

Epidemiology, Clinical Characteristics and Outcome of COVID-19 in Pediatric Patients Admitted at Aga Khan University Hospital, Karachi

Falak Abro, Javairia Khalid, Fariha Shaheen, Naureen Lalani, Ali Saleem, Fyezah Jehan
Department of Pediatrics and Child Health, Aga Khan University, Karachi.

Abstract

Background: The information on the epidemiology, clinical spectrum, and outcome of COVID-19 in children of developing countries are limited.

Objective: To identify the epidemiology, clinical characteristics of patients and outcome of COVID-19 in pediatric patients admitted to the Aga Khan University Hospital in Karachi, Pakistan.

Study type, settings & duration: A retrospective study through medical records was conducted at Aga Khan University Hospital, Karachi from March to August 2020.

Methodology: The medical record of sixty pediatric patients was used for this study. They all were positive SARS-CoV-2 by reverse transcription-polymerase chain reaction assay (RT-PCR) and were subsequently admitted at Aga Khan University Hospital Karachi, from March 2020-August 2020, and the data were analyzed using SPSS version 22.

Results: From a total of 415 suspected COVID-19 children, 60 were COVID-19 positive. Of whom, 42 (70%) children were female. About 24 (40%) children acquired COVID-19 infection through household contacts. Eight children (13.3%) were asymptomatic, whereas 35 (58.3%), 12 (20%), and 5 (8.3%) had a mild, moderate, and severe infection respectively. Respiratory symptoms were prevalent in 21 (40%) patients including pneumonia 5 (10%) and acute respiratory distress syndrome (ARDS) 3 (6%). Malignancy 7 (11%) was the most prevalent underline comorbidity. Mortality was observed in 5 (8.3%) children. Most children, 52 (87%), were discharged after a four-day median hospital stay (range 2-8 days).

Conclusion: Children with COVID-19 had mild illness. Severe illness was observed in young children and those with comorbidities. Most of the children had a good outcome with early discharge from hospital.

Key words: Children, COVID-19, disease severity, respiratory virus, developing country.

Introduction

The end of 2019 saw the emergence of a novel viral infection caused by what we now know as the Severe Acute Respiratory Distress Syndrome Coronavirus 2 (SARS-Cov-2).¹ A majority of the

infections are asymptomatic or mild, with a propensity to cause respiratory symptoms and pneumonia leading to respiratory failure, multi-organ dysfunction, and even death.

At the beginning of the pandemic, children accounted for between 1-5% of diagnosed COVID-19 cases, owing mostly to the fact that early detection and testing were focused on identifying cases with severe symptoms that were more likely to occur in the elderly. With changes to case definitions and awareness, there is now an increased detection of milder illness that occurs in the young. Therefore, it is now relatively more conspicuous that children of all ages can get COVID-19 although they are less commonly affected than adults in terms of severity.² Despite the widespread transmission of the virus, the epidemiological and clinical patterns of COVID-19 in children are still unclear. A recent study of 72,314

Corresponding Author:

Falak Abro

Department of Pediatrics and Child Health

Aga Khan University, Karachi.

Email: falak.abro@yahoo.com

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FJ & AS conceptualized the project. FA & NL did the data collection. FA & JK did the literature search. Statistical analysis was performed by FS & JK. Drafting, revision & writing of manuscript were done by FA, FJ, JK.

COVID-19 cases from the Chinese Center for Disease Control and Prevention showed that only 2% of infected cases were of children between 0-19 years of age.³ Similarly, an estimated 149,760 laboratory-confirmed cases reported from the United States also showed only 1.7% of children were infected.⁴

Likewise, a meta-analysis of children with clinical features of COVID-19 reported that 19% were asymptomatic. However, in symptomatic patients, fever (48%) and cough (39%) were the most prevalent features followed by diarrhea in 7% of cases and nausea or vomiting in 6%. Imaging abnormalities were seen in 66% of patients with 35% of children showing ground-glass opacities.⁵ The initial assumption that pediatric SARS-CoV-2 infection is rare, has given way to a more complex understanding of infectious manifestations in children, as well as awareness of a widening disease spectrum. Critical knowledge gaps persist, especially in developing countries like Pakistan, with major public policy and program implications. Inadequate data variability by age, geography and race are hindering efforts to thoroughly evaluate the prevalence of infection and disease in children and adolescents, as well as their role in disease transmission. Hence, this study aimed to identify the epidemiological and clinical trends of COVID-19 in pediatric patients admitted to the Aga Khan University Hospital in Karachi, Pakistan.

