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Coronavirus Pandemic

Prevalence of anti-SARS-CoV-2 IgG positivity and long COVID-19 in pediatric age group

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Abstract

Introduction: This study aimed to determine the prevalence and associated factors of coronavirus disease 2019 (COVID-19) and long COVID-19 in children in Duhok province and Zakho city in the Kurdistan region.

Methodology: The study was conducted as a cross-sectional study and included children aged 5–12 years in Duhok and Zakho, two major neighboring cities in the Bahdenan region of northern Iraq. A total of 330 participants were included and the study was conducted between October 2022 and April 2023. The children were tested for the presence of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G (IgG) antibodies. A questionnaire was used to collect demographic and personal data, and symptoms of each participant to determine the prevalence of long COVID-19.

Results: Out of 330 participants, 302 (91.5%) were positive for IgG, and 156 (51.7%) of them were male. Only 4 participants (1.3%) had pneumonia, and 282 (93.4%) were asymptomatic. Fourteen out of 302 (4.6%) participants had long COVID-19. There were significant associations between long COVID-19 and history of previous COVID-19 episodes ($p = 0.001$), presence of pneumonia ($p = 0.001$), and family history of COVID-19 ($p = 0.005$).

Conclusions: There was a high prevalence of COVID-19 among children in Duhok province and Zakho city, and 4.6% of them experienced long COVID-19. Factors such as prior COVID-19, pneumonia, and family history of COVID-19 were associated with long COVID-19. Continued monitoring, education, vaccination, preventive measures, and supportive care are recommended to effectively address the impact of COVID-19 on the pediatric population.

Key words: SARS-CoV-2; IgG positivity; long COVID-19; children; pediatrics.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China in December 2019, leading to the official designation of coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) on 11 February 2020. The subsequent global spread resulted in a significant health crisis, impacting health services and exacerbating the situation with reinfections [1–3]. In a broader context, the predominant demographic affected by COVID-19 comprised adults, whereas children contributed to a comparatively modest percentage of reported cases. Specifically, there was a discernible elevation in reported cases among children aged 5–14 years, constituting 6.3% (6,020,084 cases) of global instances, in contrast to the 1.8% (1,695,265 cases) observed among those under the age of 5 years, spanning the period from 2019 to 2021 [4–5]. However, it is imperative to acknowledge the potential for underestimation attributable to the proclivity of children to manifest asymptomatic infections [5,6]. The incidence of asymptomatic cases in pediatric COVID-19 has been reported to range from 10% to 90%, accompanied by diverse physio-pathological theories posited to elucidate these occurrences [7]. Besides, the evidence gaps regarding long COVID-19 in pediatric populations pose significant challenges in our understanding of the long-term consequences of SARS-CoV-2 infection in children. Critical gaps include a lack of clarity on the prevalence and duration of long COVID-19 in this age group, with limited documentation on specific symptoms and their impact on daily life [8,9]. Identification of risk factors contributing to long COVID-19 development in

children, such as initial infection severity, underlying health conditions, and genetic predispositions, remains understudied [6,10]. Moreover, the long-term consequences, encompassing both physical and mental health aspects, require thorough investigation [10,11]. Addressing these gaps is essential to inform clinical management, public health strategies, and policy decisions related to the well-being of children in the context of the ongoing COVID-19 pandemic. To date, no comprehensive study has been conducted in Iraq to address the questions surrounding the seropositivity of SARS-CoV-2 antibodies and the prevalence of long COVID-19 among children. The current study aimed at determining the prevalence of COVID-19 and long COVID-19, as well as associated factors, in the pediatric age group in Duhok city and Zakho city in Iraq.

Methodology

Study design

This study was conducted as a cross-sectional study among the pediatric age group (5–12 years) in Duhok city and Zakho City between October 2022 and April 2023. Duhok and Zakho are two major neighboring cities in the Bahdenan region of northern Iraq. All children who visited the outpatient clinics at Hevi Pediatrics Hospital and Zakho General Hospital were actively enrolled in this study. Children older than 12 years old were not included because they were part of the COVID-19 vaccination program and had already been vaccinated.

