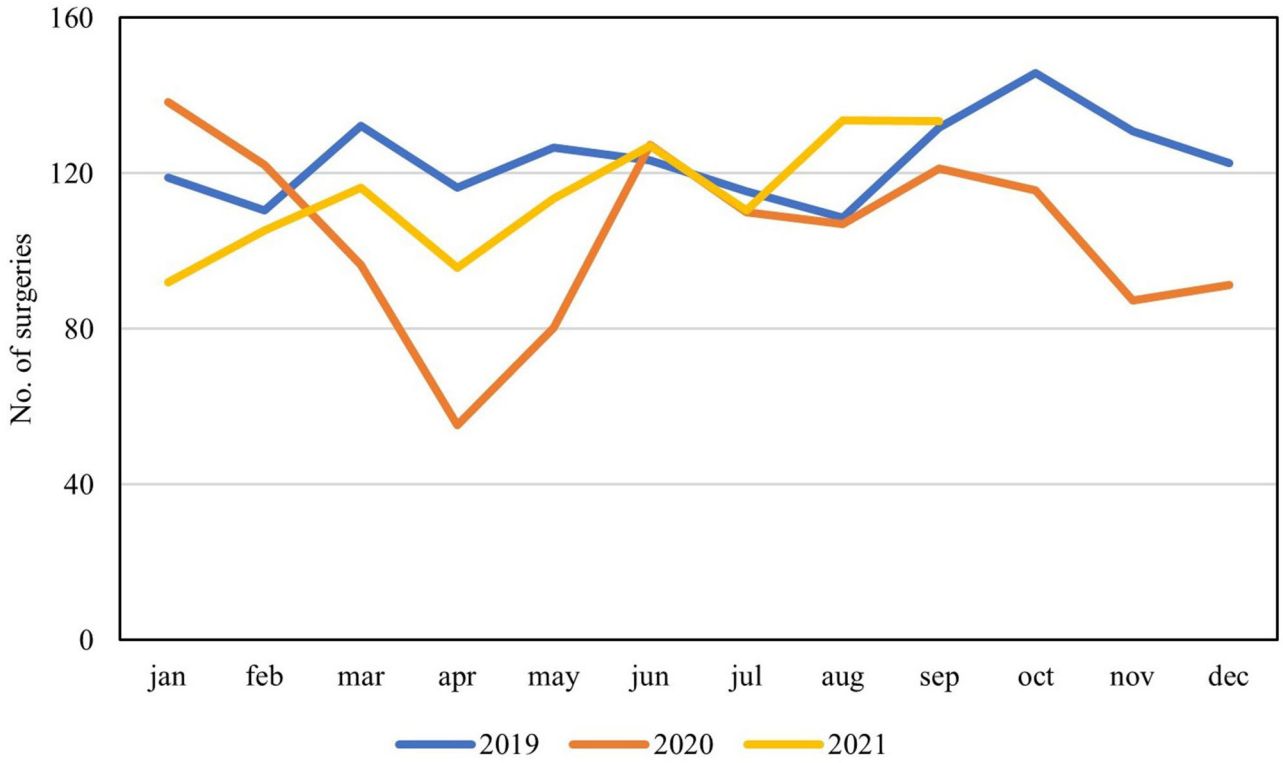


FIGURE 3 | Mean monthly number of overall surgeries performed at seven participating centers during the past 3 years presented per annum in absolute numbers.

RESULTS

A total of 10 tertiary European centers of pediatric urology, representing a background population of 21.6 million people (individually ranging from 1.2 to 3.3 million), were included prospectively in the study. According to 2019 cross European demographics, this corresponds to a total pediatric reference population <15 years of 3.26 million (9). All participating centers experienced a complete initial COVID-19 related closedown of elective pediatric urology cases, which happened medio March 2020 (effectuated between March 3rd and 17th and ended between March 20th and September 1st, respectively).

Quantitative Data

Seven centers (70%) were able to provide complete waiting list data for all timepoints, corresponding to a reference population of 17.7 million inhabitants. Results from the total counting of waiting lists at the five study timepoints across all participating centers are first presented in absolute numbers (**Figure 1**, **Table 2**). An increase in mean days waiting was seen during spring 2020 and again during late fall. This corresponded to the fluctuations of the first and second wave of infections in Europe. The total number of patients waiting for surgery did not increase on a broadscale during the first wave of infections, however it did increase during the second wave.

Both the number of patients and the mean days waiting generally decreased during the summer of 2020, after the first wave of infections, whereas a corresponding decrease was not seen after the second wave. At the end of the study, the included pediatric urology centers had increased the overall number of patients on waiting lists with 11% (from 1,010 to 1,123 patients), whereas mean days on waiting list had accumulated with 73% (from 74 to 128 days) (**Figure 1**). Over the entire course of the study period, the total accumulation of waiting days consequently attenuated with 6,102 days within the study population.

Evaluation of the proportional changes in waiting lists for high-volume procedures generally revealed clear gradual increase in the average days spent on waiting lists at the end of the study period (increasing with 62% for cystoscopy, 45% for orchidopexy, 36% for hypospadias and 70% for foreskinplasty). The changes in waiting lists corresponded to the nationwide fluctuations in the COVID-19 pandemic, although with some possible delay between new waves of infections and increasing waiting lists (**Figure 2**, **Supplementary Table 1**). The number of patients waiting remained stable until finally increasing in some procedures during the second half of the study period (final increase of 5% for cystoscopy, 7% for orchidopexy, −9% for hypospadias and 35% for foreskinplasty). These changes corresponded to a delay in seeing patients at the outpatient clinic for planning new surgical interventions.

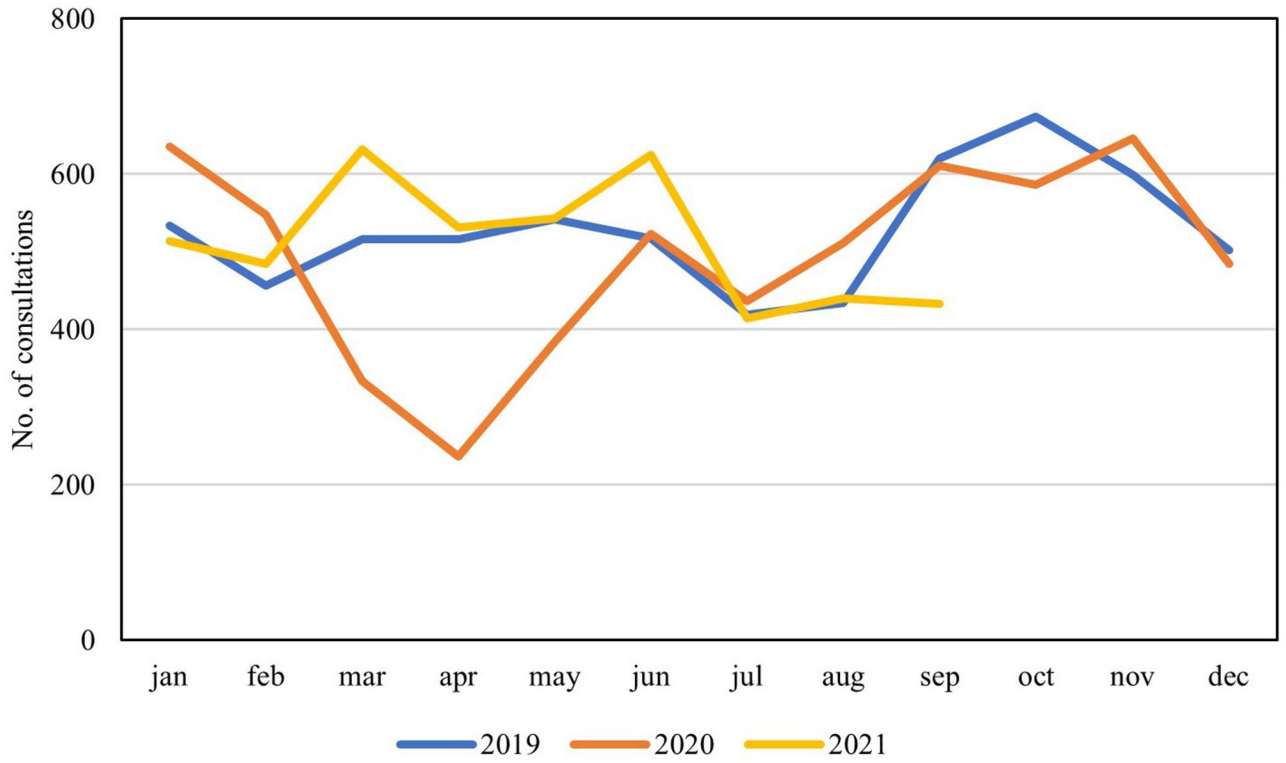


FIGURE 4 | Mean monthly number of overall consultations performed at seven participating centers during the past 3 years presented per annum in absolute numbers.

Seven centers (70%) were able to provide additional administrative data on performed surgical procedures and outpatient consultations. Tendencies confirmed decreased activities with a clear dip during the first pandemic wave, when compared to activity levels of 2019, corresponding to a stagnation in number of patients entering the waiting lists during the first part of the study (**Figures 3**, **4**). When evaluating external referrals, a corresponding decrease in activity was also seen during spring 2020 (**Figure 5**).

Qualitative Data

All 10 centers provided full survey data from each of the four survey timepoints. Financial resources remained unreduced in ∼80% of the centers during the study period but with uncertainties at the last survey. A tendency of extra funding was reported in 15% of centers during the second half of the study (**Figure 6A**). A tendency of lesser funding was reported in an equal number of centers (15%) and these centers were also more heavily burdened by the COVID-19 pandemics at a national level. Operating room (OR) capacity was reduced with at least 75% at 3-months after the closedown in 70% of centers, while 30% had been able to re-establish their capacity to 76–100% of normal. In approximately half of the centers a decrease in OR capacity clearly followed the first and second wave of infections in Europe (during the spring and fall of 2020, respectively) (**Figure 6B**). Three months after initial closedown (June 2020) 40% experienced a decrease in OR staff compared to normally, however during the remaining study period, an increasing number of centers were able to sustain or even increase the OR staff working hours to endure the increasing caseload (**Figure 6C**). Consequently, rather than lack of human or material resources, at the end of the study period, general ongoing COVID-19 situation was viewed as the main limiting factor for OR capacity throughout the study period in most centers (**Figure 6D**).

In January 2021, 60% of centers reported a second closedown (effectuated between October 5th and December 2nd and lasting on average 2–3 months, although still ongoing in two centers at the end of the study period) with a corresponding decrease in OR capacity in almost 50% of centers. Management of waiting lists was done in accordance with various guidelines depending on each center, with ∼20% of centers following ESPU guidelines and 40% following local hospital guidelines, and centers generally adhered to the same guidelines throughout the study period (**Figure 6E**).

Combined Quantitative and Qualitative Data

When evaluating the mean proportional changes for all high-volume procedures in relation to funding, a larger increase in number of patients waiting was seen in centers reporting on less funding in the final survey compared to centers reporting

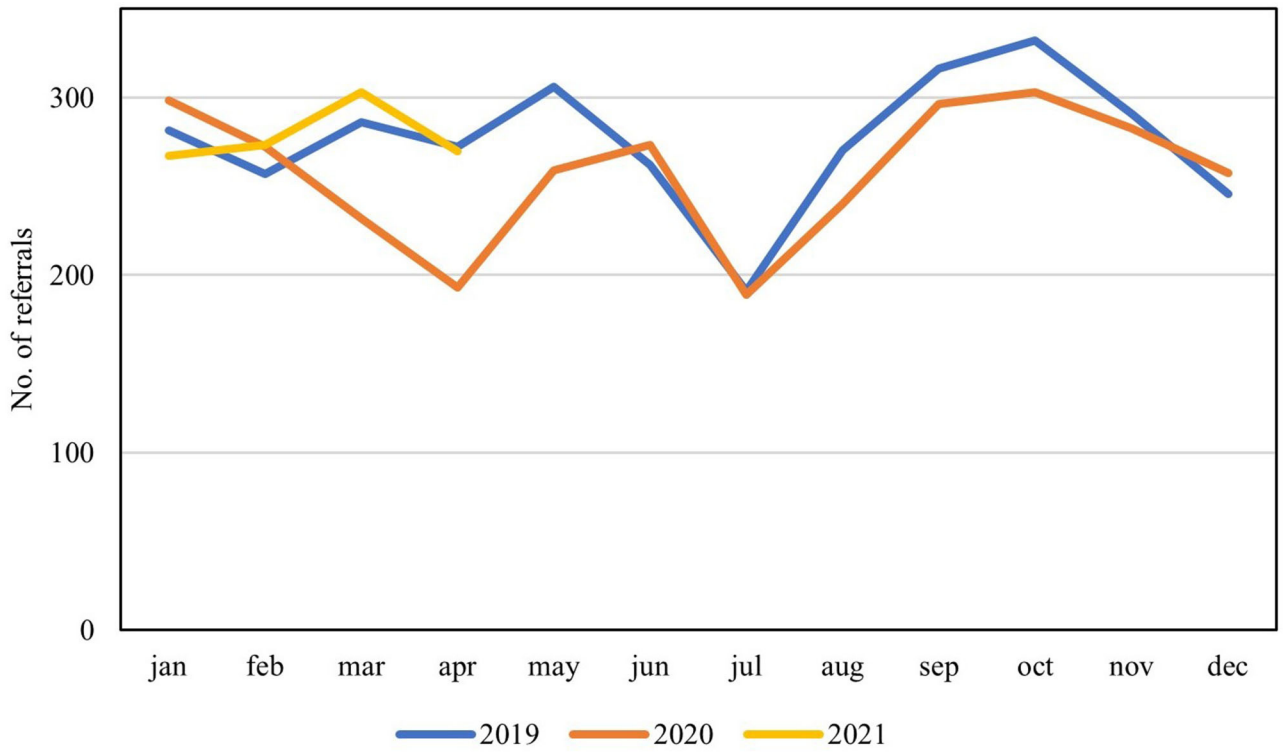


FIGURE 5 | Mean number of overall external referrals to pediatric surgical evaluation received at two participating centers during the past 3 years presented per annum in absolute numbers.

unreduced or additional funding. This tendency was not seen in relation to mean days waiting (**Figure 7**). Similar tendencies were seen when evaluating the proportional changes in relation to OR staff working hours; less ability to increase staff working hours at the end of the study was correlated with increased numbers of patients waiting, whereas this tendency was not seen in relation to mean number of days waiting (**Figure 8**).

DISCUSSION

This European multicenter study is the first of its kind to report on prospectively gathered multicenter real-time data on the ongoing impacts of COVID-19 on elective surgeries in European pediatric urological populations. Our study presents waiting list outcomes for a variety of 17 urological procedures from tertiary European referral centers for pediatric urology within the first year of the COVID-19 pandemic, covering a population of ∼22 million persons.

Since the outbreak of the COVID-19 pandemic, pediatric surgical activities has evidently been reduced worldwide (10–13) and although the quality of the surgical treatment does not seem to have diminished during the pandemic (14), increased time to surgery has been documented in various urgent pediatric cases, such as acute appendicitis (15, 16) and testicular torsion (17, 18). Further, the pandemic has impacted on the training of new pediatric surgeons (19) and presumably also on non-COVID-19 related pediatric research (20). In non-urgent elective cases however, the effect of the current administrative prioritizations, halting surgical activities, has not yet been investigated prospectively on a multicenter level.

In our material we found that during the first half of the study period, the number of patients on waiting lists for most surgeries remained stable and did not increase until the second half. This is explained by a reduced intake *via* outpatient clinics, consequently halting new OR bookings during the initial closedown.

Later during the study period, the number of patients on waiting lists and accumulated waiting time increased for most procedures, although we did encounter tendencies that some procedures were prioritized. These procedures, although many of them performed on rare diseases with consequently small sample-sizes, often represented cases with life- or organ-threatening conditions (pyeloplasty, bladder exstrophy, heminephrectomy). Still, for now, any conclusions regarding low-volume procedures can only be speculative. However, when evaluating the proportional waiting list changes at the end of the study period, we did find a clear increase in the accumulated time waiting for all four high-volume surgeries (hypospadias, cystoscopy, foreskinplasty and orchidopexy), in addition to an increase in number of patients waiting.

Attenuated waiting lists generally reflected the first and second wave of European COVID-19 infections, and indications of compensatory activities to decrease waiting lists were seen after the first wave, during summer 2020. However, similar tendencies were not found after the second wave, where waiting

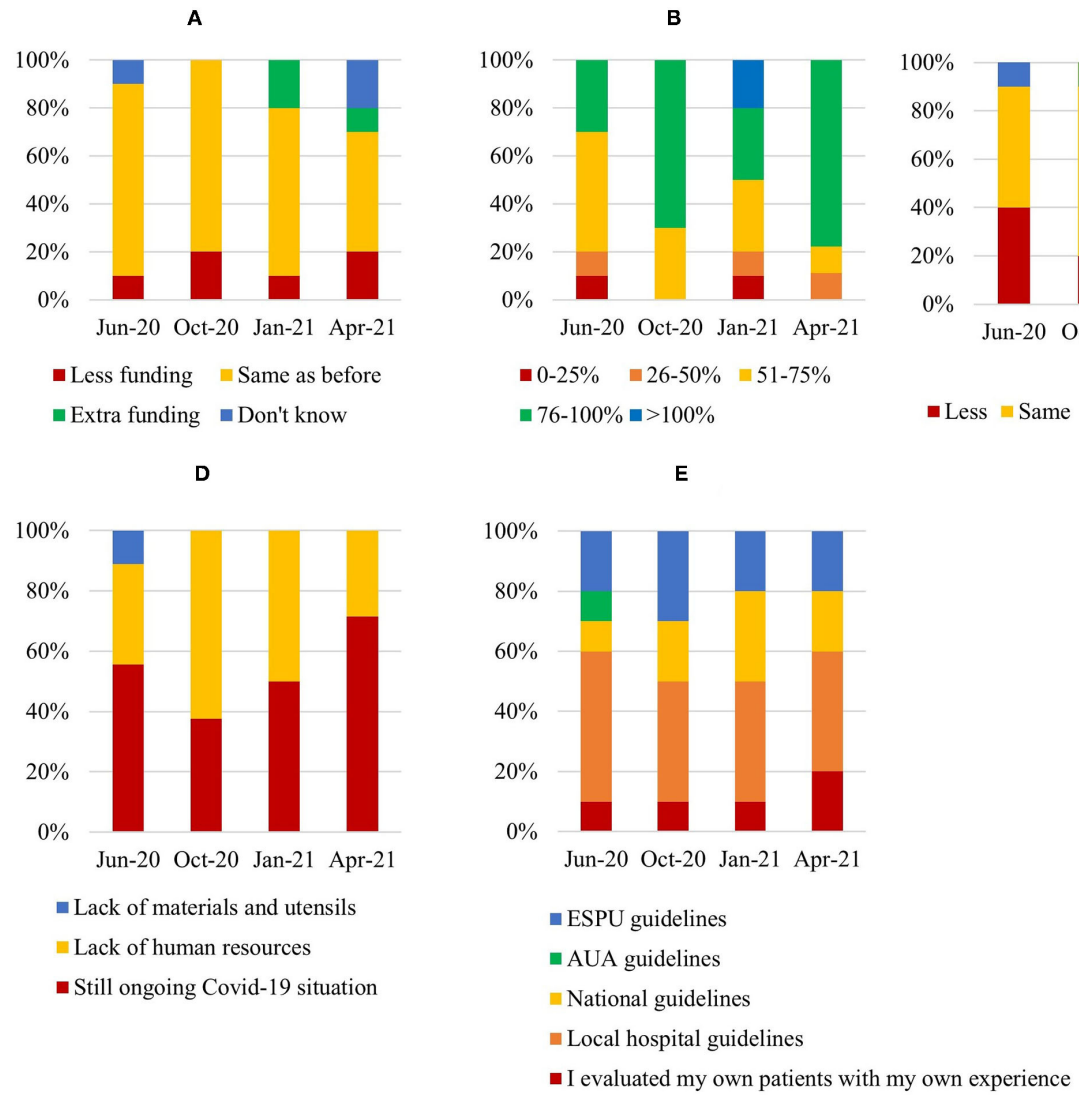


FIGURE 6 | Compiled survey data from all centers. Each subfigure represents a question from the survey: **(A)** Have your financial resources changed after the Covid-19 close-down? **(B)** Have you now reached the same OR capacity as before close-down? **(C)** Have you been able to increase team-member working hours (i.e., surgeons, anesthesiologists, OR nurses and postop team), in order to decrease the waiting list? **(D)** What is the main limiting factor right now for full OR capacity? **(E)** Did you follow ESPU or national guidelines to deal with the waiting list during and after closedown?

list continued to increase, which may indicate an exhaustion of the center capacities, limiting the ability to compensate for attenuated waiting lists with more elective operating room time. This exposes a limit of robustness in the health care systems with regards to compensatory means that might have reached an upper limit in many centers at that time. Although the data material obtained in this study was largely explorative, allowing only for descriptive statistical analysis, the gradually attenuating waiting lists during the first year of COVID-19 were convincing, and in general corresponded to similar reports from adult surgery waiting lists in the same period (21–24).

According to the survey data, OR capacity decreased in more than half of the participating centers, however, most centers were able to maintain or increase their financial budget (60–80%), as well as OR staffing (70%), during the second half of the study period. Still, at the end of the study, half of the centers still reported an OR capacity below 75%, due to an ongoing COVID-19 situation. Guideline adherence for prioritizing surgical cases, varied greatly within the study group, however, remained unchanged throughout the study period. Our findings related to high-volume cases support that prioritization was quite similar between centers, although different guidelines were used.

Not all centers reported on a 2nd closedown (60%), but waiting lists were markedly increased at the second wave, much more than after the first. This may be due to closing of elective

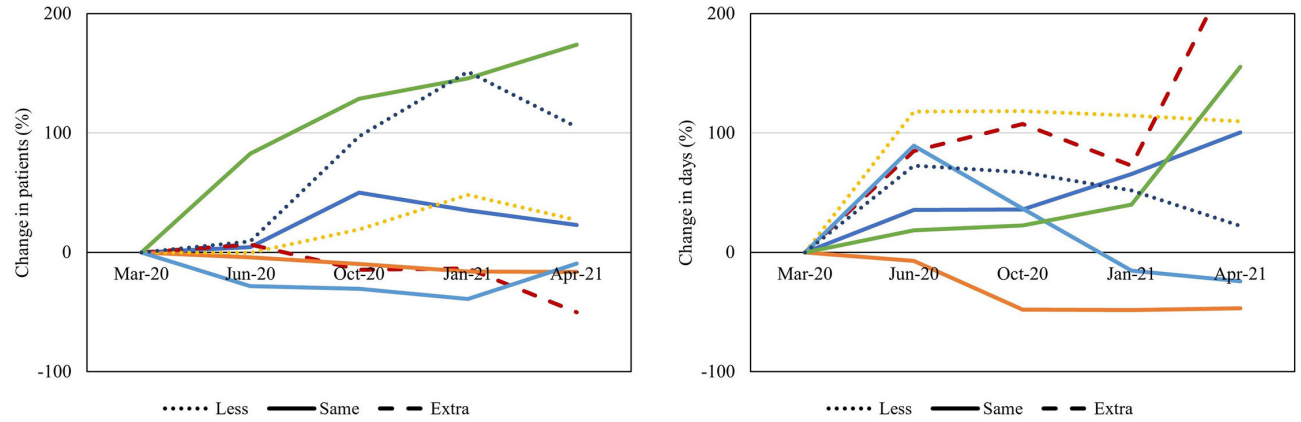


FIGURE 7 | Funding during the study period. Proportional changes in number of patients and mean days waiting for the mean of all high-volume procedures presented in percentage for each center (represented in colors) in relation to funding status at the end of the study (dotted, dashed and straight lines, respectively).

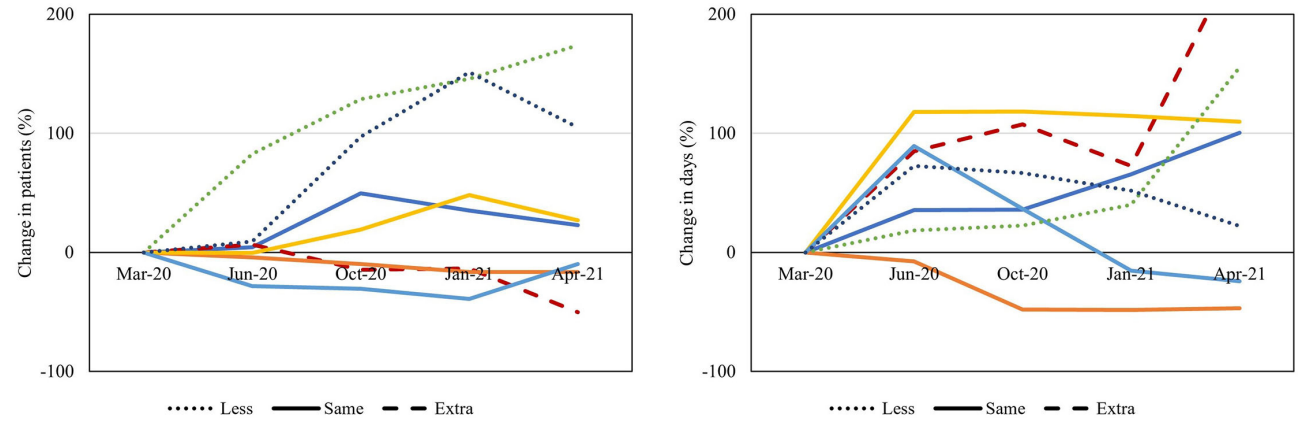


FIGURE 8 | Ability to increase operating room staff working hours. Proportional changes in number of patients and mean days waiting for the mean of all high-volume procedures presented in percentage for each center (represented in colors) in relation to staff working hours at the end of the study (dotted, dashed and straight lines, respectively).

surgeries but still performing the outpatient clinics. One of the most critical measures of the quality of a country's health care system is how long patients must wait to access medical care. Our study demonstrated a waiting time of ∼2.5 months for a surgical intervention in general anesthesia before the pandemic, to more than 4 months for the average pediatric patient after 1 year of the pandemic.

Patients perspectives have been reported to play an important role in the rate of hospital contacts during the pandemic, and although this was not possible for us to evaluate in the current study, we do suspect that fear of seeking healthcare, as seen in other studies on emergency conditions, has also influenced elective waiting lists (12, 15, 17, 18, 25, 26). Several new advances have been implemented in many clinics during the pandemic, to meet with the emerging challenges. Telemedicine for one has proven to be a valuable tool in the reduction of physical outpatient activity by replacing actual meetings with either telephone, video or online consultations. Surveys have demonstrated acceptable user satisfaction rates despite short-notice introduction of the new technique (27, 28), although possibly susceptible to social and economic disparities (29). New telemedical guidelines have been proposed and might very well find a more permanent place in future pediatric practices (30).

European centers will ongoingly need to plan more elective surgeries to address the currently increased caseload. This study should be understood in the context of an ongoing worldwide health crisis from which the full impact on healthcare systems are yet to be seen, warranting further monitoring and analysis. In respect to waiting time for interventions in patients which we know have morbidity in delay for treatment, we do not have tools for estimating loss of quality of life, and neither cost related to postponing surgeries (i.e., medications, monitoring, outpatient visits, parents needing to stay home from work to take care of their child, children not attending

school). It is feasible, however, that the impact of patients and parents staying home longer, while waiting for surgery, will have social, educational and economic consequences for the families, as well as possible progression of the underlying medical conditions (31).

At present, some European countries are still facing a heavy burden on healthcare due to the COVID-19 situation. In addition, we do not know how the European health care systems will react during a post-COVID-19 period, in the sense that health care workers have been exhausted by the emergency of high workload and long working hours. In addition, patients that are subjected to post-COVID-19 symptoms may cause further challenges to the healthcare systems to provide and prioritize care of patients (32, 33). By these means, pediatric urology waiting lists may further increase before it can go back to the same level as before COVID-19.

The prospective study design ensured that data was gathered consistently throughout the study period. By including a variety of centers throughout Europe, we believe that the waiting list tendencies found among the participating centers can indeed be translated to other countries and other regions or continents with similar socio-economic health resources. If looking at the whole population of the European Union (447 million), and if our data provided could represent the whole union, then an extrapolation with a 30-fold increment would represent the whole union; waiting lists could be expected to increase with 183 060 accumulated waiting days due to the pandemic (3 390 new pediatric patients waiting and an increased waiting time of 54 days).

In conclusion, closure of elective interventions affected the pediatric urology population by an increased number of patients waiting for surgery and an increase in time on waiting lists (70% longer) for surgical interventions. Some centers dealt with the problem by increasing their operating resources off-hours, however, it is still not known how many more patients will suffer from delays before it turns back to normal again. Political decision-making and unified forces will be needed to restore a reliable health care system that attends the pediatric population in a timely manner.

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 review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

NJ, MF, AC, and NK developed the study design. NJ and MF analyzed the data and drafted the manuscript. All authors contributed with study data from their own center and critically reviewed and accepted the final manuscript.

FUNDING

NJ and MF has received unrestricted research grants from the Novo Nordisk Foundation (NNFSA170030576).

ACKNOWLEDGMENTS

We want to acknowledge the coordinating team of eUROGEN European Reference Network on rare urogenital diseases and complex conditions (Grant Agreement 831386) and specifically coordinator prof. Wouter Feitz for valuable comments on the initial study design. Further, we wish to thank economist Franciska Holm Clausen from Rigshospitalet, Copenhagen, for reviewing the data and manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.874758/full#supplementary-material

REFERENCES

1. Recommendations from the EAU/ESPU Paediatric Urology Guidelines Panel applicable during the COVID-19 pandemic Diagnosis and outpatient clinics for paediatric urology cases. Available online at: https://www.espu.org/members/publications/380-changes-in-paediatric-urology-practice-in-the-context-of-the-covid-19-outbreak
2. Tur AB, Prieto JC, Gómez-Fraile A, Corbetta JP. The effect of the Covid-19 Pandemic on pediatric urology. *Int Braz J Urol.* (2020) 46:133–44. doi: 10.1590/s1677-5538.ibju.2020.s112
3. Campi R, Tellini R, Grosso AA, Pecoraro A, Mari A, Raspollini MR, et al. Exploring the diversity and predictors of histopathological findings across the European association of urology guidelines office rapid reaction group priority groups for patients with renal tumors: implications for individualized prioritization of renal cancer care. *Eur Urol Open Sci.* (2021) 34:5–9. doi: 10.1016/j.euros.2021.09.009
4. Esposito C, Masieri L, Castagnetti M, Crocetto F, Escolino M. Letter to the editor: robot-assisted and minimally invasive pediatric surgery and urology during the COVID-19 pandemic: a short literature review. *J Laparoendosc Adv Surg Tech.* (2020) 30:915–8. doi: 10.1089/lap.2020.0251
5. Cini C, Bortot G, Sforza S, Mantovani A, Landi L, Esposito C, et al. Paediatric urology practice during COVID-19 pandemic. *J Pediatr Urol.* (2020) 16:295–6. doi: 10.1016/j.jpurol.2020.04.023
6. Fernandez N, Caicedo JI. Impact of COVID-19 on the future of pediatric urology practice. Do guidelines apply to medical practice worldwide? *J Pediatr Urol.* (2020) 16:291–2. doi: 10.1016/j.jpurol.2020.05.001
7. Implementing decision containing criteria for establishing and evaluating ERNs, including the exchange and dissemination of information about

the ERNs. Available online at: https://ec.europa.eu/health/publications/implementing-decision-containing-criteria-establishing-and-evaluating-erns-including-exchange-and_en (accessed Febraury 26, 2022).
8. Publications & Data | European Centre for Disease Prevention and Control. Available online at: https://www.ecdc.europa.eu/en/publications-data (accessed June 10, 2021).
9. Population structure and ageing - Statistics Explained. Available online at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_structure_and_ageing (accessed Febraury 25, 2022).
10. Garriboli M, Mishra P, Taghizadeh A, Paul A. The response of a tertiary paediatric urology unit to the COVID-19 Pandemic in central London: what have we learned? *Br J Surg.* (2020) 107:e578–80. doi: 10.1002/bjs.11978
11. Gunadi, Idham Y, Paramita VMW, Fauzi AR, Dwihantoro A, Makhmudi A. The Impact of COVID-19 pandemic on pediatric surgery practice: a cross-sectional study. *Ann Med Surg.* (2020) 59:96–100. doi: 10.1016/j.amsu.2020.09.020
12. Farooq MA Al, Kabir SMH, Chowdhury TK, Sadia A, Alam MA, Farhad T. Changes in children's surgical services during the COVID-19 pandemic at a tertiary-level government hospital in a lower middle-income country. *BMJ Paediatr Open.* (2021) 5:e001066. doi: 10.1136/bmjpo-2021-001066
13. Wei Y, Yu C, Zhao TX, Lin T, Dawei HE, Wu S de, et al. The impact of the COVID-19 pandemic on pediatric operations: a retrospective study of Chinese children. *Ital J Pediatr.* (2020) 46:155. doi: 10.1186/s13052-020-00915-3
14. Merino-Mateo L, Tordable Ojeda C, Cabezalí Barbancho D, Gómez Fraile A. Impact of the COVID-19 pandemic on the surgical activity of Pediatric Urology: analysis of postoperative complications according to the Clavien-Dindo classification. *Actas Urol Esp.* (2020) 44:659–64. doi: 10.1016/j.acuro.2020.09.003
15. Schäfer F-M, Meyer J, Kellnar S, Warmbrunn J, Schuster T, Simon S, et al. Increased incidence of perforated appendicitis in children during COVID-19 pandemic in a bavarian multi-center study. *Front Pediatr.* (2021) 9:683607. doi: 10.3389/fped.2021.683607
16. Montalva L, Haffreingue A, Ali L, Clariot S, Julien-Marsollier F, Ghoneimi A El, et al. The role of a pediatric tertiary care center in avoiding collateral damage for children with acute appendicitis during the COVID-19 outbreak. *Pediatr Surg Int.* (2020) 36:1397–405. doi: 10.1007/s00383-020-04759-0
17. Holzman SA, Ahn JJ, Baker Z, Chuang K-W, Copp HL, Davidson J, et al. A multicenter study of acute testicular torsion in the time of COVID-19. *J Pediatr Urol.* (2021). doi: 10.1016/j.jpurol.2021.03.013
18. Pogorelić Z, Milanović K, Veršić AB, Pasini M, Divković D, Pavlović O, et al. Is there an increased incidence of orchiectomy in pediatric patients with acute testicular torsion during COVID-19 pandemic?–A retrospective multicenter study. *J Pediatr Urol.* (2021) 17: 479.e1–6. doi: 10.1016/j.jpurol.2021.04.017
19. Mariani A, Tiryaki S, Harms M, Orlov V, Enache T, Bidault-Jourdainne V, et al. What we learned from the Covid-19 first wave: a survey from Young Pediatric Urology Committee (YPUC) from ESPU. *Minerva Pediatr.* (2021). doi: 10.23736/S2724-5276.21.06325-4. [Epub ahead of print].
20. Harper L, Kalfa N, Beckers GMA, Kaefer M, Nieuwhof-Leppink AJ, Fossum M, et al. The impact of COVID-19 on research. *J Pediatr Urol.* (2020) 16:715–6. doi: 10.1016/j.jpurol.2020.07.002
21. Ashfaq A, Gray GM, Carapellucci J, Amankwah EK, Ahumada LM, Rehman M, et al. Impact of coronavirus-2019 on pediatric and adult heart transplantation waitlist activity and mortality in the United States: a descriptive approach. *Lancet Reg Heal Am.* (2021) 3:100060. doi: 10.1016/j.lana.2021.100060
22. Muschol J, Gissel C. COVID-19 pandemic and waiting times in outpatient specialist care in Germany: an empirical analysis. *BMC Health Serv Res.* (2021) 21:1076. doi: 10.1186/s12913-021-07094-9
23. García-Rojo E, Manfredi C, Santos-Pérez-de-la-Blanca R, Tejido-Sánchez Á, García-Gómez B, Aliaga-Benítez M, et al. [Impact of COVID-19 outbreak on urology surgical waiting lists and waiting lists prioritization strategies in the Post-COVID-19 era]. *Actas Urol Esp.* (2021) 45:207–14. doi: 10.1016/j.acuro.2020.11.001
24. Uimonen M, Kuitunen I, Paloneva J, Launonen AP, Ponkilainen V, Mattila VM. The impact of the COVID-19 pandemic on waiting times for elective surgery patients: a multicenter study. *PLoS ONE.* (2021) 16:e0253875. doi: 10.1371/journal.pone.0253875
25. Amparore D, Campi R, Checcucci E, Piana A, Sica M, Grosso AA, et al. Patients' perspective on the use of telemedicine for outpatient urological visits: Learning from the COVID-19 outbreak. *Actas Urol Esp.* (2020) 44:637–8. doi: 10.1016/j.acuro.2020.06.008
26. Campi R, Tellini R, Grosso AA, Amparore D, Mari A, Viola L, et al. Deferring elective urologic surgery during the COVID-19 pandemic: the patients' perspective. Urology. (2021) 147:21–6. doi: 10.1016/j.urology.2020.09.015
27. Gan Z, Lee SY, Weiss DA, Van Batavia J, Siu S, Frazier J, et al. Single institution experience with telemedicine for pediatric urology outpatient visits: adapting to COVID-19 restrictions, patient satisfaction, and future utilization. *J Pediatr Urol.* (2021) 17:480.e1-480.e7. doi: 10.1016/j.jpurol.2021.05.012
28. Schmidtberg LC, Grindle C, Hersh DS, Rowe C, Healy J, Hughes CD. Telehealth in pediatric surgical subspecialties: rapid adoption in the setting of COVID-19. *Telemed e-Health.* (2021) 28:344–52. doi: 10.1089/tmj.2021.0080
29. Winkelman AJ, Beller HL, Morgan KE, Corbett ST, Leroy SV, Noona SW, et al. Benefits and barriers to pediatric tele-urology during the COVID-19 pandemic. *J Pediatr Urol.* (2020) 16:840.e1–6. doi: 10.1016/j.jpurol.2020.09.028
30. Charnell AM, Hoen L't, Sforza S, Spinoit AF, Radford A. Remote consultations in paediatric urology–Not just for pandemics? *J Pediatr Urol.* (2021) 17:260–2. doi: 10.1016/j.jpurol.2021.01.001
31. Forner D, Leslie PK, Aldaihani A, Bezuhly M, Noel CW, Horne D, et al. Psychosocial distress in parents with children awaiting surgery during the COVID-19 pandemic. *Child.* (2022) 9:87. doi: 10.3390/children9010087
32. Saloner B, Parish K, Julie Ward MA, Grace DiLaura R, Sharon Dolovich J. Persistent symptoms in patients after acute COVID-19. *JAMA.* (2020) 324:603–5. doi: 10.1001/jama.2020.12603
33. Tenforde MW, Kim SS, Lindsell CJ, Billig Rose E, Shapiro NI, Files DC, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with covid-19 in a multistate health care systems network—United States, March–June 2020. *Morb Mortal Wkly Rep.* (2020) 69:993–8. doi: 10.15585/mmwr.mm6930e1

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 | Frontiers in Public Health

PERSPECTIVE
published: 30 May 2022
doi: 10.3389/fpubh.2022.874687

COVID-19 Vaccination in Pediatric Population: A Necessity or Obstruction to the Protection of the Right to Health? Biojuridical Perspective

*Clio Bilotta†, Giulio Perrone†, Stefania Zerbo and Antonina Argo**

Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Section of Legal Medicine, University of Palermo, Palermo, Italy

One of the most recently debated topics worldwide is the mass vaccination of children against coronavirus disease 2019 (COVID-19). Next, the risk/benefit ratio of COVID-19 vaccination and infection in children are compared. Nonetheless, the real question in this debate is as follows: Does the vaccine represent a necessary tool or is it an obstacle in protecting the right to health? From a public health point of view, the Supreme Court of Nova Scotia, in Canada, recommends COVID-19 vaccination in the pediatric population. Based on Article 25 of the Draft Articles on State responsibility, vaccination can be considered a social act necessary for protecting the individual's right to health. The 1989 New York Convention on the Rights of the Child and the European Regulation number 219/1111 state that the opinion of a minor aged >12 years is considerable. However, this validity of opinion is related to age and degree of discernment. The onset of adverse events following the administration of the COVID-19 vaccine may lead to compensation in the near future. Recent studies have identified a new COVID-19-related pediatric pathology, known as multisystem inflammatory syndrome. Other studies have demonstrated that myocarditis in the pediatric population might occur following COVID-19 vaccine administration. In June 2021 in the USA, the Center for Control and Prevention of Infectious Diseases Advisory Committee on Immunization Practices declared that the benefits of vaccination against COVID-19 in the pediatric population outweighed the risks. In the meantime, whereas the bioethical debate remains open, monitoring the real risk/benefit ratio of vaccination in the pediatric population is crucial.

Keywords: COVID-19 vaccination in pediatric population: bioethical controversy COVID-19 vaccination, pediatric population, children, right to health, bioethical controversy

OPEN ACCESS

Edited by:
Antonio Oliva,
Università Cattolica del Sacro Cuore, Italy

Reviewed by:
Dario Sacchini,
Università Cattolica del Sacro Cuore, Italy
Adrien Schvartz,
Bicêtre University Hospital, France

***Correspondence:**
Antonina Argo
antonina.argo@gmail.com

†These authors share first authorship

Specialty section:
This article was submitted to Children and Health, a section of the journal Frontiers in Public Health

Received: *12 February 2022*
Accepted: *22 April 2022*
Published: *30 May 2022*

Citation:
Bilotta C, Perrone G, Zerbo S and Argo A (2022) COVID-19 Vaccination in Pediatric Population: A Necessity or Obstruction to the Protection of the Right to Health? Biojuridical Perspective.
Front. Public Health 10:874687.
doi: 10.3389/fpubh.2022.874687

INTRODUCTION

The ongoing coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which first began in 2020, led several countries worldwide to adopt drastic preventive measures to reduce infection rates and mortality. The pandemic led to profound changes. Most individuals were subjected to restrictive measures that affected their freedom, to protect their health, which is considered

a legally protected right. Various debates are ongoing regarding the legitimacy of the preventive measures taken during the COVID-19 pandemic and their concordance with the protection of human rights. In fact, the content of several decree laws, such as Decree Law No 28/2020 and Decree Law No 6/2020, created a dichotomy between the right to personal freedom and the right to health.

In the wake of the COVID-19 pandemic, one of the most recently debated topics worldwide concerns the mass vaccination of children against COVID-19. It is certainly not the first time that the literature addresses the thorny issue regarding the dichotomy between individual freedom and public health, in the case of massive and/or mandatory vaccinations. The erroneous connection between the measles-mumps-rubella vaccine and autism, which was reported by Andrew Wakefield et al. in 1998, despite the subsequent official denials (1, 2), contributed to the no-vax movement, decreasing vaccination rates (3, 4), and resurgence of vaccine-preventable diseases (5).

The spotlights on the mass vaccination of children against COVID-19 are relatively recent, since the vaccination campaign first involved elderly people. In fact, as it is now well-known, the lethality of COVID-19 is significantly higher in older individuals. Around 80% of COVID-19-related deaths in China predominantly involved individuals aged >60 (6), and the highest mortality rate was recorded in Europe in individuals aged ≥75 years (7, 8). Consequently, several questions arose regarding COVID-19 vaccination in the pediatric population. In fact, a debate was present regarding the age groups to be vaccinated. When the Food & Drug Administration in America authorized mRNA vaccines in the pediatric population aged ≥12 years, both the American Academy of Pediatrics and the Center for Control and Prevention of Infectious Diseases recommended vaccination in this age group. On the other hand, Great Britain recommended vaccination in children aged 12–17 years, only in cases of severe chronic disease, or if they were living with vulnerable individuals. The Public Health Agency maintained a prudent approach by watching the impact of vaccination in other countries such as Sweden. Most recently, both the Food & Drug Administration and European Medicines Agency authorized the use of mRNA vaccines in the 5–11-year age group. The discussion that followed was regarding the comparison of the risk/benefit ratio of COVID-19 vaccination and the risk of infection in children.

Previous epidemiological data, which drive the current opinion that is adverse to the administration of COVID-19 vaccines to pediatric population, showed an asymptomatic or paucisymptomatic course of SARS-COV-2 infection in children and adolescents (9, 10), with a hospital admission rate of <2% (11) and a low mortality (12). Nonetheless, subsequent studies demonstrated that the initial data underestimated COVID-19-related pediatric hospitalizations and mortality (13). These studies noted that the hospital admission rate was 11.7%, with severe manifestations of infection in 3.6% of cases (14). Over 5.7 million pediatric cases of SARS-CoV-2 were diagnosed in 2021 in the USA, with 21,814 hospitalizations and 498 deaths (9).

Abbreviations: COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome; PIMS-TS, pediatric inflammatory multisystem syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

While monitoring 15 hospitals, the Association of Italian Pediatric Hospitals pointed out that in January 2022, pediatric patients' admission rate to the intensive care unit and/or any other medical floor, due to COVID-19 infection, was much greater than in the three previous pandemic waves[1].

The Italian Society of Pediatrics encouraged pediatric COVID-19 vaccinations. They argued that, although symptoms from COVID-19 infection in children are commonly milder than in the adult population, several cases of severe infection required urgent hospitalization in the intensive care unit, and deaths occurred in the pediatric population. For this reason, the Italian Society of Pediatrics raised the issue of protecting children's health by administering the vaccine. This gave the pediatric population the same rights as the adult population. The vaccine was therefore considered a necessary element in protecting the health of the pediatric population [2].

However, all medication, including the COVID-19 vaccine (15), are not exempt from adverse effects. In fact, they sometimes carry even serious and/or lethal consequences. Therefore, the question that arises is that "is it really necessary to administer a vaccine, with unknown side effects, in a young population, in which the incidence of COVID-19-related complications and deaths seem low?" However, when considering this argument, it is necessary to evaluate the late complications of COVID-19 infection, to be able to compare them with those of the vaccine. It is clear that the answer to these questions is inherent in the evaluation of the risk/benefit ratio, which could currently be distorted by early data from inconclusive studies.