Methodology

An retrospective analysis of medical records was conducted at Aga Khan University Hospital (AKUH). Clinical criteria of a suspected case included the presence of either fever, cough, sore throat, respiratory distress, radiographic presentation of pneumonia, or prior hospitalization within the last 14 days. Epidemiological criteria included travel history outside the city or abroad, living in epidemic areas, or contact with confirmed COVID-19 patients within the last 14 days. All children with any of the clinical or epidemiological criteria were screened for COVID-19. We included all pediatric patients (aged 0–18 years) from March to August 2020 with laboratory-confirmed COVID-19 positive SARS-CoV-2 nasopharyngeal PCR (polymerase chain reaction) assay.

Data was extracted from medical records on a structured questionnaire and included demographic details, clinical and epidemiological features and comorbidities etc. The guidelines of Ministry of National Health Services & Regulation were used to categorize cases as asymptomatic, mild to moderate, and severe diseases (Supplement

Table-1).⁶ We also identified cases with the multisystem inflammatory syndrome (MIS-C) in children and adolescents using standard World Health Organization definitions (Supplement Table-2).⁷ Information on specific laboratory parameters was collected. Radiology (chest x-ray and CT scan) reports were reviewed for the presence of effusion, pneumothorax, consolidation or bilateral patchy opacities. Outcome measures included PICU stay, survival, disease severity, need for ventilation and length of stay.

Descriptive analysis was used for demographic characteristics with median and interquartile range (IQR) for quantitative variables like age and duration of hospital stay, while frequencies (percentage) for qualitative variables like gender, co-morbid conditions and mortality. SPSS version 22 was used for data analysis.

The Ethical approval was obtained from Ethical Review Committee of Aga Khan University Hospital, Karachi.

Results

Between March to August 2020, from a total of 415 suspected COVID-19 children (18 years and younger) admitted to the hospital from the emergency department, an aggregate of 60 (14%) tested positive for SARS-CoV-2. Of whom, 42 (70%) children were female, demographics are shown in Table-1 and laboratory findings are depicted in Table-2. Twenty-four (40%) children acquired COVID-19 infection through household contact, 3 (5%) had travel history abroad and 33 (55%) children had neither contact history nor travel history on admission.

Among 60 patients, 8 (13.3%) children were asymptomatic, 35 (58.3%) were mild, 12 (20%) were moderate and 5 (8.3%) were in a severe category. Clinical symptoms in children on admission are shown in Figure-1. Two neonates (3.3%) contracted the virus with mild respiratory symptoms and required oxygen support. Human Metapneumovirus was incidentally co-detected in one patient (2%) as not all children with respiratory symptoms were screened for other viruses, five (8.3%) were diagnosed with pneumonia, and three (6%) with acute respiratory distress syndrome (ARDS). Gastrointestinal symptoms were observed in 13 (21.6%) patients. Two (3%) with acute appendicitis, one (2%) with intussusception. Seizures or altered mental status were noted in 6 (10%) children. Significant comorbidities 20 (33%) were found in children with positive SARS-CoV-2 infection (Figure-2). Of the total, 7 (11.6%) children had underlying malignancy with a diagnosis of acute

lymphoblastic leukemia in 5 (8%) children and most common morbidity. Fifty-five (91%) children were discharged with a median length of stay of 4 days (2-8 days) in the hospital. Fourteen children (27%) required intensive care at the time of admission, with the median length of stay of two days. While 5 (10%) children required mechanical ventilation. The overall mortality was 8.3%, i.e. five children presented with severe illness and four of them had underlying co-morbid and expired with multi-organ failure.

