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Original Article

Investigation of Laboratory Indicators, Clinical Symptoms, and COVID-19 Vaccination History in Children Referred to Imam Khomeini Hospital in Jiroft City, South Iran

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Abstract

Background: The commencement of COVID-19 vaccination has had an impact on hospitalizations and deaths of patients. This study aims to investigate the effect of COVID-19 vaccination on children›s hospitalizations and deaths.

Methods: This cross-sectional study examined 893 children infected with COVID-19 referred to Imam Khomeini hospital in Jiroft City in the south of Iran in 2022. Data collected and analyzed included demographic variables including age, sex, place of residence, underlying disease, vaccination status, injection dose of vaccine, history of contact with a patient with COVID-19, and clinical and laboratory characteristics such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), creatinine (CR) and days of hospitalization. The data were analyzed using SPSS-v20 software.

Results: The average age ± SD of the patients is 4.6 ± 3.9 years. There were 302 (33.81%) children in the age group of 9 to 12 years and 133 (14.89%) of children were in the age group under one year. The most common clinical symptoms in children with COVID-19 were fever (67.41%), diarrhea (38.63%), and cough (30.57%). ESR and CRP were 27.72 ± 20.8, and 25.51 ± 32.8 respectively amongst the participants. Out of 893 children, 480 (53.75%) were vaccinated and 413 (46.24%) had not received the vaccine. Out of 480 vaccinated children, 460 (95.83%) were outpatient, and only 20 (4.16%) were hospitalized, and out of 413 non-vaccinated children, 241 (58.35%) were outpatient, and 172 (41.64%) were hospitalized.

Conclusion: The results showed that vaccination led to a 95.83% reduction in hospitalization and a 100% reduction in long-term hospitalization. The COVID-19 vaccination is very effective in preventing the harmful effects of COVID-19 in future trends and pandemics.

Keywords: Hospitalization, COVID-19, Vaccination, Children

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Introduction

In December 2019, an epidemic of a new virus occurred in China, which was later named SARS-CoV-2. On March 11, 2020, the World Health Organization (WHO) announced that this virus had caused a worldwide pandemic (1). The WHO announced the epidemic of this virus as the sixth public health emergency that required international attention (2).

This virus can cause severe respiratory, intestinal, cardiac, and neurological symptoms (3,4). In humans, the coronavirus mainly causes respiratory and digestive manifestations, which range from a simple cold to severe clinical conditions such as bronchitis, pneumonia, acute respiratory distress syndrome, diffuse coagulation disorders, failure of several organs at the same time, asthma, and fibrocystic and chronic obstructive pulmonary diseases, and death (5).

Most findings indicate that the course and clinical symptoms are milder and the prognosis is better in children, but many of them are not diagnosed in the early stages of this infection; thus children can play an important role in transmitting this virus to others (2,5). Also, due to the predominance of gastrointestinal symptoms in infants and children, in some cases, the spread of this virus through feces continues for several weeks after diagnosis in children, and it can also spread in kindergartens or elementary schools (5). In addition, in 41% of cases, intra-hospital transmission has been

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reported (6). Children with underlying diseases such as cancer, asthma, obesity, neurodevelopmental disorders, certain mental health conditions, etc, are at a higher risk of hospitalization and have certain conditions, as well as medical complexity, were associated with a higher risk of severe COVID-19 illness (7,8).

Simultaneously with the progress of clinical manifestations, there is often a significant increase in inflammatory cytokines such as intercholine (2,7,9) as well as granulocyte colony growth factor, tumor necrosis factor-alpha, and macrophage inflammatory protein (10).

Based on a large study conducted on 2143 children more than 90% of patients with confirmed COVID-19 were asymptomatic and had mild, or moderate forms of the disease, and 5% of children had severe disease (8). Due to the missed diagnosis of many cases of COVID-19 in children in the early stages of infection and the important role of children in transmitting this virus to others (5), it is necessary to pay special attention to the complete vaccination of COVID-19 in children.

The availability of an effective and safe pediatric COVID-19 vaccine seems imperative for clinical and epidemiological reasons (11) because serious complications from COVID-19 are rare among children who receive the COVID-19 vaccine (12). The incidence of adverse reactions to the COVID-19 vaccine in children is not higher than that of adults and the available evidence confirms that the COVID-19 vaccines are safe and effective for children (13). Therefore, it is necessary to vaccinate children against COVID-19.

