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Clinical Characteristics of Novel Coronavirus Disease in the Pediatric Population

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ABSTRACT

Objectives: To assess the clinical characteristics of COVID-19 Virus disease in the pediatric population in Pakistan.
***Study Design*:** Cross-sectional study.
***Place and Duration of Study*:** Pak Emirates Military Hospital, Rawalpindi Pakistan, from Mar 2020 to Jan 2021.
***Methodology*:** All children presenting to the department with symptoms consistent with COVID-19 disease were tested for the virus. Patients who tested positive on the PCR were included in the study. Patients with non-consistent symptoms of COVID-19 and those who tested negative on the PCR were excluded from the study. All clinical data, including the age of the child, the onset of symptoms, the gap between the onset of symptoms and presentation as well as clinical symptoms, were documented on a predefined proforma.
Results: A total of 106 patients were enrolled on the study. The mean age of patients was 5.6±2.5 years. The most frequent symptoms were fever (63, 59.6%) and cough (49, 46.2%). There were 3(2.9%) cases with severe or critical illness. The most frequent abnormal laboratory findings were leukopenia (29, 27.4%) and increased creatine kinase (38, 36.0%). Ground-glass opacities were observed in the HRCT chest of 17(65.3%) cases, out of 26 children diagnosed with pneumonia. The majority (70, 66%), had a positive exposure history. 88(83%) cases did not abide by the precautionary measures against the COVID-19 disease.
***Conclusions*:** The current study indicates that children usually present with mild symptoms but can present as severe diseases, as observed in this study.
Keywords: COVID-19, Fever, Pediatric population, MIS-C.

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INTRODUCTION

In the days after the COVID virus was identified in the city of Wuhan, no children were affected, which indicated that children perhaps did not suffer from the common symptoms of the disease. However, by June 2020, there were 7.8 million confirmed cases, of which 2% were confirmed in children.[1,2] According to the study conducted by the Chinese Center for Disease Control and Prevention, it was found that of the 44,672 confirmed cases of COVID-19 that were studied, only one death was reported of an individual aged 19. In contrast, 80% of all deaths occurred in the elderly population.[3,4] No child below the age of 10 died of the disease, apart from a one-year-old child who had suffered from severe symptoms. Only one death was reported amongst the age group of 10-19 years.[5] In addition, since the detection of the first case and its rapid spread throughout the world, the clinical progression of COVID-19 and its epidemiology, especially among children, is still not entirely understood.[6]

Children of all ages can get COVID-19.[8,9] However, the incidence increases with advancing age. Among children<18 years of age in the United States, there were >1.2 million positive tests for SARS-CoV-2 between March and December 2020.[7-9]

The primary aim of this study was to evaluate and present the common and severe clinical manifestations of pediatric COVID-19 disease so that it would be helpful for paediatricians in our setups as well as in other countries in the timely diagnosis and management of the disease. Several drugs are used to treat the coronavirus or prevent its complications in the pediatric population. The most commonly used drugs are Remdesivir, Tocilizumab, Intravenous immunoglobulins (IVIG), Steroids, Anticoagulants/Heparin, Ivermectin and Azithromycin (Not recom-mended nowadays). Multiple ongoing trials are currently being conducted in Europe, India and US, and the results of those trials are awaited. However, current trials show promising results with significant viral load reduction and symptom relief with the above-mentioned medications.

METHODOLOGY

This was a cross sectional study conducted from Pak Emirates Military Hospital, Rawalpindi Pakistan, from March 2020 to January 2021. Data collection was started after obtaining approval from the Ethical

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Review Committee (A/28/EC/338/2021). In addition, informed verbal and written consent was obtained from the guardians of the children. All the patients were assessed at the time of presentation, while the patients admitted were assessed daily for signs and symptoms throughout their hospital stay. The non-probability convenience sampling technique was applied to enroll children in the study.

Inclusion Criteria: All children between the ages of 2 to 12 years, presented to the hospital with symptoms consistent with COVID-19 diseases, such as fever, cough, diarrhoea and shortness of breath, and were tested for the virus and tested positive on the PCR were included in the study.