Table 1: Epidemiological data and clinical characteristics of COVID-19 in pediatric patients admitted at Aga Khan University Hospital, Karachi.

Epidemiological Data	N (%)
N	60
Gender	
Female	42 (70)
Age, Years (Median, IQR)	4 (1, 13)
Age Categories (Years)	
<1	15 (25.9)
1-5	19 (32.8)
6-10	5 (8.6)
11-18	19 (32.7)
Household contact with confirmed COVID-19 cases	24 (40)
Travel History	3 (5)
Hospitalization history in the last two weeks	37 (62)
Clinical Findings	
Anemic (≤ 11 g/dl)	25 (44.64)
Fever (Body Temperature $>38.5^{\circ}\text{C}$)	10 (16.7)
Oxygen Saturation (%)	98 (98, 99)
Duration of Hospitalization (days)	4 (2, 8)
PICU stay duration (days) (n=14)	2 (1, 5)
Chest X-ray	8 (19)
CT Chest	2 (66.7)
Mechanical Ventilation	5 (10)
Only COVID-19	37 (61.6)
COVID-19 with other Comorbidities	20 (33)
MISC COVID-19	3 (5)
Death	5 (10)

Data presented as median (IQR) and n (%). PICU= Pediatric Intensive care unit, MISC= Multi-system inflammatory syndrome in children.

One, 15-year-old male child with chronic kidney disease, presented with multi-organ failure, required mechanical ventilation and died. Second, a 14-year-old girl with underlying malignancy expired with multi-organ involvement. Third, a 5-month-old male with no prior comorbid, presented with respiratory failure and died with multiple organ failure. Fourth, a 4-year-old male child received from the peripheral hospital due to complications of gut perforation developed multiple organ failure and died. Fifth, a 6-month-old male with non-traumatic coma, intracranial bleed, and herniation (sudden onset of vomiting, seizures, and drowsiness) expired within 12

hours of admission. Tocilizumab was administered to two patients (3.3%), both patients could not survive due to underlying co-morbid and severity of illness. Three patients (5%) with MISC COVID-19 were given methylprednisolone and intravenous immunoglobulin (IVIg), all of them were recovered and discharged.

Table 2: Laboratory findings of COVID-19 in Pediatric patients admitted at Aga Khan University Hospital, Karachi.

Laboratory Tests	Median Value (Range)
White Blood Cells ($\times 10^9/\text{L}$)	8 (6.25, 12.1)
Lymphocytes (%)	36 (18.6, 46.4)
Neutrophil: Lymphocyte ratio	2 (1.1-3.8)
Procalcitonin (ng/ml)	0.3 (0.11, 4)
C-Reactive Protein (mg/L)	15 (1.69, 93.8)
D-Dimer (mg/L)	2.4 (0.5, 4.3)
Erythrocyte Sedimentation Rate (mm/1st hr)	12.5 (1.7, 21)
Alanine Aminotransferase (U/L) (n=28)	32 (15.5, 70.5)
Aspartate Transferase (U/L) (n=12)	40 (27, 138)
Creatinine (mg/dl) (n=44)	0.4 (0.3, 0.6)
Blood Urea Nitrogen (mg/dl) (n=35)	10 (8, 16)
Ferritin (ng/ml) (n=20)	450 (244.6, 795)
LDH (IU/L) (n=21)	337 (244, 431)

Data presented as median (IQR), LDH= Lactate dehydrogenase

Discussion

We report sixty children, who were hospitalized with confirmed SARS-CoV-2 infection. Since it was the initial phase of the pandemic with strict lockdown and closure of schools, the major source of contact for children would be an infected family member.⁸ We detected female predominance among COVID-19 positive children. More than 50% of children had mild symptoms, and most of them were discharged with a shorter stay in the hospital, and the need for mechanical ventilation remained rare but few children have had severe illness. The important clinical characteristics of COVID-19, evident in our patient cohort were fever, cough, vomiting, diarrhea, and pneumonia. Respiratory symptoms were more commonly found than gastrointestinal symptoms. This trend differed slightly from another observation from Wuhan, which reported predominantly the presence of gastrointestinal symptoms in patients from a cohort of 244 pediatric cases.⁹ A 10-month-old baby with intussusception died from multi-organ failure and a 5-year-old boy with acute suppurated appendicitis perforation had also been reported in a study from Wuhan.¹⁰ A spectrum of features of atypical appendicitis was observed in a study report of eight children in the UK.¹¹