The purpose of this study was to determine laboratory indicators clinical symptoms and history of COVID-19 vaccination in children referred to Imam Khomeini Hospital in Jiroft City in the south of Iran.

Methods

This study was a cross-sectional (descriptive) study and the study population included all children infected with COVID-19 with a positive polymerase chain reaction (PCR) test on an outpatient basis or hospitalized in the special department for corona patients of Imam Khomeini Hospital in 2022. Once a license was obtained from Jiroft University of Medical Sciences, patient records were utilized to collect the data. The inclusion criteria included all people under 14 years of age who were referred to Imam Khomeini hospital, as well as the completeness of the patients' files and the positiveness of the RT-PCR test. Exclusion criteria included age over 14 years and incompleteness of patient file information. The data was collected by census method from all the children referred to the hospital who met the inclusion criteria. To collect data, clinical records, laboratory findings, and children's immunization status were extracted using a checklist. The collected data included demographic variables including age, sex, place of residence, underlying disease, vaccination status, injection dose of vaccine, history of contact with a patient with COVID-19, clinical and laboratory characteristics including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), creatinine (CR), as well as days of hospitalization. Quantitative data were reported as mean ± standard deviation (SD) and qualitative data were reported as numbers (percentage). The collected data remained confidential and was used only for research. The data was analyzed using SPSS version 22 statistical software.

Results

In total 893 children infected with COVID-19 were enrolled. The average age ± SD of the patients was 4.6 ± 3.9 years. There were 302 (33.81%) children in the age group of 9 to 12 years, and 133 (14.89%) children were in the age group under one year. More children 463 (51.84%) were boys and 824 (92.27%) were urban residents (Table 1).

In the admitted children, the mean ± SD of temperature was 37.6 ± 0.53 degrees Celsius. The most common symptom was fever in 602 (67.41%), 273 (30.57%) had a cough, and 58 (6.49%) had muscle pain. The level of consciousness decreased in 91 (10.19%). 13 (1.45%) of children, experienced convulsions, 16 (1.79%) had stomachache, 9 (1%) had nausea, 26 (2.91%) had vomiting, 345 (38.63%) had diarrhea, 6 (0.67%) had anorexia, 33 (3.69%) had headache, and 9 (1%) had chest pain.

Out of 893 investigated individuals, 11 people (1.23%) had asthma, 6 people (0.67%) had neurological diseases, 26 (2.91%) had cardiovascular disease, 5 (0.55%) had diabetes, 1 (0.11%) had bowel obstruction, 4 (0.44%) had seizures, 9 (1%) had hypertension, 2 (0.22%) had thyroid disorders, and 8 (0.89%) had other chronic diseases.

The results of Table 2 show that the normal range of ESR is 1-20 mm/h, and in the present study, the average ESR was 27.72 ± 20.8. The normal range of creatinine (Cr) is 1.2-0.5 mg/dL, and, in the present study, the average Cr

Table 1. The demographic information and contact history of children with COVID-19 referred to Imam Khomeini Hospital in Jiroft in 2022

Variables		Frequency	Percent
Gender	Girls	430	48.15
	Boys	463	51.85
Age	1>	133	14.89
	2-5	261	29.23
	6-8	197	22.06
	9-12	302	33.82
Residence	City	824	92.27
	Village	69	7.73
Contact history	Yes	784	87.79
	No	109	12.21

was 0.78 ± 0.232.

The normal range of WBC is 5 to 10 $\times 10^3$ μ/L, and, in the present study, the average WBC count was 8.85 $\times$ 10^3 μ/L, ± 5.82.

The normal range of CRP is less than 10 mg/L, and in the present study, the average CRP was 25.51 ± 32.8.

Regarding intubation, out of 893 investigated children, 5 (0.5%) were intubated (all were not vaccinated), and among 480 children with a history of COVID-19 vaccination, only 20 (4.1%) were hospitalized.

The results of Table 3 show out of out of 893 children with COVID-19, 480 (53.75%) were vaccinated and 413 (46.24%) were not vaccinated. In total, 724 (81.07%) children were outpatients and 169 (18.92%) children were hospitalized. Out of 480 vaccinated children, 460 (95.83%) were outpatient, and only 20 (4.16%) were hospitalized, and out of 413 non-vaccinated children, 241 (58.35%) were outpatient, and 172 (41.64%) were hospitalized ($P < 0.001$).