Blood samples and questionnaire

Blood samples were collected from all participants aged between 5 to 12 years who visited the outpatient clinics at Hevi Pediatric Teaching Hospital and Zakho General Teaching Hospital.

We employed a comprehensive questionnaire to collect crucial information regarding the participants. Data were collected through face-to-face interviews with the guardians of the children. Demographic details recorded through the questionnaire included age, gender (categorized as male or female), socioeconomic status (categorized as good, acceptable, or poor), and mother's occupation. We also assessed the family structure by inquiring about the number of family members. Health-related parameters encompassed birth weight, premature labor history (with options for yes or no), and the method of infant feeding (breastfeeding, formula feeding, or a combination of both). The participants were asked about any known chronic illnesses which were verified using official chronic disease identification documents provided by local health authorities. The current weight and height were measured, and the body mass index (BMI) was calculated. We recorded information on the history of documented prior COVID-19 episodes, by classifying the severity as mild, moderate, or severe; and the presence of pneumonia. The hospital discharge card was verified for evidence of pneumonia.

In addition, we recorded the immunization status (categorized as complete, partial, or unimmunized), mother's education level, family history of documented COVID-19, and the contact person if applicable (mother, father, siblings, grandparents, other relatives, or neighbors). SARS-CoV-2 antibody profiles, specifically immunoglobulin G (IgG), were examined. Participants with a history of documented COVID-19 were asked to indicate whether they had symptoms during the infection.

The symptoms under investigation were meticulously documented during two distinct time frames: (1) the period of infection, and (2) continuation of symptoms 4 weeks after the infection. The long COVID-19 cohort comprised individuals who exhibited ongoing symptoms lasting beyond 4 weeks post infection, and were unaffected by alternative diagnoses [10]. Participants were queried about various symptoms, including fatigue, post-exertional malaise/poor endurance, high temperature, loss or change in the sense of smell or taste, hair loss, problems with memory or concentration, difficulty sleeping, dizziness, headache, mood changes, dyspnea, cough, chest pain, joint or muscle pain, rhinorrhea, loss of appetite, red eyes, and change in bowel habits. Moreover, an open-ended category labeled "others" was included to capture any additional symptoms that may not have been covered by the predefined list. This comprehensive approach ensured a thorough exploration of potential symptoms experienced by the participants, both during the active infection period and in the subsequent weeks.

In order to determine their socioeconomic status, the participants underwent a food security assessment utilizing a set of questions pertaining to the preceding 3 months. These inquiries addressed concerns about potential food shortages, financial constraints impacting food availability, and the repercussions on dietary habits. Participant classification was determined by their responses to these questions, providing a comprehensive evaluation of varying levels of food security within the surveyed population.

IgG detection

The VIDAS-SARS-CoV-2 IgG (bioMérieux, Grenoble France) is an assay that employs the enzyme linked fluorescent assay (ELFA) technique. Its primary objective is to quantitatively detect IgG antibodies specific to SARS-CoV-2 in serum or plasma. The test was conducted following the manufacturer's instructions. The methodology included a two-step ELFA method with final fluorescence detection by utilizing a single-use solid phase receptacle (SPR) as both the solid phase and pipetting device which streamlined the process. Ready-to-use reagents pre-dispensed in sealed single-use strips facilitated automation of all assay steps. The reaction medium cycled in and out of the SPR device multiple times. Following sample dilution, SARS-CoV-2 IgG was captured by the recombinant SARS-CoV-2 antigen within the SPR device. The washing steps removed unbound components. In the second step, specifically labeled anti-human IgG with alkaline phosphatase detected the captured IgG. Further washing steps eliminated unbound components, ensuring a precise and automated assay process.

Ethical considerations

The study protocol and the consent were approved

Table 1. Association of IgG positivity with different variables.

