

The Outcome of Hospitalized Children with COVID-19 in a Referral Center in Yazd, Iran

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ARTICLE INFO	ABSTRACT
<p>Article type: Original Article</p> <hr/> <p>Article History: Received: 11 Jun 2023 Accepted: 05 Oct 2023</p> <hr/> <p>Key words: COVID-19, Outcome, Hospitalized Children, SARS-CoV-2, Iran.</p>	<p>Introduction: As there is limited research on COVID-19 in children, and reports have indicated low adverse clinical outcomes and mortality rates, our team conducted this study to investigate the clinical outcomes in hospitalized children with COVID-19.</p> <p>Materials and Methods: This historical cohort study included children aged 1 month to 18 years with COVID-19. They were admitted to a referral hospital in Yazd, Iran, over a year from February 2020. Demographic information such as age and sex, the length of hospitalization, and the reverse transcription-polymerase chain reaction (PCR) test results were recorded. We also evaluated Patients' outcomes, including admission to the pediatric intensive care unit (PICU), need for mechanical ventilation, and mortality.</p> <p>Results: Our study included 94 patients, of which 52.1% were female and 29.8% were under one year old. Children aged 1-59 months accounted for more than half of the sample (53.2%). The most common symptoms reported were fever (85.1%), respiratory problems (47.9%), and gastrointestinal symptoms (46.8%). The mean duration of hospital stay was 6.4±5.7 days. About 38.3% of cases required admission to the PICU, and 11.7% needed mechanical ventilation. 75% of deaths occurred in children with confirmed COVID-19 who had an underlying disease. Moreover, respiratory distress at the time of referral was significantly associated with admission to the intensive care unit (P=0.008), requiring mechanical ventilation (P=0.003), and mortality (P=0.02).</p> <p>Conclusion: Our findings suggest that children under one year old, patients with underlying diseases, and those experiencing respiratory distress at the time of referral are high-risk groups and require special attention in care and treatment.</p>
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Introduction

The coronavirus disease 2019 (COVID-19), arising from acute respiratory syndrome coronavirus2 (SARS-CoV-2), became a worldwide pandemic within months of its local outbreak in China (1). COVID-19 clinical manifestations in children can differ from adults, from asymptomatic to respiratory or gastrointestinal involvement presentations. Sometimes, in severe cases, it occurs with shock or coagulation disorder (2). Early reports indicate that children (under 18 years of age) are relatively less likely than adults to have COVID-19-related adverse clinical outcomes and mortality (3-5). Since the onset of the pandemic, various manifestations of COVID-19 have been observed in children, including pneumonia caused by COVID-19, whether with acute respiratory distress syndrome or without it, and multisystem inflammatory syndrome in children (MIS-C), meningoencephalitis, and appendicitis (6).

Moreover, children, like adults, are more prone to severe COVID-19 if they have comorbid conditions, consisting of chronic kidney or lung disease, malignancy, diabetes, Immunodeficiency, heart disease, and obesity (7). Some studies suggest that children, differently from adults, increase the angiotensin-converting enzyme (ACE2) expression and the number of lymphocytes. In addition, they experience multiple viral infections and programmed vaccinations that can improve their innate and adaptive immunity (8,9). According to researchers, the prevalence of COVID-19 in children is believed to be lower compared to that in adults. Moreover, mortality rates in children are generally low and tend to occur primarily in patients with underlying diseases. Similar to adults, children who have comorbidities such as chronic kidney and lung diseases, malignancies, diabetes, obesity, hematologic or immune disorders, heart disease, or congenital malformations are at a higher risk of developing severe conditions due to COVID-19 (10,11). Since COVID-19 is an emerging disease, more information about the course of the disease and the outcome of affected children in different areas can help find risk factors in each area and will be effective in developing appropriate interventions.

The recent study aimed to investigate the hospital outcome of children with SARS-CoV-2 in a referral center in Yazd, central Iran.

Materials and Methods

This study was executed from February 2020 to February 2021 in a referral hospital in Yazd, central Iran. All patients aged 1 month to 18 years with confirmed or suspected COVID-19 admitted to this center were included in the study. Some participants were referred to our center from other hospitals for advanced medical care. Data were extracted from the medical records of the studied children.

Definition of Items

1. COVID-19 confirmed cases: These are patients who have tested positive for COVID-19 through a reverse transcription-polymerase chain reaction (RT-PCR) test conducted on a nasopharyngeal specimen.

2. Suspected cases: These are patients who exhibit consistent clinical signs or symptoms of COVID-19 and have a history of contact with a known COVID-19 patient.

3. Probable cases: These are patients who have chest computed tomography (CT) findings that align with COVID-19, in addition to displaying clinical signs or symptoms of the virus. We reported the outcome of patients, consisting of admission to the pediatric intensive care unit (PICU), the requirement for mechanical ventilation, and death. Patient information was collected and analyzed, including demographics, chief complaints, medical histories, underlying diseases, and clinical outcomes.

