

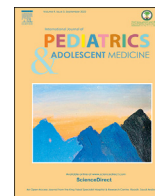
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## Original Article

## Epidemiological characteristics, clinical course, and laboratory investigation of pediatric COVID-19 patients in a tertiary care center in Saudi Arabia

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## ABSTRACT

**Background:** Since the initial emergence of the novel SARS-CoV-2 coronavirus responsible for the 2019 coronavirus disease (COVID-19) pandemic, many studies have been exploring the nature and characteristics of this virus and its associated clinical manifestations. The present study aimed to describe the clinical presentation and outcomes of COVID-19 infections in pediatric patients.

**Methods:** A retrospective review of findings associated with 143 pediatric patients (age <14 years) with a confirmed COVID-19 diagnosis who had undergone inpatient or outpatient treatment at King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia, between March 2020 and October 2020, was conducted. The analyzed data included patient demographic information, pre-existing medical conditions, symptoms, interventions, and outcomes.

**Results:** The median age of this patient population was 7 years. Of these 143 patients, 67 (46.8%) had known pre-existing medical conditions including bronchial asthma (12.8%), chronic lung disease (CLD) (3%), congenital heart disease (CHD) (17%), primary immunodeficiencies (1.5%), malignancies (9.8%), and 7.5% were post-transplant patients. Thirty-seven patients (26%) were overweight or obese. Sixty-three of these patients (51%) were symptomatic, with the most common symptom being fever (55%). Ultimately, 45 patients (31%) required admission to the hospital, with a median duration of hospitalization of 9.6 days for admitted patients. There were no documented cases of infection-related mortality among this pediatric cohort, although 11 patients experienced post-infectious complications that primarily manifested as a loss of taste and smell.

**Conclusion:** These findings suggest that pediatric COVID-19 patients tend to experience mild forms of the disease, without any significant differences in disease severity as a function of patient gender or immune status.

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**Abbreviations:** COVID-19, 2019 coronavirus disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; CLD, chronic lung disease; CHD, congenital heart disease; MOH, Saudi Ministry of Health; PCR, polymerase chain reaction; BCG, Bacillus Calmette–Guérin; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; SOT, solid organ transplantation.

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## 1. Introduction

In December 2019, an outbreak of a severe respiratory disease in Wuhan, China, was linked to a novel coronavirus [1]. The International Committee on Taxonomy of Viruses designated this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease it caused was named 2019 Coronavirus Disease (COVID-19). Within months of its initial discovery, SARS-CoV-2 had spread rapidly throughout the world, forcing the World Health

Organization (WHO) to declare the outbreak a pandemic on March 11, 2020 [2–5]. The virus is highly transmissible and contagious, affecting all age groups including children [6].

The disease has a wide variety of presentations ranging from asymptomatic to severe respiratory distress, respiratory failure, and even death. To date, the number of affected patients is increasing, reaching up to more than two hundred and thirty million people, and the mortality rate is reported to be more than four million deaths globally [7].

The American Academy of Pediatrics (AAP) recently reported that children represent 14.2% of total accumulated cases since the beginning of the pandemic in the USA [8]. This lower incidence rate among children may be attributable to children having fewer opportunities for exposure due to school, daycare, and activity closures, as well as a lower probability of their being tested if they are exposed [9]. In addition, children exhibit a higher rate of asymptomatic infection. Despite this, transmission studies examining the risk of secondary infection from children and adolescents to household contacts demonstrate that transmission from these asymptomatic children does occur [10,11].

Several studies have described the characteristics of COVID-19 in children. One systematic review incorporated 62 studies and 3 reviews published between January 2020 and May 2020, with a total sample size of 7480 pediatric patients, with authors concluding that children were less affected by this disease than adults and were more likely to experience milder forms of COVID-19 [12]. However, relative to the intensive study of COVID-19 infections in adults, there remains a paucity of information regarding pediatric patient populations.