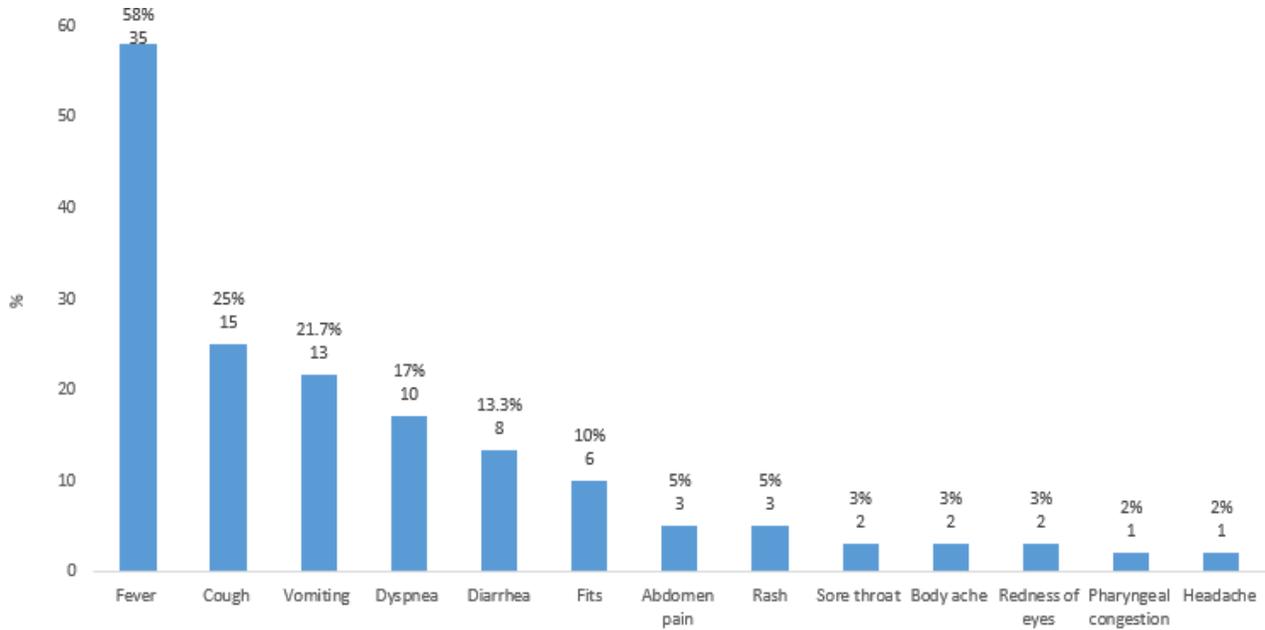


Figure-1 Clinical symptoms of COVID-19 in pediatric patients admitted at Aga Khan University Hospital, Karachi.

