Original Article :

Clinical manifestations and general characteristics of pediatric patients with COVID-19: A single-center study in the Makkah region, Saudi Arabia

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Abstract

Background and Aims:

The clinical presentations of pediatric patients infected with COVID-19 vary from mild to acute. The most commonly reported signs and symptoms are fever, cough, headache, myalgia, shortness of breath, nausea, vomiting, abdominal pain, and diarrhea. While pediatric hospitalizations are lower than those for adult patients, there is still inadequate data related to the general features of pediatric patients with COVID-19 in Saudi Arabia.

This study aimed to identify clinical presentations, laboratory abnormalities, duration of hospitalizations, need for intensive care unit (ICU) admissions, and incidence of death and possible risk factors of mortality in pediatric patients.

Methods:

A retrospective study was conducted at the Maternity and Children's Hospital in Makkah, Saudi Arabia, from March 2020 to December 2021. Pediatric patients under 18 years of age who had positive Polymerase Chain Reaction (PCR) test results for COVID-19 were included. Clinical presentations, laboratory results, medications, and any radiological abnormalities were extracted from electronic medical records and a chart review.

Results:
A total of 95 patients with a confirmed diagnosis of COVID-19 were included in the study. Of the patients, 50 (52.6%) were male, 64 (67.4%) were Saudi, and 31 (32.6%) were non-Saudi. The patients' mean (SD) age was 3.71 (3.69) years. Their mean temperature rose to 38.34°C (0.8^{O}C), and the mean duration of their fever was 2.97 (2.8) days. The most commonly observed manifestations were diarrhea, vomiting, and abdominal pain. Of the patients, 24.2% needed ICU admission, 12.6% required mechanical ventilation, 9.5% were given vasoactive agents, 2.1% required dialysis for acute kidney injury (AKI), and 5.3% passed away. The incidence of death was significant in non-Saudi patients (P = .038).

Conclusions:
COVID-19 equally affected males and females. Most of the pediatric patients who died had co-morbidities. Fever, diarrhea, vomiting, and abdominal pain were the most prevalent symptoms.

Introduction

Coronavirus disease 2019 (COVID-19), which was initially reported in China at the end of 2019, has affected more than 7.5 million people and resulted in more than 6 million deaths worldwide. Moreover, more than 13 billion vaccine doses have been administered. [1,2] The first case of COVID-19 in Saudi Arabia was identified in early March 2020, and since then, this newly discovered virus has affected more than 830 thousand people in this country. However, it has a high recovery rate, reaching 96%. [3] The clinical manifestations of this virus vary among pediatric patients ranging from a mild, asymptomatic presentation to a critical disease. [4,5] The most commonly reported signs and symptoms in children are fever, cough, headache, sore throat, myalgia, shortness of breath, nausea, vomiting, abdominal pain, and diarrhea. [6,7] The laboratory manifestations generally found in this group of patients are a reduction in white blood cells, lymphopenia, and increased inflammation parameters, including ferritin, C-reactive protein, erythrocyte sedimentation rate (ESR), fibrinogen, and D-dimer. [8] The majority of pediatric patients have mild to moderate symptoms, and they have not been hospitalized as often as adult patients. [9] In Saudi Arabia, the general characteristics of pediatric patients with this virus were reported in a small number of studies, and one study found that the most common symptoms among this age group were fever, cough, and mild infection (in the majority of cases). [10] Another study conducted in the central region of Saudi Arabia described the same finding that most pediatric patients infected with COVID-19 experienced mild disease. [11] Yet, data on the general features of pediatric patients with COVID-19 in Saudi Arabia are still inadequate. [12] Therefore, our study aimed to identify clinical presentations, laboratory abnormalities, treat-

ments, duration of hospitalizations, need for intensive care unit (ICU) admissions, and the incidence of death and possible risk factors of mortality, including chronic diseases and underlying conditions, among pediatric patients with COVID-19.

Materials and Methods

We conducted an observational retrospective descriptive study at the Maternity and Children's Hospital in Makkah, Saudi Arabia, to examine the clinical and general features of pediatric patients with COVID-19 from March 2020 to December 2021.

Ethical approval was obtained from the ministry of health before commencing the study (approval number: H-02-K076-0621-519). Pediatric patients under 18 years of age who had positive PCR tests for COVID-19 were included in the study. Their clinical presentations, laboratory results, medications, and any radiological abnormalities seen on chest computed tomography were extracted from electronic medical records and reviewed by a radiologist.

Data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows) version 25 (IBM Corp., Armonk, N.Y., USA). Frequencies and percentages were used to display the categorical variables. Means and standard deviations were employed to present the continuous variables, and logistic regression was undertaken where appropriate. The chi-squared test was used to ascertain if there were any associations between gender, nationality, and death, and $P < 0.05$ was considered statistically significant.