Therefore, similar to the adult population, a pertinent question still weighs on this very complex issue: Does the vaccine represent a necessary tool to protect the right to health of children and the global population, or rather an obstacle against the protection of the same right?

MULTIFACTORIALITY OF THE RIGHT TO HEALTH

One of the aspects of each vaccination campaign is protecting the right to health of the global population and the individual himself. The first two international sources that included the right to health among other human rights were the Universal Declaration of Human Rights (The Universal Declaration of Human Rights – United Nations General Assembly of 10 December 1948), which mentioned health as an essential element for an adequate standard of living (Article 25) and the WHO Constitution (Constitution of the World Health Organization – 7 April 1948), which declared that health is "a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity." This right was further recognized as a human right in the International Covenant on Economic Rights Social and Cultural events in

[1] Available online at: https://www.aopi.it/news/pazienti-pediatrici-covid-al-via-il-monitoraggio-di-aopi-il-76-dei-bambini-ricoverati-non-e-vaccinato/.

[2] Available online at: https://sip.it/2021/12/03/bambini-e-vaccino-covid-19-cosa-ce-da-sapere.

1966 (International Covenant on Economic, Social, and Cultural Rights – General Assembly of 16 December 1966).

Many subsequent conventions, such as the European Social Charter, the American Convention on Human Rights, and the International Convention on Economic, Social, and Cultural Rights, contain an article or a clause relating to the right to health. The International Convention on Economic, Social, and Cultural Rights established in article 12 that states should "recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health" that they are able to achieve. Regarding minors, paragraph 1 of article 24 of the International Convention on the Rights of the Child and Adolescent reports that the states recognize the right of the minor to secure the best possible state of health and to benefit from medical services and rehabilitation. This convention strives to ensure that no minor is deprived of the right to have access to such health-related services.

COMPARISON OF CASE-LAW TREND ABOUT PEDIATRIC VACCINATION

If the jurisprudence is already favorable to mandatory vaccination, despite scientifically proven adverse effects secondary to vaccines' administration, it is understandable how the same jurisprudence could be in favor of the vaccination campaign against COVID-19 in the pediatric population. In fact, recent judgments in Italy link vaccination to the aforementioned concept of health, which is understood as a set of socioeconomic benefits, as well as health, establishing that the non-fulfillment of the vaccination obligation constitutes an obstative reason, in itself, to access the schools of the childhood (pursuant to art.3 paragraph three of Legislative Decree no. 73/2017), to protect the minors and the entire school community (Regional Administrative Court of Piedmont, judgment no. 1034/2018). Comparative jurisprudence deals with the same theme: in England, the Family Division (Lincoln) of the High Court of Justice, sided in favor of the administration of mandatory vaccines, going against the doctrine that the potential risks of vaccines are greater than their benefits in children. The uncertainty regarding the long-term side effects was not given much importance. These currents of thought would be based, according to the judges, on general public knowledge, rather than on academic scientific knowledge.

The same judgment was issued by the Family Division of the Supreme Court of Nova Scotia, in Canada, which, in the decision reasons, highlights the positions of the Public Health Agency of Canada and the World Organization of Health, recommending the vaccinations in support of public health and arguing that contrary opinions are not supported by any scientific evidence and, therefore, not suitable for the protection of the best interest of the minor.

THE STATE OF NECESSITY: A JURISPRUDENTIAL EXEMPTION?

In the case of the COVID-19 pandemic, the concept of necessity is relevant. The need to counter the spread of the COVID-19 pandemic within one's own territory can erase the unlawfulness of certain conducts, opposing international laws. Article 25 of the Draft Articles on State Responsibility of the International Law Commission (2001) discusses the following state of necessity to commit the deed to avoid a serious, imminent, and involuntary danger, which is not punishable. The proclamation of a state of emergency in 2020 led to a succession of numerous sources of law, differing in strength and effectiveness. Examples of such laws are the resolutions of the Council of Ministers, decree laws, ministerial decrees and Prime Ministerial decrees, ministerial orders, civil protection orders, and trade union ordinances. The questions that arise are the relationship between these sources and the Constitution, and whether it is legitimate to apply these non-legislative sources to a fundamental constitutional right (16). The Constitutional Court specified that such acts must respect the general principles of the legal order and constitutional rights and that they must be in accordance with the state of emergency. Failure to comply with these conditions would determine the constitutional illegitimacy of these measures.

THE INFORMED CONSENT OF THE MINOR

The Italian legislation states that the consent of a single parent is sufficient when it comes to ordinary acts involving a minor. In contrast, the consent of both parents is required for extraordinary acts. Based on these legislations, routine treatments, such as, mandatory medications and vaccinations represent ordinary acts. All other medical acts are classified as extraordinary. Vaccination against COVID-19 constitutes an extraordinary act, since it is not yet compulsory. As such, consent from both parents is required, and a mandatory double signature is requested in a filled format provided by the National Health Ministry.

In the event of a conflict between the parents, or between them and the minor, the conflict is resolved by the judge of the Juvenile Court. In the case of disagreement of the minor, who is "capable of discernment," a large proportion of jurists considers that a health treatment contrary to the minor's will infringes the principle enshrined in article 32 of the Constitution.

In fact, the 1989 New York Convention on the Rights of the Child, the 1997 Strasbourg Convention on the Rights of the Child, the European Constitution, and the European Regulation no. 219/1111 expressly state that the opinion of the minor who aged >12 years has its weight. However, the age of the minor and his degree of discernment are taken into consideration (17). Medico-legal doctrine addressed this topic while having a similar position, taking into account the opinion of minors aged ≥ 14 years, when it comes to the topic of preventable infectious diseases (18).

COVID-19 VACCINATION: FUTURE PROSPECTS OF COMPENSATION?

The onset of any acute adverse event following COVID-19 vaccination may lead to consequences in the near future. In fact, constitutional judges are based their reasoning on the existence of the duty of social solidarity with those who have to undergo a certain act of prophylaxis for the protection of

the global health. In this regard, the Italian sentence no. 107 of the Constitutional Court, which took place on 26 April 2012, declared the unconstitutionality of article 1, paragraph 1, Lex 25 February 1992, no. 210. This was done because the latter article does not provide the right to compensation, under the conditions and in the manners established by the same law, in respect of those who have suffered consequences following vaccination against measles, mumps, and rubella.

COMPARISON OF RISK/BENEFIT RATIO OF COVID-19 INFECTION AND VACCINE

Although with a rather low incidence, COVID-19 still can cause complications in the pediatric population. In fact, recent studies have identified a new entity, known as multisystem inflammatory syndrome (MIS-C), or pediatric inflammatory multisystem syndrome (PIMS-TS). This syndrome was considered a sequelae of COVID-19 based on the very short time interval between the infection and the onset of this syndrome. In some cases (3–25%), patients had comorbidities, such as immunological diseases, immunosuppression, cancers, and respiratory diseases. Severe complications of this syndrome include respiratory and myocardial failure (19). Other complications of COVID-19, commonly in the adult population, concern the onset of long-term effects, up to 6 months after infection, consisting of multiple symptoms, including fatigue, muscle, bone and joint pains, palpitations, insomnia, and breathing problems (20). These findings are also seen in the pediatric and adolescent population.

Although the vast majority of subjects in the pediatric and adolescent population did not report complications following COVID-19, both MIS-C and prolonged COVID-19 could have permanent effects, especially for patients with comorbidities, influencing their future development and health (21, 22). As such, vaccination is crucial to prevent these negative outcomes.

Vaccination would also allow social reintegration (23), further lowering the rate of spread of the virus within the population. Nevertheless, some studies demonstrate the presence of adverse reactions following COVID-19 vaccination, such as the onset of myocarditis (24). The incidence rate can be high, especially in males aged 12–29 years (25). Nevertheless, all myocarditis cases resolved shortly after occurrence.

As such, in June 2021 in the USA, the Center for Control and Prevention of Infectious Diseases Advisory Committee on Immunization Practices declared that the benefits of vaccination against COVID-19 for the pediatric population outweighed the risks and therefore recommended vaccination in subjects aged $\geq$12 years (26).

Finally, a point worthy of consideration in this emerging ethical debate is the position of some authors who highlighted the presence of masqueraded childism while deprioritizing children vaccination in the face of a vulnerable adult population (27). The arguments for a better natural immunity generated through infection, and the possible risk of vaccination in children, seem to be related to this unequal moral approach. Therefore, to fight hidden childism, more efforts should be put into combatting injustice against children's health (28, 29).

COMPARISON WITH OTHERS VACCINES: JUDICIAL ASPECTS

In 2017, in an attempt to counter the outbreak of epidemics caused by lower vaccination rates in the pediatric population, the Italian Parliament extended the list of mandatory vaccinations to include those against pertussis, measles-mumps-rubella, chickenpox, and Hemophilus influenzae type B (30, 31). In fact, pediatric vaccination rates had reached percentages much lower than the 95% coverage target vaccination rate (32). Mandatory vaccination resulted in the prohibition of access to pre-school education services for children aged <6 years, if they were not vaccinated. Although this law allowed an increase in the rate of vaccination, the idea of mandatory vaccination remains a controversial and debated issue (33). Prior to the introduction of this new law, the communication campaigns were completely inadequate (34). Meanwhile, France also made some pediatric vaccinations mandatory to reduce the increased mortality secondary to decreased vaccination rates (35). Similar legislative measures have been adopted by California's government in 2015, forcing the country to pass Senate Bill 277/2015, a law that removes non-medical exemption from school vaccinations (36). Although measles vaccination coverage increased to over 95% since the introduction of these laws in the aforementioned countries, the debate on the ethical and legal issues surrounding mandatory vaccinations remains open.

DISCUSSION

All sources of international law highlight that the right to health is a progressive right, whose "progressive realization" cannot be achieved in the short term. To protect this right in cases of pandemics or epidemics, it is necessary to achieve herd immunity. This is attained through widespread vaccination, which includes the pediatric population, allowing an indirect protective effect through a lower spread of infection. In fact, children develop better immunity than older adults. Vaccination of the pediatric population thereby balances the lower immunity of older adults (37). The role of herd immunity has already been demonstrated in cases of other infectious diseases, such as influenza, rotavirus, and pneumococcal disease (38–40). For this reason, vaccination of the pediatric population is important to reduce cases of MIS-C and PIMS-TS and to protect the older adults.

The COVID-19 vaccine plays a major role in protecting the population's health, reducing contagion, and accelerating the regression of the pandemic. This vaccine may become compulsory. However, compulsion is problematic in liberal democracies, which are founded on individual freedom. Jurisprudence often uses several expedients, including the fact that non-vaccination of the child will directly affect him/her, not the decision-maker. As such, compulsion might be justified in certain circumstances. In addition, extraordinary factors must be present, such as a threat to the community; the impossibility of defending a legally protected right without the restriction of freedoms (41).

Furthermore, the right to health is not the mere absence of disease, but instead includes other factors, such as those that are socioeconomic. This global model of the right to health, as the crisis between several psychophysical and socioeconomic factors, should encourage vaccination in children, since it can be a tool capable of improving their quality of life. In fact, vaccination guarantees psychological and social well-being, through the resumption of usual sociocultural activities, that were suspended during the pandemic. This suspension had some psychological repercussions, especially in the young population (42, 43). Vaccination also provides physical well-being, reducing hospital admissions and serious manifestations of infection. In fact, the authors currently support children's vaccination, believing that very often, the complications arising from highly diffusive events have a much higher incidence than the adverse effects of vaccination. Therefore, the scientific data currently available, promotes vaccination in children, since its most serious adverse effects were limited to sporadic episodes of myocarditis, with favorable prognosis. In contrast, COVID-19-related MIS-C or PIMS-TS led to severe heart and respiratory failure. In fact, although rare, the sequelae of COVID-19 infection in the pediatric population were not free from fatal outcomes (44, 45). Therefore, the risk/benefit ratio would currently be in favor of a large-scale vaccination of the pediatric population. However, in the case of "mature minors" with sufficient intelligence to understand the consequences of the proposed medical treatment, and holding the capability of discernment, the vaccine should be administered only in the presence of the will of the minor, as well as with the consent of the parents.

Furthermore, vaccination could be considered a social act equivalent to that used in a state of emergency and is necessary for the protection of the population's health. In this context, it is crucial to assess the consequences of free-riding, which endangers public health. In fact, it implies the absence of a moral duty to accept burdens, despite the benefits of a collective action (41, 46). Therefore, the COVID-19 vaccine could be considered a duty to protect public health. In this sense, vaccine-related adverse effects should be not exempt from future remediation.

Healthcare workers, for whom vaccination was mandatory, will most probably have access to compensation for vaccine-related complications. However, the judicial profile regarding vaccination compensation should be updated and expanded, including among the cause of compensation also the complications secondary to non-compulsory vaccinations, but recommended during emergencies, such as pandemics.

Further monitoring and studying late complications of the COVID-19 vaccine and infection in the pediatric population is needed. It will be possible to understand the risk/benefit ratio in the pediatric population only after obtaining more relevant scientific data. For this reason, the authors reserve the right to change their opinion if new and relevant scientific data regarding this topic emerges. Meanwhile, the bioethical debate remains open, where one wonders whether the vaccine represents a necessary tool to protect the right to health of children and the global population.

DATA AVAILABILITY STATEMENT

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

AUTHOR CONTRIBUTIONS

CB and GP conducted the researches and wrote the draft. SZ and AA oversaw and revised the draft. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Quick D, Larson H. The Vaccine-Autism myth started 20 years ago. here's why it still endures today. *TIME*. (2018). Available online at: http://time.com/5175704/andrew-wakefield-vaccine-autism/ (accessed March 11, 2019).
2. J. Belluz. 20 Years ago, research fraud catalyzed the anti-vaccination movement. Let's not repeat history. *Vox*. (2018). Available online at: https://www.vox.com/2018/2/27/17057990/andrew-wakefield-vaccines-autism-study (accessed March 11, 2019).
3. Vaccinations of US Children Declined after Publica- tion of Now-Refuted Autism Risk. *ScienceDaily*. (2012). Available online at: https://www.sciencedaily.com/releases/2012/06/120604142726.htm (accessed March 11, 2019).
4. Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the united states: a review of measles and pertussis. *JAMA*. (2016) 315:1149–58. doi: 10.1001/jama.2016.1353
5. Sifferlin. Four diseases making a comeback thanks to anti- vaxxers. *TIME*. (2014). Available online at: http://time.com/27308/4-diseases-making-a-comeback-thanks-to-anti-vaxxers> (accessed March 11, 2019).
6. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi*. (2020) 41:145–51. doi: 10.3760/cma.j.issn.0254-6450.2020.02.003
7. Gabutti G. d'Anchera E, De Motoli F, Savio M, Stefanati A. The Epidemiological Characteristics of the COVID-19 Pandemic in Europe: Focus on Italy. *Int J Environ Res Public Health*. (2021) 18:2942. doi: 10.3390/ijerph18062942
8. *Rapid Risk Assessment: Increase in Fatal Cases of COVID-19 Among LongTerm Care Facility Residents in the EU/EEA and the UK*. Stockholm: European Centre for Disease Prevention and Control (2020).
9. Principi N, Esposito S. Reasons in favour of universal vaccination campaign against COVID-19 in the pediatric population. *Ital J Pediatr*. (2022) 48:4. doi: 10.1186/s13052-021-01192-4
10. de Souza TH, Nadal JA, Nogueira RJN, Pereira RM, Brand P MB. Clinical manifestations of children with COVID-19: a systematic review. *Pediatr Pulmonol*. (2020) 55:1892–9. doi: 10.1002/ppul.24885
11. American Academy of Pediatrics and the Children's Hospital Association. Children and COVID-19: state data report. Version: 9/16/21. Available online at: https://downloads.aap.org/AAP/PDF/AAP%20and%20CHA%20-%20Children%20and%20COVID-19%20State%20Data%20Report%209.16%20FINAL.pdf
12. Abu-Raya B, Migliori GB, O'Ryan M, Edwards K, Torres A, et al. Coronavirus disease-19: an interim evidence synthesis of the world association for infectious diseases and immunological disorders. *Front Med*. (2020) 7:572485. doi: 10.3389/fmed.2020.572485
13. Esposito S, Marchetti F, Lanari M, Caramelli F, De Fanti A, et al. Working group on COVID-19 in pediatrics of the Emilia-Romagna region (RE-CO-Ped). COVID-19 management in the pediatric age: consensus document of the COVID-19 working group in paediatrics of the Emilia-Romagna

region (RE-CO-Ped), Italy. *Int J Environ Res Public Health*. (2021) 18:3919. doi: 10.3390/ijerph18083919
14. Preston LE, Chevinsky JR, Kompaniyets L, Lavery AM, Kimball A, Boehmer TK, et al. Characteristics and disease severity of US children and adolescents diagnosed with COVID-19. *JAMA Netw Open.* (2021) 4:e215298. doi: 10.1001/jamanetworkopen.2021.52988
15. Bilotta C, Perrone G, Adelfio V, Spatola GF, Uzzo ML, Argo A, et al. COVID-19 vaccine-related thrombosis: a systematic review and exploratory analysis. *Front Immunol.* (2021) 12:729251. doi: 10.3389/fimmu.2021.729251
16. Calamo Specchia, Marina. Principio di legalità e stato di necessità al tempo del COVID-19. *Osservatorio Costituzionale AIC 3.28*. (2020):142–73.
17. Quagliariello C, Fin C. *Il consenso informato in ambito medico: un'indagine antropologica e giuridica*. Societariello C, Fin C, editors. Turin: Il mulino (2016).
18. Prestileo T, Argo A, Triolo V, Zerbo S, Procaccianti P. Informed consent to perform the HIV diagnostic test: how to behave when minors are involved. *Infezioni in Medicina*. (2008) 16:200–3.
19. Dembiecem embiecember Issue 4, Pages 200ages 200 200Pages, et al. SARS-CoV-2 vaccination in children and adolescents-a joint statement of the european academy of paediatrics and the european confederation for primary care paediatricians. *Front Pediatr*. (2021) 9:721257. doi: 10.3389/fped.2021.721257
20. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, et al. Preliminary evidence on long COVID in children. *Acta Paediatr.* (2021) 110:2208–11. doi: 10.1111/apa.15870
21. Thomson H. Children with long covid. *New Sci.* (2021) 249:10–1. doi: 10.1016/S0262-4079(21)00303-1
22. Munblit D, Simpson F, Mabbitt J, Dunn-Galvin A, Semple C, Warner JO. Legacy of COVID-19 infection in children: long-COVID will have a lifelong health/economic impact. *Arch Dis Child*. (2021) 107:e2. doi: 10.1136/archdischild-2021-321882
23. Kamidani S, Rostad CA, Anderson EJ. COVID-19 vaccine development: a pediatric perspective. *Curr Opin Pediatr.* (2021) 33:144–51. doi: 10.1097/MOP.0000000000000978
24. Hause AM, Gee J, Baggs J, Abara WE, Marquez P, Thompson D, et al. COVID-19 vaccine safety in adolescents aged 12–17 years - United States, December 14, 2020-July 16, 2021. *MMWR Morb Mortal Wkly Rep*. (2021) 70:1053–8. doi: 10.15585/mmwr.mm7031e1
25. Oster ME, Shay DK, Su JR, Gee J, Creech CB, Broder KR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. *JAMA*. (2022) 327:331–40. doi: 10.1001/jama.2021.24110
26. Gargano JW, Wallace M, Hadler SC, Langley G, Su JR, Oster ME, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the advisory committee on immunization practices - United States, June 2021. *MMWR Morb Mortal Wkly Rep.* (2021) 70:977–82. doi: 10.15585/mmwr.mm7027e2
27. Autzen, B., Dineen, K., Vaughan, D. Vaccinating children: fairness and childism. *Lancet Infect Dis*. (2021) 21:1354–5. doi: 10.1016/S1473-3099(21)00483-7
28. Nisreen A Alwan. We must call out childism in Covid-19 policies. *BMJ*. (2021) 375:n2641. doi: 10.1136/bmj.n2641
29. Adami R, Dineen K. Discourses of childism: how covid-19 has unveiled prejudice, discrimination and social injustice against children in the everyday. *Int J Child Rights*. (2021) 29:353–70. doi: 10.1163/15718182-29020001
30. D'Ancona F, D'Amario C, Maraglino F, Rezza G, Iannazzo S. The law on compulsory vaccination in Italy: an update 2 years after the introduction. *Euro Surveill.* (2019) 24:1900371. doi: 10.2807/1560-7917.ES.2019.24.26.1900371
31. D'Ancona F, D'Amario C, Maraglino F, Rezza G, Ricciardi W, Iannazzo S. Introduction of new and reinforcement of existing compulsory vaccinations in Italy: first evaluation of the impact on vaccination coverage in 2017. *Euro Surveill.* (2018) 23:1800238. doi: 10.2807/1560-7917.ES.2018.23.22.1800238
32. Chirico F. The new Italian mandatory vaccine Law as a health policy instrument against the anti-vaccination movement. *Ann Ig.* (2018) 30:251–6. doi: 10.7416/ai.2018.2217
33. Giambi C, Fabiani M, D'Ancona F, Ferrara L, Fiacchini D, Gallo T, et al. Parental vaccine hesitancy in Italy - Results from a national survey. *Vaccine.* (2018) 36:779–87. doi: 10.1016/j.vaccine.2017.12.074
34. Cattarin M, Bellè M, Bergamini M, Gallo L. Suspension of mandatory vaccination and public health preserving: Rovigo local health unit experience after appliance of Veneto regional law 7/2007. *J Prev Med Hyg*. (2013) 54:181–6.
35. L47838995H D, Fonteneau L, Vaux S, Barret AS, Antona D, Bonmarin I, et al. Assessment of the impact of the extension of vaccination mandates on vaccine coverage after 1 year, France, 2019. *Euro Surveill.* (2019) 24:1900301. doi: 10.2807/1560-7917.ES.2019.24.26.1900301
36. Barraza L, Reiss D, Freeman P. Legal and policy responses to vaccine-preventable disease outbreaks. *J Law Med Ethics*. (2019) 47(2_suppl):11–4. doi: 10.1177/1073110519857307
37. Velavan TP, Pollard AJ, Kremsner PG. Herd immunity and vaccination of children for COVID-19. *Int J Infect Dis.* (2020) 98:14–5. doi: 10.1016/j.ijid.2020.06.065
38. Kim TH. Seasonal influenza and vaccine herd effect. *Clin Exp Vaccine Res.* (2014) 3:128–32. doi: 10.7774/cevr.2014.3.2.128
39. Pittet LF, Posfay-Barbe KM. Pneumococcal vaccines for children: a global public health priority. *Clin Microbiol Infect.* (2012) 18(Suppl 5):25–36. doi: 10.1111/j.1469-0691.2012.03938.x
40. Lopman BA, Payne DC, Tate JE, Patel MM, Cortese MM, Parashar UD. Post-licensure experience with rotavirus vaccination in high and middle income countries; 2006 to 2011. *Curr Opin Virol.* (2012) 2:434–42. doi: 10.1016/j.coviro.2012.05.002
41. Sheather J. Should childhood MMR vaccination be compulsory? *Rights, duties and the public interest Hum Vaccin Immunother.* (2013) 9:1389–91. doi: 10.4161/hv.24691
42. Scapaticci S, Neri CR, Marseglia GL, Staiano A, Chiarelli F, Verduci E. The impact of the COVID-19 pandemic on lifestyle behaviors in children and adolescents: an international overview. *Ital J Pediatr.* (2022) 48:22. doi: 10.1186/s13052-022-01211-y
43. Achdut N, Refaeli T. Unemployment and psychological distress among young people during the COVID-19 Pandemic: psychological resources and risk factors. *Int J Environ Res Public Health.* (2020) 17:7163. doi: 10.3390/ijerph17197163
44. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19 associated multisystem inflammatory syndrome in children - United States, March-July 2020. *MMWR Morb Mortal Wkly Rep*. (2020) 69:1074–80. doi: 10.15585/mmwr.mm6932e2
45. Siebach MK, Piedimonte G, Ley SH. COVID-19 in childhood: transmission, clinical presentation, complications and risk factors. *Pediatr Pulmonol.* (2021) 6:1342–56. doi: 10.1002/ppul.25344
46. Hart HLA. Are there any natural rights? *Philos Rev*. (1955) 64:175–91. doi: 10.2307/2182586

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 | Frontiers in Public Health

TYPE Original Research
PUBLISHED 25 August 2022
DOI 10.3389/fpubh.2022.950870

OPEN ACCESS

EDITED BY
Biagio Solarino,
University of Bari Aldo Moro, Italy

REVIEWED BY
Hongwei Hu,
Renmin University of China, China
Tianyu Wang,
Renmin University of China, China
Chao Wang,
China University of Mining and Technology, China

*CORRESPONDENCE
Zangyi Liao
cu192043@cupl.edu.cn

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

RECEIVED 23 May 2022
ACCEPTED 22 July 2022
PUBLISHED 25 August 2022

CITATION
Yang J, Shen Y, Deng Y and Liao Z (2022) Grandchild care, inadequate medical insurance protection, and inequalities in socioeconomic factors exacerbate childhood obesity in China. *Front. Public Health* 10:950870. doi: 10.3389/fpubh.2022.950870

Grandchild care, inadequate medical insurance protection, and inequalities in socioeconomic factors exacerbate childhood obesity in China

Jing Yang[1], Yun Shen[2], Yue Deng[3] and Zangyi Liao[4]*

[1]School of Public Administration, Hunan University, Changsha, China, [2]School of Economics, Sichuan Agricultural University, Ya'an, China, [3]Institute of Quality Development Strategy, Wuhan University, Wuhan, China, [4]School of Political Science and Public Administration, China University of Political Science and Law, Beijing, China

This study examines the influences of grandchild care and medical insurance on childhood obesity. Nationally representative longitudinal data—from the China Family Panel Studies 2010–2020—of 26,902 school-age children and adolescents aged 6–16 years and China's new reference standard ("WS/T586-2018") are used to identify a child's obesity status. Using binary mixed-effects logistic regression models and the Blinder–Oaxaca decomposition method, this study explores the roots of obesity inequalities and finds that at least 15% of Chinese children aged 6–16 were obese in the 2010s. The logistic regression analysis results indicate that grandchild care, public medical insurance, and commercial medical insurance are key risk factors of child obesity. However, the influences are heterogeneous in different groups: Grandchild care and public medical insurance increase urban–rural obesity inequalities because of a distribution effect, and grandchild care may also exacerbate children obesity inequalities between left-behind and non-left-behind children owing to the event shock of parental absence. Inequalities in socioeconomic status (SES) factors such as income, education, and region also cause obesity inequalities. These results indicate that child obesity and its inequalities are rooted in multidimensional environmental inequalities, including medical protection policies and its benefit incidence; intergenerational behavior and family SES factors; and urban–rural and left-behind risk shocks. This study provides new evidence for the development of population-based interventions and equitable medical insurance policies to prevent the deterioration of child obesity among Chinese school-age children and adolescents.

KEYWORDS

childhood obesity, grandchild care, medical insurance, socioeconomic factors, obesity inequalities, left-behind children

Introduction

As an important evaluation index of social development, children's nutrition and health have attracted much attention globally. At present, millions of children face nutritional imbalance, healthcare service shortages, and exposure to COVID-19. Some studies show that annually, malnutrition contributes to 3 million child deaths worldwide, and one in four children under age five have stunted growth due to nutritional problems (1). Meanwhile, obesity is a chronic nutritional disease caused by the excess of energy intake over energy consumption, and just like malnutrition, it is harmful to children's physical and mental health. Childhood obesity has become one of the most serious public health challenges in the 21st century (2), which is gradually transforming from a biological problem to a complex social problem (3, 4). Weight is impacted by genetic factors, environmental security, social status, and behavioral outcomes (5). Studies conducted in recent years have shown that during the COVID-19 lockdown, the rate of childhood obesity increased with the change in lifestyle (6, 7). However, compared with malnutrition, childhood obesity in developing countries is relatively overlooked (8). As poor countries escape from poverty traps and flee from famine, obesity rates rise (9). Although the overall rate of overweight and obesity among children in developing countries is lower than that in developed countries, obesity risk is accumulatively increasing at an alarming rate. In recent decades, China's situation is rapidly changing—from facing malnutrition to becoming the fastest growing obese population. Moreover, owing to population aging and parental migration (10), the phenomenon of intergenerational caring for grandchildren is relatively common (11). More importantly, the obesity costs of dependency burden and obesity-related medical care have increased astronomically, while the instability of family care continues to exacerbate the child obesity crisis (12). In 2020 and 2021, the COVID-19 pandemic severely affected the lives of children and young people worldwide, with public health measures taken to reduce community transmission of SARS-CoV-2, including unprecedented school closures and stay-at-home orders (13). As COVID-19 continues to spread globally, healthcare systems worldwide are overwhelmed, exacerbating the crisis of medical accessibility targeted at child obesity, thus making it urgent to address how to improve child obesity governance policies among generations.

Children's health and its risk factors

A long-published study has documented that genetic factors (14) and the family socioeconomic environment (15–19) are risk factors affecting child health. Currie and Stabile (20) report that children with lower family socioeconomic status have difficulty recovering from adverse health shocks to a healthy state. Miller et al. (21) find the mediating effects of caregiver mental and physical health on children's mental health. Some studies document that mother-related characteristics of family functioning are also associated with children's mental health (22–24). Especially in early childhood, children's caregivers play an extremely important role in improving children's eating behavior and physical health (25). Aristides et al. (26) find that income inequities strongly contribute to healthcare inequalities and private health insurance, to inequalities of medicine use. Pickett et al. (27) find that social gradients and inequalities in almost all morbidities are the "causes of the causes" of child health. Few studies explore the health problems of left-behind children (28–31), finding that left-behind children are more likely to have poor health status due to parental absence. Some studies find that health services are beneficial to increasing the health-related outcomes of child health (32, 33). However, Paul et al. (34) find that maternal education remains an important determinant of child health outcomes in India, while a poor healthcare system weakens its effect. Although the impacts of medical factors on child health are widely discussed, few studies focus on the effects of multi-level medical systems and their benefit incidence heterogeneity on child obesity.

Childhood obesity and family-based intervention

In recent years, the prevalence of childhood obesity has raised concerns because of the possible clinical and public health consequences (35). Childhood obesity leads to an increased risk of chronic diseases and seriously affects children's health (36). Previous studies find many factors affecting childhood obesity. Income and education socioeconomic status (SES) factors are inversely associated with child and adolescent obesity as measured by high body mass index (BMI) levels in developing countries (37–40). Zenab et al. (41) find that parental education, health insurance coverage, female gender, and language spoken at home other than Spanish were protective against overweight or obesity among children in the United States. Gopalan et al. (42) examine the spillover effects of parental public health insurance on the decrease of children's BMI, especially for girls. In some developing countries, especially in China, obesity risk is an important public health problem threatening child health (43, 44). Survey data show that between 1985 and 2010, the detection rates of obesity among male and female Chinese children and adolescents increased from 0.63 and 0.60% in 1985 to 11.60 and 5.59% in 2010, respectively (45). However, grandchild care exerts a certain negative impact on early childhood health of children aged 0–6 years (46). The spoiling effect of grandparents' indulgence on left-behind children produced negative effects on the children's BMI through an increase in unhealthy food consumption (47). Recent literature finds that childhood obesity also depends on emotional eating and family stability (48, 49).

Moreover, recent studies of children have raised concerns about family parental factors and increased SES risk factors. Although the proportion of intergenerational-care families in China has been increasing in recent years (50), the influence of grandchild care on childhood obesity among school-age Chinese children and adolescents is underrepresented in the existing literature. Few studies focus on school-age children and adolescents and identify the link between intergenerational factors and childhood obesity (51). Thus, it remains unclear whether an interaction exists between grandchild care and child obesity in different groups. China continues to face special child obesity risks that are rooted in socioeconomic and population-based inequalities. Without an effective intervention, the prevalence of overweight and obesity among Chinese school-aged children and adolescents will reach 31.80% by 2030 (52). Since 2011, the Chinese government has enacted a series of "Child Development Plans" (2011–2020) and related health improvement policies to prevent childhood obesity effectively (53), and the trend of childhood obesity shows staged mitigation features. Although the prevention and treatment of obesity among children and adolescents were the focus in the 2010s (54, 55), the intervention policies targeting the roots of child obesity differences require further investigation.

The present study

This study investigates the influences of grandchild care and medical insurance on child obesity using nationally representative longitudinal data between 2010 and 2020. We propose the following hypotheses: (1) Grandchild care increases the probability of childhood obesity; (2) medical insurance is positively associated with children's obesity risk; and (3) factors influencing child obesity are heterogeneous owing to group differences.

We take the following steps for our analysis: (1) investigate the recent prevalence trend of obesity rate among Chinese school-age children and adolescents and compare the differences among different groups; (2) examine the risk factors of childhood obesity inequalities and identify the associations among grandchild care, medical insurance, and child obesity; (3) decompose these factors' contributions and reveal how children are impacted by inequalities in different ways and the most important influencing factors, specifically, inequalities among urban–rural and left-behind children.

Our contributions to the literature are summarized as follows: 1) We explore the potential association between child obesity and grandchild care using new data from a nationally representative survey in China, the "China Family Panel Studies 2010∼2020"; (2) we empirically identify the relationship between child obesity and medical insurance among Chinese school-age children and adolescents and evaluate the effectiveness of multi-level medical insurance programs; and (3) we decompose the factor inequalities of child obesity due to the urban–rural gap and left-behind experience. Our findings could help reduce the intergenerational spoil effect and enhance the health improvement effect of medical insurance on child obesity and then provide policy implications for improving population-based obesity intervention systems.

Materials and methods

Study population

The data for this study come from the CFPS (2010–2020) collected by the Institute of Social Science Survey, Peking University (https://opendata.pku.edu.cn/dataverse/CFPS). The CFPS is a ten-year longitudinal survey of a nationally representative cohort of Chinese communities, families, and individuals. In the 2010 baseline survey, the CFPS dataset included almost 15,000 families and 30,000 individuals within these families. Because of its systematically stratified sampling method and large-sample characteristics, these studies have provided one of the most nationally representative survey databases in China. The CFPS has the highest-quality survey database for children aged 0–16. A total of 26,902 school-age children and adolescents aged 6–16 years are included in our analysis.

Statistical methods

We propose the following research hypotheses. First, grandchild care is associated with child obesity because of grandparental spoiling and unhealthy care practices. Second, medical insurance is related to the reduction of child obesity. Third, there is heterogeneity in the factors influencing child obesity because of environmental differences. In our investigation, we take the following steps: Step 1. We measure child obesity using the BMI index; Step 2. We analyze the influential factors of child obesity; Step 3. We apply the Blinder–Oaxaca decomposition method (BO) to compare the obesity inequality. Based on the regression results, we provide an in-depth discussion of the full empirical results.

A binary mixed-effects logistic regression model is employed to identify the influential factors of child obesity, in which the log odds of the binary outcome variable is modeled as a linear combination of the predictor variables when data are clustered or when both fixed and random effects exist[1].

$$Obesity_{it} = IR_{it}\alpha + MS_{it}\beta + P_{it}\gamma + R_{it}\rho + \epsilon_{it} \quad (1)$$

1 See https://stats.oarc.ucla.edu/r/dae/mixed-effects-logistic-regression/.

In Equation (1), the dependent variable $Obesity_{it}$ is the obesity status of child i at time t. IR_{it}represents grandchild care. MS_{it} represents medical insurance. P_{it} is a set of control variables that represent child-level (age and gender) and family-level (education and income) characteristics. R_{it} includes two-way fixed effects: region and year dummy variables. ε_{it} is the error term. A $p < 0.05$ means that the results are significant.

In addition, this study examines the heterogeneity of different factors influencing child obesity after distinguishing the types of Chinese school-age children and adolescents (e.g., urban vs. rural children and left-behind vs. non-left-behind children). Because traditional regression analysis is unable to derive directly the mean differences between groups, and the Shapley decomposition value method only yields the magnitude of the contribution of each factor in a linear regression model, neither of these models can decompose the differences between groups for models where the explanatory variable is a categorical variable. Therefore, we use BO for this analysis to investigate the coefficient effects of the urban–rural split and parental absence (or left-behind experience), and the characteristic effects of intergenerational parenting and health insurance on childhood obesity. BO is used to examine comparatively the determinants of childhood obesity differences among different groups. BO decomposes the differences in the dependent variables between groups into two components: changes in the distribution of levels of these determinants (E, explainable differences) and the consequence of the changes in the influence (U, unexplained differences).

$$E(Obesity_A) - E(Obesity_B) = X_A\beta_A - X_B\beta_B = (X_A - X_B)\beta^* + X_A(\beta_A - \beta^*) + X_B(\beta_B + \beta^*) \quad (2)$$

In Equation (2), M and F represent different groups. E($Obesity_A$) and E($Obesity_B$) represent the child obesity status in different groups, and X_M and X_F are the influential factors in the different obesity models. In our table, the term (X_A-X_B)β^* represents changes in the levels or values of a specific variable between different groups (distributional effect), while the term X_A (β_A-β^*)+X_B (β_B-β^*) captures the changes in the influence of a specific variable for determining obesity inequalities between these two groups (coefficient effect).

Following Powers et al. (56) and Yun (57), this study further extends Equation (2) to decompose and explain the estimated binary value of each coefficient.

$$E(Obesity_A) - E(Obesity_B) = E + U = \Sigma_{K=1}^{P} W_{\Delta X\beta_k} U = \Sigma_{K=1}^{P} E_k + \Sigma_{K=1}^{P} U_k \quad (3)$$

In Equation (3), $W_{\Delta x_k}$represents the contribution share of the mean change of the k explanatory variable. $W_{\Delta x_{\beta_k}}$ reflects the contribution share of the coefficient estimated value change of the k explanatory variable.

Measures

Measurement of childhood obesity

Child obesity is a dependent variable. We use BMI as the obesity indicator, which may dynamically reflect the childhood obesity status. BMI = weight (kg)/height^2 (m^2); it is a common clinical measurement indicator of physical health for assessing the status of child obesity. The recommended age-gender-specified BMI standard is used in our analysis to assess the trend of obesity rate for children and adolescents aged 6–16 years. The cutoff points of BMI are shown in Table 1. We use the determination criteria scale of the "WS/T586-2018 overweight and obesity screening of school-age children and adolescents," established by the National Health Commission of China in 2018. Compared with the old criteria in versions 1985 and 2000, the recent standard, "WS/T 586-2018," is more practical in terms of identifying the latest obesity prevalence in Chinese school-age children and adolescents.

Independent variables

Grandchild Care. Chinese families generally have a traditional culture of grandchild care, in which parents are busy with their work, and older people help families raise their grandchildren. Intergenerational care is an important way for Chinese families to care for their children. Consequently, the development and health of children may be affected by the intergenerational care from the grandparents. Based on the items in the CFPS questionnaire, specifically, "Who mainly takes care of the child during daytime or at night" or "Who takes care of the children during the month when the parents are not on vacation," if the child's grandparents mainly take care of the grandchild, the value of *grandchild care* is set to 1 and 0 otherwise.

Medical Insurance. (1) For *public medical insurance*, insured = 1, and uninsured = 0. In China, the public insurance system (including resident basic medical insurance, new rural cooperative medical insurance, and other social medical items) is usually organized by the local and central governments. These provide institutional support for basic medical care for residents and cover medical costs incurred when individuals receive outpatient and inpatient care. (2) Regarding *commercial medical insurance*, the commercial medical insurance system is a supplementary medical insurance plan, which is managed by a commercial insurance company. Based on an item in the CFPS, specifically, "In the past 12 months, did the family buy any commercial medical insurance for the child?", participated = 1, and did not participate = 0. (3) Regarding *medical utilization*, the variable is measured by the frequency of going to the hospital to see a doctor within a year.

Covariates. Child-level factors include age and sex. SES factors in our study include *income* and *education*. *Income* is measured by the household income status: if the family's income

TABLE 1 Cutoff points for obesity screening.

Child's age	Boys	Girls	Child's age	Boys	Girls
6	17.7	17.5	12.5	24.7	24.5
6.5	18.1	18.0	13	25.2	25.0
7	18.7	18.5	13.5	25.7	25.6
7.5	19.2	19.0	14	26.1	25.9
8	19.7	19.4	14.5	26.4	26.3
8.5	20.3	19.9	15	26.6	26.6
9	20.8	20.4	15.5	26.9	26.9
9.5	21.4	21.0	16	27.1	27.1
10	21.9	21.5	16.5	27.4	27.4
10.5	22.5	22.1	17	27.6	27.6
11	23.0	22.7	17.5	27.8	27.8
11.5	23.6	23.3	18	28.0	28.0
12	24.1	23.9			

TABLE 2 Baseline characteristics.

		Child obesity rate, n(%)		P-value by using chi-square test
		No	Yes	
Grandchild care	Yes	5,429 (78.04%)	1,528 (21.96%)	Pearson chi2(1)=12.41, $P = 0.000$
	No	17,130 (85.89%)	2,815 (14.11%)	
Basic Medical insurance	Insured	16,935 (84.32%)	3,150 (15.68%)	Pearson chi2(1) = 234.77, $P = 0.000$
	Uninsured	5,624 (82.50%)	1,193 (17.50%)	
Commercial medical insurance	Participated = 1	3,524 (86.86%)	533 (13.14%)	Pearson chi2(1) = 31.89, $P = 0.000$
	Unparticipated = 0	19,035 (83.32%)	3,810 (16.68%)	

is greater than the median income, the value of the *income* variable is set to 1 and 0 otherwise. *Education* is represented by the value of the average education years of all the adult family members at the last interview. Region and year fixed effects are controlled for in every regression model. *Region* represents the survey address: east = 1, central = 2, and west = 3; *year* includes 2010, 2012, 2014, 2016, 2018, and 2020.

Results

Baseline characteristics and general trend

Table 2 shows that children cared for by their grandparents were more likely to suffer from obesity (21.96% are obese) compared with their counterparts. The chi-square ($\chi 2$) results of the chi-square test show significant differences in child obesity due to grandchild care ($\chi 2 = 12.41$, $p < 0.001$). The average obesity rate of children covered by public medical insurance was 15.68%, while that of uninsured children was 17.50%. The average obesity rate of children who participated in commercial medical insurance was also lower than those who did not participate. The $\chi 2$ test results document differences in child obesity due to public medical insurance ($\chi 2 = 234.77$, $p < 0.001$) and commercial medical insurance ($\chi 2 = 31.89$, $p < 0.001$).

Table 3 presents the descriptive statistics, including the means, standard deviations (SDs), and range of all the variables included in the analysis. The average grandchild care for the children surveyed was more than one in four. The participation rate in basic health insurance was more than 70%, while the participation rate in commercial health insurance was only 15%. The results of the chi-square test or analysis of variance (ANOVA) show significant obesity differences based on the demographic variables ($p < 0.05$).

Figure 1 shows the prevalence change in child obesity between 2010 and 2020. We find that at least 15% of children aged 6–16 years were obese in the past 10 years. The obesity rate of grandparent-raised children rose from 18.96 to 23.25% from 2010 to 2020, while the non-grandparent-raised children's obesity rate was always below 15%. The results of the trend analysis indicate that the obesity rate of children raised by their grandparents is greater than that of the non-grandparent-raised group. Between 2010 and 2020, the obesity rate of children that did not participate in the commercial medical insurance

TABLE 3 Demographic variables.

	2010 (n = 4,967) Mean (SD) or n (%)	2012 (n = 4,460) Mean (SD) or n (%)	2014 (n = 4,514) Mean (SD) or n (%)	2016 (n = 4,484) Mean (SD) or n (%)	2018 (n = 4,825) Mean (SD) or n (%)	2020 (n = 3,652) Mean (SD) or n (%)	2010∼2020 (n = 26,902) Mean (SD) or n (%)
Grandchild care							
Grandparent-raised = 1	1,139 (22.93%)	1,075 (24.10%)	1,185 (26.25%)	1,261 (28.12%)	1,510 (31.30%)	787 (21.55%)	6,957 (25.86%)
Non-grandparent-raised = 0	3,828 (77.07%)	3,385 (75.90%)	3,329 (73.75%)	3,223 (71.88%)	3,315 (68.70%)	2,865 (78.45%)	19,945 (74.14%)
Public medical insurance							
Insured = 1	3,145 (63.32%)	2,435 (54.60%)	3,088 (68.41%)	4,021 (89.67%)	4,368 (90.53%)	3,028 (82.91%)	20,085 (74.66%)
Uninsured = 0	1,822 (36.68%)	2,025 (45.40%)	1,426 (31.59%)	463 (10.33%)	457 (9.47%)	624 (17.09%)	6,817 (25.34%)
Commercial medical insurance							
Participated = 1	875 (17.62%)	567 (12.71%)	676 (14.98%)	539 (12.02%)	637 (13.20%)	763 (20.89%)	4,057 (15.08%)
Unparticipated = 0	4,092 (82.38%)	3,893 (87.29%)	3,838 (85.02%)	3,945 (87.98%)	4,188 (86.80%)	2,889 (79.11%)	22,845 (84.92%)
Medical utilization (range 0∼60)	1.39 (2.37)	0.93 (1.94)	1.67 (3.64)	1.71 (3.10)	1.74 (3.69)	1.17 (2.39)	1.45 (2.96)
Age (range 6∼16)	10.59 (2.92)	10.41 (2.92)	10.37 (2.90)	10.13 (2.86)	10.25 (2.88)	10.31 (2.85)	10.35 (2.89)
Gender							
Male	2,571 (51.76%)	2,335 (52.35%)	2,384 (52.81%)	2,430 (54.19%)	2,583 (53.53%)	1,950 (53.40%)	14,253 (52.98%)
Female	2,396 (48.24%)	2,125 (47.65%)	2,130 (47.19%)	2,054 (45.81%)	2,242 (46.47%)	1,702 (46.60%)	12,649 (47.02%)
Income							
High-income	2,571 (51.76%)	2,335 (52.35%)	2,130 (52.81%)	2,430 (54.19%)	2,583 (53.53%)	1,950 (53.40%)	13,490 (50.14%)
Low-income	2,396 (48.24%)	2,125 (47.65%)	2,384 (47.19%)	2,054 (45.81%)	2,242 (46.47%)	1,702 (46.60%)	13,412 (49.86%)
Education (range 0∼30)	5.98 (3.96)	6.18 (3.68)	5.86 (3.45)	6.17 (3.47)	6.87 (3.21)	7.27 (3.41)	6.36 (3.58)
Region							
Eastern	1,766 (35.55%)	1,594 (35.74%)	1,502 (33.27%)	1,448 (32.29%)	1,652 (34.24%)	1,301 (35.62%)	9,263 (34.43%)
Middle	1,526 (30.72%)	1,390 (31.17%)	1,477 (32.72%)	1,462 (32.60%)	1,545 (32.02%)	1,143 (31.30%)	8,543 (31.76%)
Western	1,675 (33.72%)	1,476 (33.09%)	1,535 (34.01%)	1,574 (35.10%)	1,628 (33.74%)	1,208 (33.08%)	9,096 (33.81%)

Chi-square test for heterogeneity(categorical variables), ANOVA test for differences in the mean (continuous normally distributed variables). SD, standard deviation.

was greater than that of their counterparts. Meanwhile, since 2016, the obesity rate of the group that participated in public medical insurance was greater than that of their counterparts. In addition, before 2020, the obesity rate of urban children was lower than that of children from rural areas. However, the obesity rates of left-behind and non-left-behind groups stayed largely the same since 2010. Thus, the results show inter-group differences in child obesity.

