ORIGINAL ARTICLE



Clinical Profile, Hospital Course and Outcome of Children with COVID-19

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Received: 8 August 2020 / Accepted: 12 November 2020 / Published online: 13 February 2021 $\ensuremath{\mathbb{C}}$ Dr. K C Chaudhuri Foundation 2021

Abstract

Objectives To describe the epidemiological and clinical characteristics and outcome of hospitalized children with COVID-19 during the initial phase of the pandemic.

Methods This was a cross-sectional descriptive study conducted at the dedicated COVID-19 hospital of a tertiary care referral center in North India. Consecutive children aged 14 y or younger who tested positive for SARS-CoV-2 by RT-PCR from nasopharyngeal swab between 1 April 2020 and 15 July 2020 were included.

Results Of 31 children with median (IQR) age of 33 (9–96) mo, 9 (29%) were infants. About 74% (n = 23) had history of household contact. Comorbidities were noted in 6 (19%) children. More than half (58%) were asymptomatic. Of 13 symptomatic children, median (IQR) duration of symptoms was 2 (1–5.5) d. Fever (32%) was most common followed by cough (19%), rapid breathing (13%), diarrhea (10%) and vomiting (10%). Severe [n = 4, 13%] and critical [n = 1, 3%] illnesses were noted more commonly in infants with comorbidities. Three (10%) children required PICU admission and invasive ventilation; one died. Median (IQR) length of hospital stay was 15 (11–20) d. Follow up RT-PCR before discharge was performed in 17 children and the median (IQR) duration to RT-PCR negativity was 16 (12–19) d.

Conclusions In the early pandemic, most children with COVID-19 had a household contact and presented with asymptomatic or mild illness. Severe and critical illness were observed in young infants and those with comorbidities.

Keywords Children · COVID-19 · India · SARS-CoV-2 · PICU

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Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) causing coronavirus disease (COVID-19) has spread globally, posing immense challenges to every country's healthcare system. The main reasons for the huge impact of COVID-19 are lack of preparedness for unprecedented and unexpected spread, intrinsic virulence of the pathogen and its contagiousness, asymptomatic spreaders, lack of immunity and effective vaccine, and nonavailability of proven and effective antiviral drugs. The first adult case in India was reported by the end of January 2020 among returning travelers from China, but by August, the number of cases has steadily increased to reach 2,088,611. Globally, children are less frequently affected by the disease. As per WHO-China joint mission report, children <18 y of age accounted for only 2.4% of 55,924 laboratory confirmed cases of COVID-19 in China, most of whom were household contacts of positive cases [1]. Similarly, Centers for Disease Control (CDC) from USA reported 2572 patients aged <18 y amounting to 1.7% of total COVID-19 cases [2]. Data from India showed comparatively higher incidence; ICMR laboratory surveillance network reported 3.6% and 8.1% of total cases in age group 0-9 y and 10-19 y, respectively between 22 January 2020 and 30 April 2020 [3]. The illness severity in pediatric age group also seems to be milder as compared to adults [4-8]. Hospitalization rates for patients <18 y ranged from 5.7% to 20% in USA with only 0.6%-2% requiring intensive care [2]. Of the 731 pediatric patients with confirmed SARS-CoV-2 infection reported from China, 12.9% were asymptomatic and 43.1% had only mild upper respiratory illness (URI). Moderate disease defined as lower respiratory tract signs in addition to URI symptoms, but without shortness of breath or hypoxemia was noted in another 41%. Only 2.5% children had severe disease with hypoxemia and 0.4% had critical illness with organ dysfunction [9]. Despite the daily reportage of total and statewise tally of cases by Ministry of Health and Family Welfare (MOHFW), the epidemiology and clinical characteristics of COVID-19 in pediatric age group remains less known. Since, symptomatology, severity and outcome of COVID-19 have been variable in different countries, local data on epidemiology, clinical manifestations, disease investigations, treatment modalities, and outcome will be useful to plan clinical services including screening, testing, isolation, and intensive care facilities to manage these children in face of escalating pandemic. Therefore, the authors conducted this study to present information on clinical characteristics and outcome of children with confirmed COVID-19 admitted to their tertiary centre during early pandemic.