Relatively, little data are available relating to COVID-19 infection rates and related outcomes among immunocompromised patients. One multicenter study of pediatric solid organ transplant (SOT) patients conducted across five institutions in Texas, Florida, and California found that the prognosis of these patients largely mirrors that of the general immunocompetent patient population [13]. A separate report reviewed the available literature pertaining to COVID-19 incidence among patients with malignancies, SOT recipients, patients with primary immunodeficiencies, and patients undergoing treatment with biological immunosuppressive agents. These researchers concluded that immunocompromised patients seem to exhibit typical clinical manifestations of COVID-19, whereas patients with malignancies may be at a higher risk of more severe COVID-19 disease, and patients undergoing biologic treatment may not be at an elevated risk of severe disease [13].

In Saudi Arabia, there have been a few studies describing COVID-19 in children. One published analysis of COVID-19 cases in Saudi Arabia reported that 74 (4.8%) of 1519 included cases were diagnosed in children aged 14 years or younger. However, the clinical characteristics and outcomes in these children were not reported as this was a large review of all COVID-19 cases including adults [14]. Another study conducted in King Abdullah Specialized Children's Hospital, a tertiary care children's hospital in Riyadh, Saudi Arabia, described 742 pediatric cases and found that children infected with SARS-CoV-2 tended to exhibit mild disease manifestations and a good overall prognosis [15]. In a separate study of 88 children (0–14 years of age) who were admitted to Prince Sultan Military Medical City (PSMMC) in Riyadh, Saudi Arabia, between April and June of 2020, 5.7% exhibited Multisystem Inflammatory Syndrome in Children (MIS-C) [16]. Another 88 cases in children were reported from King Abdulaziz University in Jeddah, where the majority of hospitalized children reportedly experienced a brief febrile illness and made a full recovery, although a minority suffered from severe disease [17].

The aim of the present study was to describe the clinical, epidemiological, laboratory, management, and outcome

characteristics of pediatric patients infected with SARS-CoV-2, and to better clarify the risk factors associated with severe COVID-19 disease and mortality in children. Our institution is unique in that we have the highest population of immunocompromised children as we care for cancer, bone marrow transplant (BMT), and SOT patients. As such, we additionally sought to better define the clinical features and outcomes of COVID-19 in an immunocompromised pediatric population.

## 2. Methodology

### 2.1. Inclusion criteria

This was a single-center, retrospective cohort study. Patients eligible for inclusion were pediatric patients (defined as individuals <14 years old) with a confirmed COVID-19 diagnosis evaluated in an inpatient or outpatient setting. COVID-19 test, admission criteria, and related investigations were conducted in accordance with the guidelines of the Saudi Ministry of Health (MOH) and hospital protocol. These criteria evolved continuously as new information pertaining to the pandemic emerged, introducing variability into our data. Our patient cohort included patients evaluated between March 1, 2020, and October 30, 2020, at King Faisal Specialist Hospital and Research Center, Riyadh, Kingdom of Saudi Arabia, with 143 patients fulfilling our inclusion criteria. The study was approved by the institutional review board (Reference number 2201079).

### 2.2. COVID-19 testing

Nasopharyngeal and oropharyngeal swabs were obtained from all patients who were either symptomatic or had been exposed to a confirmed case of COVID-19. Testing criteria were based on contemporaneous MOH protocols. Samples were processed in the microbiology and molecular laboratory of King Faisal Specialist Hospital and Research Center for polymerase chain reaction (PCR) testing to confirm the diagnosis of SARS-CoV-2 infection. Several methods were available for COVID-19 PCR testing, including the GENEXPERT (CEPHID) rapid COVID-19 kit, QIAstat rapid multiplex respiratory kits (QIAGEN), where COVID-19 is tested among other respiratory pathogens, and BIOFIRE testing system (BIOFIRE Salt Lake City, USA).

### 2.3. Data collection

Patient electronic medical records were retrospectively accessed to collect relevant epidemiological data, including basic demographic data such as age, nationality, weight, and height, as well as pre-existing medical conditions including immunocompromising diseases, congenital heart disease (CHD), chronic lung disease (CLD), and others. History and date of exposure, if known, were documented. The patient's record numbers were retrieved from the infection control department logs, which kept track of all the COVID-19 tested patient's at King Faisal Specialist Hospital and Research Center. Symptoms, requirement for admission, and length of stay criteria changes with protocol changes over time, and data were collected from patient charts when available.

Patient body weight values were plotted on Saudi growth charts, and overweight patients were defined as those whose weight was at or above the 85th percentile [18].