Results

Ninety-five patients with a confirmed diagnosis of COVID-19 were included in the study. Table 1 summarizes the socio-demographic profiles of the patients:

Table 1 Socio-Demographic Profile of Patients (n = 95)

Demographical Characteristics	n	%
Gender		
Male	50	52.60
Female	45	47.40
Nationality		
Saudi	64	67.40
Non-Saudi	31	32.60
Age: 3.71 years ± 3.69		

Fifty (52.6%) were male and 64 (67.4%) were residents of Saudi Arabia. The mean age (SD) of the patients was 3.71 (3.69) years. The majority of the patients (n = 43; 45.3%) had no relevant medical history, 16 (16.8%) had a primary immunodeficiency, 11 (11.6%) had an autoimmune disease and/or were using immuno-suppressants before COVID-19, and 4 (4.2%) had chronic kidney disease.

The children's mean body temperature was 38.34^{O}C (0.8^{O}C) upon admission, and the mean duration of fever was 2.97 (2.8)

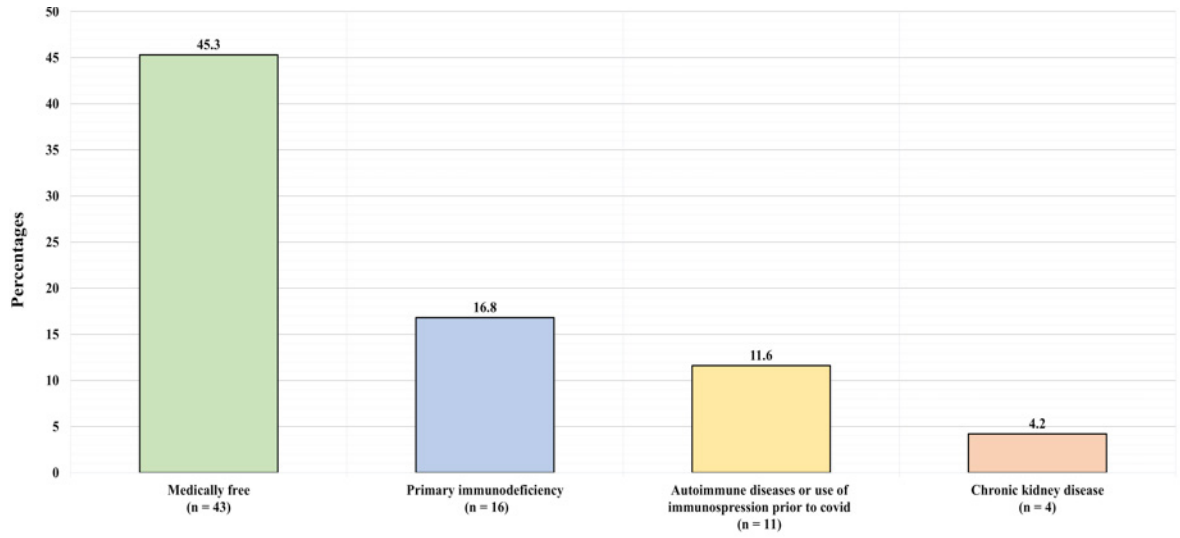


Figure 1: Medical history of the patients

days. The most commonly observed symptoms were diarrhea, vomiting, and abdominal pain (n = 49; 51.6%); cough (n = 34; 35.8%); and dyspnea (n = 29; 30.5%). The least observed manifestations were headache (3 = 3.2%) and conjunctivitis (n = 5; 5.3%), Moreover, 11 (11.6%) patients were asymptomatic. (Table 2)

Table 2: Clinical manifestations (n = 95)

Clinical signs	n (%)
Asymptomatic	11 (11.6)
Nasal discharge	10 (10.5)
Cough	34 (35.8)
Dyspnea	29 (30.5)
Diarrhea, Vomiting or abdominal pain	49 (51.6)
Anosmia	24 (25.3)
Headache	3 (3.2)
Conjunctivitis	5 (5.3)
Cutaneous rash	10 (10.5)
Neurological (seizure)	18 (18.9)
Hypoxemia	19 (20)
Fever: mean ± SD	38.34 ± 0.8
Duration of fever (days): mean ± SD	2.97 ±2.796
Minimum–maximum	0-14

Regarding the laboratory values 17 (17.98%) patients who had their troponin level measured, 6 (6.3%) had elevated troponin. Of the 8 (8.4%) patients who had their fibrinogen level tested, 2 (2.1%) had elevated fibrinogen. Chest imaging showed that 29 (30.5%) patients had a lung abnormality. (Table 3)