Grandchild care

Table 4 shows that the impact of grandchild care on child obesity is significant (OR = 1.15, 95% CI: [1.07, 1.25], p = 0.000). Compared with the case of non-grandparent-raised children, grandchild care is significantly positively associated with child obesity. A possible explanation is that these grandparents had difficulty providing reasonable care for their grandchildren because of the decline in their bodily functions. In addition, majority of these grandparents likely had poor health awareness (58), such that they tended to provide excessive food to the child. Unhealthy grandchild-caring habits such as unhealthy diets, too much television, too little activity, and too little sleep were likely detrimental to the Chinese children's weight management.

Medical insurance

Over 74% of children were covered by public medical insurance, while over 15% of the children participated in

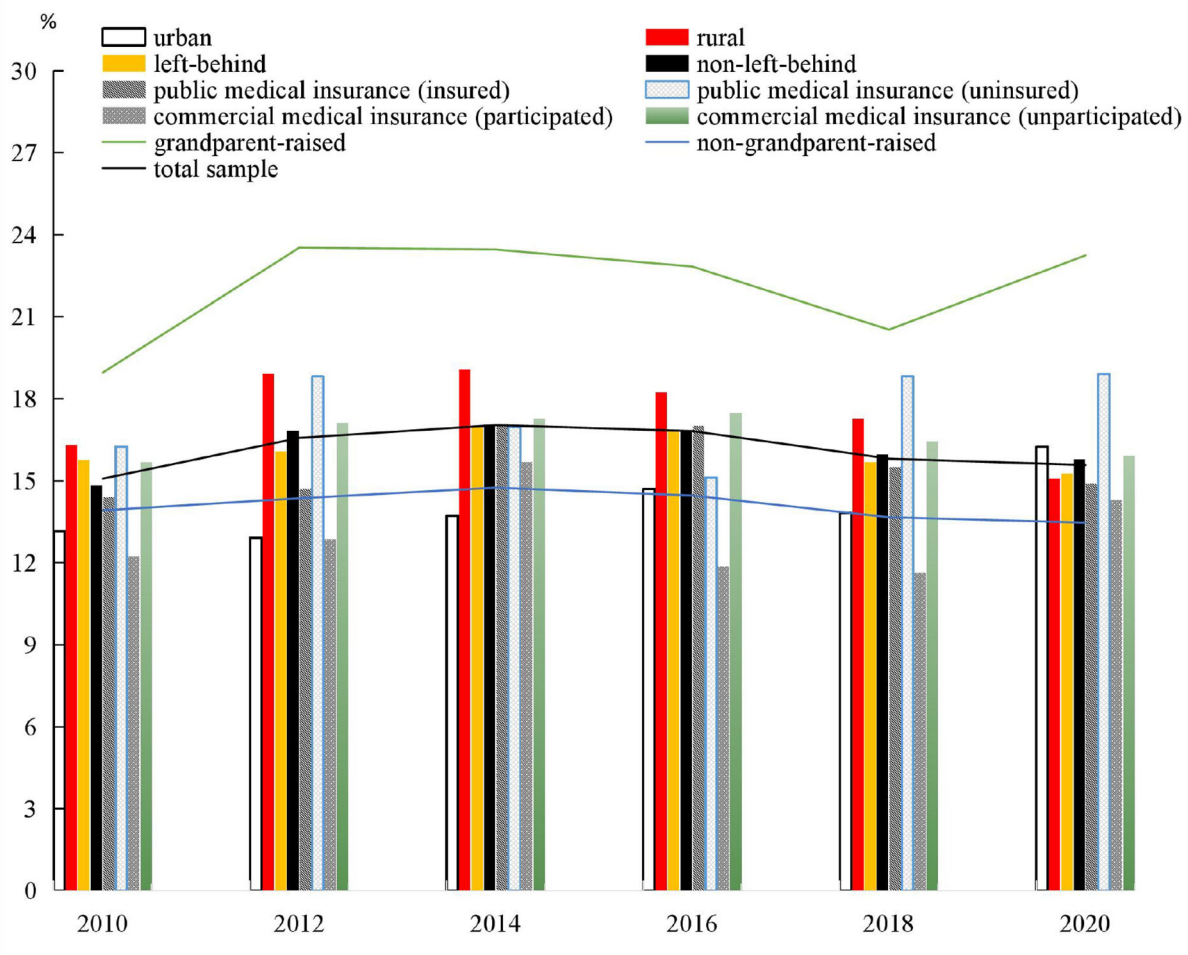


FIGURE 1
Child obesity rate during 2010–2020(%).

commercial medical insurance. Uninsured children were more likely to be obese than insured children (OR = 0.87, 95% CI: [0.80, 0.95], p = 0.002; OR = 0.84, 95% CI: [0.76, 0.93], p = 0.001). The results indicate that although most Chinese children had commercial medical insurance, the implementation of a multi-level medical insurance system could decrease the probability of Chinese school-age children and adolescents becoming obese. It is widely discussed that China's various types of medical insurance are useful in alleviating the cost of obesity-related medical care, fostering the healthy eating behaviors, and increasing the level of children's medical use, which may eventually reduce child obesity. Since the medical insurance reform was implemented in the 2010s, the increasing supportive policies for healthcare providers have improved the medical environment for insured children. Medical utilization is also a risk factor affecting child obesity (OR = 0.97, 95% [CI: 0.95, 0.98]), which indicates that a lesser frequency of medical utilization is associated with a higher prevalence of obesity, suggesting that increasing the accessibility and quality of children's medical utilization may help in timely mitigating obesity risks and reducing the damage of chronic diseases. More importantly, the medical advice provided by doctors also widens both the child's and parents' awareness of obesity risks, leading to an improvement in the child's daily weight management. Thus, it is necessary to improve the social insurance system and develop a specific commercial medical insurance for child obesity management.

Covariates

The study finds that the child's gender is associated with elevated levels of BMI. In China, boys are usually spoiled by the family, which may result in gender differences in childhood obesity (OR = 1.32, 95% CI: [1.23, 1.42], $p < 0.001$). Child obesity is influenced significantly by child age, but the impact of

TABLE 4 Influencing factors of child obesity.

	Odds Ratio	Std. Err.	z	P>|z|	[95% confidence interval]	
Grandchild care	1.1547	0.0448	3.71	0.000	1.0702	1.2460
Public medical insurance	0.8735	0.0377	−3.13	0.002	0.8026	0.9506
Commercial medical insurance	0.8397	0.0453	−3.24	0.001	0.7555	0.9333
Medical utilization	0.9655	0.0063	−5.36	0.000	0.9532	0.9780
Age	0.9159	0.0531	−1.51	0.130	0.8175	1.0262
Age-square	0.9866	0.0030	−4.51	0.000	0.9808	0.9924
Gender	1.3227	0.0479	7.72	0.000	1.2320	1.4200
Income	0.8797	0.0338	−3.33	0.001	0.8158	0.9486
Education	0.9439	0.0054	−10.16	0.000	0.9334	0.9545
Middle	1.0290	0.0476	0.62	0.536	0.9399	1.1267
Western	1.3710	0.0627	6.90	0.000	1.2534	1.4997
Year FE	YES	YES	YES	YES	YES	YES
Constant	1.9573	0.5401	2.43	0.015	1.1397	3.3614

TABLE 5 Obesity difference between urban and rural children.

	Urban children ($N = 10,869$)				Rural children ($N = 16,033$)			
	Odds Ratio	$P > \|z\|$	[95% confidence interval]		Odds Ratio	$P > \|z\|$	[95% confidence interval]	
Grandchild care	1.2065	0.003	1.0654	1.3663	1.1285	0.014	1.0246	1.2429
Public medical insurance	0.8469	0.017	0.7392	0.9703	0.9001	0.058	0.8074	1.0034
Commercial medical insurance	0.9404	0.413	0.8117	1.0894	0.7365	0.000	0.6323	0.8579
Medical utilization	0.9696	0.005	0.9489	0.9907	0.9654	0.000	0.9501	0.9809
Age	0.7419	0.001	0.6228	0.8837	1.0661	0.406	0.9167	1.2397
Age-square	1.0003	0.956	0.9914	1.0092	0.9769	0.000	0.9693	0.9847
Gender	1.5318	0.000	1.3648	1.7193	1.2045	0.000	1.1006	1.3183
Income	0.9198	0.189	0.8119	1.0419	0.8626	0.003	0.7828	0.9507
Education	0.9567	0.000	0.9410	0.9726	0.9345	0.000	0.9195	0.9498
Middle	1.0691	0.322	0.9368	1.2202	0.9913	0.890	0.8758	1.1220
Western	1.2899	0.001	1.1147	1.4927	1.3789	0.000	1.2266	1.5501
Year FE	Yes				Yes			
Constant	3.3374	0.005	1.4305	7.7862	1.2542	0.532	0.6159	2.5539

age-square shows an inverted U curve (OR = 0.99, 95% CI: [0.98, 0.99], $p < 0.001$). The results also show an obvious relationship between endowment disadvantage and child obesity. SES factors (income and education) are significantly associated with an elevated obesity status (OR = 0.88, 95% CI: [0.82, 0.95], p = 0.001; OR = 0.94, 95% CI: [0.93, 0.95], $p < 0.001$, respectively), which indicates that a lower SES is associated with a higher obesity rate. One explanation may be that children with a lower family SES tend to choose foods with higher calorie, which in turn leads to child obesity. Another possible explanation is that families with lower SES invest less resources in weight management for the child. In addition, child obesity is higher in the western economically underdeveloped region than in the eastern developed provinces (OR = 1.37, 95% CI: [1.25, 1.50], $p < 0.001$).

Obesity differences and blinder–oaxaca decomposition

Heterogeneity analysis of urban–rural differences

The results of the study show urban–rural differences in the influential factors of child obesity (Table 5). Risk factors that influence obesity among urban children include grandchild care (OR = 1.21, $p < 0.01$), public medical insurance (OR =

0.85, $p < 0.05$), medical utilization (OR = 0.97, $p < 0.01$), age-square (OR = 1.00, p = 0.001), gender (OR = 1.53, $p < 0.001$), education (OR = 0.96, $p < 0.001$), and a western location (OR = 1.29, p = 0.001). Risk factors influencing rural children's obesity include grandchild care (OR = 1.13, $p < 0.05$), commercial medical insurance (OR = 0.97, $p < 0.001$), medical utilization (OR = 1.21, $p < 0.001$), age-square (OR = 0.98, $p < 0.001$), income (OR = 0.86, $p < 0.001$), education (OR = 0.93, $p < 0.01$), and a western location (OR =1.38, $p < 0.001$). The results show that public medical insurance has a more significant effect on urban than on rural children, but we have not confirmed the statistically significant effect of commercial medical insurance on reducing urban children's obesity risk. Thus, the association between medical insurance and child obesity is heterogeneous for urban and rural children. The disparity in healthcare conditions may contribute to the differences in child obesity status and its influential factors when comparing rural and urban children. Medical utilization is significantly associated with both urban and rural children, while the income and age-square variables only have significant effects on rural children. This means that intervention policies should focus either on the improvement of SES or the medical environment. Our study confirms that the effects of public medical insurance are significant only on urban children's obesity, while the effects of commercial medical insurance and income are significant only on rural children. Thus, for urban children, the aim should be to improve public medical insurance and medical utilization, while for the latter, it should be to increase the commercial medical insurance coverage and income status. Therefore, policies are urgently needed to combat these obesity inequalities, and population-based and family-focused interventions on childhood obesity should be implemented in a coordinated manner.

Left-behind event shock

Compared with non-left-behind children, the phenomenon of intergenerational care in China among left-behind children is more widespread. Specifically, the data show that in 2020, more than 67% of left-behind children were mainly cared for by their grandparents. In our study, left-behind children are those whose parents stayed outside the home for a long time and rarely went back home to care for their children. A child is considered left-behind in this study if one or both parents did not live with them for <6 months in 1 year or left home for at least 1 month. Because of the shock of being left behind, the instability of the family structure may exacerbate the childcare crisis, leading to parents spending less time caring for left-behind children, and the raising burden being transferred to the elderly. Because of parental absence and grandchild care vulnerability, the influence of grandchild care on child obesity may differ between left-behind and non-left-behind children.

The results in Table 6 show that the factors influencing left-behind children's obesity include grandchild care (OR = 1.27, $p < 0.001$), medical utilization (OR = 0.96, $p < 0.001$), age-square (OR = 0.99, $p < 0.01$), gender (OR = 1.18, $p < 0.01$), income (OR = 0.81, p = 0.001), education (OR = 0.95, $p < 0.001$), and a western location (OR = 1.43, $p < 0.001$). The factors influencing non-left-behind children's obesity include public medical insurance (OR = 0.85, $p < 0.05$), commercial medical insurance (OR = 0.85, $p < 0.01$), medical utilization (OR = 0.97, $p < 0.05$), age-square (OR = 0.99, p = 0.001), gender (OR = 1.41, $p < 0.001$), education (OR = 0.94, $p < 0.001$), and a western location (OR = 1.34, $p < 0.001$).

We confirm that grandchild care increases the obesity risk of left-behind children, but there is no significant association between grandchild care and child obesity for non-left-behind children. Moreover, public and commercial medical insurance may lower the child obesity rate only for non-left-behind children (OR < 1, $p < 0.05$), while the effects on left-behind children are not significant. This indicates no significant protective effects of medical insurance in reducing the risk of obesity among left-behind children in China. Income is only associated with left-behind children's obesity, while the effect of income on non-left-behind children is not significant. Thus, the obesity effects of grandchild care, medical insurance, and other SES factors are heterogeneous.

Decomposition of childhood obesity inequalities

We further apply BO to identify the contribution share of the above-mentioned factors on the differences in child obesity. The explainable endowment effect reflects the percentage increase in the probability of urban children being obese when they have similar endowment characteristics as rural children. The results show that the obesity rate of rural children is higher than that of urban children. The decomposition of the obesity gap shows that the unexplained share related to differences in individual characteristics is −0.0141, or 39.90% of the total wage gap. The decomposition of the obesity gap shows that the explained share associated with differences in individual characteristics is −0.0212, or 60.10% of the total wage gap. The urban–rural decomposition results in Table 7, panel A, indicate that the proportion of endowment differences is larger than the coefficient differences (unexplained component). The obesity gap between urban and rural children is largely due to the explained part of the BO.

Considering the decomposition of the different variables in Table 7, the significant contribution shares of some of the endowment effect on child obesity are significant ($p < 0.05$), including grandchild care (C = −0.0005, $p = 0.003$), public medical insurance (C = −0.0001, $p = 0.025$), gender (C = −0.0001, p =0.000), education (C = −0.0133, $p = 0.000$), and a western location (C = −0.005, $p = 0.004$). The factors above

TABLE 6 Child obesity difference between left-behind children and non-left-behind children.

	Left-behind children ($N = 9,916$)				Non-left-behind children ($N = 16,986$)			
	Odds Ratio	P > |z|	[95% confidence interval]		Odds Ratio	P > |z|	[95% confidence interval]	
Grandchild care	1.2673	0.000	1.1221	1.4314	1.0994	0.085	0.9871	1.2244
Public medical insurance	0.9172	0.245	0.7929	1.0610	0.8490	0.002	0.7646	0.9427
Commercial medical insurance	0.8232	0.051	0.6773	1.0006	0.8480	0.011	0.7472	0.9624
Medical utilization	0.9607	0.000	0.9419	0.9798	0.9690	0.000	0.9526	0.9856
Age	0.9085	0.321	0.7516	1.0981	0.9092	0.193	0.7878	1.0493
Age-square	0.9862	0.005	0.9767	0.9958	0.9874	0.001	0.9801	0.9947
Gender	1.1759	0.007	1.0444	1.3239	1.4150	0.000	1.2939	1.5474
Income	0.8110	0.001	0.7156	0.9191	0.9297	0.136	0.8448	1.0232
Education	0.9490	0.000	0.9304	0.9680	0.9388	0.000	0.9260	0.9518
Middle	0.9848	0.847	0.8422	1.1515	1.0656	0.269	0.9522	1.1925
Western	1.4326	0.000	1.2255	1.6748	1.3447	0.000	1.2045	1.5013
Year FE	YES				YES			
Constant	1.8516	0.183	0.7484	4.5807	2.0295	0.041	1.0290	4.0027

TABLE 7 Decomposition of child obesity differences due to characteristic endowment.

	Panel A: Reference group (Urban children) vs. Comparison group (rural children)		Panel B: Reference group (Left-behind children) vs. Comparison group (non-left-behind children)	
	C	Pct. (%)	C	Pct. (%)
Overall difference	−0.0353(0.000)	100	0.0005(0.902)	100
Explainable differences	−0.0212(0.000)	60.10	0.0089(0.000)	1644.70
Unexplained differences	−0.0141(0.010)	39.90	−0.0083(0.095)	−1544.70
Due to Difference in Characteristics				
Grandchild care	−0.0005(0.003)	1.42	0.0088(0.000)	1633.16
Public medical insurance	−0.0001(0.025)	0.32	−0.0003(0.250)	−63.79
Commercial medical insurance	−0.0006(0.455)	1.69	0.0015(0.062)	269.43
Medical utilization	0.0002(0.003)	−0.61	−0.0015(0.000)	−280.39
Age	0.0005(0.000)	−1.51	−0.0113(0.002)	−2093.15
Age-square	−0.0002(0.149)	0.69	−0.0047(0.322)	−871.74
Gender	−0.0001(0.000)	0.32	−0.0001(0.005)	−21.15
Income	−0.0030(0.139)	8.40	0.0027(0.002)	497.75
Education	−0.0133(0.000)	37.72	0.0095(0.000)	1753.93
Middle area	0.0002(0.407)	−0.56	−0.0002(0.792)	−43.99
Western area	−0.0050(0.004)	14.16	0.0019(0.000)	351.23

The results related to the coefficient effect (unexplainable part) are not listed.

are both negative components that can increase the obesity difference between urban and rural children. Overall, the obesity rate is lower for urban than for rural children, while public medical insurance is higher for urban than for rural children. Thus, identifying an uninsured child is important to alleviate the obesity difference among urban and rural Chinese children. In addition, grandchild care, which is negatively associated with child obesity, contributes to widening the inequalities in obesity between urban and rural children, as urban children have lower levels of intergenerational parenting than rural children. The endowment differences in education and gender are also major contributors to the changes in obesity differences between urban and rural children. Moreover, medical utilization ($C = 0.0002$, $p = 0.003$) and child age ($C = 0.0005$, $p = 0.000$) importantly contribute to the decrease in the obesity inequalities between urban and rural children. In China, the difference in

medical utilization may decrease the obesity difference resulting from the integration of China's urban–rural public welfare system. The urban–rural differences in obesity among Chinese school-age children and adolescents shrink with age because of physiological factors.

In Table 7, panel B, the contribution share of the endowment effect is slightly larger than that of the coefficient effect between left-behind and non-left-behind children. Specifically, medical utilization ($C = -0.0015$, $p = 0.000$), age ($C = -0.0113$, $p = 0.002$), and gender ($C = -0.0001$, $p = 0.005$) are significantly negative, owing to the endowment difference. The results indicate that these are the main factors for reducing the obesity difference between non-left-behind and left-behind children. However, the influence of grandchild care ($C = 0.00881$, $p = 0.000$), income ($C = 0.0027$, $p = 0.002$), education ($C = 0.0095$, $p = 0.000$), and a western location ($C = 0.0019$, $p = 0.000$) is significantly positive, indicating that the differences in these variables exacerbate the obesity inequality. The results show that changes in the distribution of grandchild care in different families are the major contributors to changes in children obesity inequalities because of the distribution effect. Because the incidence of obesity and grandchild care in left-behind children is higher than that in non-left-behind children, unbalanced grandchild care behavior may worsen the obesity inequality in left-behind children. Moreover, although the alleviation effect of education on child obesity for left-behind children and non-left-behind children is both significant, the inequality in education is still a source of obesity difference. The previous results suggest that income has a suppressive effect on obesity only for left-behind children, not for non-left-behind children; therefore, the income disparity may exacerbate obesity inequalities between left-behind and non-left-behind children. Moreover, medical utilization can reduce the obesity difference. In addition, the effects reflected by individual variables (age and gender) can decrease the inequalities in child obesity.

Discussion

Over recent decades, the overweight and obesity situation among Chinese children has become serious. According to the "WHO child growth standards (2006)" for school-aged children and adolescents, the results of the "China childhood obesity report (2017)" meant that the obesity rate among Chinese children aged 7–18 years in 1985 and 2000 was 0.5 and 4.6%, respectively, and the predictive value of obesity rate may reach only 8.5% in 2020 (10). However, using the "WS/T586-2018" as a reference, Song et al. (59) find that the obesity rate rose from 2.3 to 15.2% from 1991 to 2015, and the obesity rate for girls rose from 2.5 to 10.1%, which is worse than what Ma et al. (10) predicted. Our findings are closer to those of Song et al. (59). We document that at least 15% of Chinese children aged 6–16 years were obese during 2010–2020. Although the difference in the results may be related to the measurement tools and data sources, the obesity risk is clearly becoming a serious public problem threatening child development; thus, it is necessary to take urgent obesity control measures from different perspectives.

Our results indicate that left-behind children and rural children who are cared for by grandparents have a higher probability of being obesity. Some studies find a consistent conclusion that parental absence made left-behind children in rural areas become a high-risk group prone to nutrition and health problems (60, 61). A study confirms that the mechanisms by which grandchild care affects the physical health of left-behind children are complex (47). Although grandchild care may have some positive effects in offsetting children's psychological loss due to parental absence (50), the negative effect of grandchild care on child obesity remains dominant in our study. We further determine that differences exist in the intergenerational mechanisms on child obesity among different groups, and we believe that policies that support and optimize the behaviors of intergenerational care may be a key measure for preventing children's obese status.

In fact, child obesity is not caused only by child-related factors. Aside from child-level differences, child obesity is also closely related to socio-political factors (18). Some studies have confirmed that social medical insurance in rural areas could reduce preventive savings by increasing the uncertainty of future medical expenditures, increase consumption, and improve nutrition intake and the child's health (62, 63). Our study also finds that having medical insurance can reduce the risk of child obesity, especially for urban and non-left-behind children. However, we find no significant association between public medical insurance and child obesity for rural and left-behind children, while public medical insurance is an important factor to the obesity inequalities between urban and rural children. The outcome disparities reflect that the inequalities in the benefits of medical insurance are still obvious because of the differences in the children's growth environment, which means that the role of public medical insurance in protecting the physical health of vulnerable children (rural and left-behind children) is inefficient. We find that commercial medical insurance is significantly associated with the obesity status of rural children. Therefore, the family and political environments are important to the prevention of child obesity. This means that governments at all levels should further improve the design of the medical insurance systems for different children and strengthen the complementary role of commercial health insurance to prevent the obesity risk of rural children. In addition, policies supporting primary grandchild caregivers should be made to prevent child obesity.

In line with previous research (64–66), we find that the prevalence of child obesity is higher in families with a lower SES. Especially for rural and left-behind children, family income and education are important in reducing childhood obesity rates. A study finds an inverse relationship between BMI and

SES and that low school SES and rural locality of the school are school-level risk factors of child obesity (65). Thus, we recommend family-based education on healthy eating and exercise. In families with insufficient investment in education and poor income, children's obesity reduction is difficult because of the restrictions of SES factors; thus, children from lower-SES families tend to eat excessive and poor-quality foods, including fried foods. Therefore, we confirm that children from lower-SES families are more vulnerable to obesity risk than other children, especially in China's rural and western areas. Thus, related policies targeting to improve the equitable development of SES factors are strongly recommended.

A study finds that majority of the inequality in childhood obesity is explained by parental socioeconomic gradients (67), with socioeconomic factors accounting for 75.8% of the existing inequalities. Residential areas and education provided by the mother were the most important causes of inequality (68). It is important to tailor policies that target child obesity/overweight to tackle not only the prevalence of this disease but also its distribution (69). The results of our study support the findings discussed above. Our study also confirms that the effects of family income and education significantly dominate child obesity inequalities. The results indicate that inequalities in socioeconomic factors measured by family income play a critical role in mitigating the obesity rate among rural and left-behind children, while income differences contribute to the obesity inequalities among left-behind and non-left-behind children. In our analysis, the level of family education is an important contributing factor that increases the obesity inequalities between urban and rural children. In addition, family income and education are the major contributors to changes in the obesity differences between left-behind and non-left-behind children. Thus, we believe that childhood obesity differences are rooted in socioeconomic inequalities, including urban–rural shocks, left-behind shocks, and family capital. Population-based interventions are important in preventing the prevalence of childhood obesity, but policies that target vulnerable groups are also needed to alleviate the inequalities in SES factors.

A study finds that the experience of being left behind or of parents' migration may reduce the care provided to Chinese children and thus affect the health of children (70). Kristin (71) confirms that cumulative adverse childhood experiences may exacerbate existing social disparities in children's health. Jessica et al. (72) confirm that rural children experience health and healthcare disparities compared with their urban peers and represent a unique and vulnerable pediatric patient population. The root causes of health inequalities (obesity, anxiety, infectious diseases, injuries, prematurity, and low birth weight) of children are complex, and interventions to address child health inequalities must consider the structural determinants (73). We also find that the negative experience of being left-behind has a detrimental consequence for child physical health, and grandchild care is significantly associated with child obesity because of the early negative experience of parental absence. Thus, it is necessary to take effective family-level measures to decrease childhood obesity caused by cumulative adverse experiences.

Some scholars claim that children's age and gender are risk factors of childhood obesity (74). We document that gender and age are significantly associated with child obesity and its inequalities among Chinese school-age children and adolescents.

This study has several notable strengths. We apply the new determination criteria using ten-year survey datasets to explore the obesity inequalities in China. The findings could help people reduce the intergenerational spoil shock and increase the improvement effect of medical insurance on child health. In addition, this study provides new evidence for the development of population-based interventions and equitable medical insurance policies to prevent the deterioration of child obesity among Chinese school-age children and adolescents. However, some points are worth improving such as data limitations and the lack of information on physical exercise and sleeping habits, as well as parental overweight. Because of the cross-sectional limitation of the data, although this study confirms that children's family environment and SES factors contribute to child obesity differences, these factors cannot explain all the mechanisms of obesity inequalities. Given the complexity of family-based intergenerational care in China, more in-depth analysis is needed in future.

Conclusion

We document the influences of grandchild care and medical insurance on child obesity using unique CFPS data (2010–2020). Our results indicate that the epidemiological status of obesity among Chinese school-age children and adolescents has become more severe than in the last decades. Thus, measures that prevent and control the epidemiological trend are urgently needed. We confirm that child obesity among Chinese school-age children and adolescents is caused by many risk factors, including family characteristics, SES factors, and genetic influence. Grandchild care is significantly positively associated with child obesity, while the implementation of medical insurance can decrease the probability of being obese for Chinese school-age children and adolescents. Our study has policy implications. Specifically, improving the medical insurance coverage of children is likely to alleviate the obesity risks among Chinese school-age children and adolescents.

Another significant finding of this study is that inequalities in obesity are rooted in socioeconomic environmental differences and policy efficiency, including household education, income, urban–rural segmentation, and left-behind risk shocks.

Using BO to decompose childhood obesity inequalities, we find that the role of grandchild care and public medical insurance and grandchild care may increase the obesity inequalities between urban and rural children, while grandchild care may increase the obesity inequality between non-left-behind and left-behind children because of the shock of parental absence. With the gradual widening of the gap between urban and rural areas in China, the urban–rural structural barriers may set an obvious barrier for the health equality and obesity prevention among different Chinese children. More importantly, children from urban areas can efficiently enjoy better educational resources and sound medical systems than rural children. We recommended tailoring policies to target child obesity and tackle not only the prevalence of obesity but also its distribution. Therefore, it is important to break down the barriers between urban and rural areas and ensure the fairness in public healthcare resource provision and medical accessibility. We should ensure that children from the rural areas and left-behind families equally benefit through a renewed focus on inequalities.

We suggest that relevant government departments comprehensively consider the effects of these risk factors and develop a systematic family risk assessment tool for child obesity among Chinese school-age children and adolescents. First, family-level public intervention measures should be implemented among Chinese school-age children and adolescents. The vulnerable children should be made a priority for obesity prevention, especially among rural and left-behind children. Governments at different levels should optimize the school-based obesity prevention program and strengthen the comprehensive family support mechanism to develop a health-supported environment for child obesity prevention. On the one hand, the government should improve the unified standards of diagnosis, assessment, treatment, prevention, and management of child obesity for primary care providers. On the other hand, health education, diet control, and scientifically planned exercise regimens should be promoted among Chinese school-age children and adolescents. Moreover, the quality and efficiency of children's healthcare must be improved to prevent the factors caused by school lockdown and home isolation during the COVID-19 outbreak. Because of the potential absence of parental supervision and the affordability of healthcare resources, it is advised to improve the quality of grandchild care among Chinese school-age children and adolescents. For obese children, a comprehensive and systematic intervention approach is needed, focusing on a multi-level intervention model and fully strengthening the responsibilities of families, schools, medical institutions, and the government, to achieve the goal of preventing and controlling child obesity. The government can also help prevent obesity by purchasing services and allowing relevant social organizations to provide professional care services for rural and left-behind children.

Second, we recommend that the multi-level medical insurance system be designed to alleviate the obesity illness's economic burden by constructing a more inclusive medical insurance system for the affected children. In addition, clinicians should conduct an overall assessment of the obesity risk factors and then prescribe a holistic approach for obesity treatment of these children. Moreover, considering the difficult situations of insured children, the government can explore the integrated medical insurance systems, establish a gradient commercial medical insurance plan for different groups of children, and focus on improving the coverage scope of the medical insurance system.

Third, the obesity inequalities should be alleviated by improving the SES of disadvantaged families and gradually integrating the effects of the medical insurance systems. Some related social policies targeted at child obesity inequalities among Chinese school-age children and adolescents are advised as follows: (1) increasing the financial input in child healthcare and implementing a mutual fund system specifically for these vulnerable groups; (2) improving nutrition, the health environment, and medical conditions for disadvantaged children to avoid obesity inequalities due to urban–rural and left-behind experiences; (3)improving the fairness of basic medical insurance and scientifically defining the reimbursement scope of children's medical insurance systems; (4) establishing a laddered policy rate of reimbursement to address SES inequalities and providing care subsidy for grandchild-care families in need; (5) improving the left-behind children's medical accessibility of healthcare insurance payments in different-grade hospitals and popularizing children's commercial medical insurance system; and (6) promoting the social environment to prevent and control the prevalence of child obesity.

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.

Ethics statement

The studies involving human participants were reviewed and approved by Peking University Biomedical Ethics Committee (No. IRB00001052-14010). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. The animal study was reviewed and approved by Peking University Biomedical Ethics Committee (No. IRB00001052-14010). Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication

of any potentially identifiable images or data included in this article.

Author contributions

JY: conceptualization, methodology, validation, formal analysis, reviewing, and editing. YS: conceptualization, methodology, validation, writing, reviewing, and editing. YD: conceptualization, methodology, validation, formal analysis, and funding acquisition. ZL: conceptualization, reviewing and editing, supervision, and funding acquisition. All authors contributed to the article and approved the submitted version.

Funding

This research was funded by the National Social Science Foundation of China (Grant No. 21CSH011) and Qian Duan-sheng Outstanding Scholars Support Program of China University of Political Science and Law. This work was supported by CFPS of the Institute of Social Science Survey of Peking University. The data from China Family Panel Studies (CFPS), is funded by Peking University.

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. Irena AH, Mwambazi M, Mulenga V. Diarrhea is a major killer of children with severe acute malnutrition admitted to inpatient set-up in Lusaka, Zambia. *Nutr J.* (2011) 10:110. doi: 10.1186/1475-2891-10-110

2. World Health Organization(WHO). Noncommunicable diseases: Childhood overweight and obesity. Available online at: https://www.who.int/news-room/questions-and-answers/item/noncommunicable-diseases-childhood-overweight-and-obesity (accessed August 10, 2022).

3. Sorof J, Daniels S. Obesity hypertension in children: a problem of epidemic proportions. *Hypertension.* (2002) 4:44–7. doi: 10.1161/01.HYP.0000032940.33466.12

4. Ng M, Fleming T, Robinson M. Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013: a Systematic Analysis for the Global Burden of Disease Study (2013). *Lancet.* (2014) 384:766–81. doi: 10.1016/S0140-6736(14)60460-8

5. Heitkamp M, Siegrist M, Molnos S, Brandmaier S, Wahl S, Langhof H, et al. Obesity genes and weight loss during lifestyle intervention in children with obesity. *JAMA Pediatr.* (2021) 175:e205142. doi: 10.1001/jamapediatrics.2020.5142

6. Wudeneh M, Laboni H. Impact of the COVID-19 lockdown on weight status and associated factors for obesity among children in Massachusetts. *Obesity Medicine.* (2021) 22:100325. doi: 10.1016/j.obmed.2021.100325

7. Samur B M, Samur T G, Gul-Sir U, Hatipoglu N. Vicious cycle between severity of childhood obesity and pandemic: Potential impact of metformin. *Obesity Medicine.* (2022) 33:100433–100433. doi: 10.1016/j.obmed.2022.100433

8. Wang F, Lin L, Lu J, Cai J, Xu J, Zhou X. Mental health and substance use in urban left-behind children in China: A growing problem. *Children Youth Services Rev.* (2020) 116. doi: 10.1016/j.childyouth.2020.105135

9. Popkin B M, Adair L S, Ng S W. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev.* (2012) 70:3–21. doi: 10.1111/j.1753-4887.2011.00456.x

10. Ma G, Mi J, Ma J. Childhood obesity report in China 2017. *People's Medical Publishing House.* (2017). Available online at: https://www.pmphmall.com/gdsdetail/609728-284355

11. Chen F, Liu G, Mair CA. Intergenerational ties in context: grandparents caring for grandchildren in China. *Social Forces.* (2011) 2:571–94. doi: 10.1093/sf/sor012

12. Yue J, Fan X. China's child care policy system: review, reflection and reconstruction. *Social Sciences in China* 2018. Available online at: https://navi.cnki.net/knavi/journals/ZSHK/detail

13. Moore J B. COVID-19, childhood obesity, and NAFLD: colliding pandemics. *Lancet Gastroenterol Hepatol.* (2022) 7:499–501. doi: 10.1016/S2468-1253(22)00100-5

14. Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *Bull World Health Organ.* (1987) 65:663–737.

15. Gibson J, Rozelle S. How elastic is calorie demand? Parametric, nonparametric, and semiparametric resultsfor urban papua new Guinea. *J Dev Stud.* (2002) 6:23–46. doi: 10.1080/00220380412331322571

16. Stansfeld SA, Clark C, Lopez-Barrio I. Aircraft and road traffic noise exposure and children's mental health. *J Environ Psychol.* (2009) 29:203–7. doi: 10.1016/j.jenvp.2009.01.002

17. Tian X, Yu X. Using semiparametric models to study nutrition improvement and dietary change with different indices: the case of China. *Food Policy.* (2015) 53:67–81. doi: 10.1016/j.foodpol.2015.04.006

18. Zhou C, Sylvia S, Zhang L, Luo R, Yi H, Liu C, et al. China's left-behind children: impact of parental migration on health, nutrition, and educational outcomes. *Health Aff.* (2015) 11:1964–71. doi: 10.1377/hlthaff.2015.0150

19. Fledderjohann J, Erlam J, Knowles B, Broadhurst K. Mental health and care needs of British children and young people aged 6-17. *Child Youth Serv Rev.* (2021) 126:106033. doi: 10.1016/j.childyouth.2021.106033

20. Currie J, Stabile M. Socioeconomic status and child health:why is the relationship stronger for older children? *The American Economic Rev.* (2003) 5. doi: 10.3386/w9098

21. Miller KM, Orellana ER, Briggs HE, Quinn A. Influence of caregiver substance dependence and serious mental illness on children's mental health: moderating effects of social support. *Child Adolesc. Soc. Work J.* (2014) 5:435–54. doi: 10.1007/s10560-014-0326-8

22. Janke K. Air pollution, avoidance behaviour and children's respiratory health: evidence from England. *J. Health Econ.* (2014) 38:23–42. doi: 10.1016/j.jhealeco.2014.07.002

23. Nikolaev EL, Baranova EA, Petunova SA. Mental health problems in young children: the role of mothers' coping and parenting styles and characteristics of family functioning. *Procedia Soc Behav Sci.* (2016) 17:94–9. doi: 10.1016/j.sbspro.2016.10.152

24. Murnan A, Wu Q, Slesnick N. The impact of parenting on child mental health among children of prostituting mothers. *Child Youth Serv Rev.* (2018) 89:212–7. doi: 10.1016/j.childyouth.2018.04.042

25. Skouteris H, Hill B, Mccabe M, Swinburn B, Busija L. A parent-based intervention to promote healthy eating and active behaviours in pre-school children: evaluation of the MEND 2∼4 randomized controlled trial. *Pediatr Obes.* (2016) 1:4–10. doi: 10.1111/ijpo.12011

26. Aristides AM, Perelman J, Jacinto PA, Tejada C, Barros A, Bertoldi AD, et al. Income-related inequality and inequity in children's health care: A longitudinal analysis using data from Brazil. *Soc Sci Med.* (2019) 224:127–37. doi: 10.1016/j.socscimed.2019.01.040

27. Pickett KE, Yassaman V. Mathew M. The social determinants of child health and inequalities in child health. *Paediatr Child Health.* (2022) 32:88–94. doi: 10.1016/j.paed.2021.12.003

28. Schmeer K. Father absence due to migration and child illness in rural mexico. *Soc Sci Med.* (2009) 8:1281–6. doi: 10.1016/j.socscimed.2009.07.030

29. Yao L. Internal migration, international migration, and physical growth of left-behind children: a study of two settings. *Health &Place.* (2015) 36:118–26. doi: 10.1016/j.healthplace.2015.09.008

30. Michaella V, Valentina M, Melissa S. Left behind' but not left alone: parental migration & the psychosocial health of children in Moldova. *Social Sci Med.* (2015) 132:252–60. doi: 10.1016/j.socscimed.2014.08.040

31. Nguyen CV. Does parental migration really benefit left-behind children? Comparative evidence from Ethiopia, India, Peru and Vietnam. *Social Sci Med.* (2016) 153:230–9. doi: 10.1016/j.socscimed.2016.02.021

32. Yu X, Shangguan Y W. Liu H. New rural social endowment insurance, intergenerational care and children's health chinese. *Rural Eco.* (2019) 7:125–44. Available online at: http://zgncjj.crecrs.org/Magazine/Show/69545

33. Singh A, Vellakkal S. Impact of public health programs on maternal and child health services and health outcomes in India: a systematic review. *Soc Sci Med.* (2021) 274:113795. doi: 10.1016/j.socscimed.2021.113795

34. Paul S, Paul S, Gupta AK, James KS. Maternal education, health care system and child health: evidence from India. *Soc Sci Med.* (2022) 296:114740. doi: 10.1016/j.socscimed.2022.114740

35. Townsend N, Scriven A. The health consequences of obesity: public health mini-guides. *Obesity.* (2014) 9:48–66. doi: 10.1016/B978-0-7020-4634-6.00003-0

36. Song PH, Xu WY, Chisolm DJ, Alexy ER, Ferrari RM, Hilligoss B, et al. How does being part of a pediatric accountable care organization impact health service use for children with disabilities? *Health Serv Res.* (2019) 5:1007–15. doi: 10.1111/1475-6773.13199

37. Goodman E. The role of socioeconomic status gradients in explaining differences in US adolescents' health. *Am J Public Health.* (1999) 10:1522–8. doi: 10.2105/AJPH.89.10.1522

38. Wang Y, Zhang Q. Are American children and adolescents of low socioeconomic status at increased risk of obesity? Changes in the association between overweight and family income between 1971 and (2001). *Am J Clini Nutr.* (2006) 4:707–16. doi: 10.1093/ajcn/84.4.707

39. Wang X, Liu Y, Wen D. Childhood obesity epidemic characteristics and its influencing factors. *Int J Pediatr.* (2016) 3:197–201.

40. Buoncristiano M, Williams J, Simmonds P, Nurk E, Ahrens W, Nardone P, et al. Socioeconomic inequalities in overweight and obesity among 6- to 9-year-old children in 24 countries from the World Health Organization European region. *Obesity Rev.* (2021) 22:e13213–e13213. doi: 10.1111/obr.13213

41. Yusuf ZI, Dongarwar D, Yusuf RA, Bell M, Harris T, Salihu H M. Social determinants of overweight and obesity among children in the United States. *Matern. Child Health J.* (2020) 9:22–33. doi: 10.21106/ijma.337

42. Gopalan M, Lombardi C, Bullinger LR. Effects of parental public health insurance eligibility on parent and child health outcomes. *Econ Hum Biol.* (2022) 44. doi: 10.1016/j.ehb.2021.101098

43. Zhang C, Cui L. Influencing factors of childhood obesity. *Int J Pediatr.* (2019) 2:113–5.

44. Xu H, Sun J, Ma G. Promoting childhood obesity prevention and control through social environment optimization. *Chin J Sch Health.* (2021) 11:1601–4,

45. Rong F, Jun-Qing W, Yu-Yan L. Correlations between relevant indexes of chronic diseases and overweight and obesity in childhood. *Chin J Public Health.* (2015) 4:506–9.

46. Man X, Wang X, Meng F. Influence of grandparenting on early childhood health. *Chin J Public Health.* (2019) 12:1671–4.

47. Liu B, Ping Q, Xiao S, Liao F. The influence of grandparents' indulgence on the health status of the Left-behind children in rural areas from the perspective of food consumption: a case study from Hubei province. *Chinese Rural Econ.* (2019) 1:32-46.

48. Heijden L, Feskens E, Raat H, Janse A. Quality of life of children and adolescents with clinical obesity, perspectives of children and parents. *Obes Res Clin Pract.* (2021) 10:466–72. doi: 10.1016/j.orcp.2021.07.001

49. Ju S, Iwinski S, Fiese BH, McBride BA, Bost KK. Influences of child temperament and household chaos on preschoolers' emotional eating. *Childhood Obes.* (2022) 1–10. doi: 10.1089/chi.2021.0237

50. Deng Y, Zhi R, Wang J. The effect of intergenerational raising on labor wages: an empirical evidence based on the data of CEES. *J Beijing Normal University (Social Sciences).* (2021) 2:144–58. Available online at: http://wkxb.bnu.edu.cn/CN/Y2021/V0/I2/144

51. Costa-Font J, Gil J. Intergenerational and socioeconomic gradients of child obesity. *Social Sci Med.* (2013) 93:29–37. doi: 10.1016/j.socscimed.2013.05.035

52. Wang Y, Zhao L, Gao L, Pan A, Xue H. Health policy and public health implications of obesity in China. *Lancet Diabetes Endocrinol.* (2021) 7:446–61. doi: 10.1016/S2213-8587(21)00118-2

53. Hu H, Gao J, Jiang H. Xing, P. Injuries among schooling left-behind, migrant and residential children in China. *Int J Equity Health.* (2018) 17:47. doi: 10.1186/s12939-018-0767-3

54. Moreno L A, Bel-Serrat S, Santaliestra-Pasías A M, Rodríguez G. Obesity prevention in children. *World Rev Nutr Dietetics.* (2013) 3:119–26. doi: 10.1159/000342560

55. Schur EA, Melhorn SJ, Scholz K, DeLeon MRB, Elfers C T, Rowland M G, et al. Child neurobiology impacts success in family-based behavioral treatment for children with obesity. *Int J Obes.* (2020) 44:2011–22. doi: 10.1038/s41366-020-0644-1

56. Powers DA, Yoshioka H, Yun M. Mvdcmp: multivariate decomposition for nonlinear response models. *Stata J.* (2011) 4:556–76. doi: 10.1177/1536867X1101100404

57. Yun M. Decomposing differences in the first moment. *Econ Lett.* (2004) 82:275–80. doi: 10.1016/j.econlet.2003.09.008

58. Zhang YF, Wang W, Zhu YN, Yang LF, Zhang H. Effects of grandparenting on infants' physical and psychological development. *Chin J Child Heal Care.* (2015) 10:1044–6.

59. Song Y, Xi B, Ma l, Luo DM. Annual report on Chinese children's development (2020) : The trend of overweight, obesity and abdominal obesity rate in Chinese children. *Social Sciences Academic Press (China).* (2020) 11:1–22.

