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SARS-CoV-2 infection in children, clinical characteristics, diagnostic findings and therapeutic interventions at a tertiary care center in Riyadh, Saudi Arabia

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A B S T R A C T

Background: Coronavirus disease 2019 (COVID-19) pandemic caused by SARS-CoV-2 was first identified in Wuhan, China. All ages are susceptible to SARS-CoV-2 infection. Few studies had reported milder course in children however, severe course of illness has been reported. We aimed to describe the clinical features of COVID-19 in pediatric patients including diagnostic findings and therapeutic interventions in severe disease manifestation.

Methods: We retrospectively reviewed 742 patients with SARS-CoV-2 proven infection at King Abdullah Specialist Children’s Hospital, from April 2020 and July 2020. Inpatients, outpatient, including those with severe manifestation treated at the Intensive Care Unit (ICU) were included. We collected data including demographic data, comorbidities, symptoms, imaging data, laboratory findings, treatments and clinical outcomes of patients with COVID-19.

Results: Among of 742 patients, 71 (9.6%) were hospitalized. The median age of patients was 75 months old and 53.6 were male. A total of 461 (62.1%) had close contact with confirmed cases, 45 (6.1%) had no contact history, and 236 (31.8%) with unknown exposure risk. The most common symptoms at the onset of illness were fever (32.5%), respiratory symptoms (21%) and gastrointestinal symptoms (10.3%). Among the entire cohort, 7 patients were admitted to PICU with COVID-19 related symptoms, five patients diagnosed with MIS-C, one patient with Kawasaki, and one patient with pneumonia. All patients received supportive therapy, no antiviral treatment had been used however, in MIS-C patients IVIG had been given to all patients, five patients received Anakinra; and one patient received tocilizumab.

Conclusions: In this study, children infected with SARS-CoV-2 are less likely to develop symptomatic or serious diseases. Among symptomatic children, the most common clinical features were fever and respiratory symptoms followed by gastrointestinal manifestations. The majority of infected children have reported contact with an infected individual. MIS-C associated with COVID-19 is a severe presentation of SARS-CoV-2 infection and of a major concern as an overlapping features with other diseases could happen, making the diagnosis challenging.

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Abbreviations: CDC, Center for Disease Control and Prevention; COVID-19, 2019 novel coronavirus disease; SARS-CoV, severe acute respiratory syndrome coronavirus; WHO, World Health Organization; ICU, Intensive Care Unit; IVIG, Intravenous Immunoglobulin; MIS-C, Multisystem Inflammatory.

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Introduction

The SARS-CoV-2 coronavirus responsible for the Corona Virus Infectious Disease-2019 (COVID-19) pandemic is an enveloped, single-stranded positive-sense RNA virus [1]. On December 31, 2019, the World Health Organization (WHO) China Country Office was informed of cases of pneumonia secondary to a new type of coronavirus [2]. On February 11, 2020, the International Committee on Taxonomy of Viruses named this new virus “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2), while WHO announced COVID-19 as the name of this new disease on the same date [3]. At the time of this writing, 14,765,256 cases have been reported globally [4].

Children represent a small proportion of the population diagnosed with laboratory-confirmed SARS-CoV-2 infection, accounting for an estimated 2–5% of the cases [5]. In the only published study of COVID-19 cases in Saudi Arabia, 74 (4.8%) of the 1519 cases were in children aged 14 years or younger [6]. However, clinical characteristics and outcomes in these children was not reported. Internationally, several descriptive reports have appeared regarding COVID-19 in children. One of the first detailed studies came from China and described 2135 pediatric patients with suspected COVID-19, of which 728 were lab-confirmed cases. Of the lab-confirmed cases, 12.8% were asymptomatic, 43.1% had mild symptoms, 40.9% had moderate symptoms, and 2.9% had severe symptoms or critical disease. The proportion of severe or critical cases was higher in children less than 1 year of age [7]. Similarly, a multinational, multicenter cohort study of COVID-19 in children and adolescents in Europe reported 582 children with PCR-confirmed SARS-CoV-2 infection. Sixty-two percent of those children were admitted to hospital, 25% had pre-existing medical conditions, and 48 children (8%) required intensive care admission [8]. Significant risk factors for intensive care unit (ICU) admission were age less than 1 month, male sex, pre-existing medical conditions, and presence of lower respiratory tract infections signs or symptoms on presentation [8]. A systematic review of 7780 pediatric patients with COVID-19 currently in press reports fever and cough (at 59.1% and 55.9%, respectively) as the most frequent symptoms of COVID-19 in children. Almost 20% of children with COVID-19 were asymptomatic, and only 7 deaths were reported [9].