Exclusion Criteria: Patients with non-consistent symptoms of COVID-19, such as evidence of a bacterial infection, headache, burning micturition and those who tested negative on the PCR were excluded from the study.

All clinical data, including the age of the child, the onset of symptoms, the gap between the onset of symptoms and presentation as well as the clinical symptoms, were documented on a predefined pro forma. The pro forma was pilot tested on ten residents to look for inconsistency and redundancy. After critically revising the pro forma, the authors started data collection. The data was then converted to Patients with non-consistent symptoms of COVID-19, and those who tested negative on the PCR were excluded from the study to electronic data using an excel sheet.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were summarized as mean±SD and qualitative variables were summarized as freque-ncy and percentages.

RESULTS

The total number of patients presenting to our department with suspected COVID-19 disease was 140. PCR revealed 120 positive cases, while 106 patients were enrolled in our study. There were 70 (66%) male children and 36(33.9%) females. 15(14.1%) children had asthma as comorbidity. The mean age of patients was 5.6±2.5 years. The mean heart and respiratory rates were 93.96±20.52 and 27.96±12.2 per minutes, respectively. The most frequent abnormal laboratory findings in pediatric patients were leukopenia in 29(27.4%) patients and increased creatine kinase in 38(36.0%). The mean leukocyte count was 11.62±8.8/L, and the mean haemoglobin was 9.2±4.4 X 109g/dl (Table-I).

Table-I: Laboratory Characteristics in Pediatric Patients with COVID-19 Disease (n=106)

Laboratory Characteristics	Mean±SD
Age	5.60±2.50
Heart Rate (per minute)	93.96±20.52
Respiratory Rate (per minute)	27.96±12.20
Hemoglobin (g/dl)	9.20±4.40 X 109
Leukocyte Count (per L)	11.62±8.80 X 109

Majority of the patients presented with fever 63(59.4%) and cough 49(46.2%). Fever was the most frequent symptom. The other common symptoms were diarrhoea 44(41.5%), anosmia 13(12.6%), and rash 15 (14.1%) children Table-II.

Table-II: Clinical Sign and Symptoms of Study Population (n=106)

Clinical Signs/Symptoms	Frequency (%)
Fever	63 (59.4)
Diarrhea	44 (41.5)
Vomiting	49 (46.2)
Cough	49 (46.2)
Rhinitis	27 (25.4)
Rash	15 (14.1)
Anosmia	13 (12.6)
Wheezing	26 (24.5)
Bradycardia	29 (27.3)
Tachycardia	19 (17.9)

There were 3(2.9%) cases with severe or critical illness. A single death was reported in an 11-year-old male without any known co-morbid, who had presented with fever and diarrhoea. The child was initially treated as a case of suspected enteric fever. However, the child eventually developed multisystem inflammatory syndrome secondary to COVID-19 (MIS-C), a rare form of the disease reported only in a few places worldwide. Furthermore, two other patients had presented with the same condition but recovered because of timely diagnosis and management, namely IVIG and steroids. All of these children fulfilled the criteria for MIS-C devised by the World Health Organization.

Ground-glass opacity was observed in the CT scan of the lungs in 17(65.3%) out of 26 children diagnosed with pneumonia. The majority (70, 66%) had a positive exposure history. 88(83%), did not abide by the precautionary measures against the COVID-19 disease. In three patients who had developed a more severe form of the disease (MIS-C), the cardiac echography of 1(33%) patient revealed cardiomegaly, left ventricular systolic dysfunction, and coronary aneurysms. In addition, the time lag between the onset of symptoms and the presentation was 4.0±3.0 days.

