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Clinical Profile and Short-Term Outcome of Children Admitted with COVID-19 During the Second Wave in a Tertiary Care Centre in Kerala

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ABSTRACT

Background

COVID-19, caused by SARS-CoV-2, emerged in Wuhan, China in December 2019 and was declared a pandemic by the WHO on March 11, 2020. In India, the second wave occurred between March and June 2021, affecting children across all age groups with presentations ranging from mild symptoms to severe multisystem involvement. This study describes the clinical profile and short-term outcomes of children admitted with COVID-19 in a tertiary care center in Kerala.

Methods

A descriptive study was conducted among 246 children aged 1 month to 13 years, admitted to the COVID-19 isolation ward between May and July 2021, with laboratory confirmed COVID-19. Socio-demographic details, clinical features, and short-term outcomes were analysed.

Results

Among the 246 children studied, aged 1 month to 13 years, the median age was 48 months (IQR: 16–99 months), with a slight male predominance. A positive contact history was reported in 81% (n=200), and 28% (n=70) had severe disease. Common symptoms included fever (67%), cough (27%), and seizures (27%). The mortality rate was 0.8%. Comorbidities were present in 38% (n=93), with these children requiring significantly more respiratory support ($p<0.001$, OR=6.1). Neurological comorbidities were notably associated with severe disease ($p<0.001$, OR=4.6).

Conclusions

Children admitted with COVID-19 presented with a wide clinical spectrum, from mild illness to severe multi system involvement. The disease affected all age groups, with a slight male preponderance. Children with neurological comorbidities exhibited more adverse outcomes.

Keywords: COVID-19; clinical profile; short term outcome; children.

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INTRODUCTION

An outbreak of pneumonia of unknown origin emerged in Hubei, China, in December 2019, later identified as COVID-19 caused by SARS-CoV-2.[1] The WHO declared it a pandemic on March 11, 2020. India reported its first case in Kerala on January 30, 2020, with the state becoming one of the most affected. COVID-19 affects all ages, with children presenting a spectrum from mild illness to severe multiorgan involvement. Coronaviruses primarily cause respiratory and gastrointestinal symptoms in humans[1,2] and spread mainly through droplets.[3] Globally, chidren account for fewer cases than adults. As of October 2021, WHO data showed 2% of global cases in children under five and 7% in those aged 5–14.[4] In India, ICMR reported 3.6% of cases in children aged 0–9 and 8.1% in those aged 10–19 between January and April 2020.[5,6] Although often milder, severe and atypical cases are reported.[7,8] This study analyses the clinical profile, complications, and short-term outcomes of children hospitalized with COVID-19 in a tertiary care centre in Kerala.

METHODS

This descriptive study was conducted in tertiary care referral centre of Kerala, India. Ethical approval was taken from Institute Ethics Committee (HEC No. 05/05/2021/MCT). All hospitalised children aged between 1 month to 13 years admitted in COVID-19 isolation ward, who are laboratory confirmed COVID-19 positive between 1st May 2021 and July 2021 (2nd wave of COVID-19) were enrolled under the study. This centre was designated as a referral facility for COVID-19 patients, so patients of all severity were referred for admission. Besides this, the institute was located near the Regional Cancer Centre and hence was referral centre for COVID-19 positive children undergoing cancer treatment. Patients were triaged in casualty and admitted in isolation ward or COVID-19 intensive care unit based on severity of illness. Children were categorised as category A, category B and category C according to Kerala state guidelines for management of COVID-19. Category A included those with mild sore throat, cough, rhinorrhea, diarrhoea, and vomiting. Category B included patients with fever, severe sore throat, and increasing cough. It also included category A patients with comorbidities like chronic heart, kidney, lung, neurological or liver diseases, obesity, children on long-term steroids, and those with congenital or acquired immunosuppression. Category C included patients with breathlessness, inability to feed, reduced activity or lethargy, altered sensorium, seizures, breathlessness, cyanosis, hypotension, respiratory distress, and SpO_2 less than 94%. Adolescents with obesity are at higher risk of having severe disease. The information regarding symptoms and course in hospital were assessed using questionnaire. Information regarding demographic and clinical details including age, sex, history of contact, type of contact, comorbidities, clinical features and laboratory investigations were recorded. Severity of illness, respiratory involvement, chest imaging findings, type of respiratory support, use of antibiotics, steroids and vasoactive drugs, immunomodulators were noted. Short term outcome was defined as outcome during hospital stay. Outcome measures included duration of hospital stay, need for invasive ventilation, discharge and mortality. Clinical categories, quarantine, testing and discharges were based on Kerala state guidelines. Participants were given no economic motivation and anonymity was maintained to make sure data confidentiality.