60. Chen Z. The health status of the left-behind children in rural China. *Chin Populat Sci.* (2009) 5:95-112.

61. Zheng D, Gong J, Zhang C. Efficiency of medical service systems in the rural areas of Mainland China: a comparative study from 2013 to (2017). *Public Health.* (2019) 171:139–47. doi: 10.1016/j.puhe.2019.04.003

62. Bai C, Wu B. Health insurance and consumption: evidence from China's new cooperative medical scheme. *J Comp Econ.* (2014) 2:450–69. doi: 10.1016/j.jce.2013.07.005

63. Peng X B, Conley D. The implication of health insurance for child development and maternal nutrition: evidence from China. *Eur J Health Econ.* (2016) 5:521–34. doi: 10.1007/s10198-015-0696-7

64. Samiya F. A socio-economic study on the determinants and status of child malnutrition in rural areas of Bangladesh. *China Agricultural college.* (2014). Available online at: https://kns.cnki.net/kcms/detail/detail.aspx?dbName=CDFD2014&filename=1014221271.nh

65. Yasuo M. Maria S. Examining individual and school characteristics associated with child obesity using a multilevel growth model. *Social Sci Med.* (2015) 128:57–66. doi: 10.1016/j.socscimed.2014.12.032

66. Arendt JN, Christensen ML, Hjorth-Trolle A. Maternal education and child health: causal evidence from Denmark. *J Health Econ.* (2021) 80:102552. doi: 10.1016/j.jhealeco.2021.102552

67. Brendan W, John C. Decomposing socioeconomic inequalities in childhood obesity: Evidence from Ireland. *Econ Hum Biol.* (2015) 16:60–72. doi: 10.1016/j.ehb.2014.01.003

68. Kelishadi R, Qorbani M, Heshmat R, Djalalinia S, Sheidaei A, Safiri S, et al. Socioeconomic inequality in childhood obesity and its determinants: a Blinder-Oaxaca decomposition. *J Res Health Sci.* (2017) 3:e00391. Available online at: http://jrhs.umsha.ac.ir/index.php/JRHS/article/view/3309

69. Carlota Q, Joana O. Socioeconomic inequalities in child obesity and overweight in Portugal. *Int J Soc Econ.* (2017) 10:1377–89. doi: 10.1108/IJSE-11-2015-0291

70. Zhao Q, Yu X, Wang X, Thomas G. The impact of parental migration on children's school performance in rural China. *China Economic Rev.* (2014) 31:43–54. doi: 10.1016/j.chieco.2014.07.013

71. Kristin T. Cumulative adverse childhood experiences and children's health. *Children and Youth Services Rev.* (2020) 119. doi: 10.1016/j.childyouth.2020.105538

72. Bettenhausen JL, Courtney DO, Jeffrey JD. Health and poverty of rural children: an under-researched and under-resourced vulnerable population. *Acad Pediatr.* (2021) 21:S126–33. doi: 10.1016/j.acap.2021.08.001

73. Halfon N, Russ A S, Kahn S R. Inequality and child health: dynamic population health interventions. *Curr Opin Pediatr.* (2021) 1:33–8. doi: 10.1097/MOP.0000000000001087

74. Mirae JF, Timothy R, Anna M E, Christine N M. Weight status, medication use, and recreational activities of treatment-Nai ve transgender Youth. *Childhood Obes.* (2022) 18. doi: 10.1089/chi.2021.0155

frontiers | Frontiers in Pediatrics

TYPE Original Research
PUBLISHED 06 September 2022
DOI 10.3389/fped.2022.966901

OPEN ACCESS

EDITED BY
Tim S. Nawrot,
University of Hasselt, Belgium

REVIEWED BY
Desiree Caselli,
Azienda Ospedaliero Universitaria Consorziale Policlinico di Bari, Italy
Davide Ferorelli,
University of Bari Medical School, Italy

*CORRESPONDENCE
Simone Grassi
simone.grassi@unifi.it

†These authors have contributed equally to this work and share first authorship
‡These authors share senior authorship

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

RECEIVED 11 June 2022
ACCEPTED 12 August 2022
PUBLISHED 06 September 2022

CITATION
Vetrugno G, Grassi S, Clemente F, Cazzato F, Rossi V, Grassi VM, Buonsenso D, Filograna L, Sanguinetti M, Focardi M, Valentini P, Ozonoff A, Pinchi V and Oliva A (2022) Microbiological screening tests for SARS-CoV-2 in the first hour since the hospital admission: A reliable tool for enhancing the safety of pediatric care. *Front. Pediatr.* 10:966901. doi: 10.3389/fped.2022.966901

Microbiological screening tests for SARS-CoV-2 in the first hour since the hospital admission: A reliable tool for enhancing the safety of pediatric care

Giuseppe Vetrugno[1†], Simone Grassi[2*†], Francesco Clemente[1,3], Francesca Cazzato[1], Vittoria Rossi[1], Vincenzo M. Grassi[1], Danilo Buonsenso[4], Laura Filograna[5], Maurizio Sanguinetti[6], Martina Focardi[2], Piero Valentini[4], Al Ozonoff[7,8], Vilma Pinchi[2‡] and Antonio Oliva[1‡]

[1]Section of Legal Medicine, Department of Health Surveillance and Bioethics, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica Del Sacro Cuore, Rome, Italy, [2]Section of Forensic Medical Sciences, Department of Health Sciences, University of Florence, Florence, Italy, [3]Section of Legal Medicine, Department of Interdisciplinary Medicine, Bari Policlinico Hospital, University of Bari, Bari, Italy, [4]Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [5]Department of Diagnostic and Interventional Radiology, Molecular Imaging and Radiotherapy, PTV Foundation, "Tor Vergata" University of Rome, Rome, Italy, [6]Laboratory of Microbiology, "A. Gemelli" Hospital, Catholic University of the Sacred Heart, Rome, Italy, [7]Precision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital, Boston, MA, United States, [8]Department of Pediatrics, Harvard Medical School, Boston, MA, United States

Introduction/purpose: Since a significant proportion of SARS-CoV-2 infections occur within healthcare facilities, a multidisciplinary approach is required for careful and timely assessment of the risk of infection in asymptomatic patients or those whose COVID-19 diagnosis has not yet been made. The aim of this study was to investigate whether an adaptative model based on microbiological testing can represent a valid risk management strategy.

Material and methods: We collected data from the risk management unit database of a 1,550-bed tertiary hospital (Fondazione Policlinico Gemelli IRCCS, Rome, Italy) concerning pediatric admissions to the Emergency Department (ED) from 1 March 2020 to 31 December 2021. The study period was subdivided in period A and period B according to the technique used for the microbiological screening, respectively reverse-transcription polymerase chain reaction (RT-PCR) and antigen-detection test.

Results: In Period A, 426 children (mean age: 6 years) underwent microbiological screening at the ED. The total number of molecular tests performed was 463. 459/463 tested negative at the molecular test. In Period B, 887 children (mean age: 6 years) underwent microbiological screening in the ED. The total number of molecular tests performed was 1,154. 1,117/1,154 tested negative at the molecular test. Neither in Period A nor in Period B hospital-acquired SARS-CoV-2 infections were reported.

10.3389/fped.2022.966901

Discussion and conclusion: Despite high volumes, no cases of hospital-acquired SARS-CoV-2 infection have been reported. SARS-CoV-2 antigen-based tests can be used as a first-line option as they provide rapid results compared to RT-PCR, reducing the risk of infection in ED waiting rooms.

KEYWORDS

risk management, SARS-CoV-2, COVID-19, hospital-acquired infection, RT-PCR

Introduction

A significant share of SARS-CoV-2 infections are known to occur within healthcare facilities, thus representing simultaneous public health and medico-legal challenges (1–4). Indeed, enhancing safety policies during the pandemic can allow for regular delivery of healthcare services and protect particularly vulnerable populations like immunocompromised and oncological patients (2, 3). In order to avoid nosocomial infections, it is needed a careful and timely assessment of the risk of having been infected in the asymptomatic patients or in those whose COVID-19 diagnosis has not been already made (5–7). This demands a multidisciplinary approach using a combination of anamnestic, clinical, microbiologic, and radiologic data to establish the earliest possible diagnosis (8–11).

In this paper, we describe and evaluate the experience of a 1,550-bed tertiary hospital in Italy, where two different risk assessment policies were adopted during the pandemic. Our aim is to investigate and discuss whether an adaptive model chiefly based on microbiological testing can represent a valid risk management strategy from both a public health and medico-legal perspective.

Materials and methods

We collected data from the Risk Management Unit of Fondazione Policlinico Gemelli IRCCS, Rome, Italy. This is one of the two central hubs in Rome for pediatric COVID-19 cases since the beginning of the pandemic. Data of interest included: number of children admitted at the Emergency Department (ED) from 1 March 2020 to 31 December 2021; age at admission; results of the molecular test; number of hospital-acquired SARS-CoV-2 infections reported.

The definition of "hospital-acquired SARS-CoV-2 infection" is based on the positive result of the molecular test in patients hospitalized for at least 10 days in the ward, who had previously tested negative on the molecular admission test in ED (12–16).

The study period was subdivided in two sub-periods on the basis of what technique was used for microbiological screening: period A (1 March 2020 – 31 October 2020) and period B (1 November 2020 – 31 December 2021). In period A, amplification of SARS-CoV-2 RNA using reverse-transcription polymerase chain reaction (RT-PCR) was used, while in period B antigen-detection test – SD Biosensor antigen-detection test (South Korea), namely the STANDARD F COVID-19 Ag fluorescent immunoassay (FIA) – was adopted (the results of antigen-tests – positive or negative – were then confirmed through RT-PCR).

In both periods, the PCR test administered to the patients upon admission to the emergency room provided a result within 5 h.

During Period B, antigen testing was performed within the first hour after Emergency Department admission, with a corresponding hospital management of pediatric population flow to limit intra-hospital contagion from the Emergency Department (ED) to pediatric ward. The decision algorithms adopted in Period A and Period B are reported, respectively in Figures 1, 2.

Elective hospitalizations were allowed in no-COVID pediatric wards following a mandatory negative result of the PCR test performed in the previous 48 h. Since 7 July 2021, the risk management procedure requires hospitalized patients to repeat the PCR test every 5 days until discharge. This protocol is also the same for the parents of children admitted to the ward.

Hospitalized patients who tested positive were placed in specific respiratory isolation wards at negative pressure, separated from the remaining hospitalization areas for non-COVID children. Furthermore, the medical and nursing teams were also separated, with a staff dedicated exclusively to confirmed positive COVID-cases. The First Aid team integrated the staff of the pediatric COVID-wards.

In period A, waiting for the results of the molecular swab, the patients' assignment of risk class was also supported by clinical and epidemiological characteristics. Indeed, patients were dislocated in areas/paths specific for the risk class depending on the positive response of specific parameters including: presence in the last 14 days of symptoms compatible with SARS-CoV-2 infection: fever, cough, sore throat, conjunctivitis, loss of smell, taste, diarrhea, etc.; family members with coronavirus positive swab; area of residence in quarantine; prolonged contact (>20 min) with a probable or confirmed case of COVID 19 infection in the past 21 days.

In period B, patients with symptoms suggestive of SARS-CoV-2 infection (fever or chills, cough, congestion or runny nose, loss of taste or smell, shortness of breath or difficulty

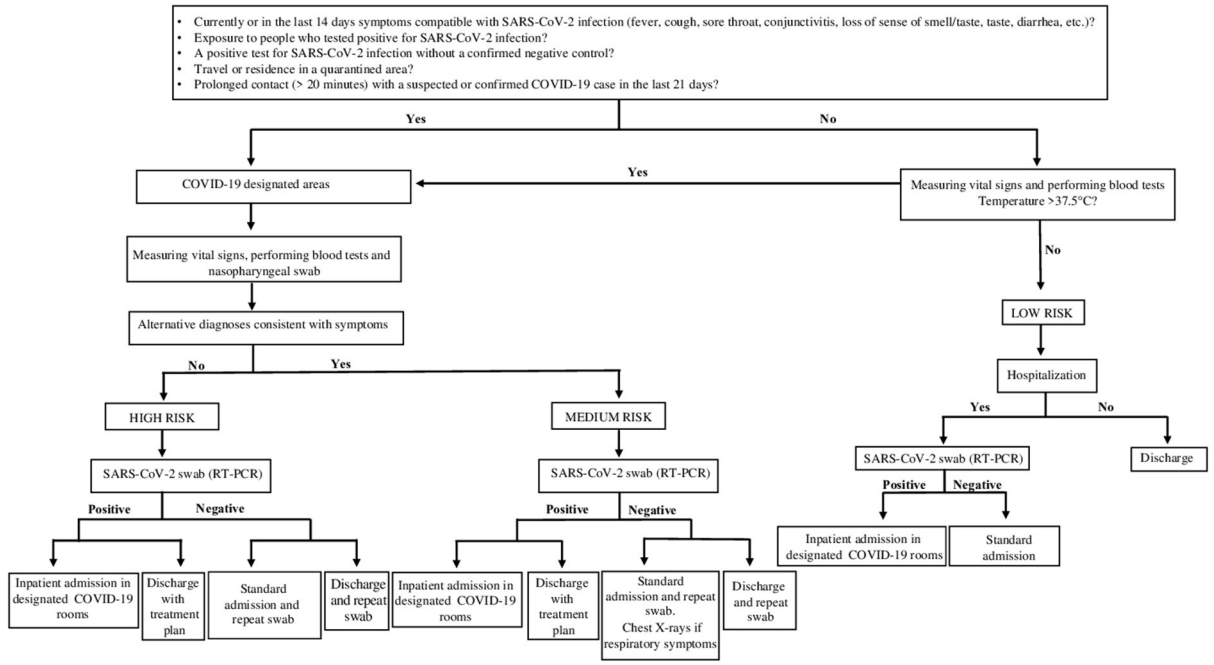


FIGURE 1
Testing algorithm for diagnosis SARS-CoV-2 infection in patients who presented to the ED from 1 March 2020 – 31 October 2020 (Period A). The standardized screening strategy was molecular swab only (RT-PCR). Waiting for the results of the molecular swab (RT-PCR), patients according to their clinical and epidemiological characteristics were divided into corresponding risk classes (High Risk; Medium Risk; Low Risk).

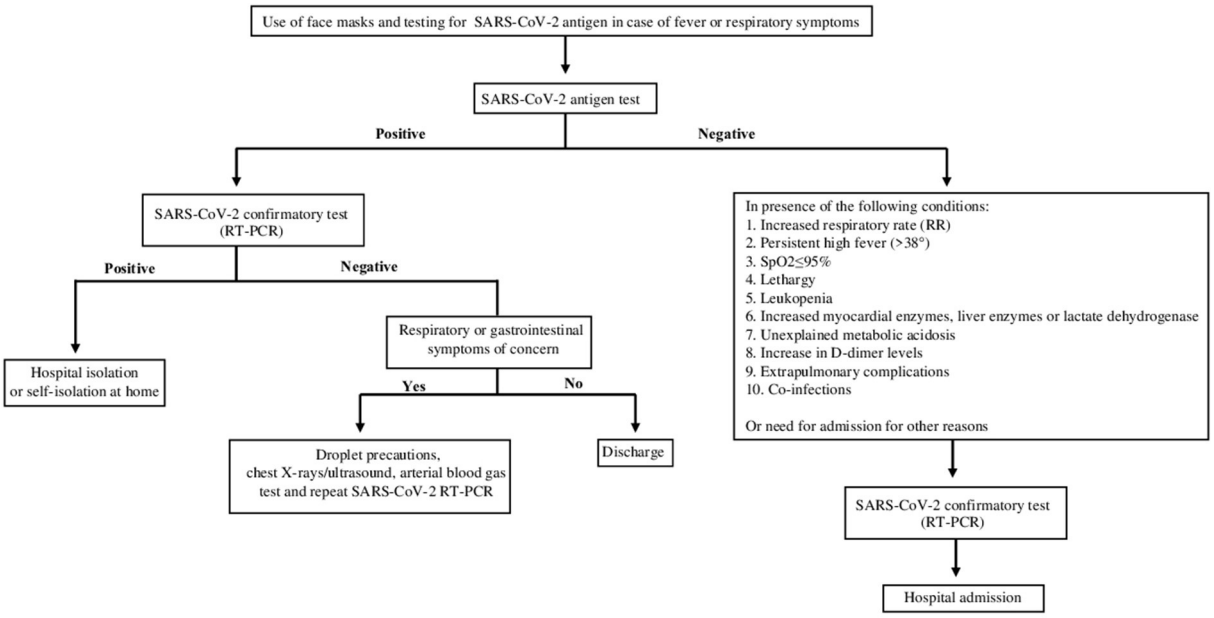


FIGURE 2
Algorithm for diagnosis SARS-CoV-2 infection in patients who presented to the ED from 1 November 2020 – 31 December 2021 (Period B). The patients with symptoms suggestive of SARS-CoV-2 infection were tested initially by antigenic-test with the SD Biosensor STANDARD F COVID-19 Ag. Then, patients with a positive antigen result and those with a negative antigen result but with one of the following clinical or laboratory criteria shown in the figure were subsequently evaluated by molecular swab (RT-PCR).

in breathing, body aches, tiredness or headache, sore throat, nausea, vomiting or diarrhea) were analyzed with antigen-test. Then, patients with a positive antigen result and those with a negative antigen result but with one of the following clinical or laboratory criteria (increased respiratory rate (RR):> 50 (2–12 months),> 40 (1–5 years),> 30 (> 5 years); persistent high fever (> 38 °) for 3–5 days or more than 1 week of illness with no improvement in symptoms; $SpO_2 \leq 95\%$ at rest; hyporeactivity, lethargy; leukopenia; myocardial enzymes, liver enzymes, lactate dehydrogenase progressively increased; unexplained metabolic acidosis; a significant increase in D-dimer levels; extra-pulmonary complications; co-infection with other viruses and/or bacteria) were subsequently evaluated by molecular swab.

In either case, a pediatric patient was admitted to a non-COVID ward in the absence of a negative response to the molecular test.

Results

In Period A, 426 children (mean age: 6 years) underwent microbiological screening at the ED. There were 463 molecular tests performed (according to the risk management protocol for which some patients underwent multiple molecular swabs based on the number of days in hospital). 459/463 molecular tests (99.1%) were negative. In Period B, 887 children (mean age: 6 years) underwent microbiological screening in the ED. These patients received a total of 1,154 molecular tests according to the same risk management protocol, and 1,117/1,154 (96.8%) tested negative at the molecular test. Neither in Period A nor in Period B hospital acquired SARS-CoV-2 infections were reported among the tested children. The cumulative trend of all molecular swabs and the positivity rate are shown respectively in Figures 3, 4.

Discussion

The aim of this study was to describe and discuss the decisional algorithms used for early identification of SARS-CoV-2-infected children who arrived at our ED.

Despite the high volumes, no cases of pediatric hospital-acquired SARS-CoV-2 infection was reported during the study period. This outcome becomes more important if we evaluate period B. Indeed, while in period A the Italian government imposed a national lockdown (starting 9 March 2020) (17) with a total closure of schools and universities (since 5 March 2020), during period B the second phase of national lockdown (from 2 November 2020 to 27 March 2021) did not require the closure of nursery schools and primary schools (up to 12 years) (18). Furthermore, vaccination prophylaxis, as an additional element of protection against restrictive lockdown measures, had not yet begun to protect both pediatric and adult patients.

In our opinion, the two most important criteria to be used to evaluate risk assessment algorithms are accuracy/reliability and the time required for test results.

From a methodological point of view, RT-PCR is very accurate (Allplex TM SARS-CoV-2 Assay Seegene: Sensitivity 95.2%–Specificity 98.9%) (19) but the results are not available for several hours with the consequent risk of increased transmission (20–22). As an alternative screening method, SARS-CoV-2 antigen-based tests can significantly reduce this time, especially in crowded settings such as a full emergency room where SARS-CoV-2 infection must be confirmed as soon as possible (23–25). Although the antigen test is less sensitive than RT-PCR, it is highly specific and, more importantly, can return a result within 15–30 min (25–27). This is possible thanks to lateral flow technology, which allows identification and visualization of the SARS-CoV-2 antigen as a reactive band for immunoassay on a compact handheld device (19, 28). However, negative results from this method due to

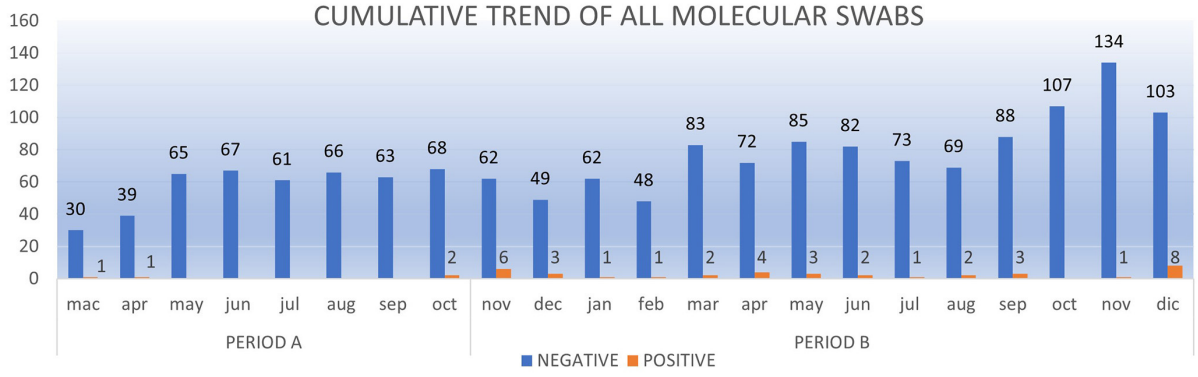


FIGURE 3
The cumulative trend of all molecular swabs (RT-PCR) from Mach 1, 2020 to December 31, 2020.

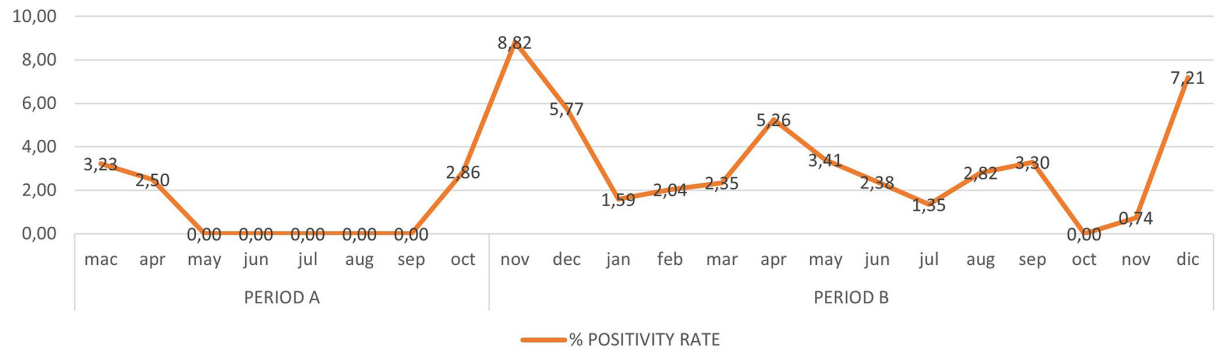


FIGURE 4
The positivity rate of all molecular swabs (RT-PCR) from Mach 1, 2020 to December 31, 2021.

the low sensitivity cannot confidently exclude SARS-CoV-2 virus infection and thus results must be verified by further RT-PCR test (29–34). As reported by Menchinelli et al. (35) in an ED, antigen-positive or antigen-negative results must be confirmed subsequently by RT-PCR testing both in patients with a low (< 10%; including patients asymptomatic or symptomatic for more than 7 days after symptom onset) and in patients with a high (> 10%; including symptomatic patients within 7 days of symptom onset) probability of testing positive.

Hence, from a public health perspective, the best option is that introduced during Period B: using the antigen test as an initial screen in order to obtain the results within an hour and, in case of a positive result, isolate the patient while waiting for result of a confirmatory RT-PCR. Indeed as noted above, another determinant of the quality of a safety protocol in this context is timeliness, since the early isolation of at-risk patients can avoid a significant spread of the infection within hospital departments. Moreover, the fact that antigen test is associated with lower sensitivity than RT-PCR is only a relative limitation, since in a pandemic context the prevalence of the infection is relatively high and thus the positive predictive value of the microbiological testing is increased.

As reported by Mönckel et al. (36) antigenic test (AGTEST) among symptomatic patients in the ED is useful for early identification of COVID-19, but for patients with negative antigen test this result must be confirmed by molecular test (RT-PCR). However, it was observed that when the prevalence of SARS-CoV-2 infection rises, the positive predictive value increases too.

Conclusion

In conclusion, our experience shows the effectiveness of a screening strategy based on rapid antigen testing in children initially assessed in the pediatric ED in order to optimize patient flow from the ED to the optimal inpatient wards. The strategy was both timely and safe, since no cases of pediatric hospital acquired SARS-CoV-2 infections were reported. Further studies will be needed to understand how this procedure can be applied with future variants of concerns and a higher vaccination coverage in children.

Limitations

Our study has some limitations to acknowledge. First, it is a retrospective study. Secondly, we could not determine the number of possible infections acquired in children while attending the pediatric ED and then discharged at home, since no follow-up data were collected for this group of children. Another relevant aspect is the increased cost of testing caused by the introduction of antigen-test screening. During our study period, the economic cost was a variable of relatively minor relevance because in that phase of the pandemic the regional health system covered all the costs for microbiological testing, thus this protocol had no direct costs for the hospital. However, if economic aspects must be considered, a modification to the protocol which might minimize cost is to conduct PCR test only on those antigen-negative patients that are at risk for other (clinical, epidemiological) reasons. This would maximize cost-benefit and reduce the overall number of tests required.

Data availability statement

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

Author contributions

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

Funding

This paper was supported by Università Cattolica del Sacro Cuore, Linea D.3.1 n. R4124501052 (Recipient: AO).

Acknowledgments

We would like to thank our colleagues Antonio Marchetti, Fondazione Policlinico Universitario A. Gemelli IRCCS, for his support in data extraction and Davide Cammarata, Fondazione Policlinico Universitario A. Gemelli, for his support in data extraction and elaboration.

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. Barranco R, Rocca G, Molinelli A, Ventura F. Controversies and challenges of mass vaccination against SARS-CoV-2 in Italy: medico-legal perspectives and considerations. *Healthcare.* (2021) 9:1163. doi: 10.3390/healthcare9091163

2. Oliva A, Caputo M, Grassi S, Vetrugno G, Marazza M, Ponzanelli G, et al. Liability of health care professionals and institutions during COVID-19 pandemic in Italy: symposium proceedings and position statement. *J Patient Saf.* (2020) 16:e299–302. doi: 10.1097/PTS.0000000000000793

3. Filograna L, Manenti G, Arena V. Dell'Aquila M, Pascali VL, Natale L, et al. Claimed medical malpractice in fatal SARS-CoV-2 infections: the importance of combining ante- and post-mortem radiological data and autopsy findings for correct forensic analysis. *Forensic Imaging.* (2021) 25:200454. doi: 10.1016/j.fri.2021.200454

4. Read JM, Green CA, Harrison EM, Docherty AB, Funk S, Harrison J, et al. Hospital-acquired SARS-CoV-2 infection in the Uk's First COVID-19 pandemic wave. *Lancet.* (2021) 398:1037–8. doi: 10.1016/S0140-6736(21)01786-4

5. Grassi S, Arena V, Cattani P. Dell'Aquila M, Liotti FM, Sanguinetti M, et al. SARS-CoV-2 viral load and replication in postmortem examinations. *Int J Legal Med.* (2022) 136:935–9. doi: 10.1007/s00414-021-02753-2

6. Li X, Xu W, Dozier M, He Y, Kirolos A, Lang Z, et al. The role of children in the transmission of Sars-Cov2: updated rapid review. *J Glob Health.* (2020) 10:021101. doi: 10.7189/jogh.10.0201101

7. Vierucci F, Bacci C, Mucaria C, Dini F, Federico G, Maielli M, et al. How COVID-19 pandemic changed children and adolescents use of the emergency department: the experience of a secondary care pediatric unit in central Italy. *SN Compr Clin Med.* (2020) 2:1959–69. doi: 10.1007/s42399-020-00532-5

8. Aquila I, Sacco MA, Abenavoli L, Malara N, Arena V, Grassi S, et al. Severe acute respiratory syndrome coronavirus 2 pandemic. *Arch Pathol Lab Med.* (2020) 144:1048–56. doi: 10.5858/arpa.2020-0165-SA

9. Chams N, Chams S, Badran R, Shams A, Araji A, Raad M, et al. Covid-19: a multidisciplinary review. *Front Public Health.* (2020) 8:383. doi: 10.3389/fpubh.2020.00383

10. O'Brien H, Tracey MJ, Ottewill C, O'Brien ME, Morgan RK, Costello RW, et al. An integrated multidisciplinary model of COVID-19 recovery care. *Irish J Med Sci.* (2021) 190:461–8. doi: 10.1007/s11845-020-02354-9

11. Gediz Erturk A, Sahin A, Bati Ay E, Pelit E, Bagdatli E, Kulu I, et al. A Multidisciplinary approach to coronavirus disease (COVID-19). *Molecules.* (2021) 26:3526. doi: 10.3390/molecules26123526

12. Lauer SA, Grantz KH Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med.* (2020) 172:577–82. doi: 10.7326/M20-0504

13. Mo Y, Eyre DW, Lumley SF, Walker TM, Shaw RH, O'Donnell D, et al. Transmission of community- and hospital-acquired SARS-CoV-2 in hospital settings in the Uk: a cohort study. *PLoS Med.* (2021) 18:e1003816. doi: 10.1371/journal.pmed.1003816

14. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Ann Intern Med.* (2020) 173:262–7. doi: 10.7326/M20-1495

15. Brandal LT, MacDonald E, Veneti L, Ravlo T, Lange H, Naseer U, et al. Outbreak caused by the SARS-CoV-2 omicron variant in Norway, November to December 2021. *Euro Surveill.* (2021) 26:2101147. doi: 10.2807/1560-7917.ES.2021.26.50.2101147

16. Jansen L, Tegomoh B, Lange K, Showalter K, Figliomeni J, Abdalhamid B, et al. Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) variant cluster - Nebraska, November-December 2021. *Morb Mortal Wkly Rep.* (2021) 70:1782–4. doi: 10.15585/mmwr.mm705152e3

17. Gazzetta Ufficiale Della Repubblica Italiana (2020) *Decreto Legge 9 Marzo*. (2020). Available online at: https://www.gazzettaufficiale.it/eli/gu/2020/03/09/ 62/sg/pdf (accessed May 09, 2022).

18. Ministero Della Salute. *COVID-19*. Available online at: https://www.salute.gov.it/portale/nuovocoronavirus/archivioNotizieNuovoCoronavirus.jsp?lingua=english (accessed May 09, 2022).

19. Dinnes J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev.* (2021) 3:Cd013705. doi: 10.1002/14651858.CD013705

20. Arshadi M, Fardsanei F, Deihim B, Farshadzadeh Z, Nikkhahi F, Khalili F, et al. Diagnostic accuracy of rapid antigen tests for COVID-19 detection: a systematic review with meta-analysis. *Front Med.* (2022) 9:870738. doi: 10.3389/fmed.2022.870738

21. Falzone L, Gattuso G, Tsatsakis A, Spandidos DA, Libra M. Current and innovative methods for the diagnosis of COVID-19 infection (Review). *Int J Mol Med.* (2021) 47:100. doi: 10.3892/ijmm.2021.4933

22. Mahendiratta S, Batra G, Sarma P, Kumar H, Bansal S, Kumar S, et al. Molecular diagnosis of COVID-19 in different biologic matrix, their diagnostic validity and clinical relevance: a systematic review. *Life Sci.* (2020) 258:118207. doi: 10.1016/j.lfs.2020.118207

23. González-Donapetry P, García-Clemente P, Bloise I, García-Sánchez C, Sánchez Castellano M, Romero MP, et al. Think of the children: evaluation of SARS-CoV-2 rapid antigen test in pediatric population. *Pediatr Infect Dis J.* (2021) 40:385–8. doi: 10.1097/INF.0000000000003101

24. Peeling RW, Olliaro P. Rolling out COVID-19 antigen rapid diagnostic tests: the time is now. *Lancet Infect Dis.* (2021) 21:1052–3. doi: 10.1016/S1473-3099(21)00152-3

25. Chaimayo C, Kaewnaphan B, Tanlieng N, Athipanyasilp N, Sirijatuphat R, Chayakulkeeree M, et al. Rapid SARS-CoV-2 antigen detection assay in comparison with real-time Rt-Pcr assay for laboratory diagnosis of COVID-19 in Thailand. *Virol J.* (2020) 17:177. doi: 10.1186/s12985-020-01452-5

26. Krüttgen A, Cornelissen CG, Dreher M, Hornef MW, Imöhl M, Kleines M. Comparison of the SARS-CoV-2 rapid antigen test to the real star SARS-CoV-2 Rt Pcr Kit. *J Virol Methods.* (2021) 288:114024. doi: 10.1016/j.jviromet.2020.114024

27. Orsi A, Pennati BM, Bruzzone B, Ricucci V, Ferone D, Barbera P, et al. On-field evaluation of a ultra-rapid fluorescence immunoassay as a frontline test for SARS-CoV-2 Diagnostic. *J Virol Methods.* (2021) 295:114201. doi: 10.1016/j.jviromet.2021.114201

28. World Health Organization. *Antigen-Detection in the Diagnosis of SARS-CoV-2 Infection Using Rapid Immunoassays.* Available online at: https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-SARS-CoV-2infection-using-rapid- immunoassays (accessed May 09, 2022).

29. Yüce M, Filiztekin E, Özkaya KG. COVID-19 diagnosis -a review of current methods. *Biosens Bioelectron.* (2021) 172:112752. doi: 10.1016/j.bios.2020.112752

30. Manzulli V, Scioscia G, Giganti G, Capobianchi MR, Lacedonia D, Pace L, et al. Real time Pcr and culture-based virus isolation test in clinically recovered patients: is the subject still infectious for Sars-Cov2? *J Clinl Med.* (2021) 10:309. doi: 10.3390/jcm10020309

31. Rahbari R, Moradi N, Abdi M. Rrt-Pcr for SARS-CoV-2: analytical considerations. *Clin Chim Acta.* (2021) 516:1–7. doi: 10.1016/j.cca.2021.01.011

32. Mak GC, Cheng PK, Lau SS, Wong KK, Lau CS, Lam ET, et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. *J Clin Virol.* (2020) 129:104500. doi: 10.1016/j.jcv.2020.104500

33. Gupta N, Augustine S, Narayan T, O'Riordan A, Das A, Kumar D, et al. Point-of-care pcr assays for COVID-19 detection. *Biosensors.* (2021) 11:141. doi: 10.3390/bios11050141

34. Sidiq Z, Hanif M, Dwivedi KK, Chopra KK. Benefits and limitations of serological assays in COVID-19 infection. *Indian J Tuberc.* (2020) 67:S163–6. doi: 10.1016/j.ijtb.2020.07.034

35. Menchinelli G, De Angelis G, Cacaci M, Liotti FM, Candelli M, Palucci I, et al. SARS-CoV-2 antigen detection to expand testing capacity for COVID-19: results from a hospital emergency department testing site. *Diagnostics.* (2021) 11:1211. doi: 10.3390/diagnostics11071211

36. Möckel M, Corman VM, Stegemann MS, Hofmann J, Stein A, Jones TC, et al. SARS-CoV-2 antigen rapid immunoassay for diagnosis of COVID-19 in the emergency department. *Biomarkers.* (2021) 26:213–20. doi: 10.1080/1354750X.2021.1876769

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 06 September 2022
DOI 10.3389/fpubh.2022.904985

OPEN ACCESS

EDITED BY
Biagio Solarino,
University of Bari Aldo Moro, Italy

REVIEWED BY
Preeti Manmohan Galagali,
Bengaluru Adolescent Care and Counseling Center, India
Arnhild Ramberg Myhr,
SINTEF Digital, Norway

*CORRESPONDENCE
Tae Hyun Kim
thkim@yuhs.ac

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

RECEIVED 26 March 2022
ACCEPTED 05 August 2022
PUBLISHED 06 September 2022

CITATION
Kim B, Kim DH, Jang S-Y, Shin J, Lee SG and Kim TH (2022) Family economic hardship and adolescent mental health during the COVID-19 pandemic.
Front. Public Health 10:904985.
doi: 10.3389/fpubh.2022.904985

Family economic hardship and adolescent mental health during the COVID-19 pandemic

Bomgyeol Kim[1], Do Hee Kim[1], Suk-Yong Jang[2], Jaeyong Shin[3], Sang Gyu Lee[3] and Tae Hyun Kim[2]*

[1]Department of Public Health, Graduate School, Yonsei University, Seoul, South Korea, [2]Department of Healthcare Management, Graduate School of Public Health, Yonsei University, Seoul, South Korea, [3]Department of Preventive Medicine, College of Medicine, Yonsei University, Seoul, South Korea

Objective: This study examined whether pandemic related family economic hardships influenced adolescents' mental health during the COVID-19 pandemic in Korea.

Methods: Data were collected from 54,948 adolescents who participated in the 2020 Korea Youth Risk Behavior Web-Based Survey. We performed a multiple logistic regression analysis to examine the association between family economic hardship and mental health (anxiety, depressive symptoms, and suicidal ideation).

Results: Among the adolescents, 39.7, 24.7, and 5.9% reported slight, moderate, and severe economic hardship, respectively. COVID-19 related family economic hardship was significantly associated with higher odds of adolescents reporting anxiety, depressive symptoms, and suicidal ideation. This association was stronger among adolescents with low to middle family economic status.

Conclusions: This study suggests that adolescents from more economically vulnerable families are likely to be at a higher risk for long-term mental health effects due to the financial consequences of the COVID-19 pandemic.

KEYWORDS

adolescent, anxiety, COVID-19, depression, economic hardship, suicidal ideation

Introduction

The COVID-19 (Coronavirus Disease 2019) pandemic has led to rapid, unprecedented changes in the lives of billions of adolescents (1). The first infection in Korea was detected on 20 January 2020, triggering a national response including school closures, home confinement, and social distancing rules (2, 3). Fluctuating school and family routines, isolation at home, stressed parents, and fear of the virus have impacted adolescents significantly. Indeed, increasing mental health problems in adolescents during the COVID-19 pandemic have been reported in Korea and other countries (4–7).

More importantly, adolescents' deteriorated mental health outcomes may reflect socioeconomic inequalities (specifically, the economic well-being of households) (8). During the prolonged COVID-19 lockdowns, many employed people faced heavily

reduced workloads, temporary work suspensions such as furloughs, and even job loss (9). Economic activities were at a standstill, which can pose enormous challenges for the mental health of affected workers and their families (10, 11). Particularly, for adolescents, COVID-19-related family economic hardship is an independent and uncontrollable life event (12). Adolescents and their parents have different perceptions of the financial situation of the family. Moreover, the perceptions of adolescents seem to have a stronger association with adolescent mental health than the perceptions of parents (12, 13).

Many families have been significantly impacted economically by COVID-19, but poor families have been affected the most (14). However, it has been reported that all groups of households, from the poorest to the richest, have experienced declines in their incomes at a similar rate (15). Economically stable middle-income households are also at risk of becoming low-income households (15). Based on the results of various studies, the key remaining question is whether there is a difference in the relationship between COVID-19-related economic hardship and mental health depending on the household income level among adolescents.

Numerous family socioeconomic hardships have been linked to placing adolescents at risk for suffering poor mental health outcomes. The existing evidence points to gender, school grade, residential area, subjective academic performance, smoking status, alcohol use, and socioeconomic status being associated with mental health (16–20). In addition, children's social, emotional, and cognitive development can be affected by experiences of instability at home and school, emotional and sexual trauma (19), and domestic and community violence (18). These negative events may permanently affect a child's mental health development if they are frequent and severe. Studies related to the post-COVID-19 mental health of adolescents have found that isolation from peers, uncertainty regarding short-term and long-term prospects, and continuous states of fear, including the fear of being infected, pose a risk for developing psychopathology (5, 21, 22).

As the COVID-19 pandemic lingers, understanding the negative impact of the economic consequences on adolescents' mental health is imperative. However, there is a lack of empirical evidence on COVID-19-related family economic hardship and its influence on mental health during the pandemic. Particularly, this issue has never been studied in Korea. Thus, the present study aimed to identify the association between COVID-19-related family economic hardship from the perspective of adolescents' mental health in Korea. We hypothesized that family economic hardship due to the pandemic is associated with mental health problems among adolescents (H1). Further, we hypothesized that the association between COVID-19-related family economic hardship and adolescents' mental health differs according to the current subjective family economic status (H2).

Abbreviations: CI, Confidence intervals; COVID-19, coronavirus disease 2019; KYRBS, Korea Youth Risk Behavior Web-Based Survey; aOR, adjusted Odds Ratios.

Methods

Data and population

For this cross-sectional study, we collected data from the 2020 Korea Youth Risk Behavior Web-based Survey (KYRBWS), a national survey on various health-related behaviors of Korean adolescents. The KYRBWS is an anonymous, internet-based, self-administered, structured questionnaire (23). To obtain a representative sample, the KYRBWS designed a complex sample technique that included multiple stages, such as stratification, clustering, and multi-step sampling (23). Additionally, the KYRBWS weighted the students who participated in the survey so that they represent Korean adolescents, thereby, estimating the level of adolescents' health behavior. A representative sample of students from the 7–12th grades, aged 13–18 years, was selected; the survey was developed for school-based samples according to city size, regional group, and school type among 16 major cities and provinces in Korea, and one sample class per grade level was randomly selected. Students were instructed to complete their questionnaire at their respective schools' computer labs during school hours, under the guidance of their teachers. Detailed information on the research design and methods of the KYRBWS is presented in a previous paper (23). From 2015, the ethics approval for the KYRBWS was waived by the Korea Centers for Disease Control and Prevention Institutional Review Board under the Bioethics & Safety Act and opened to the public for academic use.

The 2020 KYRBWS survey was conducted from 3 August 2020, to 13 November 2020. It was started about 6 months after the first confirmed COVID-19 case in Korea (20 January 2020) due to the impact of COVID-19, and the survey was conducted during the second COVID-19 wave (August to November 2020). The KYRBWS adheres to the Declaration of Helsinki and all participants provided informed consent (24). As the KYRBWS was conducted as an online survey, there were no non-response items in the original data; however, logical errors and outliers were treated as missing values. All surveyed 54,948 adolescent participants were included in the analysis without any missing values.

Measurements

Dependent variables

The main dependent variable of this study was mental health, which included anxiety, depressive symptoms, and suicidal ideation. We screened for anxiety using the seven-item

Generalized Anxiety Disorder scale (GAD-7), which is valid and reliable when applied to the general population (25, 26). The GAD-7 is rapidly becoming a gold-standard screening tool for general anxiety disorder measurements and has been shown to have acceptable specificity and sensitivity for detecting clinically significant anxiety in adolescents (27). The Cronbach's α for the GAD-7 was 0.90 in the current sample. Cronbach's alpha should be from 0.70 up to and including 0.90 to demonstrate adequate consistency in a scale (28). In this study, we used a GAD-7 cutoff score of ≥10, as this threshold provides a consistent reflection of anxiety levels (25). This study followed the questions and answers that were originally structured by the KYRBWS. We determined the presence of depressive symptoms using the question: "Have you felt sad or hopeless enough to stop your daily routine for 2 weeks in the past 12 months?" Participants responded to the question with either "yes" or "no." Suicidal ideation and suicide attempts were assessed using the following two questions from the KYRBWS: "Have you seriously considered suicide in the past 12 months?" and "Have you attempted suicide in the past 12 months? The participants responded to both the questions with either "yes" or "no."

Variable of interest

The variable of interest was COVID-19-related family economic hardship, which was assessed by the following question from the perspective of the children themselves: "Do you think the COVID-19 outbreak has caused your family economic status to be worsened?" The concept of COVID-19-related family economic hardship directly measured the nature and extent of deprivation that children were experiencing due to a lack of financial resources caused by COVID-19 and relative to their own needs (29). The variable of interest was categorized based on whether respondents answered these questions as "No," "Slight," "Moderate," or "Severe."

Control variables

The control variables used in this study were sex, school grade, residential area, co-residence with parents, subjective academic performance, subjective family economic status, subjective health status, smoking status, and alcohol use. Residential area was classified into "metropolitan," "urban," and "rural." Co-residence with parents was classified into "yes" or "no." Subjective academic performance and subjective family economic status were classified originally into: "high," "upper-middle," "middle," "lower-middle," and "low" and further classified into three categories in study, including: "high" (high and upper-middle), "middle," and "low" (lower-middle and low). Subjective health status was measured with the question: "How would you rate your health in general?" The response options were "very good," "good," "normal," "bad," and "very bad" and further classified into three categories, including: "good" (very good and good), "normal," and "bad" (bad and very bad). Smoking status and alcohol use were classified into "yes" and "no."

Statistical analysis

In this study, the statistical values were calculated using sample weights assigned to the participants. The KYRBWS constructed sample weights to represent the Korean adolescent population by accounting for the complex survey design and survey non-responses. We performed a Rao-Scott chi-square test to examine the bivariate associations between adolescents' mental health problems and selected covariates—the general characteristics of the study population. Further, we performed a multiple logistic regression analysis to analyze the association between COVID-19 related family economic hardship and mental health, after controlling for covariates. The results were reported using adjusted odds ratios (aORs) and confidence intervals (CIs). Model fitting was performed using the PROC SURVEYLOGISTIC procedure and application of cluster and strata. In addition, stratified analyses according to subjective family economic status were performed on the association between COVID-19-related family economic hardship and mental health using multiple logistic regression, adjusted by sex, grade, residential area, co-residence with parents, subjective academic performance, subjective health status, smoking status, and alcoholic drinking. All statistical analyses were performed using SAS v9.4 (SAS Institute Inc.; Cary, North Carolina). Statistical significance was set at $P < 0.05$.

