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Demographic and Clinical Profiles, Including Comorbidities, of Hospitalized Patients Under 18 Years of Age with COVID-19

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Objectives: This study was aimed to evaluate the various demographic and clinical characteristics in hospitalized children with COVID-19 as well as their comorbidities.
Methods: This cross-sectional study evaluated a total of 809 hospitalized COVID-19 patients under 18 years of age in the referral university based Ali-Asghar Hospital in 2020. Demographic and clinical characteristics of patients were extracted from the archived records and data analysis was performed using SPSS software version 26.
Results: The mean age of patients was 4.1 years and the higher percentage of patients (57%) were male. The most common symptoms of COVID-19 in children were fever, cough, and diarrhea. As well, the most common symptoms in 22.1% of patients admitted to the intensive care unit (ICU) were gastrointestinal (GI) symptoms (79%), fever (62.6%), and respiratory distress (53.6%), respectively. The majority of patients were in the age group less than one year (52%) and mortality rate was 6.3% in total and 10% in children with underlying disease. Besides, the mortality rate of intubated cases was 13 times higher.
Conclusion: The findings of present study showed that COVID-19 in children was associated with various clinicopathological manifestations. Underlying disease including respiratory distress, cancer, and kidney disease as well as GI symptoms might be guided predicting the hospitalized cases in ICU. Newborns less than one year of age are exposed to severe COVID-19 infection which is associated with higher mortality rate and it should be given special attention in the early diagnosis and management of the COVID-19 disease.
Key words: COVID-19, children, clinical manifestations, SARS-CoV-2

Introduction

The novel coronavirus has also been nominated as the pandemic 2019 coronavirus disease (COVID-19) by the World Health Organization (WHO) for global health emergency.[1,2] The pneumonia outbreak caused by SARS-coronavirus 2 (SARS-CoV-2) was started in Wuhan city, Hubei Province which was quickly released across China and subsequently in most countries or regions.[3] Although the severity and lethality of COVID-19 is less compared to severe acute respiratory syndrome (SARS), elderly patients with SARS-CoV-2 infection are disposed to experience more severe symptoms.[4,5] COVID-19 disease involved all groups of age with wide range of complications from insignificant flu-like infection to severe pneumonia including acute respiratory distress syndrome (ARDS), myocardial and acute kidney injury (AKI), multiorgan dysfunction, and shock.[6] Adolescents of any age are at risk to COVID-19, but global investigation statistics have stated that they typically account for 13% of confirmed cases in laboratory tests.[7,8] Despite the high susceptibility of pneumonia in children compared to adults, the lower level of SARS-CoV-2 infection in children may be due to the low rate of diagnosis in terms of mild and unusual clinical manifestations of infection as well as low exposure.[9,10] As a result, there are fewer hospitalized children with COVID-19 than adult patients.[3,11]

In addition, the demographics and clinicopathological manifestations of the adult hospitalized patients with COVID-19 has been fully documented.[4,12–14] Due to the limited cases of children and pediatrics with SARS-CoV-2 infection, there is little information about the clinical symptoms and demographic features of the patients.[15–17]

The current situation of the pandemic showed that children had a growing trend worldwide. As reported by several studies, a number of 2135 children with COVID-19, 74 cases admitted to intensive care units (ICU), and 176 190 infected children in China, United States and on a global scale, respectively.[18,19] However, the effect of SARS-CoV-2 infection on adults and children is totally different.[17,20,21] Despite the universal distribution of COVID-19, its clinical, geographical, and epidemiological patterns remains blurred, mainly among pediatrics and adolescents. Considering the shift of infection from the elderly population to the younger age groups and the lack of complete vaccination of children, it is pertinent to identify and discover the main clinical and outcome profiles that facilitate early diagnosis and therapeutic strategies for children potentially infected with SARS-CoV-2. Also, until now, the hospitalization rate in children has been lower and there has been less information about the COVID-19 disease in patients who have underlying diseases or pre-existing comorbidities. This study was designed to investigate the demographic and clinical characteristics and to get more detailed information for management of COVID-19 in the age group under 18 years old.