These initial studies of COVID-19 in children indicate that the disease appears to be mild in nature for the vast majority of children, with a large percentage of children in fact being asymptomatic. However, one subset of children tends to have severe disease, and reports are increasing regarding a hyperinflammatory syndrome affecting children that is temporally associated with SARS-CoV-2 infection. This syndrome has been termed multisystem inflammatory syndrome in childhood (MIS-C) [9,10]. A recently published study on MIS-C in American children and adolescents revealed 186 patients across the country. The median age was 8.3 years, and 75% were previously healthy. Coronary artery aneurysms were found in 8% of patients, and Kawasaki disease-like features were reported in 40% [10].

Internationally, many descriptive studies have been conducted on COVID-19 in children; however, we are unaware of any detailed study conducted on the characteristics of COVID-19 in children in Saudi Arabia or the Gulf region. The aim of the present study was therefore to describe the epidemiology, clinical characteristics, and outcomes of COVID-19 in children in King Abdullah Specialist Children’s Hospital, a tertiary and academic free-standing hospital in Riyadh, Saudi Arabia (Fig. 1).

Material and methods

We performed a retrospective cohort study of children (≤14 years of age) with nasal/throat swab positive for SARS-CoV-2 between April 2020 and July 2020 at King Abdullah Specialized Children’s Hospital, a tertiary care children’s hospital in Riyadh, Saudi Arabia. Our hospital has adopted universal SARS-CoV-2 testing for all patients newly hospitalized and/or undergoing surgical procedures with or without the potential for aerosol generation. Asymptomatic patients and symptomatic patients who were treated as outpatients and testing positive were also included. All testing was conducted at the National Guard Microbiology and Molecular Laboratory using a real-time reverse transcriptase–polymerase chain reaction (PCR) assay. The hospital institutional review board approved this study, and the requirement for informed consent was waived.

Patients

Electronic medical records for SARS-CoV-2 infected patients were reviewed. The inclusion criteria for detailed medical record review included (1) outpatients, (2) inpatients with symptoms consistent with COVID-19, as described in the literature [14–16], and (3) age 14 years or younger. Critically ill patients were defined as those meeting any of the following criteria: (1) respiratory failure requiring mechanical ventilation; (2) septic shock, and (3) accompanied by other organ failure requiring ICU monitoring and treatment. Patients with MIS-C were defined as per the criteria adapted from the US Centers for Disease Control (CDC) [11].

Data collection

Demographic data and clinical characteristics, including exposure history, comorbid conditions, hospital course, disease severity, laboratory parameters, radiologic findings, administered therapies, clinical course during hospitalization, and laboratory findings of each patient, and Pediatric Index of Mortality 3 (PIM 3) and Pediatric Logistic Organ Dysfunction (PELOD) scores patients admitted to intensive care unit were obtained from electronic medical records.

All symptoms and signs reported at the time of presentation were recorded, including COVID-19 symptoms as outlined by the CDC [12]. These were fever (subjective or temperature ≥ 38 °C), upper respiratory symptoms, lower respiratory symptoms, gastrointestinal symptoms, or general symptoms including decrease oral intake, decrease activity, malaise, and headache.

Pre-existing comorbidities were reviewed including specific comorbidities based on previously reported studies on COVID-19, these included asthma, cardiac issues, and immunosuppression. Immunosuppression was defined as (1) concurrent use, or use during the last 6 months, of chemotherapy and intravenous immunoglobulin.