Results

The participants included in the analysis comprised 54,948 adolescents. Among them, 16,268 (29.6%) experienced no economic hardship related to COVID-19, 21,841 (39.7%) experienced slight economic hardship, 13,583 (24.7%) experienced moderate economic hardship, and 3,256 (5.9%) experienced severe economic hardship. Refer to Table 1 for an in-depth overview of the participants' characteristics.

The greater the post-COVID-19 related family economic hardship reported by adolescents, the higher the mental health complaint scores. Anxiety was experienced by 1,419 (8.7%) adolescents who experienced no economic hardship, 2,206 (10.1%) who experienced slight economic hardship, 1,801 (13.3%) who experienced moderate economic hardship, and 673 (20.7%) who experienced severe economic hardship. Depressive symptoms were experienced by 3,435 (21.1%) adolescents who experienced no economic hardship, 5,175 (23.7%) who experienced a slight economic hardship, 3,992 (29.4%) who experienced moderate economic hardship, and 1,238 (38.0%) who experienced severe economic hardship. Suicidal ideation

TABLE 1 General characteristics of the Korean adolescents included in the analysis ($N = 54,948$).

Variables	Total		Anxiety				Depressive symptoms					Suicidal ideation				
			Yes		No		P*	Yes		No		P*	Yes		No		P*
	N (%)		N (%)		N (%)			N (%)		N (%)			N (%)		N (%)		
Total	54,948	(100.0)	6,099	(11.1)	48,849	(88.9)		13,840	(25.2)	41,108	(74.8)		5,979	(10.9)	48,969	(89.1)	
COVID-19-related family economic hardship							<0.0001					<0.0001					<0.0001
No	16,268	(29.6)	1,419	(8.7)	14,849	(91.3)		3,435	(21.1)	12,833	(78.9)		1,394	(8.6)	14,874	(91.4)	
Slight	21,841	(39.7)	2,206	(10.1)	19,635	(89.9)		5,175	(23.7)	16,666	(76.3)		2,200	(10.1)	19,641	(89.9)	
Moderate	13,583	(24.7)	1,801	(13.3)	11,782	(86.7)		3,992	(29.4)	9,591	(70.6)		1,766	(13.0)	11,817	(87.0)	
Severe	3,256	(5.9)	673	(20.7)	2,583	(79.3)		1,238	(38.0)	2,018	(62.0)		619	(19.0)	2,637	(81.0)	
Sex							<0.0001					<0.0001					<0.0001
Male	28,353	(51.6)	2,191	(7.7)	26,162	(92.3)		5,633	(19.9)	22,720	(80.1)		2,254	(7.9)	26,099	(92.1)	
Female	26,595	(48.4)	3,908	(14.7)	22,687	(85.3)		8,207	(30.9)	18,388	(69.1)		3,725	(14.0)	22,870	(86.0)	
School grade							<0.0001					<0.0001					<0.0001
7	10,005	(18.2)	880	(8.8)	9,125	(91.2)		2,030	(20.3)	7,975	(79.7)		897	(9.0)	9,108	(91.0)	
8	9,564	(17.4)	1,010	(10.6)	8,554	(89.4)		2,281	(23.8)	7,283	(76.2)		1,063	(11.1)	8,501	(88.9)	
9	9,392	(17.1)	1,055	(11.2)	8,337	(88.8)		2,429	(25.9)	6,963	(74.1)		1,053	(11.2)	8,339	(88.8)	
10	8,907	(16.2)	922	(10.4)	7,985	(89.7)		2,244	(25.2)	6,663	(74.8)		926	(10.4)	7,981	(89.6)	
11	8,907	(16.2)	1,101	(12.4)	7,806	(87.6)		2,476	(27.8)	6,431	(72.2)		1,085	(12.2)	7,822	(87.8)	
12	8,173	(14.9)	1,131	(13.8)	7,042	(86.2)		2,380	(29.1)	5,793	(70.9)		955	(11.7)	7,218	(88.3)	
Residential area							<0.0001					<0.0001					0.0008
Metropolitan	23,621	(43.0)	2,414	(10.2)	21,207	(89.8)		5,709	(24.2)	17,912	(75.8)		2,440	(10.3)	21,181	(89.7)	
Urban	26,981	(49.1)	3,175	(11.8)	23,806	(88.2)		7,026	(26.0)	19,955	(74.0)		3,069	(11.4)	23,912	(88.6)	
Rural	4,346	(7.9)	510	(11.7)	3,836	(88.3)		1,105	(25.4)	3,241	(74.6)		470	(10.8)	3,876	(89.2)	
Co-residence with parents							0.0011					<0.0001					<0.0001
Yes	52,332	(95.2)	342	(13.1)	2,274	(86.9)		13,068	(25.0)	39,264	(75.0)		5,594	(10.7)	46,738	(89.3)	
No	2,616	(4.8)	5,757	(11.0)	46,575	(89.0)		772	(29.5)	1,844	(70.5)		385	(14.7)	2,231	(85.3)	
Subjective academic performance							<0.0001					<0.0001					<0.0001
High	20,146	(36.7)	1,974	(9.8)	18,172	(90.2)		4,406	(21.9)	15,740	(78.1)		1,942	(9.6)	18,204	(90.4)	
Middle	16,585	(30.2)	1,585	(9.6)	15,000	(90.4)		3,890	(23.5)	12,695	(76.5)		1,551	(9.4)	15,034	(90.6)	
Low	18,217	(33.2)	2,540	(13.9)	15,677	(86.1)		5,544	(30.4)	12,673	(69.6)		2,486	(13.6)	15,731	(86.4)	
Subjective family economic status							<0.0001					<0.0001					<0.0001
High	21,339	(38.8)	2,024	(9.5)	19,315	(90.5)		4,926	(23.1)	16,413	(76.9)		2,008	(9.4)	19,331	(90.6)	
Middle	26,397	(48.0)	2,743	(10.4)	23,654	(89.6)		6,385	(24.2)	20,012	(75.8)		2,639	(10.0)	23,758	(90.0)	

(Continued)

10.3389/fpubh.2022.904985

10.3389/fpubh.2022.904985

TABLE 1 Continued

Variables	Total	Anxiety			Depressive symptoms			Suicidal ideation		
		Yes	No	*P**	Yes	No	*P**	Yes	No	*P**
	N (%)	*N* (%)	*N* (%)		*N* (%)	*N* (%)		*N* (%)	*N* (%)	
Low	7,212 (13.1)	1,332 (18.5)	5,880 (81.5)		2,529 (35.1)	4,683 (64.9)		1,332 (18.5)	5,880 (81.5)	
Subjective health status				<0.0001			<0.0001			
Good	38,444 (70.0)	2,842 (7.4)	35,602 (92.6)		8,065 (21.0)	30,379 (79.0)		3,049 (7.9)	35,395 (92.1)	<0.0001
Normal	12,342 (22.5)	1,955 (15.8)	10,387 (84.2)		3,892 (31.5)	8,450 (68.5)		1,799 (14.6)	10,543 (85.4)	
Bad	4,162 (7.6)	1,302 (31.3)	2,860 (68.7)		1,883 (45.2)	2,279 (54.8)		1,131 (27.2)	3,031 (72.8)	
Smoking status				<0.0001			<0.0001			<0.0001
No	52,478 (95.5)	5,663 (10.8)	46,815 (89.2)		12,741 (24.3)	39,737 (75.7)		5,432 (10.4)	47,046 (89.6)	
Yes	2,470 (4.5)	436 (17.7)	2,034 (82.4)		1,099 (44.5)	1,371 (55.5)		547 (22.1)	1,923 (77.9)	
Alcoholic use				<0.0001			<0.0001			<0.0001
No	49,056 (89.3)	5,096 (10.4)	43,960 (89.6)		11,505 (23.5)	37,551 (76.5)		4,809 (9.8)	44,247 (90.2)	
Yes	5,892 (10.7)	1,003 (17.0)	4,889 (83.0)		2,335 (39.6)	3,557 (60.4)		1,170 (19.9)	4,722 (80.1)	

*Chi-Square p value.

was found in 1,394 adolescents (8.6%) who experienced no economic hardship, 2,200 (10.1%) who experienced a slight economic hardship, 1,766 (13.0%) who experienced moderate economic hardship, and 619 (19.0%) who experienced severe economic hardship.

Table 2 reports the results of the multiple logistic regression analysis, which confirmed that COVID-19 related family economic hardship was significantly associated with increased odds of mental health problems. Adolescents who experienced a higher level of economic hardship than those without hardship showed a higher possibility of anxiety (experienced slight hardship aOR = 1.07, 95% CI: 0.98–1.17; experienced moderate hardship aOR = 1.29, 95% CI: 1.17–1.42; experienced severe hardship aOR = 2.09, 95% CI: 1.82–2.40). Similarly, among adolescents who experienced more hardship than those who did not, the likelihood of depressive symptoms increased (experienced slight hardship aOR = 1.10, 95% CI: 1.04–1.16; experienced moderate hardship aOR = 1.38, 95% CI: 1.29–1.48; experienced severe hardship aOR = 1.90, 95% CI: 1.72–2.09). Adolescents who experienced a higher level of economic hardship than those without any change in economic status exhibited a higher possibility of suicidal ideation (experienced slight hardship aOR = 1.09, 95% CI: 1.00–1.18; experienced moderate hardship aOR = 1.28, 95% CI: 1.17–1.40; experienced severe hardship aOR = 1.86, 95% CI: 1.64–2.11).

Figure 1 presents the results of the stratified analyses. Regarding anxiety, in the group with low subjective family economic status, adolescents who experienced economic hardship were more likely to report anxiety than those who experienced no hardship (experienced moderate hardship aOR = 1.33, 95% CI: 1.14–1.54; experienced severe hardship aOR = 1.96, 95% CI: 1.53–2.51). In the group with mid-level subjective family economic status, the experience of hardship was significantly associated with anxiety (experienced moderate hardship aOR = 1.30, 95% CI: 1.13–1.48; experienced severe hardship aOR = 2.19, 95% CI: 1.79–2.68). In the group with high subjective family economic status, adolescents who experienced hardship were more likely to experience anxiety (experienced severe hardship aOR = 1.82, 95% CI: 1.36–2.42).

Regarding depressive symptoms, in the group with low subjective family economic status, adolescents who experienced hardship were more likely to experience depressive symptoms than adolescents who experienced no hardship (experienced slight hardship aOR = 1.09, 95% CI: 1.01–1.18; experienced moderate hardship aOR = 1.33, 95% CI: 1.21–1.47; experienced severe hardship aOR = 1.95, 95% CI: 1.64–2.32). In the group with mid-level subjective family economic status, the experience of hardship was significantly associated with depressive symptoms (experienced slight hardship aOR = 1.11, 95% CI: 1.02–1.21; experienced moderate hardship aOR = 1.42, 95% CI: 1.29–1.57; experienced severe hardship aOR = 2.12, 95% CI: 1.82–2.47). In the group with high subjective family economic status, adolescents who experienced economic hardship were

TABLE 2 Association between COVID-19-related family economic hardship and mental health ($N = 54,948$).

Variables	Anxiety		Depressive symptoms		Suicidal ideation	
	aOR (95% CI)	*P*	aOR (95% CI)	*P*	aOR (95% CI)	*P*
COVID-19-related family economic hardship						
No	1.00					
Slight	1.07 (0.98–1.17)	0.1312	1.10 (1.04–1.16)	0.0018	1.09 (1.00–1.18)	0.0432
Moderate	1.29 (1.17–1.42)	<0.0001	1.38 (1.29–1.48)	<0.0001	1.28 (1.17–1.40)	<0.0001
Severe	2.09 (1.82–2.40)	<0.0001	1.90 (1.72–2.09)	<0.0001	1.86 (1.64–2.11)	<0.0001

We adjusted the analyses for sex, grade, residential area, co-residence with parents, subjective academic performance, subjective family economic status, subjective health status, smoking status, alcoholic use. aOR, adjusted odds ratio, CI, confidence interval.

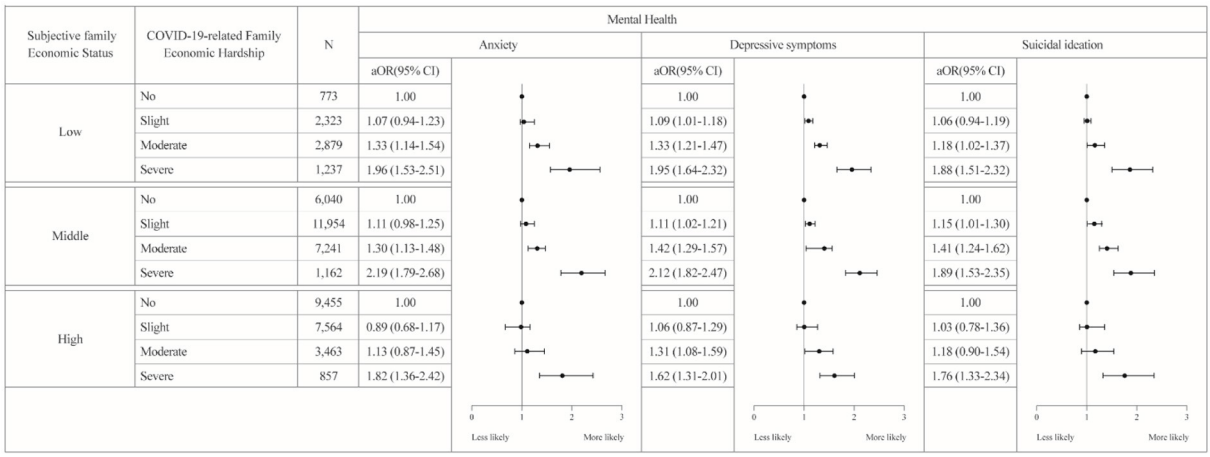


FIGURE 1
Results of the stratified analyses by subjective family economic status ($N = 54,948$). We performed stratified analyses of the association between COVID-19 related family economic hardship and mental health, stratified by subjective household economic status. We adjusted for sex, grade, residential area, co-residence with parents, subjective academic performance, subjective health status, smoking status, and alcoholic drinking.

more likely to have depressive symptoms (experienced moderate hardship aOR = 1.31, 95% CI: 1.08–1.59; experienced severe hardship aOR = 1.62, 95% CI: 1.31–2.01).

Regarding suicidal ideation, in the group with low subjective family economic status, adolescents who experienced economic hardship were more likely to have suicidal ideation than adolescents who experienced no hardship (experienced moderate hardship aOR = 1.18, 95% CI: 1.02–1.37; experienced severe hardship aOR = 1.88, 95% CI: 1.51–2.32). In the group with mid-level subjective family economic status, the experience of a downturn was associated with suicidal ideation (experienced slight hardship aOR = 1.15, 95% CI: 1.01–1.30; experienced moderate hardship aOR = 1.41, 95% CI: 1.24–1.62; experienced severe hardship aOR = 1.89, 95% CI: 1.53–2.35). In the group with high subjective family economic status, adolescents who experienced economic hardship were more likely to experience suicidal ideation (experienced severe hardship aOR = 1.76, 95% CI: 1.33–2.34).

In addition, Table 3 presents the results of the stratified analysis, which was conducted to explore the association between the family economic hardship and mental health, with a special emphasis on sex differences during the COVID-19 pandemic. Compared to the females, the males who had severe economic hardship showed more likely to have anxiety (aOR = 2.13, 95% CI: 1.75–2.60). However, compared to the males more females had depressive symptoms (aOR = 2.15, 95% CI: 1.88–2.45) and suicidal ideation (aOR = 2.04, 95% CI: 1.73–2.4).

Discussion

To the best of our knowledge, this is the first nationwide-representative study on COVID-19-related family economic hardship and mental health of adolescents during the COVID-19 pandemic. Our findings highlight that COVID-19 and its resulting economic hardships may contribute to a decrease in mental health among adolescents. As hypothesized

TABLE 3 Sex-based association between COVID-19-related family economic hardship and mental health (Male $N = 28,353$; Female $N = 26,595$).

Variables	Anxiety		Depressive symptoms		Suicidal ideation	
	Male	Female	Male	Female	Male	Female
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
COVID-19-related family economic hardship						
No	1.00	1.00	1.00	1.00	1.00	1.00
Slight	1.10 (0.96–1.26)	1.05 (0.94–1.16)	1.03 (0.95–1.12)	1.16 (1.07–1.25)**	1.00 (0.89–1.14)	1.15 (1.04–1.27)**
Moderate	1.22 (1.04–1.44)*	1.32 (1.18–1.48)***	1.28 (1.16–1.41)***	1.47 (1.35–1.60)***	1.18 (1.03–1.34)*	1.36 (1.21–1.53)***
Severe	2.13 (1.75–2.60)***	2.05 (1.72–2.44)***	1.69 (1.46–1.94)***	2.15 (1.88–2.45)***	1.67 (1.40–2.00)***	2.04 (1.73–2.41)***

We adjusted the analyses for sex, grade, residential area, co-residence with parents, subjective academic performance, subjective family economic status, subjective health status, smoking status, alcoholic use.
aOR, odds ratio, CI, confidence interval. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

in this study, we confirmed that the greater the economic hardship after COVID-19, the more severe the mental health issues (anxiety, depressive symptoms, and suicidal ideation) faced by adolescents. Furthermore, when the association of subjective family economic status with the mental health of adolescents was examined using stratified analysis, we identified that economic hardship caused by the COVID-19 pandemic had a significant impact on the mental health of adolescents belonging to the middle- to low-income economic groups.

Overall, about 11.1% of the participants of our study reported feeling anxiety, 25.2% having depressive symptoms, and 10.9% experiencing suicidal ideation. Our findings align with prior research demonstrating poor mental health during disease outbreaks, as well as with studies that reported high levels of psychological distress in other samples during the COVID-19 pandemic (30, 31) From the total, 70.4% reported experiencing economic hardship. Moreover, over 30% of our sample reported going through moderate and severe economic hardship. These findings showed that adolescents personally experience and perceive economic hardship in their families during the pandemic and highlight that majority of adolescents are experiencing COVID-19-related family economic hardship.

It was found that the greater the COVID-19-related family economic hardships, the worse the anxiety, depressive symptoms, and suicidal ideation. This link coincides with prior research on economic hardship that showed that the mental health of adolescents worsened when the economic circumstances of their parents deteriorated (32–34). Indeed, existing studies have long identified familial poverty as a risk factor for increased mental health problems among adolescents (35–37). In addition, previous studies have reported that a loss of jobs and income for parents negatively affects their children's health (38, 39).

Underemployment or job loss limits economic resources for families, thereby restricting their ability to obtain resources for ensuring consumption, education, food, housing, and a safe environment necessary for the development of adolescents (40). These deficient economic conditions can reduce the psychological resources and parenting quality of parents (41).

Furthermore, earlier studies have shown that mental health is affected by unexpected economic hardship, and that its effect varies between males and females—that is, sex is a crucial factor that must be taken into account (37, 40, 42, 43). Therefore, we analyzed the association between sex-based mental health status and family economic hardship through four subsequent categories. The results of which, demonstrated that, compared to boys, more girls with severe family economic hardship had depressive symptoms and suicidal ideation; whereas, compared to girls, boys with severe economic hardship were more likely to have anxiety. Blackwell et al. (42) reported that the economic hardship during the COVID-19 pandemic led to higher levels of stress, anxiety and depression, particularly among adolescent females. This demonstrates that family economic hardship varies based on sex-based mental health problems. Therefore, specific attention must be paid to sex differences and should be investigated in future research.

With the prolongation of the COVID-19 pandemic, uncertainty surrounding the labor market persists. Furthermore, despite the implementation of income loss compensation plans by many countries worldwide, these efforts focus on economic issues rather than those related to health (44). The potential negative impacts of COVID-19-related family economic hardship on the mental health and well-being of adolescents were evident in our study. Thus, in order to mitigate the negative consequences, health-focused policies and interventions are necessary. It must also be noted that family economic hardship itself, even if only perceived, can also have negative mental health consequences (45, 46). In addition, as poverty is inextricably linked to health, caution is necessary for adolescents in low- to middle-income households who report that they are struggling financially due to COVID-19 (47, 48). Our study emphasizes the need for governments to attend to

adolescents who are vulnerable to economic hardship as well as illness during the COVID-19 pandemic so that the discussion of social support to address the economic and health needs of families can take place.

This study has several limitations. First, this study was cross-sectional in design; hence, causal relationships between COVID-19-related family economic hardship and anxiety, depressive symptoms, and suicidal ideation could not be determined because of non-validated measures. However, related literature (49) reporting the association of suicidal ideation and depressive symptoms with household income is most likely based on self-reported responses, which may have influenced the results. Second, all data were collected through self-report questionnaires, and thus, the student-reported information may include some inaccuracy. Third, screening tools like Patient Health Questionnaire (PHQ)-2 and PHQ-9 for depression and Ask Suicide-Screening Questions-4 for suicide could not be used because of the limitations of the data. Finally, our study estimated short-term adolescent mental health responses to shock associated with COVID-19 related family economic hardship; thus, we could not address economy-wide and long-term economic hardships or examine whether the effects on mental health are transitory or persistent. However, even short-term mental health problems can have serious consequences in childhood and adolescence (50, 51). Despite these limitations, our study has several important implications. This study evaluated the association between COVID-19-related family economic hardship and adolescents' mental health during the COVID-19 pandemic using well-defined, nationally representative data in Korea.

Conclusion

In this study, we investigated the association between COVID-19-related family economic hardship and mental health issues of adolescents. Specifically, we examined anxiety, depressive symptoms, and suicidal ideation. We confirmed that the effect of family economic hardship extends to adolescents, moving beyond the participants of the labor market. These spillover effects on children's mental health suggest that the policy responses to weak economic conditions may have greater effects than anticipated. Therefore, considering the negative impact of mental health disorders (anxiety, depressive symptoms, and suicidal ideation) on daily life and health outcomes, policymakers should consider timely screening and appropriate interventions, such as online psychological counseling tailored for concerns specific to adolescents, to reduce the likelihood of emotional disturbances among adolescents during and after the COVID-19 outbreak.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: https://www.kdca.go.kr/yhs/.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was provided by the participants.

Author contributions

BK conceptualized the study, cleaned the data, performed the analyses, wrote the initial draft, and led the writing of the final draft. DHK wrote the first draft, and interpreted the results. S-YJ and JS substantially contributed to the design of the analyses, the interpretation of results, and the writing of the final draft. SGL contributed to draft writing and edited writing. THK designed and coordinated the study, supervised statistical analysis, contributed to draft writing and edited writing. All authors have read and approved the final 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

References

1. Ravens-Sieberer U, Kaman A, Erhart M, Devine J, Schlack R, Otto C. Impact of the COVID-19 pandemic on quality of life and mental health in children and adolescents in Germany. *Eur Child Adolesc Psychiatry.* (2021) 25:1–11. doi: 10.2139/ssrn.3721508

2. Crayne MP. The traumatic impact of job loss and job search in the aftermath of COVID-19. *Psychol Trauma.* (2020) 12:S180–2. doi: 10.1037/tra0000852

3. Im J, Kim J, Choeh JY. COVID-19, social distancing, and risk-averse actions of hospitality and tourism consumers: a case of South Korea. *J Destin Mark Manag.* (2021) 20:100566. doi: 10.1016/j.jdmm.2021.100566

4. Gassman-Pines A, Ananat EO, Fitz-Henley J. COVID-19 and parent-child psychological well-being. *Pediatrics.* (2020) 146:e2020007294. doi: 10.1542/peds.2020-007294

5. Xie X, Xue Q, Zhou Y, Zhu K, Liu Q, Zhang J, et al. Mental health status among children in home confinement during the coronavirus disease 2019 outbreak in Hubei Province, China. *JAMA Pediatr.* (2020) 174:898–900. doi: 10.1001/jamapediatrics.2020.1619

6. Tang S, Xiang M, Cheung T, Xiang YT. Mental health and its correlates among children and adolescents during COVID-19 school closure: the importance of parent-child discussion. *J Affect Disord.* (2021) 279:353–60. doi: 10.1016/j.jad.2020.10.016

7. Patrick SW, Henkhaus LE, Zickafoose JS, Lovell K, Halvorson A, Loch S, et al. Well-being of parents and children during the COVID-19 pandemic: a national survey. *Pediatrics.* (2020) 146:e2020016824. doi: 10.1542/peds.2020-016824

8. Li W, Wang Z, Wang G, Ip P, Sun X, Jiang Y, et al. Socioeconomic inequality in child mental health during the COVID-19 pandemic: first evidence from China. *J Affect Disord.* (2021) 287:8–14. doi: 10.1016/j.jad.2021.03.009

9. Witteveen D, Velthorst E. Economic hardship and mental health complaints during COVID-19. *Proc Natl Acad Sci U S A.* (2020) 117:27277–84. doi: 10.1073/pnas.2009609117

10. Pierce M, Hope H, Ford T, Hatch S, Hotopf M, John A, et al. Mental health before and during the COVID-19 pandemic: a longitudinal probability sample survey of the UK population. *Lancet Psychiatry.* (2020) 7:883–92. doi: 10.1016/S2215-0366(20)30308-4

11. Prime H, Wade M, Browne DT. Risk and resilience in family well-being during the COVID-19 pandemic. *Am Psychol.* (2020) 75:631–43. doi: 10.1037/amp0000660

12. Fröjd S, Marttunen M, Pelkonen M, von der Pahlen B, Kaltiala-Heino R. Perceived financial difficulties and maladjustment outcomes in adolescence. *Eur J Public Health.* (2006) 16:542–8. doi: 10.1093/eurpub/ckl012

13. Shek DT. Economic stress, psychological well-being and problem behavior in Chinese adolescents with economic disadvantage. *J Youth Adolesc.* (2003) 32:259–66. doi: 10.1023/A:1023080826557

14. Karpman M, Zuckerman S, Gonzalez D, Kenney GM. *The COVID-19 Pandemic is Straining Families' Abilities to Afford Basic Needs.* Washington, DC: Urban Institute (2020). p. 500.

15. UNICEF, UNDP, Prospera, the SMERU Research. *Analysis of the Social and Economic Impacts of COVID-19 on Households and Strategic Policy Recommendations for Indonesia.* (2021). Available online at: https://www.unicef.org/indonesia/media/9501/file/Analysis%20of%20the%20Social%20and%20Economic%20Impacts%20of%20COVID-19%20on%20Household%20and%20Strategic%20Policy%20Recommendations%20for%20Indonesia.pdf (accessed June 10, 2022)

16. Wickrama KAS, Surjadi FF, Lorenz FO, Conger RD, Walker C. Family economic hardship and progression of poor mental health in middle-aged husbands and wives. *Fam Relat.* (2012) 61:297–312. doi: 10.1111/j.1741-3729.2011.00697.x

17. Lee TK, Wickrama KA, Simons LG. Chronic family economic hardship, family processes and progression of mental and physical health symptoms in adolescence. *J Youth Adolesc.* (2013) 42:821–36. doi: 10.1007/s10964-012-9808-1

18. Sampasa-Kanyinga H, Hamilton HA. Social networking sites and mental health problems in adolescents: the mediating role of cyberbullying victimization. *Eur Psychiatry.* (2015) 30:1021–7. doi: 10.1016/j.eurpsy.2015.09.011

19. Li G, Mei J, You J, Miao J, Song X, Sun W, et al. Sociodemographic characteristics associated with adolescent depression in urban and rural areas of Hubei province: a cross-sectional analysis. *BMC Psychiatry.* (2019) 19:386. doi: 10.1186/s12888-019-2380-4

20. Assing-Murray E. Lebrun-Harris L. Associations between parent-reported family economic hardship and mental health conditions in US children. *J Child Poverty.* (2020) 26:191–214. doi: 10.1080/10796126.2020.1764188

21. Kato TA, Sartorius N, Shinfuku N. Forced social isolation due to COVID-19 and consequent mental health problems: lessons from hikikomori. *Psychiatry Clin Neurosci.* (2020) 74:506–7. doi: 10.1111/pcn.13112

22. Creswell C, Shum A, Pearcey S, Skripkauskaite S, Patalay P, Waite P. Young people's mental health during the COVID-19 pandemic. *Lancet Child Adolesc Health.* (2021) 5:535–7. doi: 10.1016/S2352-4642(21)00177-2

23. Kim Y, Choi S, Chun C, Park S, Khang YH, Oh K. Data resource profile: the Korea Youth Risk Behavior Web-based Survey (KYRBS). *Int J Epidemiol.* (2016) 45:1076–1076e. doi: 10.1093/ije/dyw070

24. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA.* (2013) 310:2191–4. doi: 10.1001/jama.2013.281053

25. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med.* (2006) 166:1092–7. doi: 10.1001/archinte.166.10.1092

26. Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care.* (2008) 46:266–74. doi: 10.1097/MLR.0b013e318160d093

27. Mossman SA, Luft MJ, Schroeder HK, Varney ST, Fleck DE, Barzman DH, et al. The Generalized Anxiety Disorder 7-item scale in adolescents with generalized anxiety disorder: signal detection and validation. *Ann Clin Psychiatry.* (2017) 29:227–34. Available online at: https://www.aacp.com/article/buy_now/?id=499

28. Nunnally JC. *Psychometric Theory*. 2nd Ed. New York, NY: McGraw-Hill (1978).

29. Mack J, Lansley S. *Poor Britain*. London: G Allen & Unwin (1985).

30. Kock M, Kuppens P, Van der Gucht K, Raes F. Mindfulness may buffer psychological distress in adolescents during the COVID-19 pandemic: the differential role of mindfulness facets. *Psychol Belg.* (2021) 61:356–76. doi: 10.5334/pb.1093

31. Sun S, Goldberg SB, Lin D, Qiao S, Operario D. Psychiatric symptoms, risk, and protective factors among university students in quarantine during the COVID-19 pandemic in China. *Global Health.* (2021) 17:1–14. doi: 10.1186/s12992-021-00663-x

32. Ananat EO, Gassman-Pines A, Francis DV, Gibson-Davis CM. Linking job loss, inequality, mental health, and education. *Science.* (2017) 356:1127–8. doi: 10.1126/science.aam5347

33. Catalano R, Goldman-Mellor S, Saxton K, Margerison-Zilko C, Subbraman M, LeWinn K, et al. The health effects of economic decline. *Annu Rev Public Health.* (2011) 32:431–50. doi: 10.1146/annurev-publhealth-031210-101146

34. Gassman-Pines A, Ananat EO, Gibson-Davis CM. Effects of statewide job losses on adolescent suicide-related behaviors. *Am J Public Health.* (2014) 104:1964–70. doi: 10.2105/AJPH.2014.302081

35. Dearing E. Psychological costs of growing up poor. *Ann N Y Acad Sci.* (2008) 1136:324–32. doi: 10.1196/annals.1425.006

36. Letourneau NL, Duffett-Leger L, Levac L, Watson B, Young-Mosrris C. Socioeconomic status and child development: a meta-analysis. *J Emot Behav Disord.* (2013) 21:211–24. doi: 10.1177/1063426611421007

37. Reiss F. Socioeconomic inequalities and mental health problems in children and adolescents: a systematic review. *Soc Sci Med.* (2013) 90:24–31. doi: 10.1016/j.socscimed.2013.04.026

38. Kalil A. Joblessness, family relations, and children's development. *Fam Matters.* (2009) (83):15–22. Available online at: https://aifs.gov.au/research/family-matters/no-83/joblessness-family-relations-and-childrens-development

39. McLoyd VC. Socialization and development in a changing economy: the effects of paternal job and income loss on children. *Am Psychol.* (1989) 44:293. doi: 10.1037/0003-066X.44.2.293

40. Yoshikawa H, Aber JL, Beardslee WR. The effects of poverty on the mental, emotional, and behavioral health of children and youth: implications for prevention. *Am Psychol.* (2012) 67:272–84. doi: 10.1037/a0028015

41. Yoshikawa H, Weisner TS, Lowe ED. *Making it Work: Low-Wage Employment, Family Life, and Child Development*. Manhattan, NY: Russell Sage Foundation (2006).

42. Blackwell CK, Mansolf M, Sherlock P, Ganiban J, Hofheimer JA, Barone CJ, et al. Youth well-being during the COVID-19 pandemic. *Pediatrics*. (2022) 149:e2021054754. doi: 10.1542/peds.2021-054754

43. Wadsworth ME, Raviv T, Santiago CD, Etter EM. Testing the adaptation to poverty-related stress model: predicting psychopathology symptoms in families facing economic hardship. *J Clin Child Adolesc Psychol*. (2011) 40:646–57. doi: 10.1080/15374416.2011.581622

44. Gray BJ, Kyle RG, Song J, Davies AR. Characteristics of those most vulnerable to employment changes during the COVID-19 pandemic: a nationally representative cross-sectional study in Wales. *J Epidemiol Commun Health*. (2022) 76:8–15. doi: 10.1136/jech-2020-216030

45. Kim TJ, von dem Knesebeck O. Is an insecure job better for health than having no job at all? A systematic review of studies investigating the health-related risks of both job insecurity and unemployment. *BMC Public Health*. (2015) 15:985. doi: 10.1186/s12889-015-2313-1

46. Kim TJ, von dem Knesebeck O. Perceived job insecurity, unemployment and depressive symptoms: a systematic review and meta-analysis of prospective observational studies. *Int Arch Occup Environ Health*. (2016) 89:561–73. doi: 10.1007/s00420-015-1107-1

47. Marmot M. Health equity in England: the marmot review 10 years on. *BMJ*. (2020) 368:m693. doi: 10.1136/bmj.m693

48. Lai ET, Wickham S, Law C, Whitehead M, Barr B, Taylor-Robinson D. Poverty dynamics and health in late childhood in the UK: evidence from the millennium cohort study. *Arch Dis Child*. (2019) 104:1049–55. doi: 10.1136/archdischild-2018-316702

49. Han JM, Song H. Effect of subjective economic status during the Covid-19 pandemic on depressive symptoms and suicidal ideation among South Korean adolescents. *Psychol Res Behav Manag*. (2021) 14:2035–43. doi: 10.2147/PRBM.S326660

50. Busch SH, Golberstein E, Meara E. The FDA and ABCs: unintended consequences of antidepressant warnings on human capital. *J Hum Resour*. (2014) 49:540–71. doi: 10.1353/jhr.2014.0016

51. Currie J, Stabile M. Mental health in childhood and human capital. In: Gruber J, editor. *The Problems of Disadvantaged Youth: An Economic Perspective*. Chicago, IL: University of Chicago Press (2009). p. 115–148.

frontiers | Frontiers in Pediatrics

TYPE Original Research
PUBLISHED 09 September 2022
DOI 10.3389/fped.2022.919061

OPEN ACCESS

EDITED BY
Biagio Solarino,
University of Bari Aldo Moro, Italy

REVIEWED BY
Susan Elizabeth Esposito,
Life University, United States
Sachiko Koyama,
Indiana University Bloomington,
United States

*CORRESPONDENCE
Leyla Namazova-Baranova
leyla.s.namazova@gmail.com
George Karkashadze
Karkga@mail.ru

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

RECEIVED 13 April 2022
ACCEPTED 25 July 2022
PUBLISHED 09 September 2022

CITATION
Namazova-Baranova L, Karkashadze G, Zelenkova I, Vishneva E, Kaytukova E, Rusinova D, Ustinova N, Sergienko N, Nesterova Y, Yatsyk L, Kratko D, Gubanova S, Gankovskiy V, Gogberashvili T, Konstantinidi T, Bushueva D, Rykunova A, Shirdanina E, Sadilloeva S, Sergeeva N, Lamasova A, Leonova E, Pankova A and Dubonosova E (2022) A non-randomized comparative study of olfactory and gustatory functions in children who recovered from COVID-19 (1-year follow-up). *Front. Pediatr.* 10:919061. doi: 10.3389/fped.2022.919061

A non-randomized comparative study of olfactory and gustatory functions in children who recovered from COVID-19 (1-year follow-up)

Leyla Namazova-Baranova[1,2]*, George Karkashadze[1]*, Irina Zelenkova[1], Elena Vishneva[1,2], Elena Kaytukova[1,2], Dina Rusinova[2,3], Natalia Ustinova[1], Natalia Sergienko[1], Yulia Nesterova[1], Leonid Yatsyk[1], Dmitrii Kratko[1], Svetlana Gubanova[1], Viktor Gankovskiy[1], Tina Gogberashvili[1], Tatiana Konstantinidi[1], Darya Bushueva[1], Anastasia Rykunova[3], Elena Shirdanina[3], Svetlana Sadilloeva[1], Natalia Sergeeva[1], Anastasia Lamasova[1,2], Elizaveta Leonova[1,2], Alina Pankova[1,2] and Ekaterina Dubonosova[1]

[1]Pediatrics and Child Health Research Institute, Russian Scientific Center of Surgery Named After Academician B. V. Petrovsky, Moscow, Russia, [2]Pirogov Russian National Research Medical University, Moscow, Russia, [3]Department of Health, City Child Polyclinics No 133, Moscow, Russia

The experimental group included 68 children over 6 years of age who had recovered from COVID-19. The control group included 22 children over 6 years of age who have never had COVID-19. Research methods included neurological examination, verification of cognitive status, examination by an otolaryngologist, and smell and taste assessment. The examination was performed 6–8 weeks after COVID-19 recovery and after 1 year in some patients. Children who recovered from COVID-19 had a reduction in their ability to smell compared to children who had never had COVID-19. The olfactory thresholds and taste identification scores after recovery from COVID-19 were identical, whether the parents had reported anosmia in their children during COVID-19 or not, and irrespective of hyperthermia level and the presence or absence of headache and hyperhidrosis during COVID-19. Analysis of correlation with neuropsychiatric symptoms showed no differences in the olfactory thresholds in children irrespective of the presence of neuropsychiatric symptoms (tics, tremors, enuresis, compulsive movements, seizures, speech disorders, attention deficit, and easy fatigability) both in general, and in particular among subjects performing or not any compulsive movements, and experiencing or not a combination of easy fatigability and daytime sleepiness. Evidence suggests that in children and adolescents, partial hyposmia is associated with depressive symptoms, varying in severity from low to high, but symptoms of depression were not caused by COVID-19 infection itself. Analysis in subgroups with different degrees

of state and trait anxiety did not reveal any significant differences in the olfactory threshold. A re-examination of 21 children was performed after 1 year. An objective olfactometric examination showed that the sensitivity to odorants increased significantly. In 1 year, we compared the thresholds of smell in children who had COVID-19 and those who did not have this disease: olfactory sensitivity after COVID-19 in children is restored to normal values. Schulte correction test showed that none of 14 children with asthenic manifestations in the form of fluctuations or exhaustion when performing the test immediately after COVID-19 had these manifestations after 1 year. Thus, asthenization of cognitive activity was recorded within the next 1.5 months after suffering from COVID-19 but was absent after 1 year.

KEYWORDS

COVID-19, children, olfactometry, cognitive functions, olfactory and gustatory functions

Introduction

Over the past few months, COVID-19 has been the focus of the global scientific community. As is well known, the olfactory disorder is considered a hallmark symptom of COVID-19 (1–4). Apparently, since children are less susceptible to SARS-CoV-2 infection, the main data currently available have been collected from cohorts of adult patients (5, 6). There is still no clarity about both the incidence (in the general population of patients with COVID-19, it can range from 32 to 69%) and the pathogenesis, as well as the outcomes of olfactory dysfunction in COVID-19 (6, 7). Research in pediatric populations is virtually non-existent worldwide; there is a paper on three pediatric COVID-19 cases where children developed anosmia and/or ageusia and an article about a multicenter study that included 10 children; yet there is no mention of any Russian studies (6, 8). We, therefore, planned and are currently conducting a study of the outcomes of olfactory disorders and associated gustatory disorders children develop during COVID-19 infection. This study is part of a larger study of the neurological outcomes of COVID-19.

When planning the study, we had a problem when selecting the method for assessment of the olfactory threshold. It is well known that the reaction to smell is mediated not only by the olfactory nerve, but also partially by the trigeminal nerve, and, possibly, by the glossopharyngeal nerve (9–11). In order to obtain information that might help to better understand the pathogenesis of olfactory dysfunction, we set the goal to investigate the olfactory threshold using three odorants, each of them being perceived *via* a different nerve. The olfactory tests most commonly used in studies worldwide are simple and convenient for clinical use, but as an assessment of the olfactory threshold, it is based on a single odorant, i.e., either n-butanol or phenyl ethyl alcohol (PEA) (12, 13). In this context, we decided to take advantage of the expertise of the Russian national school of thought in olfactometry. The method of olfactory threshold testing in adults patented by Russian authors in 1999 was taken as a basis for our research (14). The test kit required for this technique consists of serial dilutions of three odorants prepared under normal conditions, namely, (1) valerian root tincture (odor perception is mediated by the olfactory nerve), (2) acetic acid solution (odor perception is mediated by the olfactory and the trigeminal nerves), and (3) ammonia solution (odor perception is mediated by the olfactory, mainly the trigeminal, and possibly the glossopharyngeal nerve) (14).

Considering the extreme urgency of obtaining new information on the health consequences of the novel coronavirus infection, the number of subjects at the first stage of the study and, accordingly, the duration of the stage were reduced to the minimum acceptable values. The study is still underway. Due to the particular importance of the data, we present in this article the first interim results of our study.

Purpose of the study

The purpose of the study was to assess smell and taste in children after recovery from COVID-19.

Materials and methods

Study design

The experimental group included children over 6 years of age who had recovered from COVID-19 and who showed no

less than 2 weeks prior to the enrollment the first negative PCR test result for SARS-CoV-2 on nasopharyngeal or oropharyngeal swab samples, confirming the fact of recovery (in Russian clinical practice, two negative swab tests within 24 h are considered to be proof of recovery from COVID-19). The control group included children over 6 years of age who have never had COVID-19. Research methods included neurological examination, verification of cognitive status, examination by an otolaryngologist, and smell and taste assessment. To avoid excessive fatigue in children that might affect the results, the examination of each participant was carried out for 2 consecutive days. The examination was done immediately after COVID-19 recovery and after 1 year in some patients.

Eligibility criteria

Inclusion criteria for the experimental group were as follows: age of 6–18 years; a confirmed COVID-19 case; 2–5 weeks from the date of the first negative PCR test result for SARS-CoV-2 on nasopharyngeal or oropharyngeal swab samples; and informed consent to processing of personal data signed by the parents or by the subjects aged 15 years and above.

Inclusion criteria for the control group were as follows: age of 6–18 years and informed consent to processing personal data signed by the parents or by the subjects aged 15 years and above.

Non-inclusion criteria for both groups were as follows: mental deficiency and severe neuropsychiatric disorders; acute inflammation of nasopharyngeal mucosa on the day of the study; acute respiratory infection; and exacerbation of allergic rhinitis with damage to the nasopharyngeal mucosa.

General exclusion criteria were as follows: acute respiratory infection; exacerbation of allergic rhinitis with damage to the nasopharyngeal mucosa; any persisting feeling of being unwell; and refusal to continue research due to technical difficulties, for example, new circumstances preventing the parents from accompanying their child to the research center.

Study setting

The study was conducted at the Pediatrics and Child Health Research Institute, Central Clinical Hospital, Russian Academy of Sciences, Moscow. Examinations were performed in the first half of daylight hours. All subjects are Moscow residents.

Primary outcome

The endpoints of the study are data on smell and taste sensitivity in the experimental group subjects. The primary outcomes of the study are (1) comparison of the average olfactory and gustatory sensitivity test scores in the experimental and control groups and (2) correlation between olfactory and gustatory sensitivity scores.

Subgroup analysis

The experimental group was divided into two subgroups depending on the presence or absence of olfactory disorders during COVID-19, based on the results of parents' questioning by the investigator. Similarly, the experimental group was divided into two subgroups according to the presence or absence of gustatory disorders during COVID-19 infection, as reported by the parents. Additional comparative analysis of target olfactory indicators between the subgroups was carried out.

The experimental group was divided into subgroups depending on the degree of fever, the presence or absence of headache, and the presence or absence of hyperhidrosis during COVID-19 infection. A comparative analysis of olfactory sensitivity characteristics between the subgroups was carried out.

The experimental group was divided into subgroups depending on the presence or absence of neuropsychiatric microorganic symptoms (tics, tremor, enuresis, compulsive movements, seizures, speech disorders, attention deficit, and easy fatigability). Similarly, the experimental group was divided into subgroups according to the presence or absence of easy fatigability and excessive daytime sleepiness and the presence or absence of compulsive movements. A comparative analysis of olfactory sensitivity characteristics between the subgroups was carried out.

The experimental group was divided into subgroups depending on different state and trait anxiety scores and depression rates. A comparative analysis of olfactory sensitivity characteristics between the subgroups was performed.

Methods for identification of subjects meeting the non-inclusion and exclusion criteria

1. Clinical examination performed by a pediatrician, with the assessment of a child's overall health status.
2. Clinical examination performed by a neurologist, with the assessment of the neuropsychiatric mental status. The findings were also used to record additional outcomes.
3. Assessment of cognitive abilities using the Wechsler Intelligence Scale for Children (WISC). The WISC is aimed at determining the individual IQ and consists of 12 subtests. Verbal and non-verbal intelligence is measured in points, and then the Full-Scale IQ is generated. The test was administered by a clinical psychologist.

4. Examination performed by the ENT physician to assess the oropharynx and nasopharynx in terms of the status of mucosa and patency of the upper respiratory tract.

Outcome reporting methods

1. Interviewing the parents, one at a time, based on a specially developed checklist with 40 items to help identify the presence of clinical symptoms in a child with COVID-19. The results were entered into a special form. Parents were interviewed by a pediatrician.
2. Assessment of the sense of smell using the three-component olfactory test. This article presents the results of the assessment of one of the components, i.e., determination of the olfactory threshold. The olfactory threshold was tested as follows (15). The investigator presented the test tubes with serial dilutions of an odorant for 2–3 s, one at a time, to each nostril holding them at a distance of 2 cm from the subject's nose. The subject was asked to take 1–2 short sniffs while drawing in the air through the nose more actively than during common breathing, and to tell the investigator whether he or she could smell anything. First, the odorant was presented at the lowest concentration (i.e., having the weakest odor). If the subject did not smell it, he or she was presented with the odorant at the next highest concentration (2 times higher), and then at the next highest concentration, the investigator gradually increased the odorant concentration until the subject was able to smell the odor. After the subject felt the smell, the subject was asked to confirm his or her choice by making the correct choice from three pairs of test tubes, one of them containing an odorant at a given concentration and the others containing a non-odorant substance. Distilled water was used as a non-odorant substance. The procedure of triple confirmation of the right choice was necessary to exclude false sensations, which can often occur in children. After the triple confirmation of the right choice in three pairs of test tubes, the detection threshold for every given odorant was considered to be identified. The lowest concentration level of an odorant the subject was able to detect is considered the olfactory threshold.