Table 3

	Mean	Standard deviation
Hemoglobin (g/dL)	11.00	2.26
White blood cells (10^9/L)	11.96	6.79
Platelet (/mcL)	376.68	185.50
C. reactive protein (CRP) (mg/dl)	4.37	7.80
Ferritin (mico/l)	516.28	2041.57
Erythrocyte sedimentation rate (ESR) (mm/hr)	40.64	36.23
D-dimer (ng/mL)	6.42	33.20
Albumin (g/l)	37.68	6.52
Lactate Dehydrogenase (U/L)	502.98	345.40
Aspartate aminotransferase (U/L)	53.77	90.15
Alanine Aminotransferase (U/L)	24.56	25.15
Blood urea nitrogen (mg/dl)	4.52	6.54
Serum creatinine (mcg/l)	63.41	115.25
Item	n	
Troponin (n =17) pg/ml		
Normal	11	11.60
High	6	6.30
Fibrinogen (n = 8) g/l		
Normal	6	6.3
High	2	2.1
Imaging Profile		
Lung abnormality	29	30.5

The most commonly administered medications were antibiotics (n = 88; 92.6%), systemic corticosteroids (n = 34; 35.8%), and oxygen therapy (n = 26; 27.4%). The least-administered medications were aspirin (n = 2; 2.1%), tocilizumab (n = 4; 4.2%), and hydroxychloroquine (n = 4; 4.2%). (Figure 2)

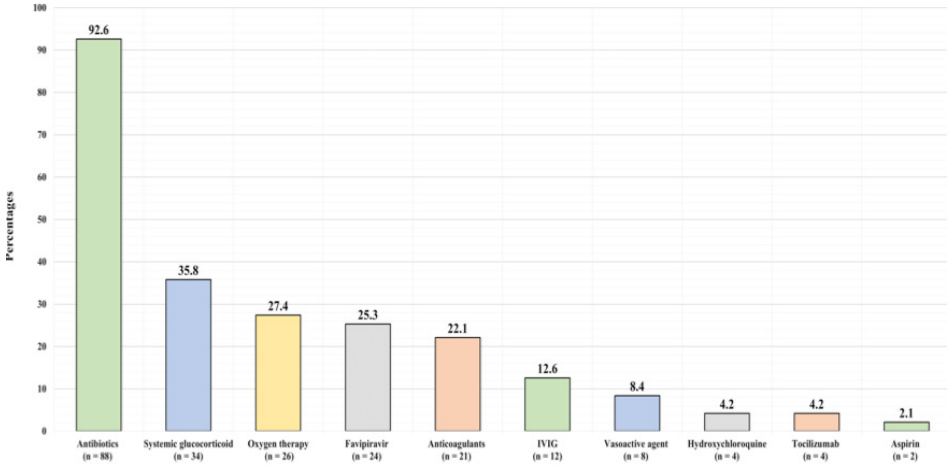


Figure 2: management of the patients:

Twenty-three patients (24.2%) needed admission to intensive care unit, 12 (12.6%) needed mechanical ventilation, 9 (9.5%) needed vasoactive agents, 2 (2.1%) needed dialysis for acute kidney injury, and 5 (5.3%) succumbed to COVID-19. Four of the deceased patients were female individuals (chi-square = 2.25); however, the difference was not statistically significant between the genders (P = 0.186). (Table 4)

Table 4: Outcomes

	n (%)		
Intensive care unit admission	23 (24.2)		
Need for mechanical ventilation	12 (12.6)		
Need of vasoactive agent	9 (9.5)		
Resolve of infection/discharge	90 (94.7)		
All-cause mortality	5 (5.3)		
	Item		P-value
	Male (1/50)	Female (4/45)	0.186
	Saudi (1/64)	Non-Saudi (4/31)	0.038*
Duration of hospitalization (days) from ER admission until discharge or death mean ± SD	12.19 ± 13.21		

Significancy < 0.05

The incidence of death was significant in non-Saudi patients compared with Saudi patients (P = .038). The SARS-CoV-2 infection resolved in 90 (94.7%) patients. The mean duration of hospitalization, from admission to discharge or death, was 12.19 (13.21) days. Further, we performed binary logistic regression analysis to examine the effects of the duration of fever and hospitalization and occurrence of diarrhea on the incidence of death (Fig. 3).