Several laboratory tests that had been conducted upon admission or during hospitalization were also reviewed; these included complete blood count (leucocytes, neutrophils, lymphocytes, hemoglobin, and platelets), serum C-reactive protein, erythrocyte sedimentation rate, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, ferritin, fibrinogen, urea, creatinine, and D-dimer. For PICU MIS-C patients, IL-1, IL-6, TNF, troponin, BNP in addition to echo findings.

Radiological finding results for the presence of patchy opacities, focal consolidation, and/or effusions were documented. We also reviewed readmissions to the hospital or ICU.

Statistical analysis

Frequencies and percentages were used to describe the categorical variables, such as gender, age category, comorbidities, signs, and symptoms. The median and percentile (Q1–Q3) values were used to describe the quantitative variables of age, weight, BMI, temperature, saturation, and laboratory values. Univariate comparisons using Fisher’s exact test and Mann-Whitney U test for non-parametric data were used for categorical and continuous variables, respectively. A P-value < 0.05 was considered statistically significant for all analyses. IBM SPSS version 26 was used to analyze the data.

Results

During the period from 7 April 2020 to 17 July 2020, a total of 742 children tested positive for SARS-CoV-2 in King Abdullah Specialized Children’s Hospital, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. A total of 71 children were hospitalized, representing 9.6% of all positive cases. There was almost equal gender distribution, with 398 males (53.6%) and 344 females (46.4%). The median age was six years (IQR: 2.8–10.6 years), and 60% of children were five years and above. One hundred fifteen children (15.5%) were known to have pre-existing comorbidity; the most common comorbidities were pulmonary diseases (45 children, 42 of them
were bronchial asthma), followed by cardiac (22 children), neurological disorders (23 children), endocrine (8 children), and the remaining 17 patients were having various comorbidities including metabolic, malignancies and others.

Almost half of the children were asymptomatic, 405 (54.6%). Common clinical signs and symptoms included upper respiratory symptoms (21%) followed by gastrointestinal symptoms lower respiratory symptoms, then general symptoms (e.g., malaise, headache, decrease oral intake). However, Fever alone was present in 32.5% of the patients.

Table 1 shows the characteristics of children in the cohort. When comparing hospitalized children with the rest of the cohort, we found that hospitalized children were older (p < 0.000), Pre-existing comorbidities were more common in admitted patients (p < 0.000), namely cardiac diseases (p = 0.001), malignancies (p < 0.000), neurological (p = 0.017) and metabolic disorders (p = 0.003). Four out of 5 children on chemotherapy and 2 out of 4 children on IVIG were hospitalized.

Majority of patients were asymptomatic (54.6%). Patients who sought medical advice presented commonly with upper respiratory symptoms followed by gastrointestinal symptoms. Fever was present in (32.5%) of patients. Hospitalized patients compared to non-hospitalized presented more with lower respiratory symptoms (p < 0.000) and gastrointestinal symptoms (p < 0.000). In addition, fever was more prevalent in hospitalized patients (71.8%) compared to non-hospitalized patients (27.4%).

Table 2 shows the characteristics of children admitted to PICU in comparison to the ward. There was no statistically significant difference in gender, age, pre-existing comorbidities, signs, and symptoms, nor in temperature on presentation among children admitted to PICU compared with those admitted to the ward.

Tables 3 shows admission, maximum, and upper laboratory values for hospitalized children. Children admitted to PICU had higher admission laboratory transaminases (alanine transaminase (ALT) and aspartate transaminase (AST)), and creatinine values. Besides, admitted children to PICU had statistically significant higher leukocytes and worse renal function during hospitalization.

Tables 4 and 5 show the Summary of patients’ characteristics and provided therapy for children admitted to PICU. Twelve patients were admitted to PICU, one neonate with VSD, and heart failure was admitted three times with worsening respiratory status due to pulmonary edema. Seven patients were admitted to PICU with COVID related symptoms, five patients diagnosed with MIS-C, one patient with Kawasaki, and one patient with pneumonia. For laboratory findings, all MIS-C patients had elevated BNP and ferritin. The echo was abnormal in one patient with low ejection fraction. All patients diagnosed with MIS-C received inotropic support. Also, all MIS-C patients were treated with IVIG, five patients were given Anakinra; and one patient received tocilizumab.