Variables	Positive IgG (n = 302)		Negative IgG (n = 28)		*p* value
	N	%	N	%	
Age group (years)					
5–7	131	43.3	13	46.4	
8–10	113	37.4	10	35.7	0.116
11+	58	19.2	4	14.3	
Gender					
Male	156	51.7	14	50.0	0.867
Female	146	48.3	14	50.0	
Birth weight (kg)					
≤ 1	4	1.3	0	0	
2–3	59	19.5	3	10.7	0.573
4–5	237	78.5	25	89.3	
5+	2	0.7	0	0	
Socioeconomic status					
Poor	64	21.2	6	21.4	
Acceptable	188	62.3	15	53.6	0.504
Good	50	16.6	7	25.0	
Mother's occupation					
Employed	35	11.6	4	14.3	0.627
Housewife	267	88.4	24	85.7	
Premature labor					
Yes	17	5.6	3	10.7	0.281
No	285	94.4	25	89.3	
Feeding					
Brest feeding	73	24.2	6	21.4	
Formula feeding	71	23.5	4	14.3	0.421
Mixed feeding	158	52.3	18	64.3	
Chronic diseases					
Yes	23	7.6	3	10.7	0.56
No	279	92.4	25	89.3	
History of documented prior COVID-19 episodes					
Yes	25	8.3	1	3.6	0.376
No	277	91.7	27	96.4	
Any evidence of pneumonia					
Yes	4	1.3	0	0.0	0.540
No	298	98.7	28	100.0	
Immunization status					
Complete	278	92.4	24	85.7	
Partial	21	7.0	4	14.3	0.348
Unimmunized	2	0.75	0	0.0	
Family history of documented COVID-19					
Yes	198	65.6	13	46.4	0.044
No	104	34.4	15	53.6	
Number of family members					
2–4	47	15.6	7	25	
5–7	175	57.9	16	57.1	
8–10	62	20.5	5	17.9	0.532
11–13	13	4.3	0	0	
14+	5	1.7	0	0.0	

COVID-19: coronavirus disease 2019; IgG: immunoglobulin G.

by the ethical committee in the College of Medicine, University of Zakho (E2022/452). Consent was obtained from the guardians of the participating children.

Statistical analyses

The data collected in this study were analyzed using SPSS version 25 (IBM Corp, Armonk, NY, USA). The Chi square test was employed to examine the relationships among the various variables. A significance level of 0.05 or lower was deemed statistically significant.

Results

IgG positivity

Out of a total of 330 participants, 302 (91.5%) cases were positive for the IgG antibody. Out of the 302 positive cases, 156 (51.7%) were male. Regarding their age distribution, 131 (43.4%) were aged between 5–7 years, 113 (37.4%) were aged between 8–10 years, and 58 (19.2%) were aged 11 years or older. Furthermore, 25 out of the 302 cases (8.3%) had a history of documented prior COVID-19 episodes; the rest denied any history of COVID-19. Only 4 cases (1.3%) showed

Table 2. Association of long COVID-19 with different variables.

Variables	Positive IgG (n = 288)	Long COVID-19 positive IgG (n = 14)	*p* value
	No. (%)	No. (%)	
Age group (years)			
5–7	126 (43.8)	5 (35.7)	
8–10	106 (36.8)	7 (50)	0.605
11+	58 (19.4)	2 (14.3)	
Gender			
Male	147 (51)	9 (64.3)	0.51
Female	141 (49)	5 (35.7)	
Birth weight (kg)			
≤ 1	3 (1)	1 (7.1)	
2–3	24 (8.3)	2 (14.2)	0.199
4–5	226 (78.5)	11 (78.6)	
5+	35 (12.2)	0 (0)	
Socioeconomic status			
Poor	59 (20.5)	5 (35.7)	
Acceptable	182 (63.3)	6 (42.9)	0.278
Good	47 (16.3)	3 (21.4)	
Mother's occupation			
Employed	32 (11.2)	3 (21.4)	0.239
Housewife	256)88.9)	11 (78.6)	
Premature labor			
Yes	15 (5.2)	2 (14.3)	0.15
No	273 (94.8)	12 (85.7)	
Feeding			
Breast feeding	69 (24)	4 (28.6)	
Formula feeding	69 (24)	2 (14.3)	0.7
Mixed feeding	150 (52)	8 (57.2)	
Chronic disease			
Yes	23 (8)	0 (0)	0.271
No	265 (92)	14 (100)	
History of documented COVID-19 episodes			
Yes	11 (3.8)	14 (100)	0.001
No	277 (96.2)	0 (0)	
Any evidence of pneumonia			
Yes	1 (0.3)	3 (21.4)	0.001
No	278 (99.7)	11 (78.6)	
Immunization status			
Complete	265 (92)	14 (100)	
Partial	21 (7.3)	0 (0)	0.546
Unimmunized	2 (0.7)	0 (0)	
Family history of documented COVID-19			
Yes	184 (63.9)	14 (100)	0.005
No	104 (36.2)	0 (0)	
Number of family members			
≤ 3	8 (2.8)	0 (0)	
4–6	173 (60.0)	7 (50)	
7–9	81 (28.1)	5 (35.7)	0.583
10–12	21 (7.3)	1 (7.1)	
13+	5 (1.7)	1 (7.1)	