Material and Methods

This was a retrospective study conducted at the dedicated COVID hospital of a tertiary care referral center of North

India. The study protocol was approved by Institute Ethics Committee. All consecutive children aged 14 y or younger who tested positive for SARS-CoV-2 by real time reverse transcription-polymerase chain reaction (RT-PCR) from combined nasopharyngeal and oropharyngeal swab between 1 April 2020 and 15 July 2020 were included in the study. The authors' center was designated as a referral facility for COVID-19 patients (both adults and children) and patients of all severity were referred for admission. Patients were received in a triage area and admitted to isolation ward, high dependent unit (HDU) or intensive care unit (ICU) based on assessment of severity of illness [10]. The severity of COVID-19 is categorized as mild, moderate, severe and critical based on clinical and/or radiological features [4]. Mild cases included children with only upper respiratory symptoms. Children with lower respiratory involvement (clinical or radiological signs of pneumonia) but without signs of severe pneumonia or hypoxemia were categorized as moderate disease. Severe disease included children with clinical features of severe pneumonia and/or hypoxemia (SpO₂ < 90%on room air) and those with severe diarrhea and dehydration. Presence of acute respiratory distress syndrome (ARDS) and/ or multiorgan dysfunction was classified as critical disease. This study included children with all severity including asymptomatic children as per the prevailing admission policy. Laboratory investigations were performed only in children with moderate to severe symptoms and/or comorbidities. Complete hemogram, liver and renal function tests, Creactive protein, chest radiograph, and RT-PCR for H1N1 influenza were the commonly ordered tests. Antibiotics were prescribed in children with pneumonia. Steroids and other repurposed therapies were used on a case to case basis. Data was collected from the case files and electronic records on a pre-designed case record form. Information regarding demographic and clinical details including age, sex, history of contact, type of contact, immunization status, 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 were noted. Outcome included length of hospital stay, recovery, and deaths.

Data regarding follow-up RT-PCR testing were recorded where available. During the initial weeks, as per hospital policy, all children underwent follow up RT-PCR testing after 4 d of asymptomatic period or 7 d after admission, whichever was later. If follow-up test was positive, test was repeated every 4 d, until negative. Patients were discharged after two consecutive negative RT-PCR tests 24 h apart. Time to RT-PCR negativity was calculated based on the duration between first RT-PCR positive test and first RT-PCR negative out of two consecutive negative tests. RT-PCR test was done on combined nasopharyngeal and oropharyngeal swabs immersed and transported in viral transport medium. RNA was extracted and RT-PCR was performed as per the standard National Institute of Virology, Pune, protocol [11].

Data entry and statistical analysis were performed using Excel (Microsoft Office 365, Redmond, WA) and SPSS software version 20 (SPSS, Inc., Chicago, IL). Descriptive statistics were used to summarize the data. Continuous variables were presented as median and interquartile range while categorical data were summarized as frequencies and percentages.

Results

A total of 1302 children were screened for COVID-19 by RT-PCR at the authors' center, of which, 5 were positive for SARS-CoV-2. Another 26 children were referred from other health care facilities after a positive RT-PCR test. Thus, a total of 31 children admitted to the center were included in this study. Table 1 describes the demographic and clinical features. Median (IQR) age was 33 (9-96) mo; about two thirds (n = 20) were under 5 y of age. Most (n = 23, 74%) had a history of household contacts with one or more affected members in the family. None of the children had a travel history or attended school or other mass gatherings. Majority (n = 26, n)84%) hailed from Chandigarh, about half (n = 14) from a single containment zone. Only a little over half (n = 17, 55%) had completed age appropriate immunization though majority had received BCG at birth (n = 29, 94%) and at least one dose of measles and rubella (MR) vaccine (n = 21, 68%). Comorbidities were noted in 6 (19%) children. More than half (58%) were asymptomatic and admitted in the initial phase as a measure of isolation and for monitoring. Of the 13 children who were symptomatic, the median (IQR) duration of symptoms was 2 (1-5.5) d. Fever (32%) was the most common symptom followed by cough (19%) rapid breathing (13%), diarrhea (10%) and vomiting (10%). Seizures and altered mental status were noted in 2 (6%) children. Eight children underwent one or more laboratory investigations. Lymphopenia was noted in one child. Three children each had elevated CRP (> 10 mg/dL) and infiltrates on chest radiography (Table 2).

The severity classification of COVID-19 is as follows; asymptomatic [n = 18, 58%], mild [n = 7, 23%], moderate [n = 1, 3%], severe [n = 4, 13%], critical [n = 1, 3%]. Three children each were admitted to HDU and ICU respectively. Of 3 children who were invasively ventilated, one child was non-hypoxemic and required mechanical ventilation due to underlying neurodevelopmental illness and status epilepticus. Other two children had underlying congenital heart disease with pneumonia, heart failure and hypoxemia. Hypotensive shock was noted in 4 children; two in children with congenital heart disease and one in a child with severe diarrhea and hypovolemia. Antibiotics (ceftriaxone and/or azithromycin)

were used in 6 children and 2 received steroids. Empirical oseltamivir was given in 3 children until H1N1 influenza infection was excluded. None of the children in the present