### Discussion

This is, to our knowledge, the first comprehensive analysis of pediatric infection with COVID-19 in Saudi Arabia. One-point worth noting is that a large number of pediatric patients from one tertiary center were studied in this analysis and both inpatients and outpatients were included. The main purpose of this study was to describe the epidemiology, clinical characteristics, and outcomes of COVID-19 in children in a pediatrics tertiary care hospital in Saudi Arabia.

The findings from the cohort showed that 10% of children who tested positive for SARS-CoV-2 were hospitalized. In the whole cohort, 60% of patients were older than 5 years; however, hospitalized children in comparison to non-hospitalized children were younger in age. Hospitalized children were known to have pre-existing comorbidities, specifically cardiac diseases, malignancy, neurologic and metabolic disorders. Lower respiratory, gastrointestinal symptoms, and fever were more common in hospitalized children. In hospitalized patients, leukocytosis and high neutrophil counts were observed in patients admitted to PICU. In addition, patients admitted to PICU were found to have high creatinine and urea in comparison to patients admitted to wards.

Since the time the World Health Organization (WHO) first announced COVID-19 as a pandemic, scientists have been exploring the specific disease characteristics, modalities of treatment, and transmission. However, the pathogenesis, variability of symptoms, and mode of transmission remained poorly understood [13]. Our data showed that patients aged below 5 years were less susceptible to SARS-CoV-2 infection (40%) compared to the ages above (60%), and the number of cases was far less in children below 2 years of age. This finding was the same as found in previous studies, where children below 5 years of age were less susceptible to COVID-19 [14]. The lower percentage of infants has no clear reason, but possibly may reflect their immune status and the lower chance of contact with adults or other children because of limited movement.

While children below 5 years of age are less susceptible to SARS-CoV-2 infection, we found that the majority of patients that fall into this category are more likely to be admitted to the hospital (49/71). Even though all age groups can be affected by SARS-CoV-2, children younger than one year of age and older than 5 years of age were more likely to be hospitalized and more likely to require critical care management.

As SARS-CoV-2 infection is predominantly transmitted via respiratory droplets [14–16], respiratory tract symptoms were commonly observed in our patients. Nonetheless, the available data, on vertical transmission to neonates were limited to small case series and showed conflicting results; some studies have demonstrated lack of transmission, whereas others were unable to definitively rule out this possibility [17,18]. We had six positive neonates and only one of the six had been delivered to a...
Table 1
Baseline characteristics in the entire cohort, outpatients and inpatients with COVID-19.

| Variable                  | Entire cohort N = 742 | Not admitted N = 671 | Admitted to Hospital N = 71 | P value |
|---------------------------|-----------------------|-----------------------|-----------------------------|---------|
| **Gender**                |                       |                       |                             |         |
| Male                      | 398                   | 353                   | 45                          | 0.083   |
| <1 month                  | 14                    | 5                     | 9                           | 12.7    |
| 2 to 12 months            | 62                    | 46                    | 16                          | 22.3    |
| 1 to 2 years              | 68                    | 62                    | 6                           | 8.5     |
| 2 to 5 years              | 151                   | 133                   | 18                          | 25.4    |
| 5–10 years                | 233                   | 220                   | 13                          | 18.3    |
| above 10 years            | 214                   | 205                   | 9                           | 12.7    |
| Below 18.5                | 401                   | 344                   | 57                          | 80.3    |
| 18.5–24.9                 | 112                   | 101                   | 11                          | 15.5    |
| BMI a                      |                       |                       |                             |         |
| 25–29.9                   | 33                    | 30                    | 3                           | 4.2     | 0.180 |
| 30–39.9                   | 15                    | 15                    | 2                           | 2.2     |         |
| 40–49.9                   | 4                     | 4                     | 0                           | 0.6     |         |
| ≥ 50 and above            | 3                     | 3                     | 0                           | 0.4     |         |
| **Pre-existing comorbidities** |                       |                       |                             |         |
| Cardiac disease           | 22                    | 14                    | 8                           | 11.27   | 0.001 |
| Malignancy                | 6                     | 6                     | 5                           | 7.04    | 0.000 |
| Neurologic disorder       | 23                    | 17                    | 6                           | 8.45    | 0.017 |
| Asthma                    | 42                    | 39                    | 3                           | 4.23    | 0.789 |
| **Symptoms and signs**    |                       |                       |                             |         |
| Asymptomatic              | 405                   | 396                   | 9                           | 12.7    | 0.000 |
| Upper respiratory symptoms| 156                   | 146                   | 10                          | 14.1    | 0.000 |
| Lower respiratory symptoms| 29                    | 19                    | 10                          | 14.1    | 0.000 |
| GI symptoms               | 77                    | 72                    | 29                          | 40.8    | 0.000 |
| Shock                     | 1                     | 0.1                   | 1                           | 1.4     | 0.096 |
| General symptoms a         | 22                    | 14                    | 8                           | 11.3    | 0.001 |
| Fever a                   | 52                    | 7                     | 4                           | 5.6     | 0.009 |
| Pyrexia                   | 241                   | 184                   | 51                          | 71.8    | 0.000 |
| Chemotherapy              | 5                     | 0.7                   | 4                           | 5.6     | 0.000 |
| Regular IVIG              | 4                     | 0.5                   | 2                           | 2.8     | 0.006 |