COVID-19: coronavirus disease 2019; IgG: immunoglobulin G.

evidence of pneumonia; while the majority, 298 cases (98.7%), had no evidence of pneumonia. Additionally, 22 cases (6.6%) were symptomatic during the infection, leaving 282 cases (93.4%) asymptomatic (Table 1).

Association between IgG positivity and different factors

This study investigated the correlation between IgG positivity and various variables. A significant association was found between a history of COVID-19 in the family and IgG positivity in the recruited sample (p = 0.044). However, no other variables exhibited statistically significant correlation (all $p > 0.05$). These non-significant factors included birth weight (p = 0.573), premature labor (p = 0.281), feeding (p = 0.421), chronic disease (p = 0.56), immunization status (p = 0.348), socioeconomical status (p = 0.504), mother's occupation (p = 0.627), and family size (p = 0.532) (Table 1).

Characteristics of patients with long COVID-19

We determined the prevalence rate of long COVID-19 cases and our findings revealed that 14 out of 302 (4.6%) participants had long COVID-19. Among them, 9 patients were male (64.3%) and 5 were female (35.7%). In terms of immunization status, all 14 participants received complete routine immunization (100%). Regarding feeding practices, 4 participants were exclusively breastfed (28.6%), 2 were formula-fed (14.3%), and 8 were on mixed feeding (57.1%). The most commonly detected symptoms among long COVID-19 patients were fatigue, (12 patients, 85.7%), followed by cough (10 patients, 71.4%), and post-exertional malaise (5 patients, 35.7%).

Additional symptoms like headache, dizziness, hair loss, reduced appetite, sleep difficulties, mood fluctuations, abdominal discomfort, changes in bowel patterns, and chest pain were also observed, albeit to a lesser extent.

Association between long COVID-19 and different variables

Significant associations were found between long COVID-19; and history of documented prior COVID-19 episodes (p = 0.001), presence of pneumonia (p = 0.001), and family history of COVID-19 (p = 0.005). However, no significant associations were observed between long COVID-19 and the other variables investigated, including age group, gender, birth weight, mother's occupation, socioeconomical status, premature labor, chronic disease, feeding type, immunization status, and family size (all $p > 0.05$) (Table 2).

Discussion

After four waves of COVID-19 and vaccination campaigns, studying the prevalence of IgG positivity in children under the age of 12 years may reflect the true prevalence of the disease in any society. It is important to recall that this age group had not been vaccinated yet [11]. The vast majority of studies investigating the prevalence of COVID-19 in children were conducted during the pandemic; and may not fully reflect the true prevalence due to the ongoing infections. Our study was performed at the end of the pandemic and the prevalence of COVID-19 IgG positivity was 91.5%. Considering the waning of immunity, the true prevalence of infection might be higher than this. In a previous study conducted in Iraq during the pandemic, IgG positivity was lower than what was found in this study [10,12]. This could indicate a consistent rise in the infection rate, even in the presence of containment measures and vaccination campaigns. We found that the vast majority of the subjects had asymptomatic infections, in line with other research studies [8,12].