Material and Methods

Demographic features of COVID-19 patients

This r cross-sectional study was performed in the university based referral center, Ali Asghar Children's Hospital in Tehran. 2019. The study population were a total of 809 children and adolescents less than 18 years of age who referred,

hospitalized, and treated due to COVID-19 disease were included in the study. Patients' demographic information and related medical history were recorded from the patients' archives. The study inclusion criteria were composed of all the population under 18 years of age who have been hospitalized with the diagnosis of COVID-19 or have been monitored on an outpatient basis. The positivity of COVID-19 patients was based on laboratory and radiological findings. Patients who refused to continue the treatment process for any reason or were transferred to another medical centers were excluded from the study.

Clinical information of COVID-19 patients

The clinical symptoms of the patients, the underlying disease and the length of hospitalization were entered in the Excel form. The definition of disease severity was based on the following criteria.[22]

Mild: symptoms limited to the upper respiratory system

Moderate: There is involvement of the lower respiratory system, but there is no need for oxygen treatment support.

Severe: need for supplemental oxygen or increase the amount of oxygen from the previous level without aggressive ventilation.

Critical: New or increased need for oxygen and invasive mechanical ventilation or having sepsis and multiple organ failure.

Ethical Approval and Considerations

Ethical approval was attained by the Ethics Committee of the Iran University of Medical Sciences (IR.IUMS. REC.1400.059) and declaration was made to keep patient's data confidential. The coded data were only available to the physician and the project manager, and were provided for treatment after the achievement of the study plan and the end of the follow-up.

Data Analysis

Data was analyzed using SPSS statistical software (version 26; SPSS). The results obtained for quantitative variables are expressed as mean and standard deviation (mean ± SD). Demographic findings of patients, clinical symptoms and para clinical findings were analyzed based on quantitative and qualitative factors. The normal distribution of the data was measured by the Kolmogorov-Smirnov test. Qualitative data in two groups were analyzed using chi-square (χ^2) test. A level of 0.05 was considered in terms of statistically significant variables.

Results

Demographic characteristics of COVID-19 patients

A total of 809 patients with COVID-19 were included in this study which had the median age of 3 (ranged 0–18) and the mean age of 4.1 ± 4.2. In addition, 57% of the patients were male and 43% of them were female. A total of 209 from 809 patients (25.8%) had underlying diseases. The most underlying diseases were chronic kidney diseases, cancer and neurological diseases, respectively. Descriptive information of the patients with COVID-19 are given in Table 1.

Table 1. **Demographic features of patients with COVID-19.**

Demographic features of patients	Total number	Percentage (%)
Age (4.1±4.2)		
Age (subgroups)		
Less than a year	154	19%
1 to 5 years	425	52.5%
6 to 10 years	136	16.8%
11 to 15 years	84	10.4%
16 to 18 years	10	1.2%
Gender		
Male	348	47%
Female	461	57%
Location		
Tehran	686	84.8%
Cities other than Tehran	123	15.2%
Inpatient ward		
special	179	22.1%
isolated	130	16.1%
Normal	500	61.8%
Type of patients' referral		
personal	738	91.2%
ambulance	71	8.8%
History of exposure with patients		29%
Comorbidity		
Chronic kidney disease	56	6.9%
dialysis	20	
cancer	53	6.6%
chemotherapy	29	
chronic liver disease	5	0.6%
diabetes	10	1.2%
asthma	5	0.6%
heart disease	8	1%
HIV	2	0.2%
Immunodeficiency	10	1.2%
chronic blood disease	27	3.3%
Chronic neurological disorders	29	3.6%
tension	10	
CP	10	
Other chronic diseases	45	5.5%

Clinical Symptoms of COVID-19 Patients

The most common clinical symptoms were fever (80.8%), cough (28.3%) and diarrhea (24.6%), respectively. In total, 40% of patients had gastrointestinal symptoms and 7.2% of them had neurological symptoms. The spearman's test was used to evaluate the association between age and clinical symptoms and it was determined that with increasing age, the probability of symptoms such as fever, muscle pain or myalgia, abdominal pain, and headache was raised. Considering that the occurrence of diarrhea is higher in the middle age, it was evaluated based on different age subgroups which was inversely related to increasing age. As well, increasing age enhanced the probability of intubation in COVID-19 patients (P-value = 0.002; r = 0.11). The frequency of clinical symptoms in COVID-19 patients are shown in Table 2.