Laboratory testing was conducted as per MOH and hospital criteria and included blood tests, including complete blood count (neutrophils, lymphocytes, hemoglobin, and platelets), C-reactive protein levels, erythrocyte sedimentation rate, liver function tests (including alanine transaminase and aspartate transaminase), renal

function tests (including BUN and creatinine), lactate dehydrogenase (LDH), ferritin, fibrinogen, and D-dimer levels. Radiologic imaging examinations including chest X-rays, computed tomography (CT), and electrocardiogram (ECG) analyses were conducted as per protocol or as indicated. Laboratory findings, radiological evidence of patchy opacities, focal consolidation, and/or effusions, and ECG changes were documented.

### 2.4. Statistical analysis

Categorical data were presented as frequencies and percentages, while continuous data were presented as medians with ranges. Univariate comparisons for categorical and continuous non-parametric data were made via Fisher's exact test and the Mann–Whitney *U* test, respectively. A *P*-value < .05 was considered to be statistically significant for all analyses. Data were analyzed using JMP (v 15) for SAS.

### 3. Results

In total, 143 pediatric patients were included in this retrospective study, all of whom had tested positive for COVID-19 infection. Of these patients, 74 were female (51%) and 69 were male (48%). The average age of the overall patient cohort was 7 years (range: 2 months–14 years). Body weight values were documented for 107 patients, among whom the median weight was in the 67th percentile (range: 3rd–99th). Asymptomatic patients were those who tested positive for COVID-19 as part of screening due to a history of exposure with an infected person, but not experiencing any symptoms at the time of testing. Complete data were available for 122 patients out of 143. Overall, 100/122 patients (90%) had known COVID-19 exposures, and 59/122 (48%) and 63/122 (51%) experienced asymptomatic and symptomatic infections, respectively.

The mean age of the asymptomatic patient population was 6.2 years (SD 3.6 years), while that of the symptomatic patient population was 7.7 years (SD 3.9 years), with a significant difference between these two values (*P* = .041; Fig. 1, Table 1).

In total, 33/143 patients (23%) were categorized as being overweight or obese, as defined by a bodyweight above the 85th percentile. Among patients for whom data were available, 22/33 patients in the obese/overweight group were symptomatic (69%),

as compared to 28/64 patients in the non-obese group (43%), with a significant difference between these two values (*P* = .014).

Moreover, 67/143 patients (46.8%) presented with pre-existing medical conditions, with complete data being available for 58 of these patients, of whom 17 (12.8%) had bronchial asthma, 4 (3%) had CLD, and 15 (17%) had CHD. In addition, 20/143 patients presented with immunocompromised status, including 2 (1.5%) with primary immunodeficiencies, 13 (9.8%) with diagnosed malignancies, 10 (7.5%) who were transplant recipients, 3 (30%) patients were liver transplant recipients, and 7 (70%) were hematopoietic stem cell transplant recipients. For further details regarding these patients and for comparisons between the symptomatic and asymptomatic patient cohorts, see Table 1.

The most common symptoms experienced by these patients included fever, which was present in 59 patients (55%), followed by cough (31%), nasal congestion (20%), and sore throat (14%). Gastrointestinal symptoms were exhibited by a smaller fraction of patients with diarrhea in 15 patients (16%) and vomiting in 7 patients (7%). Abnormal movements occurred in 2 patients, both of whom had pre-existing neurological disease, and 9 patients experienced weakness (9%). Less frequent symptoms included skin rash, conjunctivitis, and lymphadenopathy. For further details regarding the presenting symptoms in these patients as a function of whether they were immunocompromised, see Table 2.

In total, 45 patients (31%) required admission to the hospital, of whom 11 (24.4%) were immunocompromised and 34 (75.6%) were not, with a significant difference between these groups (*P* = .05). Of these 45 admitted patients, 3 were admitted to the pediatric intensive care unit (PICU), and only 1 required positive pressure ventilation. For further details regarding patient hospital admission, see Table 3.

Of the 41 patients that underwent chest x-ray imaging, 25 (60.9%) exhibited abnormal radiological findings, of whom eight were immunocompromised. Of those immunocompromised patients, 3 had pneumonic infiltrations, while the rest exhibited mild peribronchial thickening. An additional 30 patients underwent ECG, of whom two (6.6%) exhibited QT prolongation and 1 exhibited right ventricular hypertrophy, which had been diagnosed prior to infection.