1 BMI body mass index.
2 Data available for 566 children.
3 General symptoms include (Decrease oral intake, decrease activity, malaise, headache, or headache).
4 Fever as the only sign and symptom on presentation.

mother who had COVID–19 before delivery. Without amniotic fluid testing, the assumption of vertical transmission is yet to be confirmed.

To date, the available findings are clear, providing evidence that the incidence of serious illness involving hospitalization is less common in children than in adults [7–9]. Therefore, having a low threshold of suspicion is crucial for SARS-CoV-2 testing. Consequently, our assessment approach, which is identical to many other centers, has quickly shifted from the use of rigid CDC evaluation requirements to universal admission screening. We observed that positive patients in our cohort often had a history of household contacts at the time of admission, suggesting household transmission. Furthermore, our analysis showed that majority of the patients acquired the infection mainly through close contact with their relatives. This result confirms what was previously stated by Wang et al. and other studies at the outbreak of this pandemic, of which 40 pediatric patients were tested, 31 of whom were asymptomatic positive and had contact with affected family members [15,16,19].

During the period of this study, we had a few patients with one or more comorbidity. Until now, data have been insufficient for a clear establishment of certain risk factors for severe COVID–19 disease in children. Various underlying conditions have been seen in patients with COVID–19 [7,18]. Asthma was the commonest comorbidity seen in adults and pediatric patients [15,16,19]. One third (42/129) of our patients with comorbidities had underlying asthma upon diagnosis with SARS-CoV-2; however, only three required hospital admission. This proposes that although children with asthma may show symptom exacerbation in response to SARS-CoV-2 infection, asthma was not the main factor determining disease severity. Several pre-existing comorbidities diagnoses that have been associated with hospitalization in our cohort, including: cardiac diseases, malignancies, neurologic and metabolic disorders. Furthermore, the significance of obesity as an independent risk factor for severity is now being increasingly described in adult studies [20]. Therefore, a notable finding is that the majority of the hospitalized patients in this cohort had no obesity and only 5% had overweight, and none of these patients required ICU admission.

Some reports have shown a predominance of GI symptoms in children [21], but we noted dissimilar presentations among our patients, as only 10.3% had gastrointestinal symptoms. Conversely, upper respiratory tract involvement was the main clinical presentation in our cohort (21%). Fever and cough remained the most prominent symptoms, but dyspnea was less frequently observed, indicating fewer lower respiratory tract infection cases. Moreover, asymptomatic patients constituted half of our cohort (55%), as reported previously [24]. Children with acute abdomen had been reported during this pandemic, with appendicitis and intussus-
ception as the commonly described pathologies [22]. Three of our patients had appendicitis and were positive for SARS-CoV-2, with no prior concerning symptoms. Whether the infection can trigger a clinical picture consistent with acute abdomen in children should be determined by further studies.