   The study began with establishing the olfactory threshold for dilutions of 20% alcohol tincture of valerian root, for a 70% aqueous solution of acetic acid, and then for a 10% aqueous solution of ammonia. The following dilutions of these odorants in distilled water (15 for each) were proposed: for 20% alcohol tincture of valerian root and 70% aqueous solution of acetic acid: 0.00015625, 0.0003125, 0.000625, 0.00125, 0.0025, 0.005, 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1.28, and 2.56%; for 10% aqueous ammonia solution: 0.000125, 0.00025, 0.0005, 0.001, 0.002, 0.004, 0.008, 0.016, 0.032, 0.064, 0.128, 0.256, 0.512, 1.024, and 2.048%. The following conditions of the study were observed: the study was carried out in a well-ventilated room with an exhaust duct, with no aggressive odors. The subject was asked to avoid any food for 60 min prior to the test. Neither the subject nor the investigator was allowed to wear perfumes. There were 60-s breaks between tests for different odorants. After determining the olfactory detection threshold for each odorant, the investigator entered the data into the protocol. The olfactory threshold was assessed in points, and each dilution level was assigned a number of points, namely, a minimum of 1 point for the highest concentration and a maximum of 12 points for the lowest one. The higher the score, the higher the subject's ability to detect the odorant.

1. Assessment of taste sensitivity. The subject was asked to identify the taste of six different drinks. The composition of the drinks was selected based on the following requirements: ensure a maximum variety of taste sensations (acidity, sweetness, salinity, and bitterness) and recognizability of tastes for preschool and elementary school children, based on ethical considerations with regard to the young age of the subjects (preferably pleasant or neutral taste). The following drinks were presented in the order indicated: natural apple juice, water, chocolate cocktail, natural banana juice, milk, and natural cherry juice. The subjects were blindfolded and, therefore, unable to see the color of the liquid. Mechanical compression of the nasal passages was also done to exclude olfaction from participating in taste recognition. After that, the subject took a glass of liquid in his or her hands and tasted it, in no more than three sips. After identification of each liquid, the mouth was rinsed with water. Taste identification was a two-stage process. At stage I, the subject was asked to tell the taste of the liquid without any prompting. If there were difficulties or the answer was incorrect, stage II was proposed, i.e., forced choice of taste from the four proposed. The assessment was done as follows: 2 points for correct taste identification at stage I, 1 point for correct identification at stage II, and 0 points for incorrect taste identification. Taste identification data were entered into a special protocol, in which the points were summed up. The minimum possible total score was 0 and the maximum was 12. The composite score was the indicator of the child's gustatory ability. The following test conditions were ensured: the test was carried out in a room with no strong odors. The subject was asked to avoid food for 60 min prior to the test. Before testing, the subject was to rinse his or her mouth with water. Neither the subject nor the investigator was allowed to wear any perfume. The study was carried out in the presence of one of the parents or another legal representative of the child, who was to

make sure that the presented drinks were manufactured beverages and opened and poured into disposable glasses directly at the time of testing.

2. The Spielberger State-Trait Anxiety Inventory for Children (STAIC) adapted by Yu L. Khanin was used to detect the level of state and trait anxiety. The Spielberger-Khanin scale is designed for children aged 12 years and above. Rating points are scored, based on a 4-point Likert-type scale, with 4 composite score ranges corresponding to no anxiety, low anxiety, moderate anxiety, and high anxiety, respectively. The inventory was administered by a clinical psychologist.
3. The Beck Depression Inventory (BDI) is a depression rating scale designed to diagnose the level of depression. The subject responds to statements that are ranked with a gradual increase in the specific weight of a symptom in the overall severity of depression. Next, a composite score is calculated and the level of depression is determined (no depression, mild depression, moderate depression, and severe depression). The inventory was administered by a clinical psychologist.
4. The cognitive testing (Schulte correction test) was performed by a psychologist.

Ethical review

Enrollment in the study was carried out upon receipt of a signed informed voluntary consent for examination from a parent or a legally authorized representative of the child, or by the child aged 15 years and above.

Statistical analysis

Statistical analysis of the results was carried out using the STATISTICA version 11.0 software package (StatSoft Inc., Tulsa, United States). For the comparative assessment of the olfactory threshold values in the main analysis and in additional subgroups, the parametric Student's *t*-test was used for independent samples. The significance level assumed was a *p*-value of < 0.05. To determine the relationship between the smell and taste characteristics, Pearson's coefficient of linear correlation was used.

Results

Study subjects

A total of 68 children and adolescents, aged 6–18 years, were suggested for recruitment in the experimental group and 22 children of the same age were suggested for inclusion in the control group. After preliminary examinations, with the identification of subjects meeting the non-inclusion criteria, 64 participants were admitted to the experimental group and 20 participants were admitted to the control group. In the course of the study, 3 subjects were excluded from the experimental group due to the parents' inability to take the child to the research site. The study was completed by 61 subjects in the experimental group and 20 subjects in the control group (Tables 1, 2).

Main results

Note: the higher the score, the higher the olfactory sensitivity, and the lower the olfactory threshold (i.e., lower concentrations of the odorant can be detected).

The olfactory thresholds of all three odorants were significantly elevated in children with COVID-19 (Table 3). Thus, children who recovered from COVID-19 had a reduction in their ability to smell compared to children who had never had COVID-19. At the same time, the olfactory threshold for valerian root tincture was somewhat more elevated than the thresholds for the other two odorants (Table 3).

The ability to identify tastes is lower in children who recovered from COVID-19 (Table 4). Pearson's coefficient of linear correlation between the olfactory thresholds and taste identification was $r = 0.38$, which means there was a weak positive correlation between the smell and taste characteristics.

TABLE 1 Characteristics of subjects in the two groups who completed the study.

	Experimental group	Control group
Number of subjects, *n*	61	20
Average age, years	11.4 ± 3.5	11.5 ± 3.7
Gender: female, %	38.7	45

TABLE 2 Additional characteristics of the experimental group subjects.

	Total	Males	Females
Time from laboratory-confirmed onset of COVID-19 to examination of study subjects, days	45.4 ± 4.6	–	–
Time from laboratory-confirmed recovery from COVID-19 (first negative swab test) to examination of study subjects, days	27.3 ± 3.2	–	–
Hyperthermia	81.5%	59.1%	40.9%
Asthenia during COVID-19	60.4%	69.7%	31.3%
Headache during COVID-19	53.7%	51.7%	48.3%
Anosmia or hyposmia during COVID-19	41.5%	63.6%	36.4%
Ageusia or hypogeusia during COVID-19	30.2%	56.2%	43.8%
Asymptomatic COVID-19	0%	–	–

Significant gender differences were not fixed either by a sense of smell or taste.

Additional results

The olfactory thresholds after recovery from COVID-19 were identical, whether the parents had reported anosmia in their children during COVID-19 or not (Table 5).

In addition, there were no differences in taste identification scores between these subgroups. However, even more remarkably, taste identification scores after recovery were similar in subgroups of subjects who did and did not experience the loss of taste during COVID-19 infection.

Based on the results of the analysis in additional subgroups, there was no difference in the olfactory threshold and taste identification after recovery, irrespective of hyperthermia level and of the presence or absence of headache and hyperhidrosis during COVID-19. Analysis of correlation with neuropsychiatric symptoms showed no differences in the olfactory thresholds and taste identification in children, irrespective of the presence of neuropsychiatric symptoms (tics, tremors, enuresis, compulsive movements, seizures, speech disorders, attention deficit, and easy fatigability) both in general, and in particular among subjects performing or not any compulsive movements, and experiencing or not a combination of easy fatigability and daytime sleepiness.

Analysis in subgroups with different levels of depression revealed certain significant differences (Table 6).

Evidence suggests that in children and adolescents, partial hyposmia (lower olfactory sensitivity to the valerian root tincture odor and, to a lesser extent, acetic acid odor) is associated with depressive symptoms, varying in severity from low to high. At the same time, symptoms of depression are not caused by COVID-19 infection.

Analysis in subgroups with different degrees of state and trait anxiety did not reveal any significant differences in the olfactory threshold, although there was a tendency for a lower olfactory sensitivity to valerian tincture odor in the subgroup with high trait anxiety, compared to the subgroup with low trait anxiety (6.91 ± 1.3 vs. 7.95 ± 1.76 at $p = 0.09$).

We proposed a re-examination of 21 children after 1 year. None of the 9 children who had complaints of olfactory impairment at the initial examination had them at the second examination after 1 year. An objective olfactometric examination showed that the sensitivity to the three odorants increased significantly (from 5.6 to 10.4 points for valerian tincture, from 6.1 to 10.1 points for acetic acid, and from 6.6 to 9.8 points for ammonia alcohol). For 1 year, we compared the thresholds of smell in children who had COVID-19 and those who did not have this disease: among children who recovered more than 6 months ago, the thresholds of smell did not differ from those who did not get sick. Thus, olfactory sensitivity 6–12 months after suffering from COVID-19 in children was restored to normal values.

Cognitive testing (Schulte correction test) showed that none of the 10 children with asthenic manifestations in the form of fluctuations when performing the test immediately after COVID-19 had these manifestations after 1 year.

Thus, asthenization of cognitive activity, fixed by objective diagnostic methods, was recorded within the next 1.5 months after suffering from COVID-19 but was absent after 1 year. This indicates the absence of long-term consequences of COVID-19 on the cognitive activity of children in the surveyed sample but does not exclude emotional, personal, and social consequences that may follow unproductive educational activities during the period of asthenization of cognitive activity.

TABLE 3 The mean scores of olfactory threshold.

	Experimental group, points (min = 1, max = 12)	Control group, points (min = 1, max = 12)	*P*
Valerian root tincture	7.52 ± 1.68	9.05 ± 1.18	0.0008
Acetic acid solution	7.59 ± 1.79	8.79 ± 1.51	0.001
Ammonia solution	7.95 ± 2.27	9.58 ± 2.43	0.009

The higher the score, the higher the olfactory sensitivity, and the lower the olfactory threshold (i.e., lower concentrations of the odorant can be detected).

TABLE 4 The mean scores of taste identification.

	Experimental group, points (min = 0, max = 12)	Control group, points (min = 0, max = 12)	*P*
Taste identification	8.05 ± 2.19	9.93 ± 1.83	0.003

TABLE 5 Odor detection thresholds after recovery from COVID-19.

	Valerian root tincture, points	Acetic acid solution, points	Ammonia solution, points
Subjects who experienced olfactory disorders during COVID-19, as reported by parents	7.45 ± 1.37	7.68 ± 1.7	8.06 ± 1.99
Subjects with no reported olfactory disorders during COVID-19	7.54 ± 1.84	7.38 ± 2.08	7.81 ± 2.32

TABLE 6 Olfactory thresholds depending on the presence or absence of depression after recovery from COVID-19.

Assessment of depression using the Beck Depression Inventory	Valerian root tincture, points	Acetic acid aqueous solution, points	Ammonia water solution, points
Subjects with no depression	7.73 ± 1.46	8.32 ± 1.04	8.32 ± 1.68
Subjects with depression	6.29 ± 1.25	7.0 ± 2.64	8.14 ± 2.21
P	0.029	0.06	

Discussion

This study focused mainly on the assessment of the sense of smell but also taste in children with a history of COVID-19 infection. This is the first such study in Russia and one of the first in the world. Internationally, our study echoes a multicenter study (China, France, and Germany) with a slightly smaller sample size of 27 children (the main sample in that study was 367 adult participants) (6). Despite the differences in design, this multicenter study was the only one of interest for comparison of results by the time the manuscript was prepared. After a while, the results of the later studies appeared (16–19).

As reported by parents, 41.5% of children and adolescents suffering from COVID-19 had smell impairment and 30.2% had taste impairment. This is the very first data on the incidence of these disorders in Russian children, which indicates that despite the known milder course of COVID-19 in children, the olfactory and gustatory systems are widely affected by SARS-CoV-2. In the abovementioned international multicenter study, the incidence of both system disorders in children was more or less similar to our data and amounted to 37% (10 out of 27 children aged 6–17 years) (6).

The main result of our study is that based on objective examination approximately 4 weeks after recovery from COVID-19, children and adolescents had smell and taste disorders. Obviously, these changes persist after recovery from coronavirus. It is, therefore, important to assess the time to recovery of olfactory function and whether it is fully restored after recovery from COVID-19.

Another finding is that smell and taste after recovery from COVID-19 were equally affected in those who complained of impaired smell and taste during COVID-19 infection and those who did not. This indicates that complaints made by children and observations reported by parents do not fully reflect the smell dysfunction the former had. In the abovementioned international multicenter study, the authors also emphasize that 10 out of 90 participants (including one child) who underwent objective olfactory testing had olfactory dysfunction without any subjective olfactory complaints. There seems to be a cohort with extensive subclinical smell impairment, meaning that smell disorders in COVID-19 are more common than reported by patients.

No connection has been established between olfactory dysfunction and the presence of certain neurological symptoms. In addition, no connection was found between the olfactory function status and the severity of other symptoms of COVID-19 (hyperthermia, asthenia, headache, and hyperhidrosis). Colleagues from the international multicenter study came to the same conclusions, discovering that in different cohorts, correlations between olfactory dysfunction and the severity of COVID-19 were very different (6). This suggests that neither the severity of the disease nor the premorbid damage to the nervous system, but some different, unexplored factors, such as a specific viral strain, ethnicity, or phenotype, contribute to the onset of olfactory dysfunction in patients with COVID-19. In this regard, it is significant that in our study, children and adolescents with non-COVID-mediated depression experienced hyposmia. The relationship between depression and an altered sense of smell has been repeatedly shown in studies (20–22). In this case, it is important that this connection has been shown in a cohort of patients who recovered from COVID-19. Therefore, accordingly, as illustrated by depression, we can talk about the contribution of individual phenotypic factors to a person's predisposition to olfactory disorders during COVID-19.

There is a weak positive relationship between the smell and taste status. This means a partial, but not a complete overlap of olfactory and gustatory dysfunction, which is confirmed by some clinical observations. It is possible that a single etiopathogenetic factor (infection with the SARS-CoV-2 virus) and the regional proximity of receptor localization determine the relationship between olfactory and gustatory disorders; at the same time, we see individual differences in susceptibility of the two systems to such pathology, which prevents a complete synchrony of both smell and taste disorders, though given the limitations of the study, this conclusion requires further verification.

Limitations

A significant factor limiting the interpretation of the study results is the relatively small sample size. Even though the differences in study results are statistically significant, a larger sample size could increase the statistical significance of these findings.

Another limitation is retrospective questioning of parents and children about the symptoms of COVID-19 infection. On average, the survey was conducted 45 days after the onset of infection. This raises the question of the accuracy of data on the course of COVID-19 infection in children. When examining

the sense of smell, we evaluated the olfactory threshold, which to a greater extent reflects the precognitive (or extra-cognitive) part of perception, while taste testing evaluated the taste identification ability, which largely reflects the cognitive part of perception. This is why it is somewhat improper to look for a direct correlation between taste and smell testing, and it must be taken into account when interpreting the results.

Conclusion

In this study, we presented the first objective diagnostic data, indicating that in children and adolescents, changes in smell and taste sensitivity persist even 2–5 weeks after recovery from COVID-19. More importantly, these changes occur more often than reported by children and their parents. The involvement of olfactory sensitivity in the pathological process does not depend on the severity of the COVID-19 case or any premorbid neurological impairment. The study is still underway.

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 Ethics Committee of CCH RAS. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

LN-B: idea and general heading. GK: idea, study design, and head of science. IZ: olfactory test – idea and examination. EV: literature search and database. EK, DR, and NU: patients management. NS, YN, LY, DK, SG, VG, TG, TK, DB, AR, ES, SS, NS, AL, EL, AP, and ED: patients examination, database filling, and statistics. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

Publisher's note

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

References

1. Chang J, Hong C, Zhou Y, Wang D, Miao X, Li Y, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* (2020) 77:683–90. doi: 10.1001/jamaneurol.2020.1127.

2. Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: Common findings in COVID-19 patients. *Laryngoscope.* (2020) 130:1787. doi: 10.1002/lary.28692

3. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): A multicenter European study. *Eur Arch Otorhinolaryngol.* (2020) 277:2251–61. doi: 10.1007/s00405-020-05965-1

4. Kaye R, Chang CWD, Kazahaya K, Brereton J, Denneny JC III. COVID-19 anosmia reporting tool: Initial findings. *Otolaryngol Head Neck Surg.* (2020) 163:132–4. doi: 10.1177/0194599820922992

5. Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. *Head Neck.* (2020) 42:1252–8. doi: 10.1002/hed.26204

6. Qiu C, Cui C, Hautefort C, Haehner A, Zhao J, Yao Q, et al. Olfactory and gustatory dysfunction as an early identifier of COVID-19 in adults and children: An international multicenter study. *medRxiv.* (2020) [Preprint] 2020.05.13.20100198. doi: 10.1101/2020.05.13.20100198

7. Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuropathogenesis and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: A review. *JAMA Neurol.* (2020) 77:1018–27. doi: 10.1001/jamaneurol.2020.2065

8. Mak PQ, Chung KS, Wong JS, Shek CC, Kwan MY. Anosmia and ageusia: Not an uncommon presentation of COVID-19 infection in children and adolescents. *Pediatr Infect Dis J.* (2020) 39:e199–200. doi: 10.1097/INF.0000000000002718

9. Hummel T, Livermore A. Intranasal chemosensory function of the trigeminal nerve and aspects of its relation to olfaction. *Int Arch Occup Environ Health.* (2002) 75:305–13. doi: 10.1007/s00420-002-0315-7

10. Tremblay C, Frasnelli J. Olfactory and trigeminal systems interact in the periphery. *Chem Senses.* (2018) 43:611–6. doi: 10.1093/chemse/bjy049

11. Blagoveschenskaya NS. *Otoneurological symptoms and syndromes.* Moscow: Meditsina (1990). p. 432

12. Gellrich J, Sparing-Paschke L-M, Thieme T, Schwabe K, Dworschak A, Hummel T, et al. Normative data for olfactory threshold and odor identification in children and adolescents. *Int J Pediatr Otorhinolaryngol.* (2019) 123:5–9.

13. Rombaux P, Collet S, Martinage S, Eloy P, Bertrand B, Negoias S, et al. Olfactory testing in clinical practice. *B-ENT.* (2009) 5 Suppl 13:39–51.

14. Domrachev AA, Afonkin VYu, Savchenkov YuI, Amelchugov SP, Erlikh IA. *Method of threshold olfactometry. Russian federation patent RU 2169364 C1*, Moscow. (2001).

15. Karkashadze G, Namazova-Baranova L, Vishneva EA, Zelenkova IV, Kaitukova EV, et al. *The method for assessing the threshold of olfaction in children. Russian federation patent for invention*, Moscow. (2021).

16. Yan Q, Qiu D, Liu X, Guo X, Hu Y. Prevalence of smell or taste dysfunction among children with COVID-19 infection: A systematic review and meta-analysis. *Front Pediatr.* (2021) 9:686600. doi: 10.3389/fped.2021.686600

17. Elmas B, Çavdaroğlu PD, Orhan MF, Ay G, Caner I, Tarım A, et al. Evaluation of taste and smell disorders in pediatric COVID-19 cases. *Rev Assoc Med Bras (1992).* (2021) 67:789–94. doi: 10.1590/1806-9282.20200547

18. Parisi GF, Brindisi G, Indolfi C, Diaferio L, Marchese G, Ghiglioni DG, et al. COVID-19, anosmia, and ageusia in atopic children. *Pediatr Allergy Immunol.* (2022) 33:99–101. doi: 10.1111/pai.13644

19. Kumar L, Kahlon N, Jain A, Kaur J, Singh M, Pandey AK. Loss of smell and taste in COVID-19 infection in adolescents. *Int J Pediatr Otorhinolaryngol.* (2021) 142:110626. doi: 10.1016/j.ijporl.2021.110626

20. Croy I, Negoias S, Symmank A, Schellong J, Joraschky P, Hummel T. Reduced olfactory bulb volume in adults with a history of childhood maltreatment. *Chem Senses.* (2013) 38:679–84. doi: 10.1093/chemse/bjt037

21. Kohli P, Soler ZM, Nguyen SA, Muus JS, Schlosser RJ. The association between olfaction and depression: A systematic review. *Chem Senses.* (2016) 41:479–86. doi: 10.1093/chemse/bjw061

22. Uzun Cicek A, Altuntas EE, Bora A, Sarı SA. Olfactory function in depressed adolescents. *J Nerv Ment Dis.* (2020) 208:476–80. doi: 10.1097/NMD.0000000000001148

frontiers | Frontiers in Pediatrics

TYPE Opinion
PUBLISHED 16 September 2022
DOI 10.3389/fped.2022.919710

OPEN ACCESS

EDITED BY
Satinder Aneja,
Sharda University, India

REVIEWED BY
Maurizio Aricò,
Department of Pediatrics, Italy
Amrita Dosanjh,
Pediatric Respiratory, Pulmonologist, Pediatrician, United States

*CORRESPONDENCE
Marcello Benevento
marcello.benevento@uniba.it

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

RECEIVED 13 April 2022
ACCEPTED 29 August 2022
PUBLISHED 16 September 2022

CITATION
Nicolì S, Benevento M, Ferorelli D, Mandarelli G and Solarino B (2022) Little patients, large risks: An overview on patient safety management in pediatrics settings.
Front. Pediatr. 10:919710.
doi: 10.3389/fped.2022.919710

Little patients, large risks: An overview on patient safety management in pediatrics settings

Simona Nicolì[1], Marcello Benevento[1]*, Davide Ferorelli[1], Gabriele Mandarelli[2] and Biagio Solarino[1]

[1]Section of Legal Medicine, Interdisciplinary Department of Medicine, University of Bari, Bari, Italy, [2]Section of Forensic Psychiatry, Interdisciplinary Department of Medicine, University of Bari, Bari, Italy

KEYWORDS

children safety, pediatric clinical pathways, clinical risk management, children's hospital, errors

Introduction

Patient safety is an emerging healthcare discipline with the ultimate goal to reduce errors and harm to patients by implementing quality health services. In 1999, the well-known "To Err is Human: Building a safer health system" reported that between 2% and 4% of people die annually in United States hospitals for medical errors (1). Since that publication, the focus on healthcare safety has encouraged efforts by legislators, hospital government, and health professionals to promote policies and behaviors heavily to reduce errors and implement a safe provision of healthcare delivery. In 2019, the World Health Organization (WHO) declared September 17th as Patient Safety Day, confirming that as a global priority (2).

The increasing interest in patient safety has significant repercussions on scientific publications with an ever-increasing production of studies in the growing interdisciplinary field of public health. New concepts and new terms had born, such as "clinical risk," which refers to the probability that a patient can be the victim of an adverse event due to medical care, although unintentionally.

The WHO proposed to adopt a "universal vocabulary" thus standardizing the terminology and allowing effective scientific research. In clinical risk, the most explored field is adult patient safety, where growing interest is shown primarily to prevent nosocomial infections, falls, and pressure injuries. Instead, a little-explored area concerns the pediatric population (3).

This article aims to overview the spread of pediatric clinical risk management and organizational culture for healthcare quality improvement, looking at what has been done and enhancing healthcare practices to implement inpatient safety. The authors have reviewed the main concerns on pediatric patient safety and issued the main medico-legal aspects. After summarizing the relevant literature, the authors addressed their point of view by writing an opinion article.

Pediatric patient safety: The main issues

Nowadays, we are witnessing a growing interest in errors and harm in the pediatric setting, which differ from adults. Standard textbooks and research literature still give little attention to pediatric inpatient primary care and well-being. The short amount available of scientific works is due to children's particular features, characterizing their health management as different and more complex than adults. A study published in 2005 reported that adverse events occurred in children in 1% of pediatric hospitalizations and that 60% of these events were preventable. Other studies suggest that this rate may be higher (4). Table 1 summarizes the main facets of pediatric patient safety.

The assessment of decision-making capacity

Woods highlighted children's physical characteristics can affect the predisposition to errors and harm: weight-based medication dosing, significant variation in size and weight, and predisposition to medical error (5). Moreover, the number of children with chronic diseases and the obesity rate increases, so the physical features of children are sort of changing (16).

It is not unusual for physicians to ask for legal intervention when they believe that a caregiver's refusal of treatment places patients at substantial risk. This phenomenon became most dramatic in pediatric oncology, where the potential need to override caregivers' decision-making when they refuse treatment or replace it with ineffectual alternatives is well-known. Hence the question: are caregivers' rights to make medical decisions on behalf of their children absolute? Decision-making in pediatrics needs a shared approach where children, families, and healthcare multidisciplinary teams cooperate to reach a consensus on decisions in patients' best interests. This "shared" approach is fundamental in pediatric oncology to minimize children's medical and psychosocial impact (17).

The assessment of decision-making capacity for treatment and competence to consent in minors is still far to be validated (18). The acquisition of informed consent is delegated to parents or caregivers, often regardless of their ability to consent to treatment. Since children's capacities develop with growth and experience, their involvement in decisions regarding their health must also increase (19). The involvement of the minor in the diagnostic and therapeutic decision-making process is not solely based on patients' age or ability to read and write and should reduce the stress related to procedures and treatments (20). Some studies have attempted to apply to minors the MacCAT-CR and the MacCAT-T scale in various settings, including the neuropsychiatric one, with surprising results, as adolescents are likely to show the same results as adults (21). Nevertheless, these tools do not have external validation and further research is needed. Finally, all studies regarding this topic emphasize the need to implement communication between minors and parents/caregivers for therapeutic decisions (10, 22).

The outbreak of the COVID-19 pandemic addressed a challenging debate about the administration of new anti-covid vaccines for minors (23). There is a substantial heterogeneity standpoint on this topic in Western Countries. Vaccinating minors to protect them from the COVID-19 virus requires parental permission; the question arises concerning minors' decision-making capacity to consent to such preventive treatment by tracking adults' decisions. In this respect, Morgan et al. suggested a "guide" based on age groups to the consent of minors for the vaccine: is this age-based assessment sufficient? Is it enough to explain to children the benefits and burdens of procedure about a vaccine tested first? One more reason to promote research on assessing children's decision-making capacity for treatment (24).

Healthcare systems and multi-level assistance

In addition to these intrinsic factors, the setting of children's care regarding safety is also essential. Currently, the child healthcare system has different intervention levels. Family pediatricians deliver primary care; secondary care is provided in pediatric departments in general hospitals. Children's hospitals were designed to provide optimal care and a multidisciplinary approach to patients and their families (25). Settings in which patients had the most complex needs imply a higher error rate compared with ambulatorial context. The Emergency Department is the place in the pediatric Children's Hospital, where multiple factors related to staff, patients, family members, and pre-hospital communication contribute to various diagnostic and medication mistakes (26).

The healthcare activities carried out in these units often involve multiple urgent interventions for high-risk patients in a complex and stressful environment that exposes children to high frequencies of errors. Applying clinical risk management tools and methodologies changed pediatric intensive care units, reducing medical errors and adverse events and organizational, clinical, and economic impacts, contributing to safety and overall healthcare quality (27). The integrated use of proactive and reactive methods had a growing trend over time, similarly to the increasing use of proactive tools highlighted in two systematic reviews (28, 29).

The pandemic outbreak disclosed the shortages of primary care organizations resulting in inappropriate hospitalizations for non-urgent diseases, thus increasing the risk of errors and unintended harm. Many studies reported a drastic reduction in

TABLE 1 Major concerns regarding pediatric patient safety.

Matter of concern	Issues
Physical characteristics	Children's small size, weight, and morphology need a suitable healing environment (5, 6)
Capacity to consent to medical treatment/Legal Status	Cognitive development affects the capacity to choose a medical treatment/ consent to clinical research. The assessment of decision-making capacity in minors is one of the most compelling and debated topics in pediatric healthcare (7–10). The legal status of minors slightly changes between Countries. Normally, caregivers' permission is needed to choose or refuse any kind of treatment (11)
Lack of children-dedicated healthcare facilities	Settings in which patients had the most complex needs imply a high error rate. Children require healthcare focusing on their needs so they must be treated in children's hospitals (12)
Lack of pediatric guidelines	The growing lawsuits against healthcare professionals led the scientific community to great interest in drafting clinical guidelines, which have to be standardized and subjected to quality control in recent years (13, 14)
Lack of labeled medications	Most medications are not labeled for use in the pediatric population (15)

access to emergency pediatric wards, thus emerging the often inappropriate use of these services (30). The overcrowding of the emergency-urgency department, already characterized by a greater incidence of medical errors, has an even more negative impact on care safety. Therefore, it is evident the need to build a functioning network for the care of the pediatric child, especially concerning primary care (31).

But what about other settings? Although it is evident that some departments are more exposed to risk than others, no hospital ward is risk-free. An interesting article by Lynne Warda reviewed the risks of injury to children in the hospital setting, identifying that those life-threatening hazards mainly concern beds or cribs, concluding that although safety considerations are well entrenched in occupational health and safety, the needs of children are typically not addressed (32). Children require healthcare focusing on their needs. They require more time and specificities for their care; for this reason, these must be treated in children's hospitals where every detail is thought out to optimize patient safety and well-being, from the facilities to the staff specially trained for pediatric care (12).

The lack of guidelines and pediatric trials

Another pediatric "silent" crisis, as defined by Corinna Rea, concerns the lack of children's guidelines (13). Some countries favor a more centralized approach to guideline production. Others have a decentralized one, such as the US, where the American Academy of Pediatrics plays the most crucial role in developing guidelines. Decentralization seems to give rise to recommendations' production that may be overlapped, with the consequent detriment of their quality. Moreover, while there is a continuous demand for new guidelines, little importance is given to updating the old ones. Many of these results expired with all their negative consequences: the implementation of obsolete practices that can affect the quality and safety of care and distrust of clinicians and minors' families about the value of outdated guidelines. It is desirable to implement reviewing and validating procedures with greater urgency for the pediatric ones, whose development should be centralized and entrusted to a single organization. Moreover, in a broader perspective, to solve the lack of guidelines and good clinical practices, health practitioners should acquire the so-called "living guidelines" approach for ensuring inpatient high-level quality care: new evidence and recommendations are constantly monitored and possibly updated. A dynamic review approach should ensure the application of the best available practices to the pediatric population, assuring them of high-level quality care to prevent clinical risk (12).

Many barriers exist to conducting pediatric trials, so many therapies used in pediatrics are not evidence-based (15). On the other hand, recent legislation has aimed to stimulate pediatric research and drug labeling (33). In such context, the off-label use of COVID-19 vaccines rises peculiar ethical and legal concerns, as many scientific organizations cautioned against it (34).

The importance of a safety culture

In the complex working environment of Children's Hospitals, it is necessary to improve the so-called "safety culture." It consists, for professionals, in understanding e recognizing problems and risks in safety, understanding that the practice has value both for them and patients. It is also imperative for the hospital to have its safety policies, encouraging tailored and procedures baseline numbers about the safety problems before implementation (35, 36).

In light of these areas of vulnerability, pediatric clinical governance programs deserve specific attention. Several measures and tools could be implemented to reduce errors, promoting the so-called "safety culture". The efforts to be done can be synthesized in these points:

- Special attention should be paid to training new healthcare professionals and integrating patient safety into ongoing medical education.

- Studies issuing pediatric patient safety should be promoted to improve working knowledge of children's patient safety issues throughout the pediatric community, especially in searching for a validated scale assessing the decision-making capacity of minors.
- Hospitals' safety policies should implement appropriate local procedures and train multidisciplinary teams to seek quality improvement, with a greater focus on the pediatric setting.
- The development process of pediatric guidelines and recommendations should be promoted.

It is our view that one of the best tools for implementing a "safety culture" is the so-called "clinical pathway", which aims to standardize care processes and improve outcomes without increasing costs or compromising quality. Specifically, clinical pathways aim to integrate evidence into clinical practice and optimize patient outcomes while improving efficiency by translating national guidelines and the latest evidence into the local context. Multidisciplinarity and collaboration between all healthcare professionals are fundamental in the drafting and reviewing process of clinical pathways, also because they measurably improve many aspects of care for pediatric patients. As for guidelines, the spread of clinical pathways should be promoted, and where possible, it would be helpful to create a database to allow their dissemination in as many hospitals as possible and promote collaboration among these.

There is still a long way to go, but multidisciplinarity, the education of young professionals in the culture of safety, and the support of research in less explored fields are the keys to developing a safer healthcare system for pediatric patients.

Author contributions

SN and BS conceived the manuscript. SN, DF, MB, and GM wrote the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

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. Richardson WC, Berwick DM, Bisgard C, Bristow L, Buck CR. *To Err is Human: Building a Safer Health System*. Washington, D.C.: National Academy Press (2000).

2. World Health Organization. *World Patient Safety Day 2019*. (2019). Available online at: https://www.who.int/europe/news-room/events/item/2019/09/01/default-calendar/world-patient-safety-day-2019 (accessed February 11, 2022).

3. Group WAFPSD, Sherman H, Castro G, Fletcher M, Hatlie M, Hibbert P, et al. Towards an International Classification for Patient Safety: the conceptual framework. *Int J Qual Heal Care.* (2009) 21:2–8. doi: 10.1093/intqhc/mzn054

4. Greve P. Pediatrics: A unique and volatile risk. *J Healthc Risk Manag.* (2011) 31:19–29. doi: 10.1002/jhrm.20084

5. Woods DM, Holl JL, Shonkoff JP, Mehra M, Ogata ES, Weiss KB. Child-specific risk factors and patient safety. *J Patient Saf.* (2005) 1:17–22. doi: 10.1097/01209203-200503000-00006

6. Ghazali R, Abbas MY. Assessment of healing environment in paediatric wards. *Procedia - Soc Behav Sci.* (2012) 38:149–59. doi: 10.1016/j.sbspro.2012.03.335

7. van Heerden J, Delport R, Kruger M. Children's ability to consent to medical management in South Africa. *SAJCH South African J Child Heal.* (2020) 14:25–9. doi: 10.7196/SAJCH.2020.v14.i1.1621

8. Boceta R, Martínez-Casares O, Albert M. The informed consent in the mature minor: Understanding and decision-making capacity. *An Pediatr.* (2021) 95:413–22. doi: 10.1016/j.anpede.2020.10.011

9. Miano SJ, Douglas SL, Hickman RL, DiMarco M, Piccone C, Daly BJ. Exploration of decisional control preferences in adolescents and young adults with cancer and other complex medical conditions. *J Adolesc Young Adult Oncol.* (2020) 9:464–71. doi: 10.1089/jayao.2019.0135

10. Mandarelli G, Sabatello U, Lapponi E, Pace G, Ferrara M, Ferracuti S. Treatment decision-making capacity in children and adolescents hospitalized for an acute mental disorder: the role of cognitive functioning and psychiatric symptoms. *J Child Adolesc Psychopharmacol.* (2017) 27:462–5. doi: 10.1089/cap.2016.0092

11. Vrouenraets LJJJ, de Vries ALC, de Vries MC, van der Miesen AIR, Hein IM. Assessing medical decision-making competence in transgender youth. *Pediatrics.* (2021) 148:e2020049643. doi: 10.1542/peds.2020-049643

12. Casimir G. Why children's hospitals are unique and so essential. *Front Pediatr.* (2019) 7:1–5. doi: 10.3389/fped.2019.00305

13. Rea CJ, Alvarez FJ, Tieder JS. The silent crisis of pediatric clinical practice guidelines. *JAMA Pediatr.* (2021) 175:1201–2. doi: 10.1001/jamapediatrics.2021.2435

14. Cascini F, Contenti M, Scarpetti G, Gelli F, Ricciardi W. Patient safety and medical liability in Italy. *Eurohealth (Lond).* (2020) 26:34–8.

15. Meliota G, Lombardi M, Benevento M, Console V, Ciccone MM, Solarino B, et al. Off-label use of cardiovascular drugs in the home therapy of children with congenital or acquired heart disease. *Am J Cardiol.* (2022) 166:131–7. doi: 10.1016/j.amjcard.2021.11.029

16. Nittari G, Scuri S, Petrelli F, Pirillo I, Di Luca NM, Grappasonni I. Fighting obesity in children from European world health organization member states. Epidemiological data, medicalsocial aspects, and prevention programs. *Clin Ter.* (2019) 170:e223–30. doi: 10.7417/CT.2019.2137

17. Alessandri AJ. Parents know best: Or do they? Treatment refusals in paediatric oncology. *J Paediatr Child Health.* (2011) 47:628–31. doi: 10.1111/j.1440-1754.2011.02170.x

18. Hein IM, Troost PW, Lindeboom R, Benninga MA, Zwaan. C Michel, Van Goudoever JB, et al. Accuracy of the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) for measuring children's competence to consent to clinical research. *JAMA Pediatr*. (2014) 168:1147–53. doi: 10.1001/jamapediatrics.2014.1694

19. Miller VA, Drotar D, Kodish E. Children's competence for assent and consent: A review of empirical findings. *Ethics Behav*. (2004) 14:255–95. doi: 10.1207/s15327019eb1403_3

20. Coyne I, O'Mathúna DP, Gibson F, Shields L, Leclercq E, Sheaf G. Interventions for promoting participation in shared decision-making for children with cancer. *Cochrane Database Syst Rev*. (2016) 11:CD008970. doi: 10.1002/14651858.CD008970.pub3

21. Fisher CB, Puri LI, Macapagal K, Feuerstahler L, Ahn JR, Mustanski B. Competence to consent to oral and injectable PrEP trials among adolescent males who have sex with males. *AIDS Behav*. (2021) 25:1606–18. doi: 10.1007/s10461-020-03077-9

22. Ruhe KM, Wangmo T, Badarau DO, Elger BS, Niggli F. Decision-making capacity of children and adolescents–suggestions for advancing the concept's implementation in pediatric healthcare. *Eur J Pediatr*. (2015) 174:775–82. doi: 10.1007/s00431-014-2462-8

23. Ferorelli D, Spagnolo L, Marrone M, Corradi S, Silvestre M, Misceo F, et al. Off-label use of COVID-19 vaccines from ethical issues to medico-legal aspects: an italian perspective. *Vaccines*. (2021) 9:423. doi: 10.3390/vaccines9050423

24. Morgan L, Schwartz JL, Sisti DA. COVID-19 Vaccination of minors without parental consent: respecting emerging autonomy and advancing public health. *JAMA Pediatr*. (2021) 175:995–6. doi: 10.1001/jamapediatrics.2021.1855

25. Committee on Hospital Care. Family-centered care and the pediatrician's role. *Pediatrics*. (2003) 112:691–7. doi: 10.1542/peds.112.3.691

26. Kaufmann J, Laschat M, Wappler F. Medikamentenfehler bei Kindernotfällen. *Dtsch Arztebl Int*. (2012) 109:609–16. doi: 10.3238/arztebl.2012.0609

27. Mueller BU, Neuspiel DR, Stucky Fisher ER, Franklin W, Adirim CT, Bundy DG, et al. Principles of pediatric patient safety: Reducing harm due to medical care. *Pediatrics*. (2019) 143:e20183649. doi: 10.1542/peds.2018-3649

28. Pilla A Di, Specchia ML, Perilli A, Tofani N, Carini E, Ricciardi W, et al. Impact of clinical risk management in pediatric intensive care units: a systematic review. *Eur J Public Health*. (2020) 30:ckaa165-603. doi: 10.1093/eurpub/ckaa165.603

29. Specchia ML, Perilli A, Di Pilla A, Carini E, Tofani N, Ricciardi W, et al. The impact of the implementation of clinical risk management tools in pediatric or neonatal intensive care units: a systematic review. *Ig Sanita Pubbl*. (2020) 76:225–39.

30. Solarino B, Aricò M. Covid-19 pandemic and pediatric healthcare policy in Italy: time for a change. *Pediatr Rep*. (2020) 12:8823. doi: 10.4081/pr.2020.8823

31. Longhi R, Picchi R, Minasi D, Di Cesare Merlone A. Pediatric emergency room activities in Italy: A national survey. *Ital J Pediatr*. (2015) 41:1–8. doi: 10.1186/s13052-015-0184-9

32. Warda L. Is your hospital safe for children? Applying home safety principles to the hospital setting. *Paediatr Child Health*. (2004) 9:331–4.

33. Pasquali SK, Hall M, Slonim AD, Jenkins KJ, Marino BS, Cohen MS, et al. Off-label use of cardiovascular medications in children hospitalized with congenital and acquired heart disease. *Circ Cardiovasc Qual Outcomes*. (2008) 1:74–83. doi: 10.1161/CIRCOUTCOMES.108.787176

34. Lanphier E, Fyfe S. Pediatric Off-Label Use of Covid-19 Vaccines: Ethical and Legal Considerations. *Hastings Cent Rep*. (2021) 51:27–32. doi: 10.1002/hast.1296

35. Linden-Lahti C, Holmström A-R, Pennanen P, Airaksinen M. Facilitators and barriers in implementing medication safety practices across hospitals within 11 European Union countries. *Pharm Pract (Granada)*. (2019) 17:1583. doi: 10.18549/PharmPract.2019.4.1583

36. Tricarico P, Castriotta L, Battistella C, Bellomo F, Cattani G, Grillone L, et al. Professional attitudes toward incident reporting: can we measure and compare improvements in patient safety culture? *Int J Qual Heal Care*. (2017) 29:243–9. doi: 10.1093/intqhc/mzx004

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 20 September 2022
DOI 10.3389/fpubh.2022.968286

OPEN ACCESS

EDITED BY
Sreekanth Kumar Mallineni,
Majmaah University, Saudi Arabia

REVIEWED BY
Davide Ferorelli,
University of Bari Medical School, Italy
Marcello Benevento,
University of Bari Aldo Moro, Italy

*CORRESPONDENCE
Chiara Siodambro
chiara.siodambro@gmail.com

†These authors have contributed equally to this work and share first authorship

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

RECEIVED 13 June 2022
ACCEPTED 30 August 2022
PUBLISHED 20 September 2022

CITATION
Aulino G, Beccia F, Rega M, Siodambro C, Capece G, Boccia S, Lanzone A and Oliva A (2022) Child maltreatment and management of pediatric patients during COVID-19 pandemic: Knowledge, awareness, and attitudes among students of medicine and surgery. A survey-based analysis. *Front. Public Health* 10:968286. doi: 10.3389/fpubh.2022.968286

Child maltreatment and management of pediatric patients during COVID-19 pandemic: Knowledge, awareness, and attitudes among students of medicine and surgery. A survey-based analysis

Giovanni Aulino[1†], Flavia Beccia[2†], Michele Rega[1], Chiara Siodambro[1*], Giuseppe Capece[3], Stefania Boccia[2,4], Antonio Lanzone[5] and Antonio Oliva[1]

[1]Department of Health Surveillance and Bioethics, Section of Legal Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica Del Sacro Cuore, Rome, Italy, [2]Section of Hygiene, University Department of Life Sciences and Public Health, Università Cattolica del Sacro Cuore, Rome, Italy, [3]Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [4]Department of Woman and Child Health and Public Health—Public Health Area, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [5]Unit of Obstetrics and Obstetric Pathology, Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Purpose of the study: To assess perception, awareness, and attitudes regarding the medico-legal relevance of child maltreatment and management of pediatric patients during the COVID-19 pandemic in a cohort of medicine and surgery students, with a particular focus on child safety and maltreatment.

Methods: A cross-sectional, web-based survey was conducted through an anonymous questionnaire on the personal websites of Università Cattolica del Sacro Cuore medical students.

Results: The study included 1,166 participants, the majority of whom were experienced with child maltreatment and defensive medicine; only a small percentage was aware of the government's efforts to prevent child maltreatment and safeguard vaccination physicians. Moreover, there was no agreement on the use of telemedicine for non-serious pediatric patients or on the consequences it might have on their health. Finally, the detrimental impacts of lockdown on children's mental health are a major worry.

Conclusions: Knowledge of these themes is mainly implemented by deepening these concepts during the undergraduate studies since a high level of knowledge on child maltreatment and on the management of COVID-19

pandemic was significantly associated with clinical years of course. Specific seminars analyzing telemedicine and legislative protections concerning minors and those concerning vaccination doctors should be included in the study plan to raise awareness these concepts.

KEYWORDS

child maltreatment, child safety, medical liability, medical education, telemedicine, COVID-19, survey

Introduction

The first coronavirus disease (COVID-19) outbreak was announced at the end of December 2019 in Wuhan, China. The virus soon spread globally, and, for this reason, the World Health Organization declared a state of pandemic (1).

The first country that was affected in Europe was Italy. On January 31, 2020, the Italian government declared the state of emergency and established a number of measures aimed at limiting the spread of the virus.

The first nationwide lockdown was imposed on March 3, 2020, following the isolation of the first affected municipalities. Restrictions were implemented based on the regional spread of the virus until March 31, 2022 (2–4).

Many concerns have been raised about how these measures, particularly the lockdown, may affect the health, especially the mental health, of the most vulnerable individuals, including children.

Governments have taken steps to lessen the economic effects of the COVID-19 pandemic, but there has not been an adequate response to reduce domestic violence, child abuse and mental health deterioration (5). Added to this is the impact on the mental health of healthcare professionals who have been on the frontline during the pandemic and the constant risk of professional liability (6).

Doctors and medical and surgical students are probably ill-equipped to deal with the pandemic's effects on children's mental health and physician professional responsibility in the coming years.

For these reasons, the aim of this study was to assess how a cohort of medical students perceived, were aware of, and felt about the medico-legal relevance of these themes in the context of the COVID-19 pandemic, with a focus on child abuse and the treatment of pediatric patients.