The mean temperature of patients was 38 ± 0.8°C and the median was 38.2°C (33.1–40). The mean days of symptoms'

Table 2. **The frequency of clinical symptoms and their association with age of COVID-19 patients.**

Clinical symptoms	Total number (%)	*P*-value	Correlation coefficient (*r*)
Fever	645 (80.8)	0.01	0.9
Cough	229 (28.3)	0.60	
Respiratory distress	163 (20.1)	0.10	
Diarrhea	199 (24.6)	0.02	-0.08
Myalgia & muscle pain	79 (9.8)	0.001	0.29
Decreased level of consciousness	7 (0.9)		
Loss or reduction of the sense of smell	1 (0.1)	0.30	
Loss or reduction of sense of taste	2 (0.2)	0.30	
Seizure	8 (0.1)	0.50	
Abdominal pain & Cramp	64 (7.9)	0.001	0.17
Nausea	95 (11.7)		
Vomiting	125 (15.5)	0.06	
Anorexia	20 (2.5)	0.50	
Headache	42 (5.2)	0.001	
Vertigo	2 (0.2)	0.13	
Skin rash	12 (1.5)	0.4	
Paralysis of organs	1 (0.1)	0.50	
Chest pain	4 (0.5)		
Weakness and lethargy	18 (2.2)		

Table 3. **The clinical symptoms of hospitalized COVID-19 patients.**

Clinical symptoms	Total number (%)
Temperature (mean = 38 ± 0.8)	
Positive PCR test	131
Time from the onset of symptoms to referral (mean = 3.1 ± 2.8)	
Observed lung involvement in CT scan	186 (23)
Hospitalization length	10.18 ± 11.8
Oxygen therapy	145 (17.9)
Intubation	53 (6.5)
Death	51 (6.3)
Severity of symptoms	
Mild	393 (48.6)
Moderate	133 (16.4)
Intense	238 (29.4)
Critical	45 (5.6)

onset and hospital referral was 3.1 ± 2.8 days and the median was 2 (1–30) days. The length of patients' hospitalization was 10.18 ± 11.8 and median was 7 (1–134) days, as shown in Table 3. There was no significant association between age and other clinical characteristics including symptom's severity (*P*-value = 0.14) and oxygen therapy (*P*-value = 0.10).

The linear regression analysis was performed to examine the association between age and the clinicopathological factors, and there was no strong linear relationship between age and these factors. As shown in Table 4, for further evaluation, patients were divided into age subgroups. Most of patients (52%) were children aged 1 to 5 years and 179 patients (22.1%) were admitted to special wards. Seventy one patients (8.8%) were transferred to the other medical centers. Male gender was dominant in all age groups. Also, a higher percentage of patients who referred with severe and critical illness were belonged to the subgroups less than one year.

As shown in Table 4, it was found that in the age group under one year, a higher percentage of patients had severe and critical infection. The association between the COVID-19 severities in two age groups, less than one year and more than one year, was examined with Kendall's analysis. It was determined that the COVID-19 disease was more severe in younger age (*P*-value = 0.001; $r = -0.117$). In the regression analysis, mortality rate in group of under one year was significant and the probability of death in this age group was higher (*P*-value = 0.009; OR = 2.26).

According to the difference in the severity of the disease in the age groups of less than one year and more than one year, the clinical symptoms in both groups were compared. Chi-square analysis and Cramer's correlation were used for this evaluation and results were summarized in Table 5. Fever, cough, and respiratory distress were the most common symptoms in children under one year of age, and the occurrence of neurological, gastrointestinal, and skin rash symptoms was lower in this age group. Although neurological and gastrointestinal symptoms increased with age and the difference became significant, but Kramer's correlation analysis showed a weak correlation of these variables with age (<0.2), as well, in terms of fever, this correlation was moderate.