Several laboratory investigations and clinical imaging in patients with confirmed or suspected COVID-19 disease have been thoroughly discussed in previous reports. Multiple studies have reported thrombocytopenia, lymphopenia, leukopenia, elevated erythrocyte sedimentation rate (ESR), and elevated C-reactive protein (CRP), but none of these findings were specific in most instances [23–25]. Normal or low leukocyte or low lymphocyte numbers have been reported in children with SARS-CoV-2 infection [23,26]. However, in the present study, normal or high lymphocyte and neutrophil counts were more commonly observed, rather than a reduction. Since the start of this pandemic, few published reports have described radiological findings in SARS-CoV-2–positive patients. Nevertheless, Yoon et al. reported a predominance of patchy infiltrates, consolidations, and, to a lesser extent, ground-glass opacities on chest imaging [27]. In our cohort, the patients with clinically diagnosed pneumonia (n = 8) had opacity and patchy infiltrates on chest X-ray as their predominant findings.

**Table 2**
Baseline characteristics of inpatients admitted to ward and PICU.

| Variable | Admitted to ward N = 59 | Admitted to PICU N = 12 | P value |
|----------|--------------------------|--------------------------|---------|
| Gender   |                          |                          |         |
| Male     | 37 (62.7)                | 8 (66.7)                 | 1       |
| <1 month | 7 (11.9)                 | 2 (16.7)                 |         |
| 2 to 12 months | 13 (22)           | 3 (25)                   |         |
| Age      |                          |                          |         |
| 1 to 2 years | 5 (8.5)                | 1 (8.3)                  | 0.974   |
| 2 to 5 years | 16 (27.1)              | 2 (16.7)                 |         |
| 5–10 years | 11 (18.6)               | 2 (16.7)                 |         |
| above 10 years | 7 (11.9)              | 2 (16.7)                 |         |
| BMI *    | 18.5–24.9                | 9 (15.3)                 | 0.726   |
| Pre-existing |                    |                          |         |
| Cardiac disease | 6 (10.17)          | 2 (16.7)                 | 0.615   |
| Malignancy | 5 (8.47)                | – (0.00)                 | 0.581   |
| Neurologic disorder | 4 (6.78)          | 2 (16.67)                | 0.266   |
| Asthma    | 3 (5.08)                 | – (–)                    | 1       |
| Comorbidities |                    |                          |         |
| Pulmonary disease | 1 (1.69)             | – (–)                    | 1       |
| Endocrine disease | 1 (1.69)             | – (–)                    | 1       |
| Gastrointestinal |                    |                          |         |
| Hematological diseases | 2 (3.39)          | – (–)                    | 1       |
| Metabolic diseases | 2 (3.39)             | 1 (8.3)                  | 0.316   |
| Immune deficiency |                   |                          |         |
| Asymptomatic | 8 (13.6)               | 1 (8.3)                  | 1       |
| Upper respiratory symptoms | 10 (16.9)    | 0 (0)                    | 0.194   |
| Lower respiratory symptoms | 6 (10.2)       | 4 (33.3)                 | 0.058   |
| Symptoms and signs |                    |                          |         |
| GI symptoms | 24 (40.7)             | 5 (41.7)                 | 1       |
| Shock     | 0 (0)                   | 1 (8.3)                  | 0.169   |
| General symptoms • |                   |                          |         |
| Fever •   | 4 (6.8)                 | – (–)                    | 1       |
| Pyrexia   | Yes                     | 43 (72.9)                | 0.729   |
| Chemotherapy | Yes                   | 4 (6.8)                  | 0.353   |
| On regular IVG | Yes                  | 2 (3.4)                  | 0.518   |

* BMI, body mass index.
• No patients were found to have a BMI more than 30.
† General symptoms include (Decrease oral intake, decrease activity, malaise, headache, or headache).
‡ Fever as the only sign and symptom on presentation.