Materials and methods

Study design and participants

A cross-sectional, web-based survey was conducted during May 2022, in the period immediately following the end of the State of Emergency. Through outlook form, an anonymous questionnaire was administered on the personal websites of medical students attending the undergraduate course at the Università Cattolica del Sacro Cuore. As this survey was addressed to medical students, the study was based on a non-probability, voluntary sample. Participation was voluntary and unpaid.

Questionnaire design

The questionnaire (see Supplementary File 1) consisted of various sections covering the following aspects: demographic data (gender, age, course year and region of origin), knowledge and awareness of child maltreatment and, finally, the aspects of patient management during the COVID-19 pandemic. In total, the questionnaire comprised 23 questions. Students were asked to answer the questions using both binary answers and a 5-point Likert scale.

Validation of the questionnaire

To further improve the study's quality, a two-step external validation process was used. First, a heterogeneous team of students and professors from various disciplines conducted cognitive pretesting on a small sample size of 8, and then a larger cohort of 50 medical students from the course of medicine and surgery underwent pilot testing (7, 8).

Statistical analyses

The reliability of the scales was measured using the Cronbach's alpha coefficient. Using 1,000 boot-strap samples, the 95% confidence interval (CI) for each alpha value was estimated. All variables were then subjected to descriptive analyses.

Using multivariable logistic regression models, factors of knowledge and awareness on the two issues of concern (management of the COVID-19 pandemic and child abuse) were analyzed. The two tiers of the two demographic variables—region of residence and year of course—were combined from the original numerous categories.

10.3389/fpubh.2022.968286

TABLE 1 Number of responses per course year.

Course year	Number of answers	Total number of students	Percent (%)
1	152	299	50.83
2	152	295	51.53
3	187	269	69.52
4	189	270	70
5	249	286	87.06
6	237	414	57.25
Total	1,166	1,833	63.61

Regions were recoded into Center-North and South and Islands and year of course was recoded into preclinical years (1–4) and clinical ones (5 and 6). Respondents were judged to have a high degree of expertise when they correctly answered 75% of the included questions. Only dichotomic questions were included. Age, gender, course year, and region of residence were all covariates that were accounted for in the models. Multivariable logistic regression models were built using the Hosmer and Lemeshow method (9).

Each variable underwent univariable analysis using the proper statistical test (logistic regression model), and when the p-value was <0.15, it was added to the multivariable logistic model.

The influence of the independent variables on each binary outcome investigated was expressed as odds ratios (OR) and 95% confidence interval (CI).

All statistical analyses were performed using Stata software, version 14 (StataCorp LP, College Station, TX).

Ethical considerations

To participate, students had to give their informed consent. The study protocol was approved by the Ethics Committee of the Policlinico Universitario A. Gemelli IRCCS.

Results

Participants' demographic

Out of a total of 1,833 students, 1,183 questionnaires (64.54%) were collected. Seventeen of the latter were excluded because they did not provide informed consent or had incomplete information. Thus, 1,166 (98.56%) questionnaires were included in our results.

Table 1 provides a description of the response rate divided by course year. In general, a higher response rate was observed in the last 3 years compared to the first.

General characteristics of students

Table 2 provides information on the demographic characteristics of the participants. The median age of participants was 23.04 years (IQR 22–24), and females accounted for 52.74% of the total. Around 42% of the respondents attended the 5th and 6th year of course (21.36 and 20.33%, respectively). Most students were resident in Southern Italy (62.35%) and the most representative regions were Apulia, Latium, and Campania (23.41, 21.96, and 18.01% respectively) (Figure 1).

Focus on child maltreatment

The majority of students (52.06%) were familiar with child maltreatment situations; in addition, there was a strong concern among them that both the number of occurrences of child abuse has grown since the pandemic and that it may continue to rise (94.94 and 89.97%, respectively).

Contrarily, few students were aware of the government's initiatives to reduce this phenomenon (11.66%).

All students agreed on the fact that health professionals must be adequately prepared to recognize child maltreatment cases and, the majority of them believe it is advisable to further their training on this subject during their studies (100 and 88.68%, respectively).

Finally, the majority of them concurred that social distancing and lockdown have had harmful effects on children's mental health or would in the future (agree 33.28%; strongly agree 42.11%).

Management of pediatric patients during COVID-19 pandemic

The majority of students were familiar with the concept of defensive medicine (73.76%); of the latter, approximately 78% agreed on the fact that pediatricians tend to be more prone to defensive medicine (agree: 54.19%; strongly agree: 23.60%) and that pediatric patients expose pediatricians to increased use of defensive medicine (81.28%).

Only 43.65% were aware of government measures to protect vaccine doctors, despite the fact that many believed measures should be implemented, and the majority of them are concerned because they believe there will be an increase in medical-legal litigation cases as a result of the pandemic (80.45 and 79.25%, respectively).

With regard to vaccination, many agreed that it should also be extended to pediatric patients (agree: 33.05%; strongly agree: 39.66%), though a minority agreed that parents should be adequately informed on the benefits, risks, and side effects of vaccines (agree: 26.61%; strongly agree: 13.99%).

10.3389/fpubh.2022.968286

TABLE 2 Student responses to the questionnaire administered.

Variable	Category	Number	Percent (%)
General characteristics of students			
Age	Median 23.04 (S.D. 1.80, IQR 22–24)		
Gender	Male	551	47.26
	Female	615	52.74
Year of course	1	152	13.04
	2	152	13.04
	3	187	16.04
	4	189	16.21
	5	249	21.36
	6	237	20.33
Area of origin	Southern regions	654	56.09
	Center regions	313	26.85
	Islands	107	9.19
	Northern regions	92	7.9
Area of residence	Center-North	439	37.65
	South and Islands	727	62.35
Focus on child maltreatment			
Knowledge of child maltreatment situations	Yes	607	52.06
	No	559	47.94
Knowledge about the increase in child maltreatment cases during the pandemic	Yes	1,107	94.94
	No	59	5.06
Expecting an increase of child maltreatment cases in the future	Yes	1,049	89.97
	No	117	10.03
Knowledge of government measures issued child maltreatment	Yes	136	11.66
	No	1,030	88.34
Adequate preparation of health professionals regarding child maltreatment	Yes	1,166	100
	No	0	0
Under-graduate training on concepts related to child maltreatment during undergraduate studies	Yes	1,034	88.68
	No	132	11.32
Lockdown and social distancing have had, or will have in the future, consequences on children's mental health	Strongly disagree	0	0
	Disagree	19	1.63
	Neutral	268	22.98
	Agree	388	33.28
	Strongly agree	491	42.11
Focus on management of pediatric patients during COVID-19 pandemic			
Knowledge of the concept of defensive medicine	Yes	860	73.76
	No	306	26.24
Pediatricians are more prone to defensive medicine	Strongly disagree	5	0.58
	Disagree	66	7.67
	Neutral	120	13.95
	Agree	466	54.19
	Strongly agree	203	23.60
Increased use of defensive medicine due to the pandemic	Yes	699	81.28
	No	161	18.72
Knowledge of the government's measures to protect vaccine doctors	Yes	509	43.65

(Continued)

10.3389/fpubh.2022.968286

TABLE 2 (Continued)

Variable	Category	Number	Percent (%)
	No	657	56.35
Implementation of protections for frontline and vaccination doctors	Yes	938	80.45
	No	228	19.55
Increase in medical-legal litigation	Yes	924	79.25
	No	242	20.75
Extension of vaccination to the pediatric population	Strongly disagree	0	0
	Disagree	23	1.97
	Neutral	295	25.32
	Agree	386	33.05
	Strongly agree	462	39.66
The government provided adequate information to parents about COVID-19 vaccination	Strongly disagree	48	4.12
	Disagree	239	20.52
	Neutral	405	34.76
	Agree	311	26.61
	Strongly agree	163	13.99
Telemedicine should be used in the management of all non-serious patients, including pediatric patients	Strongly disagree	48	4.12
	Disagree	216	18.52
	Neutral	391	33.53
	Agree	344	29.50
	Strongly agree	167	14.32
Management of non-serious patients using telemedicine has had or will have negative effects on their health	Strongly disagree	135	11.58
	Disagree	306	26.24
	Neutral	312	26.76
	Agree	326	27.96
	Strongly agree	87	7.46
Hospital policies have been adapted to the management of pediatric patients	Strongly disagree	0	0
	Disagree	42	3.61
	Neutral	357	30.56
	Agree	393	33.73
	Strongly agree	374	32.10
Intra-hospital isolation measures taken during the pandemic have had negative effects on children's mental health, or will have in the future	Strongly disagree	1	0.09
	Disagree	25	2.14
	Neutral	280	24.01
	Agree	420	36.02
	Strongly agree	440	37.74

Moreover, there was no agreement neither on the use of telemedicine for non-serious pediatric patients nor on the consequences it might have on their health.

Finally, although many of them agreed on the hospital management of pediatric patients during the pandemic (agree: 33.73%; strongly agree: 32.10%) many of them thought that such measures have had negative effects on children's mental health or will have in the future (agree: 36.02%; strongly agree: 37.74%).

Multivariable analysis

Table 3 summarizes the results of the multivariable analysis.

A high level on knowledge on child maltreatment was significantly associated with the age of respondents ($p < 0.0001$), female gender ($p = 0.00$), clinical years of course ($p < 0.001$) and Southern regions of origin ($p = 0.061$). Testing the significant covariates in the regression, only the covariate on year of course remained statistically significant ($p < 0.0001$, adjusted OR 2.86 CI 95% [1.98–4.13]).

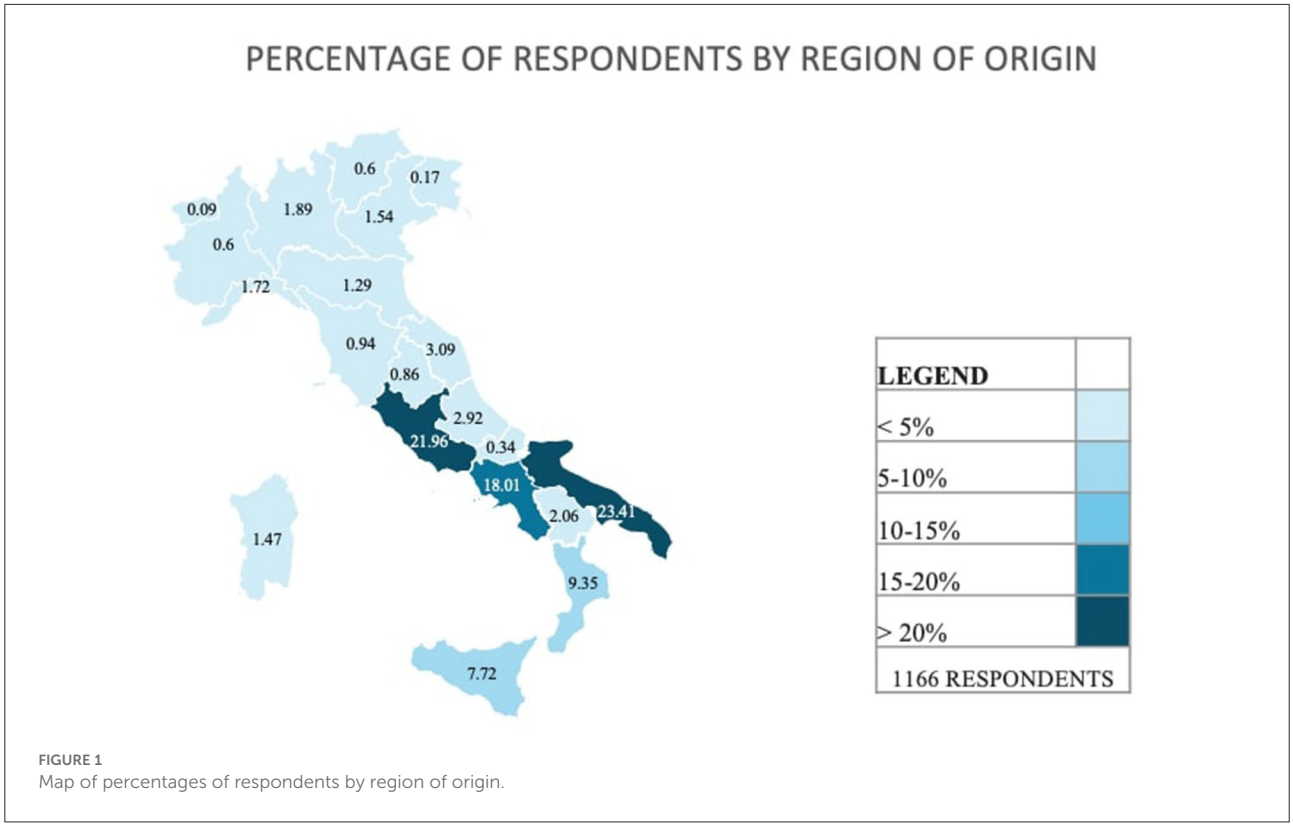


FIGURE 1
Map of percentages of respondents by region of origin.

A high level of knowledge on the management of COVID-19 pandemic was significantly associated with the age ($p < 0.001$), clinical years of course ($p < 0.0001$) and knowledge on child maltreatment ($p < 0.001$). Testing the significant covariates altogether, age and clinical years of course remained significant ($p < 0.001$ adjusted OR 1.33 CI 95% [1.20–1.47] and $p < 0.02$ adjusted OR 1.54 CI 95% [1.07–2.22] respectively).

Discussion

According to our findings, the majority of students are familiar with child maltreatment situations; additionally, furthermore, there is a strong concern among them both that cases have increased during the pandemic, and that they may increase in the future.

These results are consistent with earlier studies that showed how the COVID-19 pandemic has amplified dangerous conditions for children, families, and communities worldwide, despite the fact that no studies have ever been conducted to assess the perception of child maltreatment among undergraduate medical students (10–14).

However, it is important to emphasize that, in contrast to research done in the pre-pandemic period, medical students are more familiar with this topic, and that this knowledge is mostly tied to the year of the course to which they belong (15–17).

Indeed, after evaluating the significant variables in the regression, only the covariate on course year remained statistically significant on awareness of child maltreatment. These findings might be the fact that in the fifth and sixth years of the program, both the forensic medicine and pediatrics courses examine the risk factors of child abuse. Finally, students agree that these topics should both be known by all healthcare professionals and explored in depth during undergraduate studies.

For these reasons, we are convinced that additional seminars analyzing these topics from both a clinical and a medico-legal point of view during the degree course could be beneficial (18).

Regarding management of pediatric patients during the COVID-19 pandemic, most students that were familiar with the concept of defensive medicine agreed that pediatric patients expose pediatricians to an increased use of defensive medicine. In this regard, several studies have shown an increased risk of using defensive medicine to avoid the risk of medico-legal litigation among physicians; parental worry and anxiety, even for conditions that could be managed at home, may be the major contributing factors when dealing with pediatric patients. In such cases, unnecessary tests are also carried out with the aim of preventing the risk of complaints. It is important to acknowledge that even students, due to a lack of faith in insurance coverage, believe that defensive medicine

TABLE 3 Knowledge and attitudes on child maltreatment and management of pediatric patients during COVID-19 pandemic (adjusted *OR*, Odds Ratio; *CI*, 95% confidence interval).

		Child maltreatment		OR (IC)	OR adjusted (IC)
		No (%)	Yes (%)		
Gender	Male	257 (46.6)	294 (53.3)	–	
	Female	334 (54.3)	281 (45.7)	0.73 (0.58–0.92)	
Age		23 (22–24)	24 (22–25)	1.25 (1.17–1.33)	
Year of course	1–4	420 (61.8)	260 (38.2)	–	
	5–6	171 (35.2)	315 (64.8)	2.97 (2.33–3.79)	2.86 (1.98–4.13)
Area of residence	Center-North	238 (54.2)	201 (45.8)	–	
	South and Island	353 (48.6)	374 (51.4)	1.25 (0.98–1.59)	
		Management of pediatric patients during COVID-19 pandemic		**OR (IC)**	**OR adjusted (IC)**
		No (%)	**Yes (%)**		
Gender	Male	252 (45.7)	299 (54.3)	–	
	Female	304 (49.4)	311 (50.6)	0.86 (0.68–1.08)	
Age		22 (21–24)	24 (22–25)	1.47 (1.37–1.58)	1.33 (1.20–1.47)
Year of course	1–4	408 (60)	272 (40)	–	
	5–6	148 (30.4)	338 (69.6)	3.42 (2.67–4.38)	1.54 (1.07–2.22)
Area of residence	Center-North	213 (48.5)	226 (51.5)	–	
	South and Island	343 (47.2)	384 (52.8)	1.05 (0.83–1.33)	
Knowledge on child maltreatment	No	316 (53.5)	275 (46.5)	–	
	Yes	240 (41.7)	335 (58.3)	1.60 (1.27–2.02)	

could be a solution when dealing with pediatric patients; indeed, the lack of confidence in insurance coverage was identified as a key predictor of defensive medicine practice itself (19, 20).

On the other hand, some authors have demonstrated a greater rate of appropriateness of imaging studies during the pandemic, via a decrease in imaging investigations without evidence of bone fractures, thus implying a reduction in the use of defensive medicine (21).

In agreement with earlier research, many physicians, including vaccination doctors, are concerned about the rise in medical-legal lawsuits brought on by the epidemic (6).

This may also help explain why many physicians believe that the government's regulations for vaccination physicians should be enacted even if only a small percentage of people are aware of them (22).

A critical aspect also emerged from this survey: the lack of awareness of the legislative protections around the use of telemedicine for pediatric patients. In fact, there was no consensus about either the use for pediatric patients who weren't in a life-threatening situation or the potential effects on their health. This lack of agreement could be due to several factors, including the lack of understanding of the concept of telemedicine and the possibility that those from lower socioeconomic groups won't have access to treatment, leading to an increase in disparities (23).

In addition to this is the fact that legal issues may arise with informed consent, authorization, and accreditation profiles to the protection of patients' personal data; thus, as suggested by some authors, there is a need for governments to further develop legislations to ensure the safety of patients managed through the use of telemedicine (24, 25). Finally, a strong concern about the present and future impact of the lockdown and intra-hospital isolation measures on children's mental health emerged from the study. This strong concern is supported by evidence from the worldwide literature in addition to being perhaps related to how the lockdown affected students' mental health.

In fact, on the one hand, Nearchou et al. demonstrated how COVID-19 has had a negative impact on young people's mental health, which is primarily characterized by depression and anxiety, on the other hand, Villani et al., in a study aimed at assessing the psychological impact of the pandemic on undergraduate students, showed that 35.33% of University students had symptoms of

anxiety and 72.93% of depression, although with mild symptoms (26–28).

For these reasons, it could be beneficial to establish as many mental health support services oriented on offering measures for supporting healthy coping mechanisms throughout the current crisis as possible. The strengths and weaknesses of this study must be taken into account. Because enrollment is restricted to a single University, it is possible that it may not be accurately representative of the medical and surgical student population in Italy. This study, however, is the first to examine the perceptions, understanding of, and attitudes of medicine and surgery students toward themes of medico-legal importance in the context of the COVID-19 epidemic, with an emphasis on child safety and child maltreatment. It could offer a practical instrument to approach these subjects in training sessions and educational initiatives.

Conclusions

Our study showed that medicine and surgery students are familiar with the concepts of child maltreatment, child safety, and medical liability regarding the management of pediatric patients during COVID-19 pandemic.

This knowledge is mainly implemented by deepening these concepts during the undergraduate studies since a high level of knowledge on child maltreatment and on the management of COVID-19 pandemic was significantly associated with clinical years of course.

In addition, low level of knowledge of telemedicine, legislative protections concerning minors, and those concerning vaccination doctors emerged.

For these reasons, we believe that specific seminars analyzing these concepts should be included in the study plan, as well as multidisciplinary seminars held by forensic scientists, pediatricians, and social workers in order to raise awareness on the phenomenon of child maltreatment also among "future doctors".

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 Ethics Committee of the Policlinico Universitario A. Gemelli IRCCS. The patients/participants provided their written informed consent to participate in this study.

Author contributions

GA and AO designed, conducted, and wrote the paper. FB conducted part of the statistical part of the article. All authors reviewed and approved the draft of the manuscript and ensured the accuracy and integrity of the work before submission. All authors contributed to the article and approved the submitted version.

Funding

Funds were from Linea D1, Università Cattolica del Sacro Cuore (recipient: AO).

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

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.968286/full#supplementary-material

References

1. WHO (World Health Organization). *Coronavirus Disease (COVID-2019) Situation Reports*. Available online at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/ (accessed March 11, 2020).

2. Gazzetta ufficiale della Repubblica Italiana. *Decreto Legge 23 Febbraio 2020 N. 6*. Available online at: https://www.gazzettaufficiale.it/eli/gu/2020/02/23/45/sg/pdf (accessed February 23, 2020).

3. Gazzetta ufficiale della Repubblica Italiana. *Decreto del Presidente del Consiglio dei Ministri 11 Marzo 2020*. Available online at: https://www.gazzettaufficiale.it/eli/id/2020/03/11/20A01605/sg (accessed March 11, 2020).

4. Gazzetta ufficiale della Repubblica Italiana. *Decreto Legge 16 Maggio 2020, N. 33*. Available online at: https://www.gazzettaufficiale.it/eli/id/2020/07/15/20A03813/sg (accessed May 16, 2020).

5. Davison CM, Thanabalasingam SJ, Purkey EM, Bayoumi I. Child maltreatment and public health: do gaps in response during the COVID-19 pandemic highlight jurisdictional complexities? *Int J Environ Res Public Health.* (2021) 13:6851. doi: 10.3390/ijerph18136851

6. Oliva A, Caputo M, Grassi S, Vetrugno G, Marazza M, Ponzanelli G, et al. Liability of health care professionals and institutions during COVID-19 pandemic in Italy: symposium proceedings and position statement. *J Patient Saf.* (2020) 4:e299–302. doi: 10.1097/PTS.0000000000000793

7. Lenzner T, Neuert C, Otto W. *Cognitive Pretesting*. (2016). GESIS Surv Guidelines. GESIS Surv.

8. Hassan ZA, Schattner P, Mazza D. Doing a pilot study: why is it essential? *Malays Fam Physician.* (2006) 2–3:70–3.

9. Hosmer DW, Lemeshow S. *Applied Logistic Regression 2nd ed*. New York, NY: Wiley (2000). doi: 10.1002/0471722146

10. Katz C. What happened to the prevention of child maltreatment during COVID-19? A yearlong into the pandemic reflection. *Int J Child Maltreat.* (2021) 28:1–8. doi: 10.1007/s42448-021-00076-8

11. Lawson M, Piel MH, Simon M. Child maltreatment during the COVID-19 pandemic: consequences of parental job loss on psychological and physical abuse towards children. *Child Abuse Negl.* (2020) 110:104709. doi: 10.1016/j.chiabu.2020.104709

12. Griffith AK. Parental burnout and child maltreatment during the COVID-19 pandemic. *J Fam Violence.* (2020) 5:1–7. doi: 10.1007/s10896-020-00172-2

13. Rapoport E, Reisert H, Schoeman E, Adesman A. Reporting of child maltreatment during the SARS-CoV-2 pandemic in New York City from March to May 2020. *Child Abuse Negl.* (2021) 116:104719. doi: 10.1016/j.chiabu.2020.104719

14. Humphreys KL, Myint MT, Zeanah CH. Increased risk for family violence during the COVID-19 pandemic. *Pediatrics.* (2020) 1:e20200982. doi: 10.1542/peds.2020-0982

15. Saeed N, Sultan EA, Salama N, Galal M, Ghanem M. Child maltreatment: knowledge, attitudes and reporting behaviour of physicians in teaching hospitals, Egypt. *East Mediterr Health J.* (2021) 3:250–9. doi: 10.26719/emhj.20.126

16. Poreddi V, Pashapu DR, Kathyayani BV, Gandhi S, El-Arousy W, Math SB. Nursing students' knowledge of child abuse and neglect in India. *Br J Nurs.* (2016) 5:264–8. doi: 10.12968/bjon.2016.25.5.264

17. Li X, Yue Q, Wang S, Wang H, Jiang J, Gong L, et al. Knowledge, attitudes, and behaviours of healthcare professionals regarding child maltreatment in China. *Child Care Health Dev.* (2017) 6:869–75. doi: 10.1111/cch.12503

18. Weegar K, Romano E. Child maltreatment knowledge and responses among teachers: a training needs assessment. *School Mental Health.* (2019) 11:741–753 doi: 10.1007/s12310-019-09317-1

19. Studdert DM, Mello MM, Sage WM, DesRoches CM, Peugh J, Zapert K, et al. Defensive medicine among high-risk specialist physicians in a volatile malpractice environment. *JAMA.* (2005) 21:2609–17. doi: 10.1001/jama.293.21.2609

20. Studdert DM, Mello MM, Brennan TA. Medical malpractice. *N Engl J Med.* (2004) 3:283–92. doi: 10.1056/NEJMhpr035470

21. Bottari G, Stellacci G, Ferorelli D. Dell'Erba A, Aricò M, Benevento M, et al. Imaging appropriateness in pediatric radiology during COVID-19 pandemic: a retrospective comparison with no COVID-19 period. *Children.* (2021) 6:463. doi: 10.3390/children8060463

22. Beccia F, Amantea C, Rossi MF, Daniele A, Santoro PE, Borrelli I, et al. Responsabilità medico-legale del medico vaccinatore [Legal resposability of vaccinating doctor]. *G Ital Med Lav Ergon.* (2021) 2:93–8.

23. Katzow MW, Steinway C, Jan S. Telemedicine and health disparities during COVID-19. *Pediatrics.* (2020) 2:e20201586. doi: 10.1542/peds.2020-1586

24. Ferorelli D, Nardelli L, Spagnolo L, Corradi S, Silvestre M, Misceo F, et al. Medical legal aspects of telemedicine in Italy: application fields, professional liability and focus on care services during the COVID-19 health emergency. *J Prim Care Community Health.* (2020) 11:2150132720985055. doi: 10.1177/2150132720985055

25. De Micco F, Fineschi V, Banfi G, Frati P, Oliva A, Travaini GV, et al. From COVID-19 pandemic to patient safety: a new "Spring" for telemedicine or a Boomerang effect? *Front Med.* (2022) 9:901788. doi: 10.3389/fmed.2022.901788

26. Singh S, Roy D, Sinha K, Parveen S, Sharma G, Joshi G. Impact of COVID-19 and lockdown on mental health of children and adolescents: a narrative review with recommendations. *Psychiatry Res.* (2020) 293:113429. doi: 10.1016/j.psychres.2020.113429

27. Nearchou F, Flinn C, Niland R, Subramaniam SS, Hennessy E. Exploring the impact of COVID-19 on mental health outcomes in children and adolescents: a systematic review. *Int J Environ Res Public Health.* (2020) 22:8479. doi: 10.3390/ijerph17228479

28. Villani L, Pastorino R, Molinari E, Anelli F, Ricciardi W, Graffigna G, et al. Impact of the COVID-19 pandemic on psychological well-being of students in an Italian university: a web-based cross-sectional survey. *Global Health.* (2021) 1:39. doi: 10.1186/s12992-021-00680-w

frontiers | Frontiers in Pediatrics

TYPE Original Research
PUBLISHED 05 October 2022
DOI 10.3389/fped.2022.949922

OPEN ACCESS

EDITED BY
Joemer Maravilla,
The University of Queensland, Australia

REVIEWED BY
Antonina Argo,
University of Palermo, Italy
Tudor Lucian Pop,
Iuliu Haţieganu University of Medicine and Pharmacy, Romania

*CORRESPONDENCE
Ilenia Bianchi
ilenia.bianchi@unifi.it

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

RECEIVED 21 May 2022
ACCEPTED 16 September 2022
PUBLISHED 05 October 2022

CITATION
Focardi M, Grassi S, Raddi S, Rosati ME, Cazzato F, D'Onofrio P, Doretti V, Bianchi I, Vetrugno G, Oliva A and Pinchi V (2022) Trend in 167 cases of minors witnessing violence: The role played by COVID-19 pandemic. Front. Pediatr. 10:949922. doi: 10.3389/fped.2022.949922

Trend in 167 cases of minors witnessing violence: The role played by COVID-19 pandemic

Martina Focardi[1†], Simone Grassi[1†], Silvia Raddi[1], Maria Elena Rosati[1], Francesca Cazzato[2], Paola D'Onofrio[3], Vittoria Doretti[4], Ilenia Bianchi[1,5*], Giuseppe Vetrugno[2], Antonio Oliva[2] and Vilma Pinchi[1]

[1]Department of Health Science, University of Florence, Florence, Italy, [2]Legal Medicine, Department of Health Surveillance and Bioethics, Università Cattolica del Sacro Cuore, Rome, Italy, [3]Responsible for the Unit of the Rose Code, Area of Emergency Rooms of Careggi Hospital, Florence, Italy, [4]Head of Department Health Promotion and Health Ethics, Azienda USL Toscana Sud Est, Careggi Hospital, Florence, Italy, [5]Department of Law, University of Macerata, Macerata, Italy

Background: There currently is no evidence that COVID-19 has had an impact on the rates of psychological abuses occurring when a minor witnesses interpersonal violence.

Aim: Our aim was to describe the accesses of the last four years to the Emergency Department of a tertiary hospital (Careggi University Hospital—Florence, Italy) due to this issue and then to evaluate whether the COVID-19 has had an impact on this trend.

Methods: We collected data regarding cases of abuse in which at least a minor had reportedly witnessed the event. Medical records stored between January 1, 2018 to January 1, 2022 were analyzed, extracting sex, age and nationality of the victim; sex of the perpetrator and relationship with the victim; known previous episodes of abuse in the medical history of the victim; setting of the abuse (domestic vs. non-domestic); type of abuse (physical, psychological, sexual); whether the perpetrator was under the influence of alcohol/drugs; whether the victim was hospitalized; prognosis of the victim; number, relation with the victim and involvement in the abuse (as co-victim) of the minor(s) who witnessed the abuse.

Results: A total of 167 eligible cases were registered. 69% of victims had previous episodes of abuse. The perpetrators were all known and mainly males (96%).The abuses were mainly domestic (79%). In 74% of the cases only a type of violence was perpetrated. In 12% of the cases, the minors were also victims of physical abuse. No statistically significant relationships were found between the start of the COVID-19 pandemic and the changes in the number of cases of domestic abuse ($p = 0.07$), physical abuse ($p = 0.62$), psychological abuse ($p = 0.83$) or sexual abuse ($p = 0.88$). However, during the institutional lockdown in Italy (March-May 2022) only two cases occurred – a number that did not allow period-specific statistical inference.

Conclusions: Empowering the hospital policies specifically aimed at identifying and protecting the victims of violence/witnessed violence remains a critical goal from both a public health and medico-legal point of view.

KEYWORDS

abuse, witnessed violence, violence, children, COVID-19

Introduction

Child abuse and domestic violence represent serious public health issues associated with severe long-term physical, social and mental health outcomes along with relevant economic burden (the only cases of child sexual abuse in the United States entail lifetime economic costs for 9.3 billion $) (1–6). There are several kinds of abuse, like physical, psychological and sexual abuse (1, 7).

Witnessing violence is recognized as a form of psychological child abuse (8–11). Indeed, even only the awareness of potential violence between caregivers can be experienced by a minor in an extremely stressful fashion (10). From a legal point of view, in European Union, treaties (Istanbul Convention) and national laws (e.g., in Italy, Law n. 69/2019) recognize minors who witness violence as victims of abuse, stress the importance of combining repression and prevention and regulate mandatory reporting in these cases.

Children who witness violence – especially in case of recurrent episodes –tend to develop impaired attachment to primary caregivers and are exposed to significant physical, social and psychological issues like post-traumatic stress disorder and suicide (1, 2, 12–16). The particular vulnerability of the children is due to their scarce cognitive ability to distinguish between a threat to an adult and a threat to themselves (1).

The adverse outcomes tend to emerge during adolescence, for instance as anti-social/risky behaviors, since the scarce parental attachment and problems in the domain of externalizing (e.g., aggressivity) can lead to violent behaviors and delinquency (9, 17). On the other hand, minors who start to witness violence during adolescence are exposed to risks similar to younger children. Indeed, adolescents can be impaired in their psychological and emotional normal growth, thus being highly exposed to risks of mental and/or physical disturbances or unhealthy/anti-social/risky behaviors like the use of illicit substances (9, 18–23). Moreover, these minors are at risk of becoming authors of interpersonal violence during adulthood (1, 2, 6).

Among the factors that increase the incidence of abuses in a population, there certainly is the occurrence of disasters as a collective and highly stressful situation (7). COVID-19 pandemic is one of the most significant examples of mass disaster in human history, having imposed radical changes to the society and families from social and behavioral points of view (24). In particular, according to several authors, COVID-19 pandemic – and in particular the subsequent institutional lockdowns – has exposed the victims of domestic violence at higher risks, forcing them to remain with their perpetrators and making it difficult for them to access health/mental care facilities (1, 25). Moreover, the pandemic has increased the risk for the minors to witness domestic violence, since the schools' closure (1, 25).

However, Ferrara et al. underlined that, albeit COVID-19 led to an upward trend in domestic violence, very little attention has been paid to the effect of the pandemic on the incidence of minors witnessing domestic abuse (16).

Our aim was to describe the trend of the last four years in the accesses to the Emergency Department of a tertiary hospital (Careggi University Hospital—Florence, Italy) due to abuses in which at least a minor had reportedly witnessed the event and then to evaluate whether the COVID-19 has had an impact on this trend.

Materials and methods

We collected data regarding cases of abuse in which at least a minor had reportedly witnessed the event in the specialized section of the Emergency Department of a tertiary hospital (Careggi University Hospital—Florence, Italy). In particular, when a patient reports abuse at the hospital admission, a specific code is assigned and a specialized medical unit is alerted. In cases of abuses witnessed by minors, the information obtained from the patient is recorded and communicated to the police as required by national law.

Medical records stored between January 1, 2018 to January 1, 2022 were analyzed, extracting in anonymous way these data: sex, age and nationality of the victim; sex of the perpetrator and relationship with the victim; known previous episodes of abuse in the medical history of the victim; setting of the abuse (domestic vs. non-domestic); type of abuse as reported by the victim (physical, psychological, sexual); whether the perpetrator was under the influence of alcohol/drugs; whether the victim was hospitalized; prognosis of the victim; number, relation with the victim and involvement in the abuse (as co-victim) of the minor(s) who witnessed the abuse.

Statistical analysis (Pearson's chi-squared test) was performed to evaluate whether the pandemic has had an impact on the relationship between the primary victim and the perpetrator and on the number of cases of domestic abuse, physical abuse, psychological abuse and sexual abuse. In order to perform it, cases were grouped in four different classes: (A) cases occurred in 2018 and 2019; (B) cases occurred in 2020 and 2021; (C) cases occurred in March-May 2020 (the period of the institutional lockdown in Italy); (D) cases occurred in March-May 2019. Variables were compared between class A and class B and between class C and class D.

A p-value equal to or lower than 0.05 was set as cut-off for statistical significance. The software used for statistical analysis was IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY).

The study was approved by the competent institutional research ethics committee and was performed in accordance with the ethical standards as laid down in the 1964

10.3389/fped.2022.949922

Declaration of Helsinki and its later amendments or comparable ethical standards.

Results

683 cases of abuse in general and 167 victims of abuse witnessed by at least a minor were admitted to the specialized section of the Emergency Department during the study period (Figure 1).

Regarding the primary victims targeted by the perpetrator (Table 1), the 96% (160) of them were females and only the 4% (7) males; only the 1% (2) of them were minors; the 49% (81) were not of Italian nationality. Moreover, the 69% (116) of victims had previous episodes of abuse in their medical history. In 3 out of 167 (2%) cases the victim was hospitalized. The prognosis ranged between 0 and 40 days, with a mean value of 7 days and a median of 6 days.

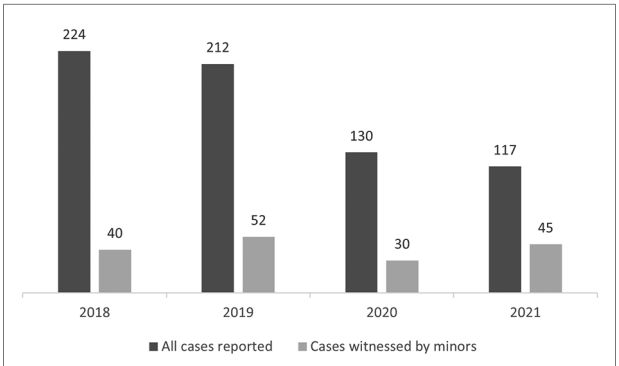


FIGURE 1
Admissions due to abuse in general and to abuse reportedly witnessed by at least a minor.

TABLE 1 Primary victims (Panel A) and perpetrators (Panel B) main characteristics.

Panel A: primary victims		
Sex	Male	96% (160)
	Female	4% (7)
Age	Minor	1% (2)
	Adult	99% (165)
Nationality	Italian	51% (86)
	Others	49% (81)
Previous episodes of abuse	Yes	69% (116)
	No	31% (51)
Hospitalized	Yes	2% (3)
	No	98% (164)
Panel B: perpetrators		
Sex	Male	96% (161)
	Female	4% (6)
Crime committed under alcohol/drug influence	Yes	5% (9)
	No	95% (158)

The perpetrators were all known and mainly of male sex (96%–161%), and only in 9 cases (5%) the perpetrator committed the violence under the influence of alcohol and/or drugs (Table 1).

The perpetrator was the partner at the time of the crime, the former partner, the son, the parent or a relative of the primary victim in, respectively, 117 (70%), 32 (19%), 4 (2%), 4 (2%) and 2 (1%) cases (Figure 2). Regarding these variables, no statistically significant relationship difference between class A and class B ($p = 0.64$).

The abuse was perpetrated more frequently in the domestic setting (132 cases – 79% vs. 35 cases –21%) (Table 2).

In 123 (74%) cases only a type of violence was perpetrated: 114 (68%) cases consisted in physical abuses and 9 (6%) in psychological ones. In the remaining 44 (26%) cases, at least two kinds of abuse co-occurred: in 42 (25%) physical and psychological; in a case physical and sexual; in a case physical, psychological and sexual (Table 2).

In 121 (72%) cases, only a child witnessed the abuse, while in the remaining 46 (28%) cases more children assisted to violence. In 12% (20) of the cases, the minors not only witnessed the violence towards other people but were also primary victims of physical abuse (Table 2).

The minor was a child or a relative of the primary victim, respectively, in 141 (84%) and 5 (3%) cases, and a child of the perpetrator in 2 (1%) cases (Figure 3).

In order to perform statistical analysis, cases were grouped in four different classes, as described in the previous section.

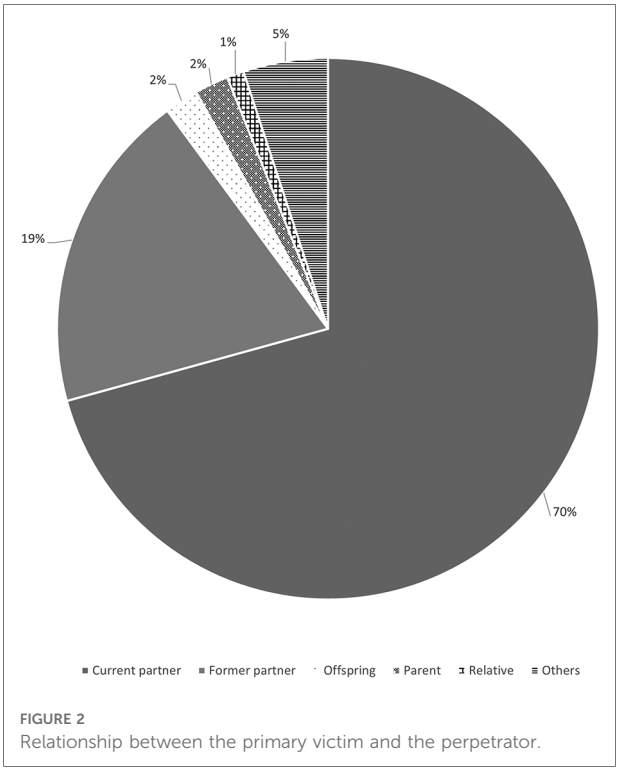


FIGURE 2
Relationship between the primary victim and the perpetrator.

TABLE 2 Abuse circumstances.

Setting	Domestic	79% (132)	
	Others	21% (35)	
Type of violence	Physical	114 (68%)	Total 123 (74%)
	Psychological	9 (6%)	
	Physical and psychological	42 (25%)	Total 44 (26%)
	Physical and sexual	1 (0.5%)	
	Physical, psychological and Sexual	1 (0.5%)	
How many minors witnessed	Only one	121 (72%)	
	More than one	46 (28%)	
Child both witnessed and primary victims		20 (12%)	

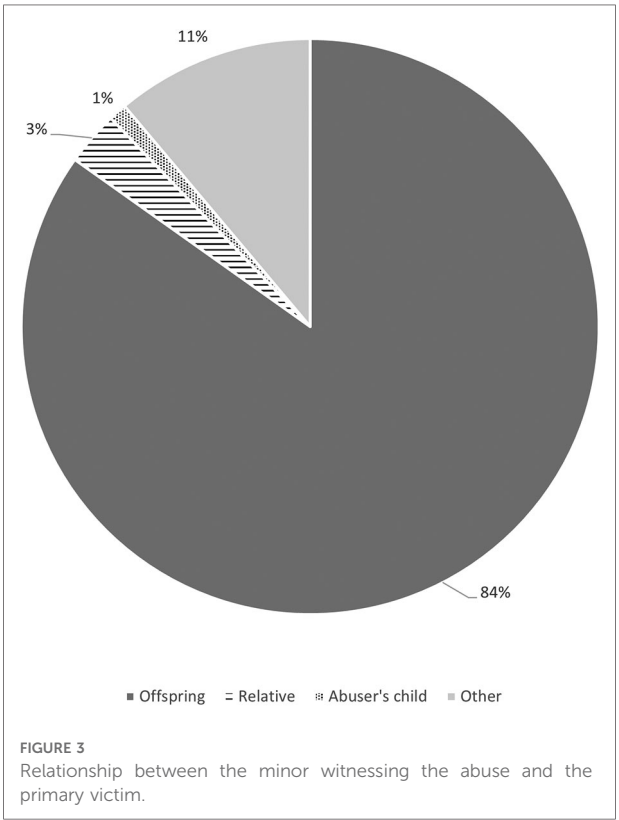


FIGURE 3
Relationship between the minor witnessing the abuse and the primary victim.

First, statistical analysis was performed comparing class A and class B (**Table 3**).

Class A consisted in 92 cases, of which 68 occurred in the domestic setting, 82 were physical abuses, 28 psychological abuses and a single case of sexual abuse.

Class B consisted in 75 cases, of which 64 occurred in the domestic setting, 65 were physical abuses, 24 psychological abuses and a single case of sexual abuse.

No statistically significant relationships were found between the start of the COVID-19 pandemic and the changes in the number of cases of domestic abuse ($p = 0.07$), physical abuse ($p = 0.62$), psychological abuse ($p = 0.83$) or sexual abuse ($p = 0.88$).

Statistical analysis on the comparison between class C and class D was not performed because, while class D consisted in 11 cases, class C consisted in only two cases (both of them were male perpetrators who perpetrated physical and psychological violence against their partners in the domestic setting).

Discussion

The research goal was to describe the trend of the last four years in the accesses to the Emergency Department of our tertiary hospital due to abuse in which at least a minor had reportedly witnessed the event and, then, to evaluate whether the COVID-19 has had an impact on this trend.

To the best of our knowledge, it is the first original research paper to describe this phenomenon focusing on the minors who witness violence and to try to make inference on the possible influence of the pandemic on it.

The role of the COVID-19 is of great scientific interest because, albeit – as said – disasters usually led to an increase in violence, the pandemic led to isolation and reduced the access to healthcare. Indeed, Viero et al. reported a downward trend in the access to the services dedicated to the victims of violence in an Italian center during the COVID-19 lockdown (7). Despite this, in 2022 Anastasia et al. performed an observational cross-sectional study on 212 mother–child dyads from February 2020 to January 2021, finding a 43.9% prevalence of intimate partner violence among the mothers at the pediatric Emergency Department (and thus inferring that there was a similar prevalence of children exposed to violence) (11).

In our study, only 30 cases were reported in 2020 (the year in which the access to health services was more difficult), while in 2021 the number of the cases (45) was even higher than that of 2018. The statistical analysis performed to compare the pre-pandemic period with the last two years failed to find a statistically significant explanation for these changes. However, if only the period corresponding to the institutional lockdown (March–May 2020) is considered, only two cases occurred, regarding women who were victims of physical and psychological abuse perpetrated by their partners in the domestic setting. This number suggests an influence of the pandemic even if, at the same time, makes impossible to perform a statistical comparison.

As said, the setting of the abuse is extremely relevant for the minor who witnesses violence. Indeed, more than 50% of the cases of physical or psychological abuse of minors is reportedly perpetrated by household members (26). In accordance with this evidence, the striking majority of our cases occurred in the domestic setting (79%).

The incidence of intimate partner violence has been reported to be higher among ethnic minorities and in cases of

TABLE 3 Statistical comparison between cases occurred in 2018 and 2019 (A) and cases occurred in 2020 and 2021 (B).

Class	Period (years)	Cases (total no.)	Domestic setting	Physical abuses	Psychological abuses	Sexual abuse
A	2018–2019	92	68	82	28	1
B	2020–2021	75	64	65	24	1
p-value			0.07	0.62	0.83	0.88

acute/chronic use of alcohol and/or drugs (1, 17, 27). Instead, in our cases the 49% of the victims belonged to an ethnic minority and only in the 5% a state of acute intoxication of the perpetrator was reported.

In the 12% of our cases, the child was not only a victim of the psychological abuse related to having witnessed violence but was also a victim of physical abuse. Minor abuse and minor exposure to violence frequently co-occur, especially when the violence is domestic (28). Moreover, about the 71, the 56% and 51% of the children who witness intimate partner violence are also victim of, respectively, sexual, physical and emotional abuse (29). In these cases of co-occurrence of different kinds of abuse, the term polyvictimization should be used. Polyvictimization represents a particularly severe issue, because it is known to relate to more severe outcomes for the minor (30).