All analyzes were performed using SPSS software (SPSS 25, SPSS Inc., Chicago, IL, USA). The value of $P < 0.05$ was considered statistically significant. The local ethics committee approved this research (Ethics Code: IR.SSU.REC.1399.076).

Results

In this study, 94 patients 1 month to 18 years have been enrolled for one year since February 2020. Of them, 52.1% were female. The highest frequency was related to participants under one-year-old (29.8%), and the lowest was related to those over 12 years old (7.4%). In other words, children

aged 1-59 months included more than fifty percent of the subjects.

COVID-19 RT-PCR was positive in 58 (61.7%) patients (confirmed cases). About 24.5% of children had only positive CT findings; in other words, they were probable cases. Fever (85.1%) and respiratory symptoms (cough, dyspnea) (47.9%) were

the most common complaint of patients, and the subsequent were gastrointestinal symptoms (vomiting, diarrhea, and abdominal pain) (46.8%). Other symptoms at admission included neurological (seizure, headache, loss of consciousness) and dermatological symptoms (Table1).

Table 1: Demographic data, clinical and paraclinical characteristics of children affected by COVID-19

Variables		No (%)
Gender	Male	45 (47.9%)
	Female	49 (52.1%)
Age	<=1 year	28 (29.8%)
	1 -5 year	22 (23.4%)
	5 -12 year	37 (39.4%)
	>12 year	7 (7.4%)
PCR	Negative	36 (38.3%)
	Positive	58 (61.7%)
Chest CT scan involvement	No	21 (22.3%)
	Yes	40 (42.5%)
	Undone	33 (35.1%)
Underlying diseases	No	59 (62.8%)
	Yes	35 (37.2%)
Signs and Symptoms	Fever	80 (85.1%)
	respiratory problems	45 (47.9%)
	gastrointestinal symptoms	44 (46.8%)

In this research, 36.6% of children had close contact with a COVID-19-infected person. The range of hospital stay was 1- 37 (mean= 6.4±5.7) days. Furthermore, 36 (38.3%) inpatient pediatric cases were admitted to the PICU during hospitalization, and 11 (11.7%) required mechanical ventilation. Underlying diseases were observed in 35 (37.2%) patients. Neurological disorders (20%), malignancies (20%), and chronic kidney disease (17.1%) were the most prevalent comorbidities observed in children hospitalized with COVID-19. Among the eight children who died with a definitive diagnosis of COVID-19 during hospitalization, 75% had an underlying disease. Chronic kidney disease was the most common underlying disease observed among the deceased children.

(28.6%) This study demonstrated a significant association between comorbidities and mortality (P= 0.02). It is worth noting that three deaths occurred in patients who exhibited lung CT involvement but tested negative on PCR (probable cases). Refer to Table 2 for a comprehensive overview of the patients' outcomes. While the study observed the highest number of deaths in infants under one year of age, there was no significant association found between age and the need for ICU admission (P=0.58) or mortality (P=0.24). However, age did show a significant correlation with the requirement for mechanical ventilation (P=0.008). In fact, patients under one year of age had a significantly higher need for mechanical ventilation compared to patients in other age groups.

Table 2: Clinical outcomes of the hospitalized children with COVID-19

Variables		No.(%)
ICU admission	No	58 (61.7%)
	Yes	36 (38.3%)
Mechanical ventilation	No	83 (88.3%)
	Yes	11 (11.7%)
Death	No	83 (88.3%)
	Yes	11 (11.7%)

Furthermore, it was found that children who presented with respiratory distress upon admission had significantly higher rates of ICU admission (P=0.008), need for mechanical ventilation (P=0.003), and mortality (P=0.02).

On the other hand, the study did not identify any significant differences in COVID-19 outcomes (mortality, ICU admission, or ventilator usage) between genders. These results are included in (Table 3).

Table 3: Association between disease symptoms, age, sex and the outcome of COVID-19 in pediatric patients