Data collection was done using a pretested questionnaire. Data entry and statistical analysis were performed using MS Excel and SPSS software version 16. Descriptive statistics were used to analyse demographic characteristics, clinical profile. Categorical variables were presented as counts and percentages; quantitative variables were expressed as mean and standard deviation or median and interquartile ranges based on the normality of the data. Pearson chi-square test was used for comparing the characteristics and outcome. A p-value less than 0.05 was considered as statistically significant. The clinical outcomes of children with comorbidities and without comorbidities were also statistically analysed. This study utilized univariable analysis using the chi-

square test to compare categorical variables between children with and without comorbidities.

RESULTS

A total of 246 children aged 1 month to 13 years who tested positive for COVID-19 during the second wave of the pandemic, from May to July 2021, were included in this study. The peak of the second wave occurred in May 2021. The demographic details, clinical features, and categorization of disease severity are summarized in Table 1.

The median age of the study population was 48 months (interquartile range [IQR]: 16–99 months). More than half of the children, 134(55%) were under five years of age. A slight male preponderance was observed, with a male-to-female ratio of 1.24. Majority of children, 200 (81%) had a history of household contact with one or more family members affected by COVID-19. Regarding disease severity, 141(57%) of the children were classified as Category B (moderate), 70 (28%) as Category C (severe), 29 (12%) as Category A (mild), and 6 (2%) were diagnosed with multisystem inflammatory syndrome in children (MIS-C). Comorbidities were present in 95 (38%) of the study population. Neurological comorbidities were the most common 28 (11%), followed closely by malignancies (10.5%).

Table 1. Demographic and clinical characteristics of children with COVID-19. (n=246)

Variables	Frequency (%)
Age	
<1 year	41 (17)
1 to 5 years	93 (38)
5 to 10 years	75 (30)
10 to 13 years	37 (15)
Gender	
Male	136 (55)
Female	110 (45)
Category	
A	29 (12)
B	141 (57)
C	70 (28)
MIS-C	6 (2)
Positive contact history	200 (81)
Fever	165 (67.1)
Nasal Congestion/ Rhinitis	68 (27.6)
Cough	67 (27.2)
Seizure	66 (26.8)
Vomiting	51 (20.7)
Diarrhoea	34 (13.8)
Breathlessness	23 (9.3)
Abdominal pain	15 (6.1)
Headache	14 (5.7)
Myalgia	11 (4.5)
Asymptomatic	10 (4.1)
Any co-infection	7 (2.8)
Pharyngitis	6 (2.4)
Poor feeding/ Poor activity	6 (2.4)
Arthralgia	4 (1.6)
Rash	4 (1.6)
Chest pain	2 (0.8)
Cyanosis	2 (0.8)
Neurological	28 (11)
Malignancy	26 (10.5)
Renal	14 (6)
Respiratory	13 (5)
Endocrine	5 (2)
Haematological	4 (2)
Cardiovascular	3 (1)
Immunological	1 (0.4)
Genetic	1 (0.4)

Table 2. Laboratory investigations in children admitted with COVID-19. (n=246)

Laboratory parameters	Median Value (Interquartile range)
Haemoglobin (g/dL)	11.40 (10.60,12.60)
Anaemia (<11 g/dL)	80 (33%)
Total Leukocyte count (cells/mm^3)	8900 (6455,11500)
Leukocytosis (>11000 cells/mm^3)	71 (29%)
Lymphopenia (< 1500 cells/mm^3)	46 (19%)
Platelet count	290,000 (220,000,340,000)
AST (U/L)	35 (32,46)
ALT (U/L	24 (17,30)
Serum Sodium (mEq/L)	137.0 (135.0, 139.0)
Hyponatremia (<135mEq/L)	56 (23%)
Serum Urea (mg/dL)	24 (19,28)
Serum Creatinine (mg/dL)	0.50 (0.40, 0.60)
CRP (mg/dL)	0.60 (0.40, 1.20)
Elevated CRP (>0.6 mg/dL)	127 (52%)

Data presented are in numbers (%) or median (interquartile range)

Fever was the most commonly reported symptom, occurring in 67.1% of patients, followed by rhinitis (27.6%), cough (27.5%), and seizures (26.8%). The mean duration of fever at presentation was 1.8 days (standard deviation [SD]: 1.376). A minority of children (4.1%) were asymptomatic and were incidentally diagnosed with COVID-19 during hospital admissions for unrelated conditions such as kerosene ingestion, snake bite, or paracetamol poisoning. Laboratory parameters are narrated in Table 2. Analysis of the laboratory parameters showed that 33% had anemia, 29% had leukocytosis. Thrombocytopenia was described in 12% population. Reactive CRP was present in 52% of the population. Leucocytosis was found have statistically significant association with severe disease with an odds ratio of 3.178 (95% CI 1.775-5.687; p value < 0.001). COVID-19-related organ involvement and treatment profiles are detailed in Table 3.