Severity of Disease and Mortality Rate in Patients With COVID-19

Mortality rate of COVID-19 patients was 6.3% and in patients with underlying disease was 10%. The highest mortality was observed in the age group of less than one year and 11% of infants who died were less than one year. As well, occurrence of underlying disease led to triple the risk of severe disease (*P*-value = 0.001; OR = 3.59). Also, in our study, occurrence of asthma was not related to the severity of disease in COVID-19 patients (*P*-value = 0.90). In examining the association between the occurrence of underlying disease and mortality rate based on different clinical factors, it was found that the risk of mortality was higher in patients with underlying disease (*P*-value = 0.01; OR = 2.1). In examining factors related to mortality using univariate analysis, differences in clinical factors such as fever, respiratory distress, decreased level of consciousness, blood and kidney diseases, and hospitalization length and intubation were significant. In the multivariate analysis shown in Table 6, by adjusting other variables, only intubation was significant, which increases the probability of death by 13 times.

Table 4. **Demographic and clinical characteristics based on the age subgroups.**

Variables	<1 year *n*=154	1–5 years *n*=425	6–10 years *n*=136	11–15 years *n*=84	16–18 years *n*=10
Gender					
Female	42.9%	43.5%	44.9%	38.1%	40.0%
Male	57.1%	56.5%	55.1%	61.9%	60.0%
Severity of symptoms					
Mild	40.3%	54.1%	44.9%	45.2%	20.0%
Moderate	10.4%	15.1%	22.8%	20.2%	50.0%
Intense	39.0%	25.6%	28.7%	33.3%	20.0%
Critical	10.4%	5.20%	3.70%	1.20%	10.0%
History of exposure	33.8%	28.5%	29.4%	27.4%	60.0%
Temperature°C	37.7	38.1	38.0	38.0	38.1
Hospitalization length (day)	12.8	9.80	10.5	9.10	12.8
Comorbidity	10.4%	25.2%	33.8%	42.9%	40.0%
Death	11.0%	6.40%	2.90%	2.40%	10.0%

Table 5. **Clinical symptoms at the age of less than one year and above one year in COVID-19 patients.**

Clinical symptoms	≤1 year age	≥1 year age	*P*-value	Correlation coefficient (*r*)	OR	95% Confidence Interval (CI)
Fever	64.3%	84.7%	0.001	0.204	0.324	0.219–0.480
Cough	30.5%	27.8%	0.498			
Respiratory distress	33.8%	16.9%	0.001	0.165		
Gastrointestinal symptoms	28.6%	43.5%	0.001	0.119		
Neurological symptoms	0.60%	8.80%	0.001	0.123		
Skin rash	0.00%	1.10%	0.225			
Decreased level of consciousness	0.60%	90.0%	0.740			

Table 6. **Association between clinical factors and mortality rate.**

Clinical factors	Univariate	Multivariate		
	P-value	*P*-value	OR	95% Confidence Interval (CI)
Fever	0.003	0.690		
Decreased level of consciousness	0.002	0.260		
Blood diseases	0.020	0.060		
Kidney diseases	0.010	0.750		
Hospitalization length	0.001	0.760		
Intubation	0.001	0.008	13.77	1.97–96.9

Mortality Rate in Patients with COVID-19 Based on PCR Results and Admission in Hospital Wards

Among the patients who had a positive SARS-CoV2 PCR results (49 patients), 6 cases (4.6%) were died and 43 cases (6.5%) were discharged. Evaluation of mortality based on PCR results did not show any significant difference (*P*-value = 0.57). In patients with negative PCR results, 125 cases (95%) and 614 cases (93.5%) were died and discharged, respectively.