Table 4 shows the comparison of the number of days of hospitalization in two groups of vaccinated and unvaccinated children, the results show that in the vaccinated group, 75% of the children were hospitalized for 1 to 2 days. and none of the vaccinated children were hospitalized for more than 8 days, but in the other group (not vaccinated), 53.69% of the children were hospitalized for 4 to 5 days, and 6.71% were hospitalized for more than 8 days.

Discussion

The findings of the present study demonstrated that the most common clinical symptoms in children with COVID-19 were fever, cough, and diarrhea. In this regard, in the study of Qasemzade et al, the main clinical presentations in children were cough, sore throat, wheezing, and fever (14). Qiu and colleagues' study, which examined 36 children with COVID-19 found that the most common symptoms in children were fever, dry cough, and pneumonia (15). In a study of 74 children with COVID-19 infection, it was found that the most common symptom in 41 cases (55.4%) was fever, and in 38 cases (51.4%) was dry cough (16). In his studies on 10 children, Jiehao et al also found that the most common symptoms in corona-positive children are fever, cough, and sore throat (17). In a review study of 11 case series and 333 samples of infants and children, it was found that the most common symptoms were fever (48%), cough (42%), and pharyngitis (30%) (18). In 20-30% of cases, in the first days of the disease, diarrhea can be the only manifestation of the disease, and pulmonary symptoms appear a few days later. In the absence of complications, the diarrhea is slimy but non-bloody and usually recovers in less than a week. Dehydration is an important complication of the disease in affected children, which may lead to hypovolemic shock. Patients hospitalized with digestive symptoms have a longer period of increased levels of inflammatory markers and liver enzymes and decreased coagulation factors (19).

Concerning the underlying diseases in our study, most cases were related to cardiovascular disease with 26 cases out of 893 patients, and asthma with 11 cases. in the study of Kompaniyets et al, the highest rate of underlying diseases was related to asthma with 4416 cases out of 43 465. In the mentioned study, the most important factor related to the severity of the disease was congenital cardiovascular disease (20).

In some studies, it is concluded that the respiratory disease caused by the COVID-19 virus may lead to severe disease in healthy children, but the presence of severe underlying diseases such as blood malignancies, diabetes, congenital heart diseases, and other underlying diseases may put the patient in a more dangerous situation (21). Heart disease in children with COVID-19 may be a sign of MIS-C or caused by a Kawasaki-like disease after COVID-19 infection, which presents as myocarditis, cardiomyopathy, coronary artery involvement, pericardial effusion, insufficiency of heart valves (especially mitral and tricuspid), diastolic and systolic dysfunction and heart failure, arrhythmia, and cardiogenic shock. There is no information about the long-term cardiac complications of the patients. However, in the studies conducted hitherto, these patients achieved complete recovery after one to two months. A case report has been

Table 2. Determination of ESR, Cr, WBC, and CRP levels in children with COVID-19 in Jiroft city in 2022

Variables	Mean	SD	Minimum	Maximum
ESR	27.72	0.8	2	96
Cr	0.78	0.23	0	2
WBC	8.85	5.82	1	48
CRP	25.51	32.8	0	134

Table 3. Outpatient and hospitalization status of children with COVID-19 referring to Imam Khomeini Hospital in Jiroft (chi-square test)

Variable	Vaccination				Total		*P* value
	Yes		No				
	Number	Percent	Number	Percent	Number	Percent	
Outpatient	460	95.83	241	58.35	724	81.08	
Hospitalized	20	4.17	172	41.65	169	18.92	0.000
Total	480	100	413	100	893	100	

Table 4. The number of hospitalization days of children infected with COVID-19 in Jiroft City in 2022

Variable		Vaccinated		Non vaccinated	
		Number	Percent	Number	Percent
Number of hospitalization days	1-2 days	15	75	38	25.50
	3-5 days	3	15	80	53.69
	6-7 days	2	10	21	14.09
	Over 8 days	0	0	10	6.71
Total		20	100	149	100

published regarding the persistent involvement of the coronary arteries in a case that appeared in the form of a giant aneurysm (20).