Laboratory result ranges from patients for whom these data were available are summarized in Table 4, with no significant differences between groups.

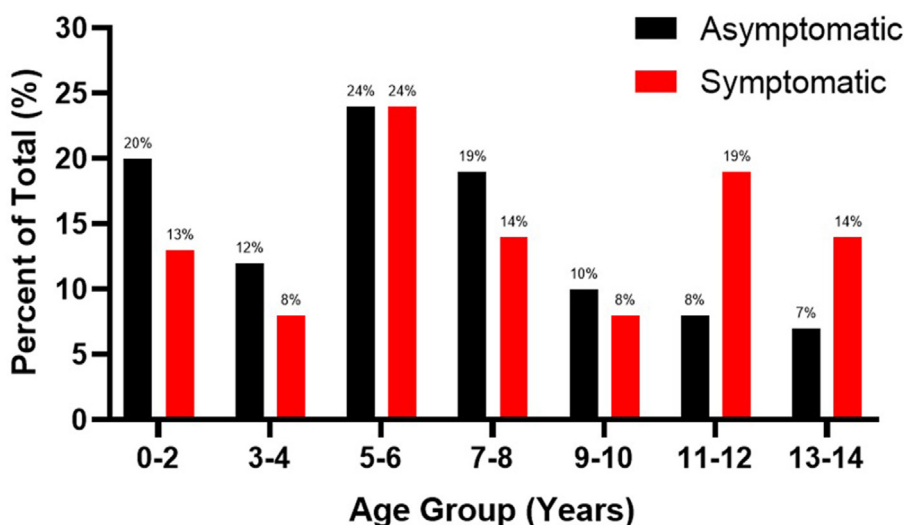


Fig. 1. Age distributions for symptomatic and asymptomatic pediatric COVID-19 patients in the study cohort.

**Table 1**  
Baseline characteristics of the overall pediatric cohort as a function of COVID-19 disease severity.

	Group	Total (n = 122)	Asymptomatic (n = 63) (%)	Symptomatic (n = 59) (%)	P-value
<b>Gender</b>	Male	60	30 (51)	30 (47.6)	.72
	Female	62	29 (49)	33 (52.3)	
<b>Mean age</b>		143	6.2 (SD ± 3.6)	7.7 (SD ± 3.9)	.041
<b>BCG vaccine</b>	Yes	79	38 (88.4)	41 (83.7)	.52
	No	13	5 (11.6)	8 (16.3)	
<b>Blood group</b>	O Positive	37	18 (44)	19 (53)	.43
	Other	40	23 (56)	17 (47)	
<b>Breast feeding</b>	Yes	56	27(72.9)	29 (65.9)	.49
	No	25	10 (27.03)	15 (34.09)	
<b>Pre-existing</b>	Yes	58	32 (55.1)	26 (44.9)	.09
<b>Medical condition</b>	No	58	23 (39.6)	35 (60.3)	
<b>Weight percentile</b>	Overweight/obese	33	10 (30)	23 (69.7)	.014
	Non-obese	64	36 (56)	28 (43.7)	

P-values were calculated using independent chi-square test.  
BCG, Bacillus Calmette–Guérin.