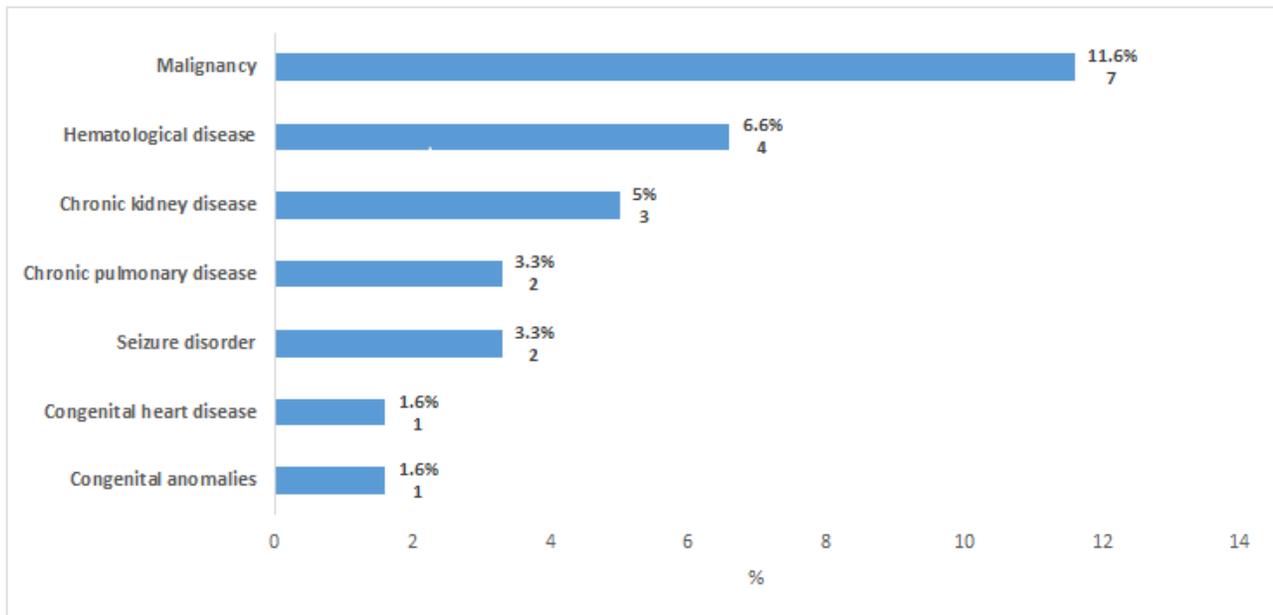


Figure 2: Comorbidities associated with COVID-19 in pediatric patients admitted at Aga Khan University Hospital, Karachi.

Among neurological features, in children, up to 28% of the cases had a headache in a CDC report of the United States.⁴ In our cohort, neurological symptoms were found in 12% of children with headache, or seizure-like activity. CT scan brain was done in two patients both of which were unremarkable. No loss of consciousness or other neurological deficits were observed in any of these cases. Almost thirty-three percent of patients

had substantial comorbidity in our study, the most prevalent of which was malignancy as compared to the study published in the where neurological comorbid was predominant.¹² In Iran, COVID-19 infection in children with underlying malignancies reported 20% mortality, most commonly identified was acute lymphocytic leukemia.¹³ It could be related to a lower immune response to infection

which leads to an increased risk of progression to the severity of illness and death.

A Multisystem inflammatory syndrome in children (MIS-C) occurs infrequently, affecting 0.14 percent of all SARS Cov-2 patients under the age of twenty-one.¹⁴ In our study, a much smaller number of children were presented with underlying cardiac dysfunction and raised inflammatory markers. Complete recovery was observed with supportive treatment and the use of IVIG with corticosteroids. In a systemic review, among 655 children with MIS-C, 1.7 % mortality was reported.¹⁵

Five children who remained critically ill required intensive care along with mechanical ventilation and vasopressor support and developed multi-organ involvement. However, a small sample size and underlying pre-existing conditions may have affected this representation. Overall severity of the COVID-19 disease reported in other studies was 1-5% of children.¹⁶ In a short report from the UK, four out of five (80%) children with comorbidities had multi-organ involvement.¹⁷ Even in one meta-analysis study, analyzed data from 27 different studies showed that severe manifestations are fewer in symptomatic COVID-19 cases in children.¹⁸ According to a study, data analyzed from seven countries on COVID-19 mortality in children, it was observed that deaths in children remained rare at 0.17 per 100,000 population.¹⁹

Our study concludes that most children with COVID-19 presented with mild illness. Severe illness was observed in young children and those with comorbidities. Most of the children had a good outcome with early discharge to home.

Our study has several limitations. First, it is a retrospective analysis of medical records. Second, its generalizability is reduced due to the small sample size and single-center study. Asymptomatic patients were also included, which may have significantly altered the proportion. Thirdly, due to exposure to prior hospitalization and widespread community transmission, COVID-19 PCR may be detected co-incidentally with other diagnoses, so we do not know the actual infectivity period of illness in critical patients.

Conflict of interest: None declared.

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