Variables		Death		P	Mechanical Ventilation		P	ICU Admission		P
		No	Yes		No	Yes		No	Yes	
Respiratory Distress No.(%)	No	61 (73.5%)	4 (36.4%)	0.02	62 (74.7%)	3 (27.3%)	0.003	46 (79.3%)	19 (52.8%)	0.008
	Yes	22 (26.5%)	7 (63.6%)		21 (25.3%)	8 (72.7%)		12 (20.7%)	17 (47.2%)	
Gatrouintestinal problems No.(%)	No	42 (50.6%)	8 (72.7%)	>0.05	43 (51.8%)	7 (63.6%)	>0.05	28 (48.3%)	22 (61.1%)	>0.05
	Yes	41 (49.4%)	3 (27.3%)		40 (48.2%)	4 (36.4%)		30 (51.7%)	14 (38.9%)	
Gender	Male	38 (45.8%)	7 (63.6%)	>0.05	39 (47%)	6 (54.5%)	>0.05	24 (41.4%)	21 (58.3%)	>0.05
	Female	45 (54.2%)	4 (36.4%)		44 (53%)	5 (45.5%)		34 (58.6%)	15 (41.7%)	
Age (Year)	≤1	22 (26.5%)	6 (54.5%)	>0.05	20 (24.1%)	8 (72.7%)	0.008	19 (32.8%)	9 (25%)	>0.05
	1-5	20 (24.1%)	2 (18.2%)		22 (26.5%)	0 (0%)		14 (24.1%)	8 (22.2%)	
	5-12	35 (42.2%)	2 (18.2%)		35 (42.2%)	2 (18.2%)		20 (34.5%)	17 (47.2%)	
	>12	6 (7.2%)	1 (9.1%)		6 (7.2%)	1 (9.1%)		5 (8.6%)	2 (5.6%)	

Discussion

This study provides essential information on the clinical features and outcomes of hospitalized children with suspected COVID-19 in our area. This study demonstrated that no significant differences between the two genders were observed. Moreover, both genders did not have statistically significant differences in PICU admission, receiving mechanical ventilation, and mortality. Consistent with our results, a study in Iran on 6610 hospitalized children with COVID-19 did not find significant gender differences in patients' outcomes (12). In another study, no gender predominance was observed, but the number of boys in the study was generally higher (63%) (13).

Our research demonstrated that the need for mechanical ventilation in children under one-year-old is significantly higher than in other age groups. A study in Iran reported that the mortality rate of under one-year-old infants was significantly higher than children between 1 and 5 years of age (12). Furthermore, another study showed that the highest proportion of severe or critical

illness was observed in infants (14). Garazzino et al. reported that hospitalization was inversely related to age, with the highest rate under one year (15).

Although, Alharbi et al. described that the hospitalized children were older than the rest. In addition, they did not report significant differences in the gender and age of children admitted to PICU compared with others (16). Overall, some studies have shown that severe SARS-CoV-2 infection is more common in infants, and others have shown that older children have critical illnesses (17-19). Madani et al. reported in their study that more than half of the hospitalized children with COVID-19 were less than 5 years old, which was consistent with our study. Although their study included only patients with a definitive diagnosis of COVID-19, ours consisted of all three categories of suspected, probable, and confirmed SARS-CoV-2 infection (12).

This study demonstrated that 38.3% of the children were admitted to PICU during hospitalization, and 11.7% underwent mechanical ventilation. Tagaro et al. found

that 16% of hospitalized children with confirmed COVID-19 were accepted to the PICU (10). A study from a single tertiary care children's hospital in New York City described that 28.3% of patients require PICU care. In a study in northern Iran, 20% of patients were transferred to the ICU (11). One of the reasons for the large number of patients admitted to the PICU is that our center is a referral hospital, and the majority of hospitalized children were referred to this center due to the need for advanced treatment and medical supervision.

Herein, underlying diseases were observed in 37.2% of patients. Neurological disorders, malignancies and kidney diseases, were the most common conditions. In the study of Mahmoudi et al., pre-existing underlying medical conditions were found in 51% of patients. Chronic kidney diseases and neurological disorders were the most common, consistent with our study (13). Alharbi et al. described that 15.5% of patients had pre-existing comorbidity. The most common comorbidities were pulmonary diseases, followed by cardiac and neurological disorders (16). Swann et al. declared Neurological comorbidity as the most common concurrent disease (20).

Moreover, we reported a significant association between comorbidities and mortality. A study conducted in northern Iran also raised comorbidities as a risk factor for the progress of the critical illness. In the study by Derespina et al., 74.3% of children transferred to PICU during hospitalization had at least one comorbid disease, and death was observed in 2.9% (21). Madani et al.'s study reported that the presence of concomitant underlying diseases tripled the mortality rate (12). This study had some limitations that we need to mention here. Our hospital was a referral center, which may justify the high number of patients admitted to the ICU and the relatively high mortality in this study. Finally, because the study inspected only hospitalized patients, it could not provide information on all children with COVID-19.

Conclusion

The findings of this study declared that although about one-third of hospitalized

children with COVID-19 were admitted to the PICU, most were discharged in good general condition. In addition, 75% of deaths in PCR-positive children had the underlying disease. It should be noted that the need for mechanical ventilation and death in under one-year patients was significantly higher than in others. Therefore, medical staff, especially pediatricians, should consider children less than one year old, patients with underlying diseases, and those with respiratory distress at the time of referral as high-risk groups and pay special attention to their management.

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