**Table 2**  
Relationship between symptoms and immunocompromised status.

Symptom	Group	Immunocompromised (%)	Non-immunocompromised (%)	P-value
Fever	Yes	11 (55)	48(55.1)	.98
	No	9 (45)	39 (44.8)	
Nasal congestion	Yes	5 (25)	14 (18.6)	.5
	No	15 (75)	61 (81.3)	
Sore throat	Yes	3 (15)	11 (14.8)	.98
	No	17 (85)	63 (85.14)	
Cough	Yes	6 (30)	26 (32.1)	.85
	No	14 (70)	55 (67.9)	
Wheezing	Yes	1 (5)	0 (0)	.05
	No	19 (95)	72 (100)	
Shortness of breath	Yes	2 (10)	4 (5.6)	.48
	No	18 (90)	67 (94.3)	
Diarrhea	Yes	2 (10)	13 (18)	.38
	No	18 (90)	59 (81.94)	
Vomiting	Yes	2 (10)	5 (6.9)	.64
	No	18 (90)	67 (93.09)	
Abnormal movements	Yes	0 (0)	2 (2.7)	.45
	No	20 (100)	70 (97.2)	
Weakness	Yes	4 (21)	5 (6.9)	.06
	No	15 (78.9)	67 (93.06)	
Skin rash	Yes	1 (5)	2 (2.8)	.62
	No	19 (95)	69 (97.2)	
Conjunctivitis	Yes	1 (5)	2 (2.17)	.6
	No	19 (95)	70 (97.2)	
Lymphadenopathy	Yes	1 (5)	0 (0)	.05
	No	18 (94.7)	70 (100)	

P-values were calculated using Fisher exact test, N (%).

**Table 3**  
Admission rates in different patient groups.

	Admitted	P-value		
		Yes (%)	No (%)	
Immunocompromised	Yes	11 (24.4)	9 (11.4)	.05
	No	34 (75.6)	70 (88.6)	
Weight percentile	<85	28 (63.7)	31 (64.5)	.92
	>85	16 (36.3)	17 (35.4)	
Age	<2	10 (22.2)	12 (15.2)	.15
	2–5	6 (13.3)	22 (27)	
	>5	29 (64.5)	45 (57)	
Gender	Male	22 (49)	36 (45.5)	.72
	Female	23 (51)	43 (54.4)	

The mean duration of hospitalization for these patients was 9.6 days (SD 9 days), while the median length of stay for the symptomatic patient cohort was 9 days as compared to 7 days for the asymptomatic patient cohort, with a significant difference between these groups ( $P = .016$ ). However, it is important to note that

protocols regarding the diagnosis, isolation, and management of COVID-19 patients have been steadily evolving since the start of the pandemic, as have the criteria for hospital admission, likely affecting this readout. In total, 8 patients experience post-infectious complications, of whom 5 experienced a persistent loss of smell, 2 exhibited unexplained weight loss, and 1 suffered from persistent headaches.

#### 4. Discussion

Since the start of the COVID-19 pandemic, researchers have sought to better understand the clinical characteristics of this disease. However, there have been relatively few studies to date describing COVID-19 infections among children in Saudi Arabia [14–17]. The present study was thus designed to explore the clinical characteristics of pediatric patients diagnosed with COVID-19 at the King Faisal Specialist Hospital and Research Center in Riyadh, which is unique in that it serves as a treatment center for a large number of immunocompromised patients.

**Table 4**  
Comparison of laboratory results between symptomatic and asymptomatic pediatric COVID-19 patients.

Variable	Total	Asymptomatic	Symptomatic	P-value
WBC	47	5.4 (0.9–15)	6 (2.03–16)	.24
Neutrophils	47	1.33 (0.01–10.5)	2.7 (0.69–12.2)	.003
Lymphocytes	47	2.4 (0.7–6.45)	1.8 (0.33–4.5)	.08
Platelets	47	258 (16–410)	277 (14–476)	.11
BUN	47	4.4 (2.1–9.1)	4.1 (2.1–6.8)	.28
Creatinine	47	32 (13–56)	39 (16–68)	.48
CRP	23	1.9 (0.2–8)	2.1 (0.3–128)	.56
ESR	29	9 (6–25)	6 (2–111)	.25
Ferritin	43	50 (5.8–1013)	49.9 (5.4–9838)	.48
D-dimer	34	0.48 (0.27–0.78)	0.42 (0.27–32)	.54
BNP	25	65.5 (35–97)	51 (6.2–2386)	.97
Fibrinogen	25	2.06 (1.86–2.8)	2.9 (1.96–5.9)	.019
AST	48	33.7 (16.9–114)	29.7 (6.6–71.8)	.44
ALT	48	19 (9.5–79.3)	17.3 (7–357)	.94
LDH	38	313 (167–478)	306 (167–1280)	.79

P-values were calculated using Mann–Whitney *U* test. Median(range).

WBC, white blood cells; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; BNP, brain natriuretic peptide; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase.