Our results are crucial for future pandemics, for aiding in devising effective containment strategies, understanding immunity dynamics, and optimizing vaccination efforts based on evolving infection trends. Children under the age of 12 years were unvaccinated, and by studying the prevalence of IgG positivity in this age group, we provided an insight into better understanding of the true extent of disease spread within the society, and insights into natural infection and immunity in this vulnerable population. In agreement with previous studies [8], household infection was found to be a risk factor for COVID-19 infection. Understanding the role of household transmission in the spread of SARS CoV-2 is crucial for implementing effective preventive measures and targeted interventions to mitigate the effect of the pandemic on vulnerable populations and curb the overall transmission of the disease.

Although the vast majority of children fully recovered from COVID-19, several studies showed that 10–25 % of them may developed persistent symptoms [13,14]. It is important to note that the prevalence rate of long COVID-19 among children varied widely in previous studies due to the studied group, research methods, and the specific definition used. In the UK, about a quarter of COVID-19 infected children continued to experience lingering symptoms for several months, and nearly 1 in 10 of them suffered from multisystem involvement [15]. In our study, 4.6% of the participants exhibited persistent symptoms, including fatigue, cough, dizziness, headache, loss of appetite,

and hair loss. To our knowledge, this study is the first investigation of long COVID-19 in children in Iraq. A study conducted in Iran reported the prevalence of long COVID-19 in children to be 10%, with the most commonly reported symptoms being fatigue, weakness, exercise intolerance, and shortness of breath [16]. However, no specific risk factor was identified for the development of long COVID-19 [16]. A study conducted in the Netherlands reported that 26% of the patients developed symptoms of long COVID-19; and identified that female gender, long duration of hospitalization, intensive care unit admission, and receiving oxygen were linked to a higher likelihood of experiencing long COVID-19 [17]. Furthermore, other studies examining factors contributing to the emergence of long COVID-19 in children revealed that age, gender, severe acute COVID-19, obesity, allergic conditions, and chronic illnesses were associated with an elevated risk of long COVID-19 [15,18–20]. In our study, we found that history of prior COVID-19 episode, development of COVID-19 pneumonia, and history of COVID-19 positive patients in the family were significant risk factors for the development of long COVID-19 in children. Our results provide insights into the characteristics of long COVID-19 pediatrics patients and offer valuable information regarding gender representation, immunization status, and feeding practices in this particular subset of participants.

The findings of our study carry significant policy implications at the local level, necessitating targeted public health interventions. The elevated prevalence of COVID-19 IgG positivity among unvaccinated children underscores the imperative for prioritizing vaccination campaigns and educational initiatives tailored for parents and healthcare providers. The identification of determinants for long COVID-19 in children holds potential to shape the formulation of precise pediatric care guidelines. The study accentuates the imperative of addressing household transmission, thereby suggesting the implementation of community health initiatives to mitigate infections within households.

Our study had limitations. First, this was a cross-sectional study that could assess changes in long COVID-19-related symptoms over time. Second, the study enrolled children who visited outpatient clinics. This could introduce sampling bias and may not have been representative of all children in the region. Third, the study relied on self-reported information, including symptoms and medical history, thus introducing the potential for recall bias. Finally, antibody response to SARS-CoV-2 can vary among individuals and studies suggest that IgG antibodies may wane over time after infection leading to missing IgG positive cases.

Conclusions

This study revealed a high prevalence of COVID-19 IgG positivity (91.5%) among children aged 5–12 in Duhok and Zakho cities, indicating substantial community exposure, even in the absence of vaccination for this age group. Long COVID-19 was observed in 4.6% of participants, with symptoms persisting beyond 4 weeks post infection. The symptoms included fatigue, cough, and headache. Risk factors for long COVID-19 in children included history of prior COVID-19 episodes, pneumonia during infection, and family history of COVID-19. Notably, other demographic and health-related factors showed no significant associations.

These findings underscore the need for ongoing research to comprehend the complexities of long COVID-19 in children, and its risk factors; while recognizing the limitations of the study's design and urging caution in generalizing the results. The study contributes valuable insights for public health strategies, emphasizing the continued impact of the pandemic on the pediatric population and the importance of understanding immunity dynamics for future outbreaks.

Disclaimer

The information in this article can be used for research purposes, and the authors disclaim no liability in connection with the use of this information.

Authors' contributions

The authors contributed equally to the study.

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Conflict of interests

No conflict of interests is declared.

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