 Table 1
 Demographic and clinical characteristics of children with COVID-19

Characteristics	N=31
Age in months	33 (9–96)
< 1 y	9 (29)
1 < 5 y	11 (36)
5 < 10 y	10 (32)
<u>></u> 10 y	1 (3)
Male sex	16 (52)
Weight (kg)	11 (8–24)
Type of contact	
Household	23 (74%)
Healthcare	0
Others/Unknown	8 (26%)
Residence	
Chandigarh	26 (84%)
Single containment zone	14 (45%)
Punjab	3 (10%)
Haryana	1 (3%)
Uttar Pradesh	1 (3%)
Referred cases	26
Medical College Hospital	3
District hospital	17
Private hospital	1
Household surveillance	5
Immunization status	
Complete	17 (55%)
Partial	12 (39%)
Not known	2 (6%)
Received BCG	29 (94%)
Received one dose of MR	21 (68%)
Breastfed	8 (61%) ^a
Comorbidities	6 (19%)
Congenital heart disease	2 (6%)
Neurodevelopmental disorders	2 (6%)
Craniopharyngioma	1 (3%)
Nephrotic syndrome	1 (3%)
Symptomatology	
Asymptomatic	18 (58%)
Symptomatic	13 (42%)
Duration of illness before admission in days $(n = 13)$	2 (1–5.5)
	Range (1–14)
Symptoms $(n = 13)$	
Fever	10 (32%)
Any respiratory symptoms	9 (29%)
Cough	6 (19%)
Rapid breathing	4 (13%)
Noisy breathing	1 (3%)
Coryza	1 (3%)
Change of voice	1 (3%)
Any GI symptoms	5 (16%)
Diarrhea	3 (10%)
Vomiting	3 (10%)
Diaper rash	1 (3%)
Any neurological symptoms	3 (10%)
Seizures and altered mental status	2 (6%)
Headache	1 (3%)

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

^a out of 13 children who are <2 y of age

cohort received hydroxychloroquine or repurposed antivirals. At the time of writing, 29 (94%) were discharged, 1 (3%) is still admitted to hospital for ongoing management of comorbidities after being tested negative for SARS-CoV-2 and 1 (3%) died. Median (IQR) length of hospital stay in survivors was 15 (11–20) d (Table 3). Follow-up RT-PCR before discharge was performed in 17 children and the median (IQR) duration to RT-PCR negativity was 16 (12–19) d. One child tested negative only after 35 d of hospitalization.

Discussion

In this study, the authors describe the clinico-epidemiological profile and outcome of an early cohort of children admitted to a dedicated COVID hospital of a tertiary level teaching hospital. As it was the initial phase of the pandemic with extended lockdown and closure of schools and outdoor activities, the primary source of infection for children was a household contact, as seen in the present cohort [12]. The authors observed that fever and respiratory symptoms predominated in the symptomatic children. Gastrointestinal symptoms were the next common manifestations. Observational studies across the world have reported similar frequency of symptoms

Table 2	Laboratory	investigations	in	children	with	CO	VID-19
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Investigations	
SARS-CoV-2 status (n = 31)	
RT-PCR for SARS-CoV-2 positive	31 (100%)
Duration of RT-PCR positivity in days $(n = 17)$	16 (12–19) Range (3–35)
Hematology and biochemistry $(n = 8)$	
Hb g/dL	10.8 (10-12)
Total leucocyte count (×10 ⁹ /L)	11,750 (4400–23,675)
Lymphocyte count $(n = 6)$ (×10 ⁹ /L) Lymphopenia (n)	4874 (2061–7301) 1 (16%)
Platelet count ($\times 10^9/L$)	138.5 (116.5–377.5)
Albumin g/dL	3.5 (1.7-4.3)
AST U/L	33 (21–53)
ALT U/L	31 (10–51)
Sodium mmol/L	140 (139–143)
Urea mg/dL	19.5 (13–27)
Creatinine mg/dL	0.37 (0.22-0.49)
CRP $(n = 7)$ mg/L Elevated CRP (>10)	4.5 (0.4–41) 3 (43%)
Chest radiograph $(n = 7)$	
Normal Infiltrates	4 (57%) 3 (43%)