**Table 3**
Maximum and minimum laboratory results in patients with COVID-19 admitted to ward and PICU.

| Variable | Admitted to ward (Median) | Admitted to PICU (Median) | P value |
|----------|----------------------------|---------------------------|---------|
| WBC *    | 6.25 (1.68–10.2)          | 6.24 (4.57–11.44)         | 0.734   |
| WBC †    | 10.2 (6.4–13.2)           | 16.8 (9.81–27.15)         | 0.012   |
| Neutrophil (lowest) | 1.67 (0.73–3.05)       | 2.745 (1.90–4.28)         | 0.099   |
| Neutrophil (highest) | 3.33 (1.73–6.81)        | 9.28 (5.68–21.18)         | 0.004   |
| Lymphocyte (lowest) | 2.085 (0.36–3.72)       | 1.16 (0.51–2.94)          | 0.555   |
| Lymphocyte (highest) | 4.46 (1.35–6.76)       | 4.82 (2.93–11.82)         | 0.286   |
| Hgb *    | 109 (94–123)              | 82 (66.25–103.5)          | 0.016   |
| Hgb †    | 125 (112–137)            | 127 (119.75–136.25)       | 0.367   |
| Platelets (lowest) | 233 (144–267)        | 126 (45.75–210.75)        | 0.053   |
| Platelets (highest) | 313 (240–444)        | 416 (168.75–541.25)       | 0.521   |
| Creatinine (highest) | 40.5 (38–48)         | 63.5 (47–81)              | 0.000   |
| BUN ‡    | 3.65 (2.735–4.78)        | 8.75 (6.475–17.4)         | 0.000   |

* WBC, White blood cells.
† Hgb, Hemoglobin.
‡ BUN, blood urea nitrogen.
**Table 4**
Profile of 6 children admitted to PICU with Kawasaki/MIS-C.

| Age (months) | Gender | PIM-3 | PELOD-2 | Inotropic support | MV (days) | LVFO (days) | Comorbidities | Admission Diagnosis | PICU LOS |
|--------------|--------|-------|---------|------------------|-----------|-------------|---------------|-------------------|----------|
| 38           | Female | 1.41% | 4       | No               | 4         | 8           | Metabolic      | Kawasaki          | 2        |
| 67           | Male   | 3.89% | 8       | Yes              | 4         | 10          | Metabolic      | MIS-C             | 2        |
| 1            | Female | 4.29% | 10      | Yes              | 12        | 2           | Metabolic      | MIS-C             | 0        |
| 3            | Male   | 62.29%| 11      | Yes              | 15        | 20          | Metabolic      | MIS-C             | 2        |
| 28           | Female | 2.5%  | 2       | No               | 0         | 2           | Metabolic      | MIS-C             | 2        |
| 144          | Male   | 32%   | 5       | No               | 2         | 0           | Metabolic      | MIS-C             | --       |

**Table 5**
Profile of 6 children admitted to PICU with COVID-19.

| Age (months) | Gender | PIM-3 | PELOD-2 | Inotropic support | MV (Days) | LFFO (Days) | Comorbidities | Admission Dx | PICU LOS |
|--------------|--------|-------|---------|------------------|-----------|-------------|---------------|--------------|----------|
| 146          | Female | 17.43%| 4       | Yes              | 3         | 1           | Spinal AV malformation / post-surgery | Cardiac, neurologic VSD and HF | 22 |
| 1            | Male   | 6.38% | 3       | No               | Non       | Non         | Post-surgery   | Cardiac, neurologic VSD and HF | 29 |
| 3            | Female | 8.95% | 5       | No               | Non       | Non         | Comorbidities | Admission Dx | 13 |
| 7            | Male   | 1.5%  | 4       | No               | Non       | Non         | Comorbidities | Admission Dx | 73 |
| 14           | Male   | 1.67% | 5       | No               | No        | Yes         | Comorbidities | Admission Dx | 6 |
| 113          | Female | 9.68% | 4       | Yes              | No        | Yes         | Comorbidities | Admission Dx | No |
| 3            | Male   | 9.68% | 8       | Non              | No        | No          | Comorbidities | Admission Dx | 22 |

Normal reference values: LDH, 125–220 U/L; Troponin, ≤34 pg/mL; Ferritin, 21.8–274.6 μg/L; BNP, ≤28.9 pmol/L.