DISCUSSION

Children of all ages can contract COVID-19.[10,11] Children, particularly those under 12 years of age, are less affected by the virus than adults, with lower positivity ratios and complications, although children are less frequently tested than adults.[12,13] In a case series done early in the pandemic, most children contracted the virus from a household contact, usually an adult as the index case.[12] In a case-control study, close contact with people infected with COVID-19 (usually a household member), having visitors at home and attending social gatherings and activities with other children were responsible for most of the COVID-19 infections in children.[14] In addition, children of all ages can transmit the virus. However, the disease transmission rate by young children is uncertain.[15,16]

There is a significant difference in the severity and mortality among pediatric and adult patients suffering from COVID-19. According to numerous pieces of research, it has been suggested that this variation may be due to the difference in Angiotensin Converting Enzyme II (ACE 2) receptors between children and adults. The ACE-2 receptor allows for the binding of the SARS-CoV.[17] According to Fang *et al*., children were protected from the severity of the virus as the ACE-2 receptors in children are largely immature.[18]

Pediatric patients respond differently to the virus due to their still-developing immune systems.[19] Children are more susceptible to developing respiratory infections and thus may have higher antibodies to fight against the virus, explaining their milder symptoms than adults.

In a study conducted in China, more than 2000 pediatric patients were evaluated for the symptoms of COVID-19. Most patients presented with mild symptoms, while critical symptoms were found in only 5.8% of children compared to the adult patients, 18.5% of whom experienced severe symptoms. Of the pediatric patients under study, only one succumbed to the illness.[20]

In a study conducted by Qiu *et al*., it was found that symptoms of COVID-19 varied between adults and children. It was highlighted that fever was experienced by 36% of the children, compared to 86% of the adults who suffered from fever. Similarly, cough and pneumonia were found in 19% and 53% of the children, respectively, while of their adult counterparts, 62% experienced cough and 95% experienced pneumonia. However, contrary to our present study, Qiu *et al*. reported no difference between pediatric and adult levels of myocardial enzymes or prevalence of leukopenia and lymphopenia.[21]

In CDC population-based surveillance, the weekly hospitalization rates of children<18 years in the United States showed a peak in January 2021 (1.4 per 100,000 population), began to decrease through mid-March, and then saw a sudden rise, particularly among adolescents age 12 years and children younger than four years.[22] Hospitalization rates vary widely from country to country. However, most of the patients treated in our setup were managed outdoors with regular follow-ups.

A study by Zachariah *et al*. evaluated chest radiographs of patients suffering from COVID-19. The results were consistent with the present study's findings and indicated that ground glass opacities were found in 69% of the patients. On the other hand, signs of pleural effusion, focal consolidation and pneumothorax were found in 25%, 22% and 5% of the patients, respectively.[23]

Lung damage in adults results from the cytokine storm induced by the virus, which results in a poor prognosis compared to children and infants. However, it has been found that such an immune-mediated response protects children due to the successful response of T cells in children, which protects them from significant lung and multisystem damage.

Recently alarm bells have been raised by the Pediatric Intensive care Society in the United States and other institutions around the world regarding the increase in the number of children presenting with this unusual inflammatory condition. In addition, it has been observed that many children manifest features overlapping with toxic shock syndrome and atypical Kawasaki disease and cardiac inflammation (MIS-C). This condition can develop during active infection and post-COVID-19 stage, mostly after 4-6 weeks of active infection.

Our study confirms all the claims mentioned earlier. Children contract COVID-19, and the majority had a positive exposure history, mostly a household contact, with signs and symptoms less severe than the adult population. However, as mentioned earlier, some patients developed MIS-C with features overlapping with atypical Kawasaki disease. However, the incidence of critical illness and mortality was fairly less compared to adults. In addition, there is a huge shortage of local studies regarding pediatric COVID-19, particularly the pediatric MIS-C, now referred to as PMIS-C. More studies locally and internationally

would help paediatricians and us all over the world better analyse COVID-19 and its complications in children.

LIMITATION OF STUDY

We did not collect data regarding socioeconomic factors. In addition, we could not follow up on the cases who were prescribed treatment on an outpatient basis to look for residual effects of the disease. Lastly, this was a cross-sectional and a single-centre study. Hence, further longitudinal studies should be done to observe any longterm effects of the illness in the diseased population.

CONCLUSION

Children usually present with milder symptoms than adults, with the most frequent symptoms being fever and cough. During these times, any child who presents with the symptoms mentioned above should be immediately tested for COVID-19. Furthermore, we now know that COVID-19 should not be taken lightly in children as the disease can progress into a multi-organ inflammatory disorder with increased morbidity.

Conflict of Intrest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MWB: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

QUM & FI: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

MTN & JB: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MG: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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