Another important evidence we found is that the 69% of the cases consisted in recurrent episodes of abuse. Indeed, abusers tend to re-perpetrate violence (1, 6). Moreover, (any form of) child abuse is a transgenerational problem, since abused minors are exposed to a higher risk of becoming abusers during the adulthood (8, 9). The relationship between recurrence of the abuse and risk of becoming a abuser is due to the fact that, according to the social learning theory, the minor who witnesses frequent episodes of violence develops the idea that using violence in the interpersonal relationships is normal and thus is prone to imitate the experienced behavior (9).

Since – as said – abuse entails a high risk of adverse outcomes for the victim and the risk of transforming the victim into a future perpetrator, exposure of a minor to violence has been included in worldwide mandatory reporting legislation (10).

Instead, from a public health point of view, several authors advocated an empowerment of the interventions targeted at enhancing the help-seeking behaviors and the identification/protection of the cases of interest, with particular regard to the high-risk categories (like institutionalized minors) (1, 7).

In particular, specialized health services dedicated to the victims of violence and to the minors who witness violence are crucial parts of a public health strategy aimed at contrasting the social/legal/economic implications of abuse and its long-term health outcomes (11). Indeed, this issue is often misrecognized and underaddressed by non-specialized healthcare professionals, leading to a failure to implement early professional-driven interventions for secondary prevention (e.g., counselling, cognitive behavioral therapy) and to report the crime(s) to the competent public authorities (7, 8, 10, 31–36). Indeed, the professionals operating in healthcare often do not have a clear idea of what should be considered reportable and they tend to avoid to report the exposure of children to interparental violence because of the fear of a further victimization of the abused parent (10). The two most important interventions to address these issues are represented by a rigorous education of the personnel and the inclusion of experts in legal/forensic medicine into the multidisciplinary teams that visit the cases of abuse (6).

A professional-driven approach to the identification of these cases is also needed because minors can be impacted in disclosing the witnessed episode, since feelings of isolation, shame, fear and guilt are very common (9, 28). As said, early identification of abused minors can limit or avoid negative outcomes enhancing their coping skills and allowing the development of a positive relationship with caring, non-abusive adults (28).

In particular, as stressed by Offidani et al., these specialized services must be provided by Emergency Departments (as in our institution), in order to allow an early identification of these cases of interest and thus to address their specific medical, social and legal needs in a proper and effective fashion (31).

Finally, as suggested by our data, pandemic can influence the accesses to these centers, and thus the adoption of evidence-based interventions to enhance the safety of the healthcare environment must be implemented to encourage the victims of violence to seek assistance and to grant them, especially in cases of domestic violence, a safe environment in which they can live.

Conclusion

Despite mass disasters usually leading to an upward trend in abuses (particularly referring to domestic abuses), there is currently no evidence that COVID-19 has had an impact on the rates of the specific form of psychological abuse occurring when a minor witnesses interpersonal violence. According to our cases, the most likely explanation is given by the extremely few cases reported during the phase of the institutional lockdown. This fact represents an issue because – as shown by our cases – most of the abuses of interest is to be classified as intimate partner violence, and during the institutional lockdown both the abused partners and

the minors were forced to stay with their perpetrators and, at the same time, tended to avoid accessing to hospitals since the pandemic. However, in order to try to overcome the limitation given by the few reported cases during the institutional lockdown, multicentric studies are needed. That being said, empowering the hospital policies specifically aimed at identifying and protecting the victims of violence and of witnessed violence is a critical goal from both a public health and medico-legal point of view.

Limitations

The results of our study stress that future research on this matter should be multicentric, needing the combination of the datasets of several centers to obtain an adequate sample for the statistical analysis regarding the specific and relatively short period of the institutional lockdown.

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 study protocol was reviewed and approved by the competent authority - Ethics Committee "Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana" (reference code: CEAVC 20058). Written informed consent to participate was not required in accordance with local and national requirements.

Author contributions

All authors contributed to the article and approved the submitted version.

Funding

Research funds of Prof. Pinchi.

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. Mazza M, Marano G, del Castillo AG, Chieffo D, Monti L, Janiri D, et al. Intimate partner violence: a loop of abuse, depression and victimization. *World J Psychiatry*. (2021) 11:215–21. doi: 10.5498/wjp.v11.i6.215

2. Fuller-Thomson E, Agbeyaka S. A trio of risk factors for childhood sexual abuse: investigating exposure to parental domestic violence, parental addiction, and parental mental illness as correlates of childhood sexual abuse. *Soc Work*. (2020) 65:266–77. doi: 10.1093/sw/swaa019

3. Solarino M, de Filippi C, Solarino B. Aspetti radiologici e medico-legali dei traumi da maltrattamento sui minori. *Radiol Med*. (2009) 114:1356–66. doi: 10.1007/s11547-009-0501-8

4. Ilenia B, Martina F, Valentina B, Pradella F, Carlo G, Francesca F, et al. Torturesalleged by migrants in Italy: compatibility and othermedicolegal challenges. *Int J Leg Med*. (2021) 135:2489–99. doi: 10.1007/s00414-021-02646-4

5. Cagetti MG, Marcoli PA, Berengo M, Cascone P, Cordone L, Defabianis P, et al. Italian Guidelines for the prevention and management of dental trauma in children. *Ital J Pediatr*. (2019) 45(1):157. doi: 10.1186/s13052-019-0734-7

6. Oliva A, Grassi S, Cazzato F, Jabbehdari S, Mensi L, Amorelli G, et al. The role of retinal imaging in the management of abusive head trauma cases. *Int J Leg Med*. (2022) 136(4):1009–16. doi: 10.1007/s00414-021-02750-5

7. Viero A, Barbara G, Montisci M, Kustermann K, Cattaneo C. Violence against women in the COVID-19 pandemic: a review of the literature and a call for shared strategies to tackle health and social emergencies. *Forensic Sci Int*. (2021) 319:110650. doi: 10.1016/j.forsciint.2020.110650

8. Carnevale S, di Napoli I, Esposito C, Arcidiacono C, Procentese F. Children witnessing domestic violence in the voice of health and social professionals dealing with contrasting gender violence. *Int J Environ Res Public Health*. (2020) 17:1–18. doi: 10.3390/ijerph17124463

9. Steketee M, Aussems C, Marshall IH. Exploring the impact of child maltreatment and interparental violence on violent delinquency in an international sample. *J Interpers Violence*. (2021) 36:NP7319–49. doi: 10.1177/0886260518823291

10. McTavish JR, MacGregor JCD, Wathen CN, MacMillan HL. Children's exposure to intimate partner violence: an overview. *Int Rev Psychiatry*. (2016) 28:504–18. doi: 10.1080/09540261.2016.1205001

11. Anastasia F, Wiel LC, Giangreco M, Morabito G, Romito P, Amaddeo A, et al. Prevalence of children witnessed violence in a pediatric emergency department. *Eur J Pediatr*. (2022) 181:2695–703. doi: 10.1007/s00431-022-04474-z

12. Oliva A, Grassi S, Zedda M, Molinari M, Ferracuti S. Forensic value of genetic variants associated with anti-social behavior. *Diagnostics*. (2021) 11:2386. doi: 10.3390/diagnostics11122386

13. Springe L, Pulmanis T, Velika B, Pudule I, Grinberga D, Villeruša A. Self-reported suicide attempts and exposure to different types of violence and

neglect during childhood: findings from a young adult population survey in Latvia. *Scand J Public Health*. (2016) 44:411–7. doi: 10.1177/1403494816631394

14. Dababnah S, Rizo CF, Campion K, Downton KD, Nichols HM. The relationship between children's Exposure to intimate partner violence and intellectual and developmental disabilities: a systematic review of the literature. *Am J Intell Dev Disabil*. (2018) 123:529–44. doi: 10.1352/1944-7558-123.6.529

15. Ferrara P, Franceschini G, Corsello G, Mestrovic J, Giardino I, Vural M, et al. Increased exposure to violence and risk of neurodevelopmental disorders in children. *J Pediatr*. (2021) 236:335–336.e2. doi: 10.1016/j.jpeds.2021.06.001

16. Ferrara P, Franceschini G, Corsello G, Mestrovic J, Giardino I, Vural M, et al. Children witnessing domestic and family violence: a widespread occurrence during the coronavirus disease 2019 (COVID-19) pandemic. *J Pediatr*. (2021) 235:305–306.e2. doi: 10.1016/j.jpeds.2021.04.071

17. Rajan S, Branas CC, Myers D, Agrawal N. Youth exposure to violence involving a gun: evidence for adverse childhood experience classification. *J Behav Med*. (2019) 42:646–57. doi: 10.1007/s10865-019-00053-0

18. Beharie N, Scheidell JD, Quinn K, McGorray S, Vaddiparti K, Kumar PC, et al. Associations of adolescent exposure to severe violence with substance use from adolescence into adulthood: direct versus indirect exposures. *Subst Use Misuse*. (2019) 54:191–202. doi: 10.1080/10826084.2018.1495737

19. Goldstick JE, Heinze JE, Stoddard SA, Cunningham RM, Zimmerman MA. Age-Specific associations between violence exposure and past 30-day marijuana and alcohol use. *J Res Adolesc*. (2019) 29:480–92. doi: 10.1111/jora.12399

20. McLaughlin KA, Basu A, Walsh K, Slopen N, Sumner JA, Koenen KC, et al. Childhood exposure to violence and chronic physical conditions in a national sample of US adolescents. *Psychosom Med*. (2016) 78:1072–83. doi: 10.1097/PSY.0000000000000366

21. Quinn K, Voisin DR, Bouris A, Schneider J. Psychological distress, drug use, sexual risks and medication adherence among young HIV-positive black men who have sex with men: exposure to community violence matters. *AIDS Care*. (2016) 28:866–72. doi: 10.1080/09540121.2016.1153596

22. Rosshandler Y, Hall BJ, Canetti D. An application of an ecological framework to understand risk factors of PTSD due to prolonged conflict exposure: israeli and palestinian adolescents in the line of fire. *Psychol Trauma*. (2016) 8:641–8. doi: 10.1037/tra0000124

23. Esposito C, Bacchini D, Eisenberg N, Affuso G. Effortful control, exposure to community violence, and aggressive behavior: exploring cross-lagged relations in adolescence. *Aggress Behav*. (2017) 43:588–600. doi: 10.1002/ab.21717

24. Oliva A, Caputo M, Grassi S, Vetrugno G, Marazza M, Ponzanelli G, et al. Liability of health care professionals and institutions during COVID-19 pandemic in Italy: symposium proceedings and position statement. *J Patient Saf*. (2020) 16:e299–302. doi: 10.1097/PTS.0000000000000793

25. Bradbury-Jones C, Isham L. The pandemic paradox: the consequences of COVID-19 on domestic violence. *J Clin Nurs*. (2020) 29:2047–9. doi: 10.1111/jocn.15296

26. Devries K, Knight L, Petzold M, Merrill KG, Maxwell L, Williams A, et al. Who perpetrates violence against children? A systematic analysis of age-specific and sex-specific data. *BMJ Paediatr Open*. (2018) 2:e000180. doi: 10.1136/bmjpo-2017-000180

27. Bordin IA, Duarte CS, Ribeiro WS, Paula CS, Coutinho ESF, Sourander A, et al. Violence and child mental health in Brazil: the itaboraí youth study methods and findings. *Int J Methods Psychiatr Res*. (2018) 27(2):e1605. doi: 10.1002/mpr.1605

28. Herrenkohl TI, Sousa C, Tajima EA, Herrenkohl RC, Moylan CA. Intersection of child abuse and children's Exposure to domestic violence. *Trauma Violence Abuse*. (2008) 9:84–99. doi: 10.1177/1524838008314797

29. Hamby S, Finkelhor D, Turner H, Ormrod R. The overlap of witnessing partner violence with child maltreatment and other victimizations in a nationally representative survey of youth. *Child Abuse Negl*. (2010) 34:734–41. doi: 10.1016/j.chiabu.2010.03.001

30. Turner HA, Shattuck A, Finkelhor D, Hamby S. Polyvictimization and youth violence exposure across contexts. *J Adolesc Health*. (2016) 58:208–14. doi: 10.1016/j.jadohealth.2015.09.021

31. Offidani C, Villani A, Reale A, Marchili MR, Aufiero LR, Moras P, et al. Early recognition of child abuse through screening indicators at the emergency department: experience of a tertiary urban pediatric hospital. *Ital J Pediatr*. (2022) 48(1):32. doi: 10.1186/s13052-022-01214-9

32. Grassi S, Mandarelli G, Polacco M, Vetrugno G, Spagnolo AG, De-Giorgio F. Suicide of isolated inmates suffering from psychiatric disorders: when a preventive measure becomes punitive. *Int J Legal Med*. (2018) 132(4):1225–30. doi: 10.1007/s00414-017-1704-5

33. Louwers ECFM, Korfage IJ, Affourtit MJ, Ruige M, van den Elzen APM, de Koning HJ, et al. Accuracy of a screening instrument to identify potential child abuse in emergency departments. *Child Abuse Neglect*. (2014) 38:1275–81. doi: 10.1016/j.chiabu.2013.11.005

34. Lindert J, Jakubauskiene M, Natan M, Wehrwein A, Bain P, Schmahl C, et al. Psychosocial interventions for violence exposed youth – A systematic review. *Child Abuse Neglect*. (2020) 108:104530. doi: 10.1016/j.chiabu.2020.104530

35. Rini MS, Colucci C, Bucci MB, Argo A. Child abuse hidden in plain sight: the dentist obligations. *Dent Cadmos*. (2017) 85(10):647–56. doi: 10.19256/d.cadmos.10.2017.06

36. Tullio V, Lanzarone A, Scalici E, Vella M, Argo A, Zerbo S. Violence against women in heterosexual couples: a review of psychological and medico-legal considerations. *Med Sci Law*. (2021) 61(1_suppl):113–24. doi: 10.1177/0025802420936081

frontiers | Frontiers in Pediatrics

TYPE Original Research
PUBLISHED 21 December 2022
DOI 10.3389/fped.2022.925520

OPEN ACCESS

EDITED BY
Antonio Oliva,
Catholic University of the Sacred Heart, Italy

REVIEWED BY
Fielding Bruder Stapleton,
University of Washington, United States
Yauhen Statsenko,
United Arab Emirates University, United Arab Emirates

*CORRESPONDENCE
Rana R Bitar
drranab@doctors.org.uk

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

RECEIVED 21 April 2022
ACCEPTED 17 November 2022
PUBLISHED 21 December 2022

CITATION
Bitar R, Alattas B, Azaz A, Rawat D and Miqdady M (2022) Gastrointestinal manifestations in children with COVID-19 infection: Retrospective tertiary center experience.
Front. Pediatr. 10:925520.
doi: 10.3389/fped.2022.925520

Gastrointestinal manifestations in children with COVID-19 infection: Retrospective tertiary center experience

Rana R Bitar, Bushra Alattas, Amer Azaz, David Rawat and Mohamad Miqdady

Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates

Objective: The majority of pediatric severe acute respiratory syndrome coronavirus 2 (COVID-19) cases demonstrate asymptomatic, mild or moderate disease. The main symptoms in children with COVID-19 are respiratory symptoms but some patients develop gastrointestinal symptoms and liver injury. We aim to review gastrointestinal symptoms and liver injury in children with confirmed COVID-19 infection.

Method: This is a retrospective case note review of children with positive COVID-19 nasal Polymerase Chain Reaction aged 0–18 years admitted to a tertiary pediatric hospital from March 1st till June 1st 2020.

Results: 180 children were identified. Mean age was 5 years (Range: 0.01–17), the majority of patients were school aged (30%). Patients were mainly from East Asia 81 (45%) and Arabs 67 (37%). Gastrointestinal symptoms were encountered in 48 (27%) patients and 8 (4%) patients had only Gastrointestinal symptoms with no associated fever or respiratory symptoms. Liver injury was seen in 57 (32%) patients. Patients with fever and cough were more likely to have gastrointestinal symptoms ($P = <0.001$ and 0.004 respectively). Fever was more likely to be associated with liver injury ($P = 0.021$). Children with abdominal pain were more likely to have elevated C-Reactive Protein ($P = 0.037$). Patients with diarrhea and vomiting were more likely to have elevated procalcitonin ($P = 0.034$ and 0.002 respectively). Children with Gastrointestinal symptoms were not more likely to be admitted to Pediatric Intensive Care Unit ($P = 0.57$).

Conclusion: COVID-19 infection in children can display gastrointestinal symptoms at initial presentation. Additionally, gastrointestinal symptoms can be the only symptoms patients display. We demonstrated that children with gastrointestinal symptoms and liver injury can develop more severe COVID-19 disease and are more likely to have fever, cough, and raised inflammatory markers. Identifying children with gastrointestinal manifestations needs to be part of the initial screening assessment of children.

What is known?

- Pediatric COVID-19 cases mostly demonstrate asymptomatic, mild or moderate disease.
- The symptoms in children are mainly respiratory but some display gastrointestinal symptoms.
- Children with COVID-19 display increased gastrointestinal symptoms when compared to adults.

What is new?

- Children with COVID-19 displaying gastrointestinal symptoms are more likely to have fever, cough and elevated inflammatory markers.
- Children with liver injury are more likely to develop fever.
- Children with gastrointestinal involvement in COVID-19 are more likely to demonstrate more severe disease but are not more likely to be admitted to PICU.

KEYWORDS

COVID-19 in children, COVID-19 clinical manifestation, COVID-19 infection, COVID-19 liver injury, COVID-19 complication

Introduction

Severe acute respiratory syndrome coronavirus 2 was the cause of a series of cases with severe pneumonia initially reported in Wuhan, China (1, 2) declared as COVID-19 by the WHO. 2.1%–5% of infected cases are children (3, 4). The pediatric population display a mild disease and majority (over 90%) have mild, moderate or asymptomatic disease (5–8) Approximately 1% of children develop severe disease requiring admission to intensive care unit (9).

The typical presentation of COVID-19 includes fever, weakness, nausea, and pulmonary symptoms such as dry cough and dyspnea. A proportion of affected patients also have digestive manifestations, such as anorexia, nausea, vomiting, diarrhea, and abdominal pain. In addition, liver injury is well described in children with COVID-19 infection. Viral fecal shedding for several weeks after diagnosis has been reported (10), COVID-19 virus was observed in rectal swabs in eight out of ten children after nasopharyngeal swabs returned negative (11). The viral shedding in stool and nasal secretions make children possible facilitators of viral transmission (5) and is one of the possible explanations for the prevalence of Gastrointestinal (GI) symptoms in CVOID-19 infected children.

GI symptoms are reported to range from 12% to 21% in the pediatric literature with varying frequencies in the United States, Europe and China (11–13). In addition, gastrointestinal symptoms are observed more frequently in children with younger age and fever (14). Children with GI symptoms show higher levels of C-reactive protein and procalcitonin this suggests that more severe COVID disease is observed with GI symptoms in children (15).

The United Arab Emirates (UAE) developed a strong testing program. They performed Polymerase Chain Reaction (PCR) nasal swab tests of 2,850 per 100,000 population per day (11), achieving identification and isolation of most paediatric COVID-19 infected children. We aim to review GI symptoms and liver injury in children with COVID-19, to evaluate risk factors predisposing for GI symptoms, and to assess if GI symptoms and liver injury are associated with more severe COVID-19 disease in our population.

Method

Approval from the Institutional Review Board Committee for COVID-19 research in the Department of Health, Abu Dhabi was obtained. We retrospectively reviewed the electronic medical records of patients with COVID-19 diagnosed based on nasal swab PCR aged 0–18 years old from 1st of March to 1st of June 2020. This study was conducted at the start of the pandemic. At the start of the pandemic all paediatric patients were admitted to hospital, Sheikh Khalifa Medical City (the only designated pediatric COVID-19 Hospital in Abu Dhabi City for children) to ensure appropriate isolation measures are carried out and the medical needs of the children are met. Patients were reviewed by a pediatrician daily and were discharged if they had two negative COVID-19 PCR test 48 h apart and were medically fit for discharge.

This patient sample has been utilized in another publication, British Medical Journal, Paediatrics open 2021, Clinical manifestation and outcome in children with COVID-19 infection in Abu Dhabi: a retrospective single centre study.

We collected patient demographics, ethnicity, Body Mass Index (BMI), length of admission, background clinical conditions, symptoms at presentation, biochemical markers, complications and mortality. Presenting symptoms reviewed were fever, cough, abdominal pain, diarrhea, and vomiting. Biochemical markers included C-reactive protein (CRP), procalcitonin, lymphocyte count, Alanine aminotransaminase (ALT) and Aspartate aminotransferase (AST). Patients with temperature >37.8 °C were considered to have fever, liver injury was defined as an increase in either AST or ALT or both above normal level for age and sex. Elevated CRP and Procalcitonin were defined as an increase above normal level for age. Lymphopenia was defined as a lymphocyte count below normal level for age and sex. Patients were classified as underweight if BMI was <18.5 kg/m^2, healthy if BMI was between 18.5 and 25 kg/m^2, overweight if BMI was 25 to 30 kg/m^2 and obese if BMI is >30 kg/m^2. All patients were followed up for 1 year for COVID related complications.

Statistical analysis

The Statistical Package for Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. Categorical variables are presented as frequency and percentage, while numerical variables are presented as mean ± standard deviation (SD), and or median (centile) with range. Correlation between categorical variables was analyzed using chi-square or Fisher's exact test, as appropriate. Comparison of non-normally distributed numerical variables was carried out using nonparametric tests including median test. A p value of <0.05 was considered to reject the null hypothesis. Sex, age, ethnicity, BMI, background medical disease, cough and fever were analyzed using multiple regression analysis to evaluate risk factors predisposing to gastrointestinal symptoms. For modeling binary outcomes, (GI complications, No GI complications), we transformed the fitted value from a linear regression to FIT in between 0 and 1. One can interpret it as a probability of a match conditional on the regressor value.

Results

180 children were identified. Patient demographic is described in **Figure 1**. 92 (51%) patients were males, mean age was 5 years (Range: 0.01–17). The majority of patients, 54 (30%) were school aged, 6–13 years old. Followed by infants, <1 year, 41 (23%) patients. Patients were mainly from East Asia, 81 (45%) patients, and Arab patient were the second common ethnicity, 67 (37%) patient. BMI was only checked for 152 patients, most patients 103 (67%) were underweight, 37 (25%) patients had normal BMI, there were 12 (8%) patients with BMI > 25 kg/m^2 and of these 12 patients, six were obese.

Clinical presentation included; fever in 84 (47%) patients, 62 (34%) patients with cough, 48 (27%) encountered GI symptoms, 32 (18%) presented with diarrhea, 20 (11%) patients suffered from vomiting, and 17 (9%) had abdominal pain (**Figure 2**). Interestingly, 8 (4%) patients only had GI symptoms with no associated fever of respiratory symptoms. The most common inflammatory marker to be elevated was CRP, 41(23%) had elevated CRP, lymphopenia was only seen in 26 (14%) patients and only 5 (3%) patients had elevated procalcitonin. Liver injury in the form of elevated ALT and/or AST was seen in 57 (34%) patients. Median ALT was 22 IU/L (Rang: 5–220), Median AST was 46 IU/L (Rang: 31–359).

Sex, age, ethnicity, BMI, background medical disease, cough and fever were analyzed using multiple regression analysis to evaluate risk factors predisposing to gastrointestinal symptoms (**Table 1**). Children with fever and cough were more likely to have GI symptoms (P = <0.001 and 0.004 respectively). Sex, age, ethnicity, BMI, and patient having a background medical disease did not predispose to the development of GI symptoms. Children with abdominal pain were more likely to have elevated CRP (P = 0.037). Patients with diarrhea and vomiting were more likely to have elevated procalcitonin (P = 0.034 and 0.002 respectively). Patients with fever were also more likely to have liver injury (P = 0.021).

Overall, 52 (29%) had comorbid medical diseases (**Figure 3**) including one of the patients with multiple organ transplantation; liver, bowel and pancreas transplant, this patient developed post COVID small intestinal rejection 10 days post COVID infection. The median length of hospital stay was 6 days (Range: 0–60). The patients were allowed to be discharged to the community if they had two COVID negative PCR tests 48 h apart. Six (3%) patients were admitted to Pediatric Intensive Care Unit (PICU) and there was no reported mortality. Of the six patients admitted to PICU; only one patient had GI symptoms, and only one patient was obese with BMI of 33.68 kg/m^2. Children with GI symptoms were not more likely to be admitted to PICU (P = 0.57).

Discussion

Respiratory illness is the main presentation of Children with COVID-19 disease and GI symptoms can also be present. GI symptoms had been reported in 24.8% of paediatric patients (16). 27% of patients in our review experienced GI symptoms. GI manifestations in COVID-19 includes; diarrhea (2%–50%), anorexia (40%–50%), vomiting (4%–67%), nausea (1%–30%) and abdominal pain (2%–6%). Diarrhea and vomiting are the most common GI symptoms described (17). We observed diarrhea in 18%, vomiting in 11% and 9% had abdominal pain. 4% of our patients had GI symptoms as the first presenting symptoms without other associated respiratory symptoms or fever. Therefore, it is important to consider COVID-19 infection in children presenting with GI symptoms with early testing, promoting patient and staff safety.

GI symptoms can be associated with severe COVID-19 in children. A multicenter study of 101 pediatric inpatients described patients presenting with GI symptoms had higher CRP, procalcitonin, ferritin values and admission to PICU (15). The levels of CRP had an expectedly high predictive value as they reflect the activity of an inflammatory process (18). In our cohort, children with GI symptoms were more likely to have fever (P < 0.001) and cough (P = 0.004). Abdominal pain was associated with elevated CRP (P = 0.037), diarrhea and vomiting were associated with elevated procalcitonin (P = 0.034 and 0.002 respectively). However, we did not observe increased PICU admissions in children with GI symptoms (P = 0.57). In addition, children with elevated liver enzymes were more likely to have fever (P = 0.021). Therefore, children with GI symptoms and liver injury in our

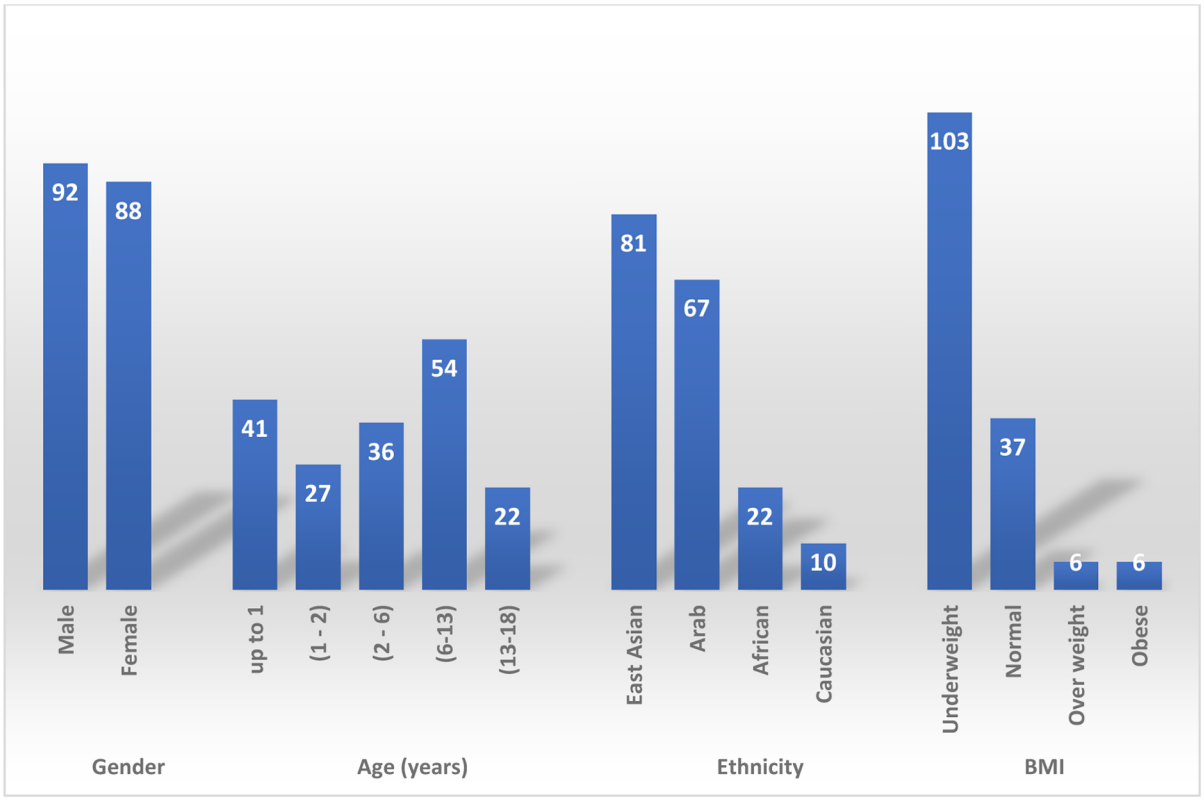


FIGURE 1
Patient demographics.

study were more likely to have abnormal inflammatory markers and display a more severe COVID-19 infection.

Previous studies performed in the United Arab Emirates demonstrated an increased risk for men of all ages to require intensive care ($p < 0.01$). Males were more likely to have at least moderate disease severity ($p = 0.0083$) and the risk of the non-mild COVID-19 was significantly higher ($p < 0.05$) in midlife adults and older adults compared to young adults (19). In addition, Al Zahmi et al. demonstrated that Caucasian or East-Asian COVID-19 patients tended to have a more severe disease despite a lower risk profile. In contrast to this, Middle Eastern COVID-19 patients had a higher risk factor profile, but they did not differ markedly in disease severity from the other ethnic groups (20). In this review, sex, age, ethnicity, BMI, and patient medical background medical disease did not predispose to the development of GI symptoms.

Approximately 1% of children with COVID-19 develop severe disease requiring admission to intensive care unit (9). Six (3%) of our patients required admission to PICU; of those 6 patients, 5 had background complex medical disease and 1 was obese. A metanalysis on 285,004 children with confirmed SARS-CoV2 infection, 9,353 (3.3%) had at least one underlying comorbidity, of which 5.4% were obese. Among 507 obese children, 64 had severe COVID-19 or required ICU admission, with a calculated risk of severity of 2.87 (95% CI 1.16–7.07) (21). Among the180 patients included in this study, 52 (29%) had background medical disease, 12 (7%) were obese. Among the 12 obese children, 1 patient developed severe COVID infection and required PICU admission. Despite this the outcome was very good with no reported mortality and only one patient developed long term complication.

The authors recognize a few limitations to this study. Firstly, this is a retrospective study and as such may be limited by inaccurate documentation. Secondly, some children with COVID-19 may not have been captured in this study despite the extensive testing and contact tracing within the United Arab Emirates. Thirdly, BMI and blood testing was not performed in all patients. Fourthly, this is a relatively small study with small sample size which may limit the power of conclusions drawn from this study. Fifthly, despite the low accuracy of the multiple regression model, it helped us to analyze statistically significant predictors and draw important conclusions about how changes in the predictor values are associated with changes in the response value. The supposed reason for the low R-squared value is the limit sample size and the high number of regressors. With an

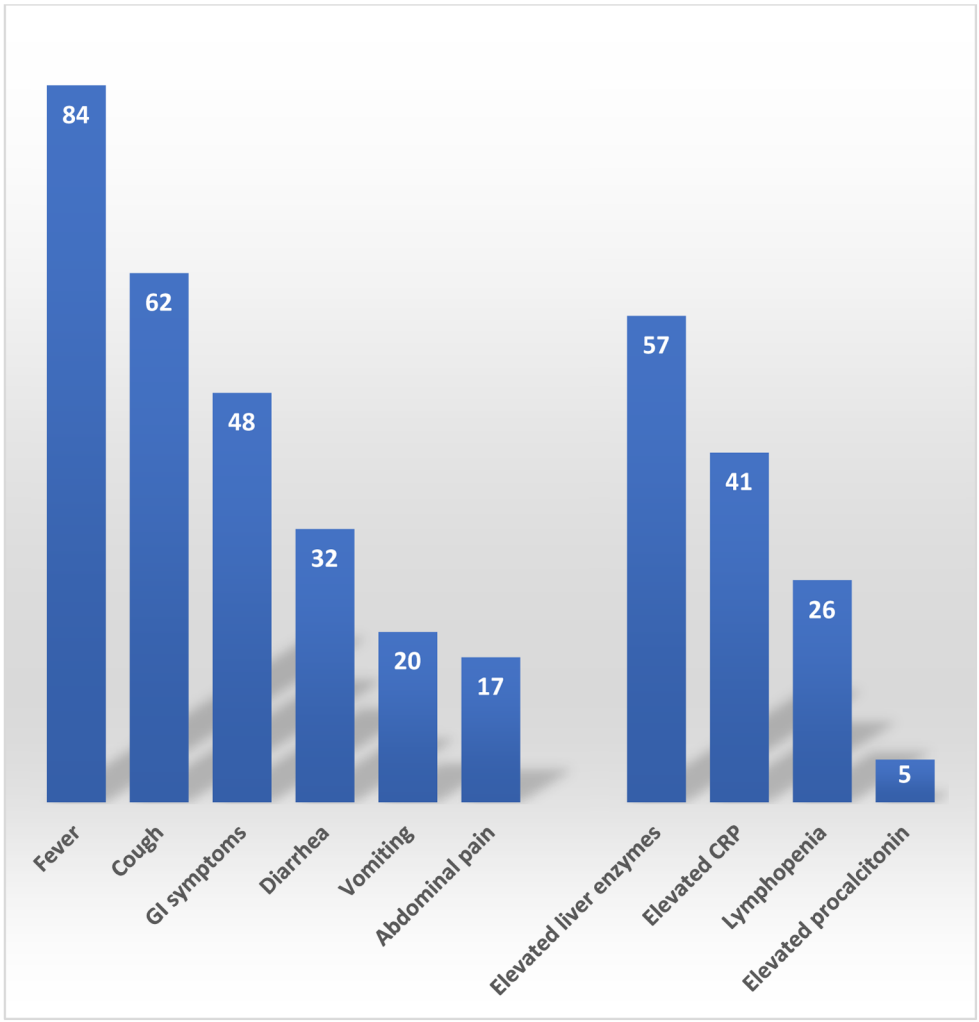


FIGURE 2
Clinical data.

TABLE 1 Regression analysis, predisposing factors to development of GI symptoms.

	Unstandardized Coefficients		Standardized Coefficients	t	*P* Value
	B	Std. Error	Beta		
(Constant)	1.678	.155		10.824	.000
Sex	−.059	.117	−.067	−.503	.616
Ethnicity	−.133	.063	−.330	−2.121	.035
Age	.070	.081	.209	.856	.393
BMI	−.006	.037	−.020	−.160	.873
Medical disease	−.053	.158	−.055	−.339	.735
Cough	−.452	.155	−.486	−2.916	.004
Fever	.745	.101	.840	7.407	.000

Dependant Variable: GI symptoms

$R^2 = .282$ F = 9.668 N = 180

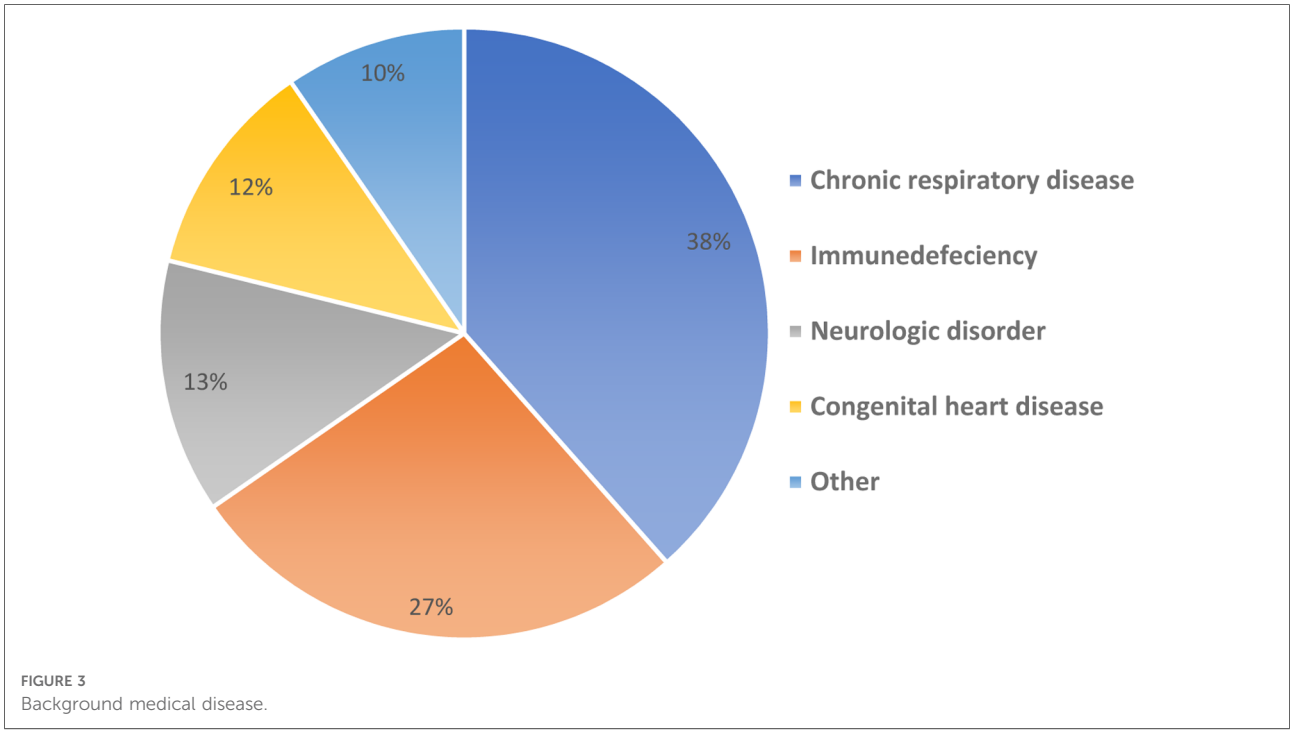


FIGURE 3
Background medical disease.

increasing number of regressors, we need an increasing amount of data to obtain reliable estimates. Finally, we also acknowledge that the study was performed at the initial time of the pandemic and there are new strains that have evolved after the study period.

This preliminary examination of GI manifestation of COVID-19 disease in children suggest that children do not always present with fever or cough. Vomiting, diarrhea and abdominal pain need to be considered as part of the screening assessment in children. Children with GI symptoms are likely to have fever, cough and raised inflammatory markers and therefore display a more sever clinical course. Although COVID-19 has a favorable clinical outcome in children, the importance of identifying pediatric cases is to reduce the spread of infection and identify high risk patients.

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 The Institutional Review Board Committee for COVID 19 research in the Department of Health, Abu Dhabi. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

RB has contribution to conception and design of work, analysis, interpretation of data and drafting and writing up the work and revisiting it critically for important intellectual content and approved the final version to be published and agrees to be accountable to all aspects of the work. BA contribution to design of work, acquisition, analysis, interpretation of data and revisiting it critically for important intellectual content and approved the final version to be published and agrees to be accountable to all aspects of the work. AA contribution to design of the work, interpretation of data and revisiting it critically for important intellectual content and approved the final version to be published and agrees to be accountable to all aspects of the work. DR: contribution to design of the work, analysis, interpretation of data and revisiting it critically for important intellectual content and approved the final version to be published and agrees to be accountable to all aspects of the work. MM: contribution to design of the work, acquisition, analysis, interpretation of data and revisiting it critically for important intellectual content and approved the final version to be published and agrees to be accountable to all aspects of the

work. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

Publisher's note

References

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *N Engl J Med*. (2020) 382(13):1199–207. doi: 10.1056/NEJMoa2001316

2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. (2020) 395(10223):497–506. doi: 10.1016/S0140-6736(20)30183-5

3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *Jama*. (2020) 323(13):1239–42. doi: 10.1001/jama.2020.2648

4. Saux NL. Current epidemiology and guidance for COVID-19 caused by SARS-co V-2 virus in children. *Can Pediatr Soc*. (2020) 39(5):355–68. doi: 10.1097/INF.0000000000002660

5. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics*. (2020) 58(4): 712–3. doi: 10.1016/j.jemermed.2020.04.006

6. Chang TH, Wu JL, Chang LY. Clinical characteristics and diagnostic challenges of pediatric COVID-19: a systematic review and meta-analysis. *J Formos Med Assoc*. (2020) 119(5): 982–9. doi: 10.1016/j.jfma.2020.04.007

7. de Souza TH, Nadal JA, Nogueira RJN, Pereira RM, Brandão MB. Clinical manifestation of children with COVID-19:a systematic review. *Pediatr Pulmonol*. (2020) 55(8):1892–9. doi: 10.1002/ppul.24885

8. Covid CD, COVID C, COVID C, Bialek S, Gierke R, Hughes M, McNamara LA, Pilishvili T, Skoff T. Coronavirus disease 2019 in children—united States, February 12–April 2, 2020. *Morb Mortal Wkly Rep*. (2020) 69(14):422. doi: 10.15585/mmwr.mm6914e4

9. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. (2020) 174:882–9. doi: 10.1001/jamapediatrics.2020.1467

10. Cai J, Xu J, Lin D, Xu L, Qu Z, Zhang Y, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin Infect Dis*. (2020) 71(6):1547–51. doi: 10.1093/cid/ciaa198

11. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med*. (2020) 26(4):502–5. doi: 10.1038/s41591-020-0817-4

12. Wang JG, Cui HR, Tang HB, Deng XL. Gastrointestinal symptoms and fecal nucleic acid testing of children with 2019 coronavirus disease: a systematic review and meta-analysis. *Sci Rep*. (2020) 10:17846. doi: 10.1038/s41598-020-74913-0

13. Chiappini E, Licari A, Motisi MA, Manti S, Marseglia GL, Galli L, et al. Gastrointestinal involvement in children with SARS-COV-2 infection: an overview for the pediatrician. *Pediatr Allergy Immunol*. (2020) 31(Suppl 26):92–5. doi: 10.1111/pai.13373

14. Xiong XL, Wong KK, Chi SQ, Zhou A, Tang J, Zhou L, et al. Comparative study of the clinical characteristics and epidemiological trend of 244 COVID-19 infected children with or without GI symptoms. *Gut*. (2021) 70:436–8. doi: 10.1136/gutjnl-2020-321486

15. Gonzalez Jimenez D, Rodríguez-Belvís MV, Ferrer Gonzalez P, Domínguez Ortega G, Segarra O, Medina Benitez E, et al. COVID-19 gastrointestinal manifestations are independent predictors of PICU admission in hospitalized pediatric patients. *Pediatr Infect Dis J*. (2020) 39:e459–62. doi: 10.1097/INF.0000000000002935

16. Cheung KS, Hung IF, Chan PP, Lung KC, Tso E, Liu R, et al. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from the Hong Kong cohort and systematic review and meta-analysis. *Gastroenterology*. (2020) 159(1):81–95. doi: 10.1053/j.gastro.2020.03.065

17. Oba J, Carvalho WB, Silva CA, Delgado AF. Gastrointestinal manifestations and nutritional therapy during COVID-19 pandemic: a practical guide for pediatricians. *Einstein (Sao Paulo)*. (2020) 18:eRW5774. doi: 10.31744/einstein_journal/2020rw5774

18. Statsenko Y, Al Zahmi F, Habuza T, NeidlVan Gorkom K, Zaki N. Prediction of COVID-19 severity using laboratory findings on admission; informative values, thresholds, ML model performance. *BMJ open*. (2022) 11(2): e044500. doi: 10.1136/bmjopen-2020-044500

19. Statsenko Y, Al Zahmi F, Habuza T, Almonasoori T, Smetanina D, Simiyu GL, et al. Impact of age and sex on COVID-19 severity assessed from radiologic and clinical findings. *Front Cell Infect Microbiol*. (2022) 11: 777070. doi: 10.3389/fcimb.2021.777070

20. Al Zahmi F, Habuza T, Awawdeh R, Elshekhali H, Lee M, Salamin N, et al. Ethnicity-specific features of COVID-19 among arabs, Africans, south asians, east asians and caucasians in the UAE. *FrontCell Infect Microbiolofy*. (2022) 11:773141. doi: 10.3389/fcimb.2021.773141

21. Tsankov BK, Alliare JM, Irvine MA, Lopez A, Sauvé L, Vallance B, et al. Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. *Int J Infect Dis*. (2021) 103:246–56. doi: 10.1016/j.ijid.2020.11.163

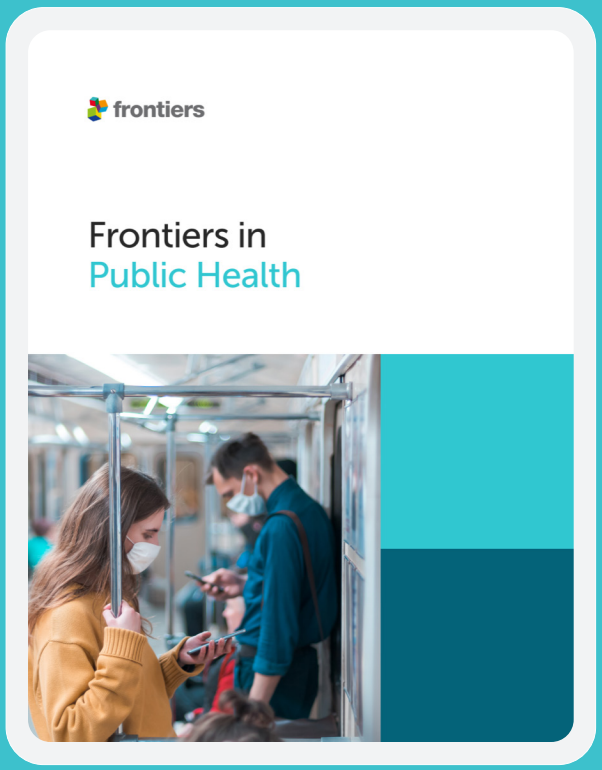
Frontiers in Public Health

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