* PIM-C, Multisystem Inflammatory Syndrome in Children.
* P IM-3, Pediatric index of mortality.
* PELOD-2, Paediatric logistic organ dysfunction.
* MV, Mechanical ventilation.
* HFO, High frequency oscillation.
* BNP, Brain natriuretic peptide.
* LDH, Lactate Dehydrogenase.
* IL1, Interleukin 1.
* IL6, Interleukin 6.
* TNFα, Tumor necrosis factor alpha.
* LOS, Length of stay.

Severe multisystem inflammatory syndrome (MIS-C) had been well described in children as an associated complication of SARS-CoV-2 infection. The syndrome first attained attention in the United Kingdom, and subsequently in Europe and the United States, where previously healthy children with severe inflammation and KD-like features were found to have evidence of SARS-CoV-2 infection [24,25]. Most reports described an age preference, as severe cases were more common in a younger age group and in children with comorbidities [23–26,28,29]. These findings were similar to what we observed in our patients, as 2 of 5 patients with MIS-C were under 3 months of age.

Multiple reports have described the laboratory characteristics in patients with MIS-C and KD, but leukopenia and high levels of ventricular natriuretic peptide (a marker of heart failure) are not clearly
defined features of KD [28–31]. Previously, Riphagen and Verdini L et al. reported pediatric MIS-C patients who developed coronary aneurysms; however, determining whether this sequela is related to MIS-C or whether these children actually had KD is challenging [30,31]. Distinguishing the two conditions can be difficult given the overlapping of clinical features and the lack of a specific diagnostic test for either condition. In our cohort, four cases (three MIS-C and one KD) met the case definition published in previous MIS-C and KD reports. The manifestation was less severe in the patient with KD than in the children with MIS-C, and none developed a coronary artery aneurysm.

At the time of writing this paper, no Food and Drug Administration-approved drugs have been released for the treatment of COVID-19. Several immune modulatory agents have been used to control the hyperactive inflammatory response associated with SARS-CoV-2 infection, including human blood-derived products and immunomodulatory therapies [32]. IVIG and steroid treatments, either alone or in combination, are currently the most commonly used immunomodulatory medications in MIS-C patients [30–34]. Anakinra (human interleukin–1 receptor antagonist) and IVIG were given to our patients diagnosed with MIS-C, and only one patient had received tocilizumab (Table 4). Although the death rates are generally reported as low [31,34], we had two deaths among our patients (a 1-month-old female) despite administration of steroids, IVIG, and anakinra, and a 12 years old child who received IVIG.

The major limitation of this study is that these data represent an early phase of SARS-CoV-2 transmission in one center in Saudi Arabia, and we had only a small number of severe or critical cases. Moreover, several key issues were changing over this period, including implementation of social distancing, national lockdown measures, and increasing testing speed, and these changes could eventually have affected the true incidence and outcome results.

Conclusion

In conclusion, our study adds to previous descriptions indicating that children with SARS-CoV-2 infection show mild clinical manifestations and have an overall good prognosis. Risk stratification for critically ill patients and especially for those with signs raising concerns of MIS-C is of crucial importance, as are early identification of the specific features and timely treatment of COVID-19 in pediatric. Additionally, the transmission of the virus and the spread of the disease are still ongoing at study rate making future studies are of a great help to understand the spectrum of this disease and the future therapeutic modalities.

Authors’ contribution

Musaed Alharbi conceptualized and designed the study and designed the data collection instruments. Alaa Alsadoon, Maria Alayed and Shahad Abu Hussien collected the data. Musaed Alharbi and Yasser M. Kazzaz coordinated and supervised data collection. Yasser M. Kazzaz carried out the initial analyses; Musaed Alharbi and drafted the initial manuscript. All authors read, reviewed and approved the manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of interest

The authors declare that there are no conflict of interests.

Ethical approval

The study was approved by the King Abdullah International Medical Research Center (KAIRMC) Institutional Review Board [RC20/454/R] and the requirement of informed consent was waived.

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