In the Lal Kheirkhah et al study, in two patients, increase in red blood cell sedimentation rate (ESR) and CRP was reported in only one child (22). In Mohammadi and colleagues' study, anemia in 48 people, thrombocytopenia in 10 people, hyponatremia in 57 people, and increased CRP in 18 people were reported as the most common laboratory abnormalities (23). In adults, the intensity of the increase in CRP indicates the systemic release of cytokines, and the increase in CRP above 41 indicates the worsening of the disease (24). Liu et al conducted research to describe the clinical manifestations and features of CT scans and laboratory results of COVID-19 disease in 15 pregnant women. Their results showed that the most common abnormal laboratory findings were a decrease in blood lymphocytes (12.15% of the patients) and an increase in CRP (10.15% of the patients) (25).

The results of the present study showed that 4.16 percent of vaccinated children were hospitalized, while 41.64% of non-vaccinated children were hospitalized due to COVID-19. This shows the effect of the vaccine on preventing hospitalization, which is consistent with the results of other studies. Mirahmadizadeh et al conducted a study comparing the effectiveness of vaccines in Iran, their results showed that the implementation of the vaccination plan, including all available vaccine options in Iran, led to a significant reduction in the incidence of COVID-19, and hospitalization related to COVID-19 was remarkedly decreased (26).

In Russell and colleagues' study, they found that serious complications from COVID-19 were rare among children who received the COVID-19 vaccine (12). Ioannidis and colleagues reviewed hundreds of pediatric hospitalizations during the summer and found that nearly all children who developed severe COVID-19 were not fully vaccinated and experienced a severe illness (27). Opel and colleagues' results showed that the COVID-19 vaccination reduced the risk of hospitalization related to this disease in children aged 5 to 11 years during the Omicron pandemic by two-thirds (28).

The results of the present study showed that the vaccination of children with COVID-19 caused a significant reduction in the hospitalization rate and the number of hospitalization days.

In the study of Bhattacharya et al, it was observed that the rate of contracting the COVID-19 disease in people who had been at least 14 days since the second dose of the COVID-19 vaccine was 0.17%, the percentage of hospitalization of these children was 0.12%, and the rate hospitalization in ICU was reported in 0.07% of them (29).

Tanveer and his colleagues examined more than 2200 children aged 12 to 15 years in a study, and at the beginning of this research, approximately half of the children received the vaccine and the other half did not receive the vaccine. One week after the administration of the second dose, no cases of COVID-19 were reported in 1005 children who received the vaccine. Among 978 children who received a placebo, 16 cases of COVID-19 were reported (30).

The results of our study showed that the average age of the examined patients was 4.6 years, the highest frequency was observed in the age group of 9 to 12 years, and the number of boys with COVID-19 was higher than girls. This is consistent with other studies; it was shown in Osmanov's study that increasing age can be considered a risk factor for COVID-19 in children, therefore, the rate of residual complications was higher in older patients (31). In Wang and colleagues' study, more boys were hospitalized due to new coronavirus infection, but this difference between the two sexes was not significant in their study (32). In the study of Lal Khairkhoeh et al, who evaluated clinical manifestations, laboratory, and radiological findings in children with COVID-19 in Esfrain city, their results showed that most children with COVID-19 were boys (22). In Mohammadi and colleagues' study, out of 70 children with COVID-19, 40 were boys and the average age of the children was 3.56 years (23).

One of the limitations of the study is the use of the recorded data of PCR-positive patients in the hospital, which cannot be used to calculate the effect of the vaccine without infection, and it fails to determine the effect of the vaccine dose on outpatient and hospitalization status with the incompleteness of vaccine doses in the studied children.

Conclusion

The results of the present study showed that the vaccine caused a 95.83% reduction in hospitalization and a 100% reduction in long-term hospitalization (more than 8 days) and intubation of patients. Therefore, completing the vaccination for COVID-19 is very effective in preventing the consequences of COVID-19 in the next possible episodes of the disease and similar epidemics in the future. It is recommended to carry out prospective studies to determine the status of future epidemics and prepare for the management of these diseases.

Authors' Contribution

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Competing Interests

The authors of this study have no conflict of interest.

Ethical Approval

The university's ethics committee's permission was also obtained with the approval ethical code IR.JMU.REC.1402.030.

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