As shown in Table 7, 179 patients (22.1%) were admitted to ICU and 630 patients were admitted to normal and isolated wards and the differences between these two groups of patients were analyzed. Although male gender comprised a higher percentage of ICU patients, the differences in gender was not statistically significant. There was a significant difference in ICU hospitalization at the age of less than one year. In univariate analysis, the risk of ICU hospitalization in age groups less than one year was 5 times higher than other groups. As well, in the multivariate analysis, fever, respiratory distress and gastrointestinal symptoms were statistically significant, and those who presented with respiratory distress and gastrointestinal symptoms had 6 and 2 times higher risk of hospitalization in ICU, respectively. Regarding the relationship between underlying diseases and hospitalization in the special ward, cancer and kidney diseases were statistically significant in univariate analysis. In the multivariate analysis, cancer or kidney disease increases the risk of hospitalization in the special ward by 2 and 1.8 times, respectively. In ICU patients, the probability of intubation was 10 times higher and the probability of death was 8 times higher.

Discussion

There are fewer treatment facilities for children and adolescents due to the possible low risk of infection and the focus on prioritizing and vaccinating young and elder patients. Therefore, the transmission of SARS-CoV-2 through the children should not be discounted. In this research we tried to explain the different clinical and epidemiological features of COVID-19 in children and adolescents to reduce the disease

Table 7. **Differences Between Hospitalized Patients in the Special and the Normal Wards.**

Clinical symptoms	ICU *N*=179	Non-ICU *N*=630	*P*-value	Correlation coefficient (*r*)	OR	95% Confidence interval (CI)
Gender						
Female	43.6%	42.9%				
Male	56.4%	57.1%				
Age						
≤1 year age	44.1%	19.0%	0.001		5.84	3.99–8.55
1–5 years	32.4%	52.5%				
6–10 years	15.6%	16.8%				
11–15 years	6.70%	10.4%				
16–18 years	1.10%	1.20%				
Clinical symptoms						
Fever	62.6%	86.0%	0.001		0.378	0.24–0.58
Cough	36.0%	25.9%	0.004	0.14		
Respiratory distress	53.6%	10.6%	0.001		6.71	4.43–10.15
Gastrointestinal symptoms	79.0%	53.9%	0.001		2.03	1.31–3.14
Neurological symptoms	6.30%	7.50%	0.190			
Comorbidity						
Cancer	2.80%	7.60%	0.027			
Liver	0.00%	0.80%	0.900			
Diabetes	2.20%	1.00%	0.180			
Blood diseases	2.80%	3.80%	0.520			
HIV	0.00%	0.30%	0.900			
Immunodeficiency	0.00%	1.60%	0.900			
Heart disease	1.10%	1.00%	0.840			
Kidney diseases	10.6%	5.90%	0.030		1.80	1.01–3.22
Asthma	0.60%	0.60%	0.900			
Neurological disorders	1.20%	0.30%	0.160			
Oxygen condition	43.0%	10.8%	0.001	0.271	0.271	0.175–0.419
Intubation	24.6%	1.40%	0.001		10.814	4.92–23.73
Death	19.0%	2.70%	0.001		8.45	4.50–15.5

complications through the effective planning and early intervention measures in this population.[22]

It has been demonstrated that the viral load of SARS-CoV-2 were 10–100 times higher in children younger than 5 years than in cases more than 5 years old and adolescents with COVID-19.[23] The incidence of COVID-19 in a series of 228 children between 1–5 years old increased by 7.4-fold.[24] Moreover, patients with COVID-19 and younger than 1 year of age and <5 years experienced severe symptoms of infection.[18,25] In this retrospective study a total of 809 children have participated which most of them had mild symptoms and were hospitalized and monitored due to concerns related to this age group as well as children referred from other cities. The mean and median age of the patients in our study was 4 ranged from infancy to the age of 18 indicating the susceptibility of all age groups to COVID-19 infection. Also, in all age groups, male gender was comprised in a higher percentage of patients, and more of this gender males were admitted to the special wards due to the severe infection. In line with other studies, difference in gender was not statistically significant.[26,27] In three studies the median age of children with COVID-19 has been reported to be 6.2, 5.3, and 8.16 years, respectively.[18,28–30] Armin et al.'s study revealed that male gender made up the majority of patients (59.4%),[28] as in Dong et al.'s and Hua et al.'s study a 56.6 % and 60.5% has been reported to be males.[18] In terms of MERS disease, females showed lower incidence and severity of the disease which can be attributed to the biological differences, protective effect of the X chromosome, and the lower expression of the ACE2 receptor in females against viral entry into the cells.[31]