Only the duration of hospitalization had

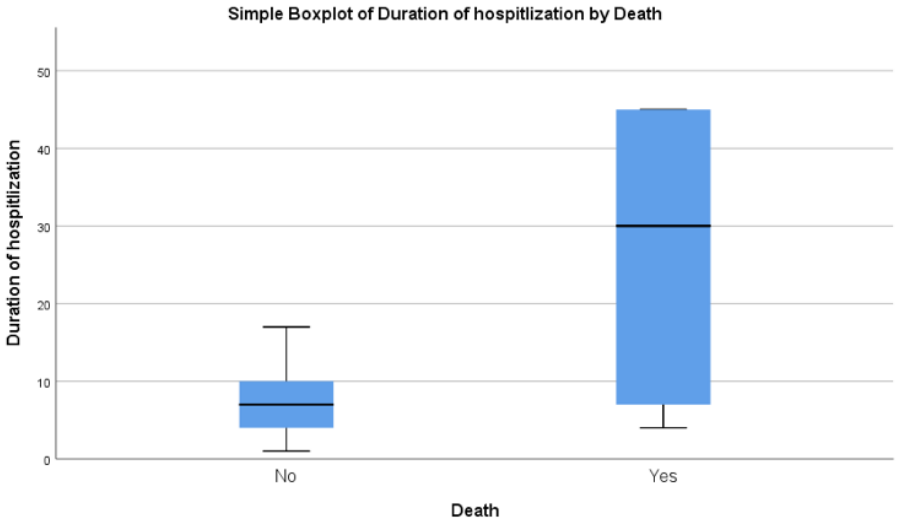


Figure 3:

a statistically significant effect on the incidence of death. The probability of a patient dying increased by 54.6% with an increased length of hospitalization (P = .008). Linear regression analysis was used to determine factors that affected the length of the hospital stay. Univariate analysis was performed to identify significant predictors that were included in the final model. The duration of fever had a significant association with patients' length of hospital stay (B = 0.643; P = .02).

Discussion

Previous studies suggest that COVID-19 equally affects individuals of both sexes and all age groups, although a more severe disease is reported in infants. The COVID-19 mortality rate in this study was 5.3%. The mortality rate for COVID-19 in pediatric patients varies between studies, ranging from 2 per million to 2.4% on other study to as high as 8.7%.13-15 This may be due to pre-existing chronic diseases and/or the severity of COVID-19. In this study, mortality was most observed in patients with prior immunodeficiency or autoimmune diseases, consumption of immuno-suppressants before COVID-19, and chronic kidney disease. Therefore, the COVID-19 mortality rates in pediatric patients are variable and affected by multiple confounders. In this study, all-cause mortality was higher in female individuals than in male individuals; however, the difference was not statistically significant due to the small number of reported deaths. This finding contradicts that of a previous study on adults that reported a higher mortality rate in men than in women.[16] however, a large descriptive study that aimed to predict the rate of hospitalization and deaths in pediatric patients in the United States found no association between sexes and death rates. [17] Also, more than fifty percent of patients in this study presented fever, diarrhea, abdominal pain, or vomiting as the most prevalent symptom of COVID-19, consistent with the previous findings. [7], [10,11] Approximately 30% of patients in this study presented with lung abnormalities on chest radiography, as opposed to 52% in another study. [18] A majority of the patients in this study had elevated levels of inflammatory biomarkers—ferritin, CRP, and ESR—consistent with findings of the study by Nino et al. [18] The WHO guidelines do not recommend antibiotic administration for mild to moderate COVID-19 [19]; however, in this study, a majority of the patients were treated with antibiotics (92.6%), followed by systemic steroids and oxygen therapy and vasoactive agents (9.5%). We examined the effects of the duration of fever and hospitalization and occurrence of diarrhea on the incidence of death; only hospitali-

zation duration had a statistically significant impact on death—the probability of a patient dying increased by more than 50% with increased duration of hospitalization, and that was expected since the sick patients will increase the hospitalization rate significantly. Furthermore, the duration of fever was the only predictor for the length of hospitalization—every increase in the duration of fever increased the length of hospital stay by 0.643 days.

This study has some limitations. First, it was a retrospective study that rationalizes the mortality and other outcomes of interest—ICU admission and the need for mechanical ventilation and vasoactive agents. Second, it was a single-center study, which limited its generalizability. Therefore, to improve the management and outcomes of COVID-19, large-scale epidemiological studies on pediatric patients are required.

Conclusion

This study suggested that COVID-19 equally affected male and female individuals. Many of the pediatric patients who died had co-morbidities. Fever, diarrhea, vomiting, and abdominal pain were the most prevalent clinical symptoms. Most of the patients received antibiotics and steroids, with fewer receiving aspirin and tocilizumab. Finally, the mortality rate was high in non-Saudis. Therefore, large-scale studies are required to improve the management of clinical outcomes in pediatric patients with COVID-19

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Availability of data and materials

Available upon request from the corresponding author.

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Ethical approval was obtained from the ministry of health before commencing the study (Approval number: H-02-K076-0621-519).

Authors' Contributions

NA conceived and designed the study, conducted research, provided research materials.

SA, SF, AA and FS collected and organized data.

MA and ME analyzed and interpreted data.

WM, Manahel and SA wrote the initial and final draft of article and provided logistic support.

All authors have critically reviewed and approved the final draft and are responsible for the

content and similarity index of the manuscript.

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