Table 3. Treatment summary and outcomes. (n=246)

Variables	Frequency (%)
Type of respiratory support	
Nasal Cannula	20 (8.0)
CPAP	9 (4.0)
NIV	6 (2.0)
Invasive ventilation	6 (2.0)
Treatment given	
Antibiotics	162 (66.0)
Steroids	21 (9.0)
Inotropes	9 (4.0)
Antivirals	8 (3.0)
Anticoagulant	6 (2.0)
Immunomodulators (IVIG)	2 (1.0)
Clinical outcome	
CNS Involvement	66 (27.0)
Shock	13 (5.0)
Transaminitis	10 (4.0)
COVID Pneumonia	5 (2.0)
Acute Kidney Injury	2 (1.0)
LV Dysfunction	2 (1.0)
Myocarditis	1 (0.4)
Outcome	
Discharged	244 (99.2)
Died	2 (0.8)

Central nervous system (CNS) involvement was observed in 66 (27%) of children, all of whom presented with seizures. Among these, four cases presented as status epilepticus, and one child was diagnosed with acute encephalitis. Shock was identified in 13 children (5%), of whom 9 (4%) required inotropic support. Acute kidney injury developed in 2 children (1%). Intravenous immunoglobulin (IVIG) was administered to 2 children, with indications being MIS-C and acute encephalitis. Steroid therapy in the form of methylprednisolone pulse was given to 21 children (9%), primarily for the management of MIS-C and acute encephalitis. Antiviral therapy with remdesivir was initiated in 8 children. Indications included severe pneumonia and acute encephalitis. In all cases, remdesivir was started within the first five days of illness. Respiratory support was required in 41 children. Non-invasive respiratory support modalities were used in 35 children (14%), while 6 children (2.6%) required invasive mechanical ventilation. The median duration of hospital stay was 4.0 days (IQR: 3.0–6.0 days).

Pre-existing comorbidities were identified in 95 (38%) of the children. Neurological disorders were the most common 28 (11%), followed by malignancies (10.5%). Children with comorbidities demonstrated a higher likelihood of requiring respiratory support. Among those with comorbidities, 12% required respiratory support-a statistically significant association with an odds ratio (OR) of 6.147 (95% CI: 2.898–13.038; p < 0.001).

The presence of comorbidities was also evaluated for its association with severe COVID-19. Severe disease was observed in 14% of children with comorbidities and 17% of those without. The distribution and association of specific comorbidities with severe disease are presented in Table 4. Neurological comorbidities were significantly associated with severe disease (OR: 4.61; 95% CI: 1.998–10.638; p < 0.001). In contrast, malignancies, despite being the second most common comorbidity, were not significantly associated with increased severity. The overall in-hospital mortality was 2 (0.8%). One death occurred in a child without comorbidities, and the

Table 4. Association of various comorbidities with severe COVID-19.

Comorbidities		Severe COVID n(%)	Non severe n (%)	χ2	p- value
Neurological	Yes	18 (7)	10 (4)	16.5	<0.001
	No	58 (24)	160 (65)		
Respiratory	Yes	2 (1)	11 (4)	1.546	0.214
	No	74 (30)	159 (65)		
Haematological	Yes	0 (0)	4 (2)	1.818	0.178
	No	76 (31)	166 (67)		
Immunological	Yes	0 (0)	1 (0.4)	0.449	0.503
	No	76 (31)	169 (69)		
Cardiovascular	Yes	2 (1)	1 (0.4)	1.82	0.177
	No	74 (30)	169 (69)		
Genetic	Yes	1(0.4)	0 (0)	2.246	0.134
	No	75 (30)	170 (69)		
Renal	Yes	5 (2)	9 (4)	0.162	0.688
	No	71 (29)	161(65)		
Malignancy	Yes	7 (3)	19 (8)	0.215	0.643
	No	69 (28)	151 (61)		
Endocrine	Yes	0 (0)	5 (2)	2.282	0.131
	No	76 (31)	165 (67)		

other in a child with medulloblastoma. The causes of death were severe viral myocarditis and multiorgan failure, respectively.

DISCUSSION

This descriptive study undertaken in a tertiary care centre in Kerala highlights the clinical profile of children admitted with COVID-19. Study was conducted during the second wave of COVID-19 pandemic from May 2021 to July 2021. A total of 246 children aged 1 month to 13 years of age who are detected to have acute SARS-COV-2 infection with positive nasopharyngeal swab for either one of the following- rapid antigen test, real-time polymerase chain reaction (RT-PCR), TrueNat or GeneXpert from May 2021 to July 2021 were included in the study. Disease affected children of all age group and its spectrum varied from mild illness to severe pneumonia with complications like shock, myocarditis, LV dysfunction, acute kidney injury, transaminitis, multiorgan dysfunction. The categorization of disease was based on the Kerala state guidelines.[9] 28% of children were belonging to category C and 2% were having MIS-C. Category C and MIS-C were considered as severe disease. The median age noted in the present study was 4 years as observed in other studies.[5,10,11] In a multicentre cohort study involving 25 European countries by Götzinger et al. noted a median age of 5.0 years and a sex ratio of 1.15 males per female.[12] A slight male preponderance was noticed in this study with a male female ratio of 1.24:1.