In our study, 29.9% of COVID-19 patients had familial exposure and the source of infection was unknown in 70.1% of children which was in contrast with the findings of other study regarding the family clusters as the main origin of the disease.[32] As well, a large percentage of children had an unknown source of infection, our study indicates that children can acquire the disease from social clusters, besides the family. Twenty three percent of children presented lung involvement in chest CT scan, and it was consistent with Ma et al. study with 22% of lung involvement in children with COVID-19. Although lung involvement in this age group was less than adults, but the pattern of glass-like opacities was similar to

them.[33] In systematic literature studies and a pediatric study in Shiraz, fever and cough has been identified as the most common clinical symptoms.[16,34,35] Findings of present study showed that fever, cough and diarrhea are common symptoms of COVID-19 infection in children. As well, a total of 40% of children had gastrointestinal symptoms such as anorexia, vomiting, abdominal pain, and diarrhea. According to Chang et al.'s and Armin et al.'s studies the uncommon gastrointestinal symptoms, diarrhea and vomiting were reported in 12%, 22.3%, and 30.3% of cases, respectively.[16,28] In the CDC report, fever, cough and shortness of breath are the most common symptoms of COVID-19 and diarrhea, myalgia and headache are uncommon in children.[26] The study of Hui Du et al. were indicated fever and cough as the most common symptoms and gastrointestinal symptoms in 11% of patients.[36] Findings of a meta-analysis study were also listed fever and cough as the most common symptoms in the age group of children and were stated vomiting as a possible symptom of COVID-19 in children under one year of age.[37] Our findings were in line with the CDC report and other studies that have mentioned fever and cough as the most common symptoms in children, but our study also was indicated the gastrointestinal symptoms and diarrhea as the common symptoms in children especially at the peak of COVID-19 infection. Although in our study, fever and cough were the most common symptoms in children under one year old, we observed that the gastrointestinal (anorexia, vomiting and diarrhea) and neurological symptoms were more common in older children. On the other hand, due to the difference in levels of immune maturity in children and adults, the prevalence and type of clinical manifestations of COVID-19 may be different.[38]

The substantial risk factors has been identified by prior studies which pave the way for severe COVID-19 in children including age younger than 1 year, underlying disease (diabetes, obesity, congenital heart disease, asthma, and neurologic conditions).[39–45] In the present study, 25.8% of the patients with COVID-19 had an underlying disease, the most common diseases were kidney diseases, neurological, blood diseases, and cancer, respectively. In the CDC study, asthma, heart, and autoimmune diseases have been mentioned as underlying diseases.[26] Singh et al.'s found that 59% of hospitalized patients had an underlying disease including malnutrition, blood malignancies, and tuberculosis as the most common diseases.[46]

In the study on 345 children with COVID-19, 23% exhibited underlying diseases and pulmonary (asthma), cardiovascular disease, and immunosuppression were the most common complications.[47] In our study, 5 cases had asthma, and it was found that it has not been effective in the severity and mortality of COVID-19 infection. In this case, our study was in line with the Hui et al. findings which showed that asthma and allergic diseases were not effective in the incidence and severity of COVID-19.[48] Therefore, the difference in COVID-19 manifestations can be attributed to the different epidemiological conditions among several studies. In a meta-analysis study, severe infection was reported in 5.1% of patients with an underlying disease and the relative risk was 1.79 (CI 1.27–2.51), and the relative risk of death in this group of patients was 2.81 (CI 1.3–6.02).[49] We observed that 46.8% of COVID-19 children had severe and critical infection, and their mortality rate was 10%. Our study found that having an underlying disease triples the risk of severe disease (*P*-value = 0.001; OR = 3.59) and doubles the risk of mortality (*P*-value = 0.01; OR = 2.1). In general, it can be concluded that children with COVID-19 and an underlying disease are at a higher risk of severe disease and death.

