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RESEARCH ARTICLE

Covid-19 In Children: A Single Centered Study

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ABSTRACT

Introduction: There is limited data available on the epidemiological features, clinical manifestations, and transmission patterns in children with COVID-19, although there has been widespread information available regarding COVID-19 in adults. The objective of our study was to report our experience in the management of children admitted with COVID-19 to our hospital.

Materials & Methods: We retrospectively reviewed the in-patient records of all children ≤ 18 years of age admitted to our COVID-19 facility during the period March 2020 till May 2021. Detailed information including demographic data, travel and contact history, living conditions and overcrowding, symptoms, and presence of co-morbid conditions were noted. The clinical symptoms, physical findings, laboratory readings and imaging data were similarly noted and analysed.

Results: During the study period a total of 67 children (30 males and 37 females) with a mean age of 11.88 ± 4.35 years were admitted to the COVID-19 facility. The presenting symptoms were fever (71.64%), skin rashes (14.93%), breathlessness (7.46%), cough (31.34%), cold (2.99%), headache (8.96%), sore throat (25.37%), loose motions (26.87%) and vomiting (8.96%). The RT-PCR was positive in 60 (89.55%) children. Sixty-one (91.045%) children recovered over a period of 10-14 days and were discharged. Six (8.955%) children died due to multisystem failure. When compared to the children who recovered, the children who died had a significantly raised serum ferritin, IL 6, C reactive proteins, D-Dimer levels, and Sr LDH.

Conclusions: COVID-19 has been affecting children, more so in the second wave, with increased hospitalizations and mortality.

Keywords: COVID-19, Children, hospitalizations, mortality

INTRODUCTION:

The first cases of COVID-19 in India were reported in the towns of Thrissur, Alappuzha and Kasargod, all in the state of Kerala, among three Indian medical students who had returned from Wuhan. [1] Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of May 2021, India has the second-highest number of confirmed cases in the world (after the United States) with nearly 20 million reported cases of COVID-19 infection and 249,992 deaths as of 11 May 2021. [2,3]

There is limited data available on the epidemiological features, clinical manifestations, and transmission patterns in children with COVID-19, although there has been widespread information available regarding COVID-19 in adults. Observations made early in the disease process plays an important role in understanding the physiological patterns and varied clinical profiles, so as to make an early diagnosis and initiate appropriate management. Sarangi et al [4] analysed the clinical characteristics of the pediatric inpatients (aged 1 month - 18 years) with COVID-19, presenting between 1 April, 2020 and 20 May, 2020 with positive nasopharyngeal swab for SARS-CoV-2 by RT-PCR (Real time polymerase chain reaction). The report consisted of 50 children (56% male) with median (IQR) age of 6 (2-12) years. Majority (56%) were from families belonging to Kuppusswamy upper lower socioeconomic class. 45 (90%) had positive household contact, and 33 (66%) had overcrowding at home. 29 (58%) children were asymptomatic while 20 (40%) had mild symptoms. Fever, cough, and sore throat were the most common symptoms. High C-reactive protein levels were seen in 15 (30%) children. There were no deaths. In this study we report our experience in the management of children admitted with COVID-19 in our hospital.

MATERIALS & METHODS:

With approval obtained from the institutional ethics committee, we retrospectively reviewed the in-patient records of all children \leq 18 years of age

admitted to our COVID-19 facility during the period March 2020 till May 2021. Detailed information including demographic data, travel and contact history, living conditions and overcrowding, symptoms, and presence of co-morbid conditions were noted. The clinical symptoms, physical findings, laboratory readings and imaging data were similarly noted and analysed. Reports of COVID-19 diagnostic tests such as RT-PCR, rapid Antigen tests, antibodies studies and high-resolution chest computed tomography (HR-CT) images were similarly noted and analysed.

Statistical analyses: The data was analysed using the Statistical Package for Social Sciences (SPSS) software version 20.0. Spearman's Rho correlation coefficient was used to determine the correlation with disease severity. A p value <0.05 was considered significant.

RESULTS:

During the study period a total of 67 children (30 males and 37 females) with a mean age of 11.88 ± 4.35 years were admitted to the COVID-19 facility of our hospital. During the same period 1733 adults were admitted to the same facility. The presenting symptoms were fever (71.64%), skin rashes (14.93%), breathlessness (7.46%), cough (31.34%), cold (2.99%), headache (8.96%), sore throat (25.37%), loose motions (26.87%) and vomiting (8.96%). Most of the children had multiple symptoms.