Children who had COVID-19 acquired so through obvious channels of transmission, such as close contact with family members, a history of exposure to epidemic areas, or a combination of the two.[13] According to studies, children mostly contract an infection via an adult contact and there is only minimal secondary transmission from children.[3] In our study 81% were having positive contact history which validates the same. The COVID-19 disease spectrum was heterogeneous and 4% were asymptomatic. The overall common symptoms were fever (67%), rhinitis (28%), cough (27%), seizure (27%), vomiting (21%). Although the clinical features of COVID-19 in children are diverse fever and cough were the most common symptoms as described in many studies.[5] Dong et.al observed that infants were more susceptible to disease and had more severe disease, but it was not observed in this study.[14] A striking observation of this study was that a high proportion of children with comorbidities required admission and among this neurological comorbidity was the most common (11%).

As in other studies, there was a considerable increase in CNS involvement in second wave.[11] The most frequent manifestation (27% of cases) was seizure. Notably, these seizures were not new-onset, as all affected children had a documented history of seizure in past. The wide variety of neurological symptoms and illnesses linked to SARS-CoV-2 are consistent with several pathogenic pathways, including post-infectious processes, cytokine storm, septic-associated encephalopathies, coagulopathy, endothelitis, and neurotropism of spike protein in SARS-COV-2.[15,16] Analysis of lab parameters shows that anemia was present in 33%,

leucocytosis in 29% and thrombocytopenia in 12%. In a study conducted by Singh et. al there was a high proportion of children with anemia (69%), leucocytosis (55%), thrombocytopenia (38%).[5] Leucopenia was seen in 12% and is comparable to other studies.[8]

In a study by Meena et. al[17] leucopenia was found to be more common than leucocytosis but in our study leucocytosis was more prevalent (29%) and it was noted that there was a statistically significant association between leucocytosis and severe COVID-19. In pediatric patients with severe COVID-19, the presence of leukocytosis may indicate a secondary bacterial infection. Elevated CRP was present in 52% of children and a similar observation was made by Nallasamy et. Al.[5] Transaminitis was observed in 4% only but a higher proportion of children with transaminitis was noted by Singh et al.[8,17] A study by Kulkarni et. al., suggests that anemia is associated with severe COVID-19 but no statistically significant association was noted in our study.[18] In our study 38% were having comorbidities and the most common comorbidity was neurological in 28(11.3%) children followed by malignancy in 26 (10.5) children. Neurological comorbidities were associated with severe disease as observed in other studies also.[11,19] No statistically significant association was noted between malignancy and severe COVID despite being the second most common comorbidity seen in the study population.

A study conducted by Ramaswamy et al.[20] states that outcome of pediatric cancer patients are favourable. Mortality in children noted was 1% which was comparable with other studies.[5,11] It was noted that mortality rate in pediatric population was less when compared to the adult population as suggested by many studies. In our study 17% children required respiratory support of which 2% required invasive ventilation. A similar observation was noted by Banerjee et al.[21] An increased requirement of respiratory support was seen in children with comorbidities and it was found to be statistically significant. A higher proportion of children requiring oxygen and respiratory support was noted in other studies also.[8] More virulent and transmissible variants, B.1.1.7 and B.1.617 were circulating during the second wave of COVID-19 pandemic and that might be reason for increased requirement of respiratory support and intensive care.[22]

CONCLUSIONS

Children of all age group were susceptible to COVID-19 disease with a slight male preponderance. Among infected, the clinical profile varied from asymptomatic or had mild symptoms to severe illness with complications like pneumonia, shock, AKI, myocarditis and multi organ dysfunction. The overall common presentations were fever, respiratory symptoms and seizure. Children with comorbidities, especially neurological comorbidities exhibited severe illness and requirement of respiratory support was more in them.

Limitations: The COVID-19 pandemic has had a catastrophic effect on global health. The clinical features and laboratory abnormalities of symptomatic patients admitted in the hospital only could be studied. As a result, it may not accurately describe mild or asymptomatic individuals who don't need hospitalisation. Lack of long-term follow-up and small sample size was a weakness of study. Single centre nature of this study could introduce case selection bias and over representation of symptomatic patients. In spite of these shortcomings, this study provides preliminary data on characteristics and outcomes of COVID-19 in children.

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