In general, studies have shown that the severity of the disease in children was less than in adults, and this can be attributed to the maturation of ACE2 receptors, the evolving immune system, and the greater prevalence of underlying diseases such as diabetes, hypertension, and heart disease in adults. ACE2 receptors act as receptors for the COVID-19 infection, and it seems that the function and maturity of these receptors in children are less sensitive to the SARS-CoV2, which reduces the entry of the virus and the severity of the disease. Similarly, due to more respiratory infections, children have more antibodies against respiratory pathogens and this may cause a protective effect.[18,50] In this study, mild, moderate, severe and critical diseases were 48.6%, 16.4%, 29.4% and 5.6%, respectively. A percentage of asymptomatic, mild and moderate COVID-19 infection has been reported as 4.4%, 51% and 38.7% in children, respectively.[18] They also showed that the severity of COVID-19 was higher at the age of less than one year and 10.6% of this age group had severe disease.[18] Moreover, severe and critical COVID-19 infection in children were verified to be 7% and 5% in a meta-analysis study.[51] As well, in breastfed infants severe and critical form of COVID-19 infection was less than 7% and 14% for one year.[37] In the present study, 39% of children under one year had severe disease and 10.4% of them had critical disease, and their mortality rate was 11%. We revealed that the severity of the disease in the age group of less than one year is more than that of older ages and it is consistent with other studies. We also observed that the risk of death in this age group is doubled (*P*-value = 0.009; OR = 2.26). Hence, the cause of severe disease and the difference in immune system in this age group is still being discussed.

Our study showed that having symptoms such as fever and decreased level of consciousness, underlying diseases including blood, kidney and neurological and hospitalization in a special ward, intubation and hospitalization length may effect on the mortality rate. In the multiple analysis, it was found that there was a correlation of mortality with intubation and hospitalization in the special ward, so that the risk of mortality in an intubated patients was 13 times higher (OR = 13.779, *P*-value = 0.008), than in a cases hospitalized in the ICU (OR = 3.33, *P*-value = 0.007). The estimated rates of intensive care unit admission, acute respiratory distress syndrome, and mortality has been reported to be 10.9%, 18.4%, and 4.3%, respectively.[52] In various studies, the admission rate in the special wards has been reported to be 10.2%, 19.4% and 17.5%.[26,53,54] In our study, 179 (22%) patients were admitted to the ICU, of which 44% were in the age group of less than one year and 22% had an underlying disease. The death rate of patients in the ICU was 8.8%. We also found that having gastrointestinal symptoms and respiratory distress increased the risk of hospitalization in ICU by 2 and 6 times, respectively. Cancer and kidney disease was associated with an increase of 2 and 1.8 times the risk of hospitalization in ICU and the probability of intubation and death was 10 and 8 times higher. In the study of Barboza et al., 41% of the patients admitted to the ICU had an underlying disease, and gastrointestinal symptoms as a risk factor for multisystem inflammatory syndrome.[55] As a result, the gastrointestinal symptoms in children with COVID-19 should be considered important and carefully monitored.

Conclusion

Our results showed that the COVID-19 infection in children is less severe and displays a better clinical outcome which is not relevant for children under one year of age, thus, having COVID-19 in this age group should be more considered. In addition, there was a strong association between the clinical outcome in COVID-19 patients and comorbidities including respiratory distress, cancer, and kidney disease and they play an important role in increasing hospitalization length and mortality rate of children. In our study, it was found that the occurrence of gastrointestinal symptoms can be associated with an increase in patients' hospitalization rate in the ICU. As well, the possibility of mortality is significantly increased in children who require invasive mechanical ventilation. Based on the current study and other studies, we suggest to postpone invasive intubation and apply the non-invasive ventilation methods as much as possible. Finally, it is important to have comprehensive information in this age group, since the age of COVID-19 exposure is shifting towards childhood and adolescence.

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