The diagnosis of SARS-CoV-2 was made by performing a rapid antigen test at the emergency services of the hospital. This was positive in 44 (65.67%) of the children and negative in 23 (34.33%). All the children had a nasal and oropharyngeal swab taken at the emergency services prior to admission into the hospital. Children testing positive for rapid antigen tests were admitted to the COVID-19 facility whereas the remaining were admitted to the holding wards awaiting the result of the RT-PCR test. The RT-PCR was positive in 60 (89.55%) and negative in 7 (10.45%) children. The antibody test was performed in 30 of these children and the results were as shown in (Table 1).

Table 1. Results of RT-PCR, RAPID ANTIGEN TEST & ANTIBODY TESTS.

	RT-PCR (n-67)	RAT (n-67)	IgM (n-30)	IgG (n-30)
Positive	60 (89.55%)	44 (65.67%)	19 (63.33%)	10 (33.33%)
Negative	7 (10.45%)	23 (34.33%)	11 (36.67%)	20 (66.66%)

The laboratory test results were as follows: mean serum ferritin levels 199.27 ± 208.01 ng/mL, mean interleukin (IL-6) levels 56.72 ± 69.22 pg/mL, mean C reactive proteins 75.76 ± 97.37 mg/L, mean D-Dimer levels were 127.507 ± 269.21 ng/mL, mean

serum LDH levels were 252.642 ± 188.147 U/L, and mean total leucocyte count was 9497.015 ± 4566.876 cells/cumm. High-resolution chest CT was performed in 64 children and the results were as shown in (Table 2).

Table 2. HR-CT.

HR-CT Results	n	%
CORAD 1	35	54.69
CORAD 2	19	29.69
CORAD 3	8	12.5
CORAD 4	2	3.13
CORAD 5	0	0

The treatment was symptomatic in most children, however additional drugs were necessary for some others which included steroids in 27 (40.299%), Remdesivir in 14 (20.896%), intravenous immunoglobulins (IVIg) in 18 (26.866%), and anticoagulants in 14 (20.896%). Sixty-one (91.045%) children recovered over a period of 10-14 days and were discharged. Six (8.955%) children died due to multisystem failure. When compared to the children who recovered, the children who died had significantly raised serum

ferritin, IL 6, C reactive proteins, D-Dimer levels, and Sr LDH. The mortality rate among the adults in our hospital during the same period was 15.63%

Figure 1 shows the admission and deaths of the children affected by COVID-19 at our hospital. The second wave of COVID-19 started in March 2021. The paediatric population seems to have been affected more in the second wave and so has the high mortality during this period as compared to the first wave in the year 2020.

Table 3. Comparison of factors between recovered and deceased children.

No	Factor	Recovered (61)	Died (6)	p-value
1	Age means (years)	12.04 ± 4.26	10.17 ± 5.31	0.3159
2	RT-PCR positive (%)	91.8%	66.67%	-
3	RAT positive (%)	31.14%	66.67%	-
4	Sr ferritin (ng/mL)	163.40 ± 168.19	563.83 ± 237.63	0.0001
5	IL 6 (pg/ml)	48.46 ± 63.32	140.67 ± 76.37	0.0014
6	C reactive protein (mg/L)	54.81 ± 66.05	288.73 ± 114.06	0.0001
7	D-Dimer (ng/mL)	63.47 ± 121.08	778.5 ± 471.33	0.0001
8	Sr LDH (U/L)	217.06 ± 120.69	614.33 ± 346.48	0.0001
9	Total leucocyte count (cells/cumm)	9275.41 ± 4200.22	11750 ± 346.48	0.2078