In our study, we found that the majority of diagnosed COVID-19 patients were over 2 years of age, with just 13% of these patients being under the age of 2 and a mean age of 7 years. Consistent with the patterns observed among adult COVID-19 patients, we found that symptomatic disease incidence increased with rising patient age. This is also in line with the results of other international studies, including pediatric age groups, wherein children over the age of 5 were found to be more affected by this disease as compared to younger patients [12,19]. Rates of symptomatic disease did not differ as a function of gender in our study cohort, with 52% and 47% of analyzed males and females, respectively, exhibiting symptomatic disease. These findings are consistent with those of other cohort studies conducted in other hospitals across the kingdom [14–17].

We found that a significant number of our patients were overweight or obese, with approximately 70% of these patients exhibiting symptomatic COVID-19 as compared to just 43% of non-obese patients. Obesity has been linked to severe illnesses caused by respiratory viruses, including the influenza virus in many studies [20], leading to the hypothesis that a similar pattern may hold true in the context of COVID-19 disease. Consistently, we were able to identify two studies conducted in the USA that demonstrated that obesity was the most common feature of patients with severe COVID-19, including one study of adult patients and one that included children in these analyses [21,22]. The relationship between obesity and the severity of COVID-19 infection is not yet fully understood, although it has been suggested to be related to the impaired immunity and decreased lung capacity observed among overweight and obese individuals [12,19].

Most patients in our study cohort were exposed either to a family member or a close contact with COVID-19, further supporting the person-to-person nature of SARS-CoV-2 transmission. Breastfeeding has been shown to play no significant role in the transmission of this virus [23,24]. In fact, many studies have found the breast milk of infected mothers to contain SARS-CoV-2-specific immunoglobulin A (IgA) antibodies up to six months post-infection, strongly suggesting a role for passive viral immunity in the protection of infants [25–27]. Consistent with these findings, we did not detect any significant differences between children as a function of whether or not they were breastfed. This suggests that future studies exploring breastmilk-mediated passive immunity and its impact on COVID-19 severity in children are warranted,

particularly now that lactating mothers are being offered COVID-19 vaccines [28].

Some reports suggest that compulsory BCG vaccination programs may help reduce the COVID-19 spread and associated mortality [29]. The idea is that a T-cell response is induced against secondary unrelated viruses which cause the formation of increased cross-reactive antibodies and increased cytokine release [30]. Our dataset did not reveal any significant difference in symptomatic disease rates when comparing individuals who did and did not receive the BCG vaccine.

The most common presenting symptom among our patient cohort was fever, followed by symptoms consistent with an upper respiratory tract infection. Gastrointestinal symptoms were less common in our patient cohort relative to other reports, with one study from China having reported that 17.6% of analyzed patients experienced gastrointestinal symptoms and 48% of patients exhibited viral shedding in their stool [31].

Sixty-seven of the patients in this study had known pre-existing medical conditions, of whom 25 patients had immunocompromising conditions, including 2 primary immunodeficiency patients, 13 patients with diagnosed malignancies, and 10 patients that were transplant recipients. Of these immunocompromised patients, 11 were admitted to the hospital, accounting for 24.4% of the total admissions.

Of the 45 total patients in this cohort who were admitted to the hospital, 4 were admitted to the PICU, and only 1 required respiratory support, with an average length of hospitalization of 9.6 days, similar to the length of stay reported in other studies.

In a large systematic review, pediatric cancer patients and those that had undergone hematopoietic stem cell transplantation were found to exhibit COVID-19 outcomes similar to those of the general population [32]. Our findings were consistent with this report. The true impact of immunosuppression on COVID-19 infection-related outcomes is particularly difficult to ascertain. In a number of reports, outcomes in immunocompetent and immunocompromised children were reported to be similar [13]. However, other reports seem to exhibit increased mortality among immunocompromised patients, particularly among cancer patients and SOT recipients [33]. The interpretation of these data is complicated by the wide array of immunomodulatory agents that individual patients may be taking, many of which are likely to have differing effects on clinical outcomes, necessitating more sophisticated statistical approaches to better delineate their effects on the disease course [34]. The heterogeneity of reported COVID-19 patient outcomes may offer some clues regarding the specific immunopathological characteristics of COVID-19 infections and the interplay between such pathology and the specific medications used by different immunocompromised patients.