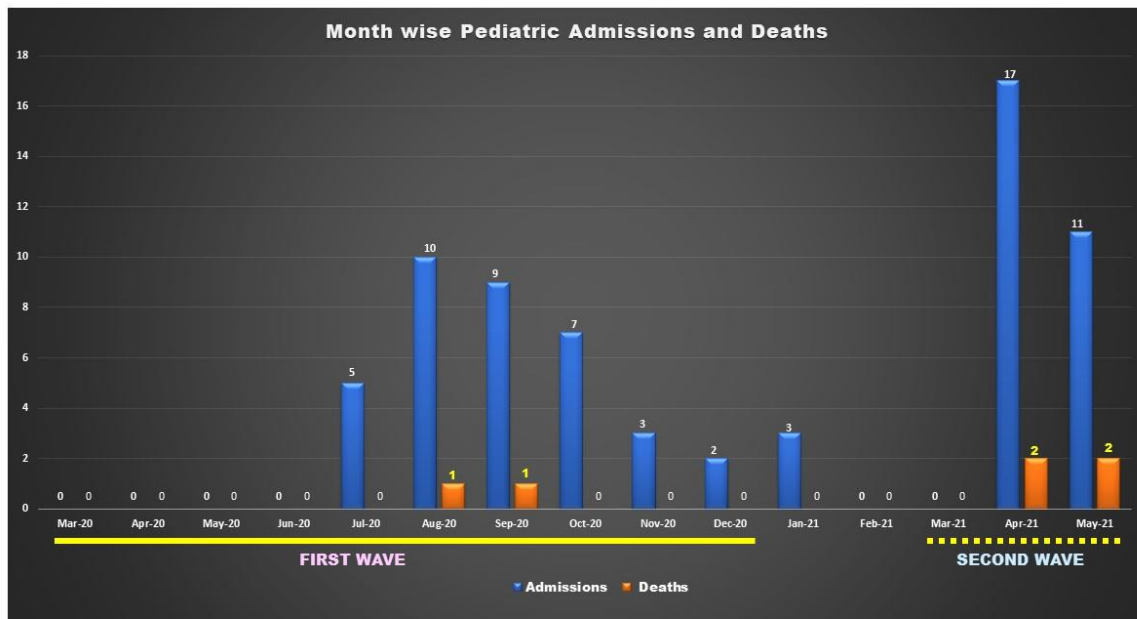


Figure 1. Admission and deaths of the children affected with COVID-19 at our hospital.

DISCUSSION:

The coronavirus is a non-segmented positive-stranded RNA virus with a roughly 30 kb genome and surrounded by a protein envelope. Most coronaviruses are known to cause diseases within their own particular host species,^[5] however viruses that can infect humans through cross-species transmission have become an important threat to mankind. Serious coronavirus disease outbreaks have happened in the past, namely severe acute respiratory syndrome (SARS) in 2003,^[6] and Middle East respiratory syndrome (MERS) in 2012.^[7] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been recognised as the causal factor in a series of severe cases of pneumonia originating in Wuhan since December 2019. By March 1, 2020, SARS-CoV-2 had led to 80 981 confirmed cases of COVID-19 in China, and 44067 cases in 117 countries.^[8] A cohort study of 44 672 Chinese cases reported that 2.1% of patients were younger than 20 years, and 1.2% were asymptomatic.^[9]

Qiu et al^[10] retrospectively retrieved data of 36 paediatric patients (aged 0–16 years) with confirmed COVID-19 from three hospitals in Zhejiang, China. The mean age of the children was 8.3 years. The route of transmission was by close contact with family members (32 [89%]) or a history of exposure to the epidemic area (12 [33%]); eight (22%) patients had both exposures. 19 (53%) patients had moderate clinical type with pneumonia; 17 (47%) had mild clinical type and either were asymptomatic (ten [28%]) or had acute

upper respiratory symptoms (seven [19%]). Common symptoms on admission were fever (13 [36%]) and dry cough (seven [19%]). Of those with fever, four (11%) had a body temperature of 38.5°C or higher, and nine (25%) had a body temperature of 37.5–38.5°C. Typical abnormal laboratory findings were elevated creatine kinase MB (11 [31%]), decreased lymphocytes (11 [31%]), leucopenia (seven [19%]), and elevated procalcitonin (six [17%]). Besides radiographic presentations, variables that were associated significantly with severity of COVID-19 were decreased lymphocytes, elevated body temperature, and high levels of procalcitonin, D-dimer, and creatine kinase MB. All children received interferon alfa by aerosolization twice a day, 14 (39%) received lopinavir–ritonavir syrup twice a day, and six (17%) needed oxygen inhalation. Mean time in hospital was 14 (SD 3) days. By Feb 28, 2020, all patients were cured.