With respect to imaging findings, only a few patients in the present study cohort exhibited abnormal x-ray results. Most of these patients exhibited peribronchial thickening, and there were no significant differences in the rates of such abnormalities when comparing immunocompromised and non-immunocompromised patients ( $P = .15$ ).

Our findings further support the conclusion that COVID-19 infections tend to be milder in pediatric patients relative to adults. The reasons for this age-related difference in disease severity remain poorly understood. Some studies have suggested that children are less sensitive to SARS-CoV-2 infection owing to reduced maturity and functionality of the viral ACE2 in children relative to adults, or due to differences in intracellular signaling responses downstream of ACE2 [35]. Other studies suggest that age-related differences in immune responses to the virus may be responsible for these differences in the severity of disease manifestations [30].

MIS-C [36] among COVID-19 patients has been described in many published reports to date. Five MIS-C patients were reported in a study conducted at King Abdullah Specialized Children's Hospital in Riyadh, all of whom were treated successfully. In addition, 5 MIS-C cases were reported among 88 patient cohorts in a study conducted in PSMC, Riyadh. However, none of the patients in our study cohort experienced this severe disease presentation. Only 1 patient who was known to have relapsed acute myeloid leukemia (AML) exhibited a severe cytokine storm-like disease presentation, with abnormal laboratory findings including elevated liver enzymes, increased ferritin levels (up to 11,752 ng/ml), and an increased IL-6 level (up to 150 pg/ml). He was otherwise clinically stable. At the time of his treatment, very limited data had been published regarding the suggested management of patients with similar cytokine storm- or MIS-C-like symptoms. In accordance with contemporaneous MOH guidelines, he was treated with tocilizumab (recombinant anti-IL-6) and dexamethasone, after which his laboratory results normalized.

In conclusion, our findings are largely consistent with those of other prior reports, confirming a milder course of COVID-19 disease among affected children, with obesity being a significant risk factor associated with symptomatic disease. Moreover, we observed significant differences in immunocompromised patients as compared to immunocompetent patients.

Limitations of our cohort study include the fact that this was a single-center study with a relatively small number of enrolled patients. In addition, there may have been many other pediatric patients with mildly symptomatic or asymptomatic cases of COVID-19 who were not included in this study. As this disease continues to be better understood, the clinical and admission policies associated therewith continue to evolve, introducing inevitable variability into our data. Together, these factors emphasize the importance of conducting additional prospective studies in children with COVID-19.

## 5. Conclusion

In summary, COVID-19 in children tends to present as a relatively mild disease, in contrast to what has been reported in adult patient populations. However, it can be a significant cause of hospital admission in pediatric populations, particularly among immunocompromised children or those with other risk factors. Studies of COVID-19 are ongoing and treatment modalities are constantly evolving. The impact of childhood vaccination on the clinical presentation of COVID-19 warrants further study, and further research regarding the changing nature and characteristics of this disease as novel SARS-CoV-2 disease variants continue to emerge within the general Saudi population will be essential [37]. There have already been some preliminary reports describing an increased risk of hospitalization among patients affected by the Delta variant of SARS-CoV-2 [38]. In addition, the Delta variant seems to more frequently affect pediatric patients as compared to the Alpha variant [38]. It would thus not be unreasonable to expect a shift in the clinical characteristics of COVID-19 infections as time goes on, making attempts to recreate this dataset in subsequent papers of particular importance.

## Ethical statement

Hereby, I, Dr. Esam Albanyan, consciously assure that for the manuscript "Epidemiological Characteristics, Clinical Course, and Laboratory Investigation of Pediatric COVID-19 Patients in a Tertiary Care Center in Saudi Arabia", the following is fulfilled:

- 1) This material is the authors' own original work, which has not been previously published elsewhere.
- 2) The paper is not currently being considered for publication elsewhere.
- 3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
- 4) The results are appropriately placed in the context of prior and existing research.
- 5) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
- 6) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

I agree with the above statements and declare that this submission follows the policies of the journal as outlined in the Guide for Authors.

## Author's statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the International Journal of Pediatrics and Adolescent Medicine.

## Declaration of conflict of interest

Each author confirms that they do not have any conflict of interest.

## Visual abstract

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