Paediatric observational studies published in literature have shown similar clinical findings with fever being the most common symptom followed by cough and sore throat. Meena et al^[11] searched four different electronic databases (MEDLINE, EMBASE, Web of Science, and CENTRAL) for articles related to COVID-19 in the paediatric population. Twenty-seven studies (4857 patients) fulfilling the eligibility criteria were included in this systematic review, from a total of 883 records. About half of the patients had fever and cough, 11% (6–17%) had fast breathing, and 6–13% had gastrointestinal manifestations. Most of the patients

had mild to moderate disease, and only 4% had a severe or critical illness. Leukopenia was the most commonest reported laboratory abnormality. They opined that severe manifestations were seen in very few children and although fever and respiratory symptoms were most common, many children also had gastrointestinal manifestations.

The Center for Disease Control (CDC) COVID-19 Response Team reported that 1.7% (2572/149,082) of the COVID-19 cases reported as of April 2, 2020, for which the age was known, occurred in paediatric patients aged < 18 years. [12] The CDC COVID-19 Response Team has estimated that 20% of all paediatric patients whose hospitalization status was known, were hospitalized, compared to 33% among all adults aged 18–64 years. Several reports have suggested that the virus has a milder effect on the paediatric population.

Chen et al [13] reported on a case series of four infants born to mothers with COVID-10, wherein none of three infants tested were positive for the virus nor developed clinical symptoms of disease, suggesting that there is a low likelihood of vertical transmission of the virus. Patel [14] systematically reviewed the literature in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines so as to gain insight into pediatric COVID-19 epidemiology. Ten studies including two case series and 8 retrospective chart reviews, altogether describing a total of 2914 pediatric patients with COVID-19 were included in this systematic review. Of the patients whose data was available, 56% were male, the age range was 1 day to 17 years, 79% were reported to have no comorbidities, and of the 21% with comorbidities, the most common were asthma, immunosuppression, and cardiovascular disease. Of pediatric patients that were tested and positive for an infection with SARS-CoV-2, patients were asymptomatic, 14.9% of the time. Patients presented with cough (48%), fever (47%) and sore throat/pharyngitis (28.6%), more commonly than with upper respiratory symptoms /rhinorrhea /sneezing/nasal congestion (13.7%), vomiting/nausea (7.8%) and diarrhoea (10.1%). Median lab values including those for WBC, lymphocyte count and CRP, were within the reference ranges with the exception of procalcitonin levels, which were slightly elevated in children with COVID-19 (median procalcitonin levels ranged from 0.07 to 0.5ng/mL. Computed tomography (CT) results suggested unilateral CT imaging findings in 36% of cases while 64% of paediatric patients with COVID-19 had bilateral findings. Of the studies with age specific hospitalization data

available, 27.0% of patients hospitalized were infants under 1 year of age. Various treatment regimens including interferon, antivirals, and hydroxychloroquine therapies have been trialled on the paediatric population but there are currently no studies showing efficacy of one regimen over the other. The mortality rate of children that were hospitalized with COVID-19 was 0.18%.

Our data clearly shows that the paediatric age group has been affected by the second wave in our country and that it appears to be severe and associated with increased mortality rate.

Multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, is a hyperinflammatory syndrome occurring in close temporal association with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children. [15, 16] As the number of COVID-19 cases has grown exponentially across the country, clinicians have started identifying this new entity more frequently. An observational study conducted at four tertiary hospitals in Mumbai, reported on 23 children (11 males) with median (range) age of 7.2 (0.8-14) years with MIS-C. COVID-19 RT-PCR or antibody was positive in 39.1% and 30.4%, respectively; 34.8% had a positive contact. 65% patients presented in shock; these children had a higher age ($p < 0.05$), and significantly higher incidence of myocarditis with elevated troponin, NT pro BNP and left ventricular dysfunction, along with significant neutrophilia and lymphopenia, as compared to those without shock. Coronary artery dilation was seen in 26% patients overall. Steroids were used most commonly for treatment (96%), usually along with intra- venous immunoglobulin (IVIg) (65%). If not identified and treated earlier, children with MIS-C are likely to have high morbidity and mortality.

Conclusion:

As the infectivity of the SARS-CoV-2 virus is very high compared to other coronaviruses reported so far, an effective vaccine is the best way to contain the rapidly escalating proliferation of this infection. There is an urgent need to expedite the development of the COVID-19 vaccine and vaccinate the population.

Conflict of Interest: The authors declare conflict of interest as None.

Compliance with Ethical Standards

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