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

[13–16]. A systematic review of 27 studies showed fever to be present in half (41%-58%) followed by cough (39%-51%) and rapid breathing (6%-17%). Gastrointestinal symptoms, particularly diarrhea was noted in 6%-13% children [17]. A wide range in severity of the disease has been reported in studies depending on the cohort (community and/or hospital based) and hospital admission criteria, but overall, severe and critical COVID-19 was less common, observed only in 1-5% of children [17–20]. About 16% (n = 5) children had severe or critical illness in the present study, a higher figure compared to other reports, however, limited sample size, underlying comorbidities and referral bias may have influenced this representation. The authors observed that the illness tended to be severe in younger infants and children with cardiovascular or respiratory comorbidities. Of the 3 children who required mechanical ventilation, 2 were infants with underlying congenital heart disease (shunt lesion and heart block) who presented with heart failure. One of them, a young infant developed acute respiratory distress syndrome and succumbed to the illness. Young children, particularly infants seem to be at increased risk of critical disease and mortality [8]. In a large pediatric study from China, the proportion of severe and critical cases were 10.6% and 7.3% for <1 and 1–5 y age groups as compared to 3%–4% for older children [4]. In common with adults, underlying

Table 3	Treatment,	and	outcome
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Variables	n (%)
Level of care	
Isolation ward	25 (80%)
HDU	3 (10%)
ICU	3 (10%)
Organ supportive therapies	
Respiratory support	5 (16%)
Supplemental oxygen	2 (6%)
^a CPAP	1 (3%)
Mechanical ventilation	3 (10%)
Shock	4 (13%)
Vasoactive/inotrope agent infusion	3 (10%)
Temporary transvenous pacing	1 (3%)
Drug treatment	
Antibiotics	6 (19%)
Azithromycin	1 (3%)
Oseltamivir	3 (10%)
Steroids	2 (6%)
Outcome	
Discharged	29 (94%)
Still in hospital	1 (3%)
Died	1 (3%)
Length of hospital stay in days. Median (IQR)	15 (11–20)

^a also received invasive mechanical ventilation

comorbidities increases the risk for severe disease and intensive care admission in children [21]. In a brief report from UK, 4 out of 5 (80%) children with comorbidities had multiorgan involvement [22]. In a study involving 48 children with COVID-19 admitted to 14 PICUs in the US, more than 80% had significant underlying medical conditions [23].

Another observation was that the median (IOR) time for RT-PCR to become negative in the present cohort was 16 (12-19) d, a finding similar to the report from Delhi on adult patients [24]. Studies on virological assessment of hospitalized patients with COVID-19 showed persistence of SARS-CoV-2 RNA in nasopharyngeal samples for a duration of about 2 wk [25, 26]. It remains to be seen whether prolonged RT-PCR positivity correlates with period of infectivity, however, these findings coupled with majority being asymptomatic, raises concern over children being potential carriers and at risk of transmitting infection to the community. The authors took a consensus decision to perform laboratory tests only as needed. Thus, the majority of children in this cohort did not undergo any investigation if they were asymptomatic. Most baseline tests were unremarkable in the present cohort. Lymphopenia was noted in only 1 (3%) child. Elevated CRP was noted in 3 (10%) children. There was no difference on course or outcome of children who did not undergo investigations. The authors suggest that it is important for clinicians caring for children to use laboratory investigations judiciously. Laboratory abnormalities have been reported in children with critical disease in conformity with underlying organ dysfunction or more commonly in COVID-19 associated hyperinflammatory syndromes (PIMS-TS/MIS-C), a delayed presentation with prominent gastrointestinal and cardiac manifestations and raised inflammatory biomarkers [27, 28]. This syndrome may be of significance in the coming months as the pandemic progresses. The authors used antibiotics in 6 children who had fever and lower respiratory involvement. None of the children received hydroxychloroquine or other repurposed antiviral drugs. Use of repurposed therapies are reported more widely in adults and in varying proportions as per severity of illness, hospital policy and local availability. Effectiveness of these agents may depend on timing of administration with respect to the course of illness and host characteristics. There is insufficient data to include them as standard care [29].

The present study is one of the early reports from India on clinical characteristics of children hospitalized with confirmed COVID-19. The data included children with asymptomatic illness, providing a true representation of disease spectrum in children. The authors have also presented data on follow-up RT-PCR results that has public health implications. A small sample size and a short study duration are notable limitations. The present study is a hospital-based study done at a tertiary level referral healthcare. The proportions described in this study with respect to clinical characteristics, severity of illness and outcome may differ in a larger sample size from a different setting.

Conclusions

In the initial phase of the pandemic, most children with COVID-19 had a household contact and presented with asymptomatic or mild illness. Severe and critical illness was observed in young infants and those with comorbidities. Majority had good outcome with recovery to hospital discharge.

Acknowledgements The authors are thankful to the COVID-19 management team at their center for their immense contribution to the clinical management and administration. The authors acknowledge the selfless work of all their nurses, administrators, laboratory technicians, hospital attendants, security personnel and sanitary attendants involved in the care of these children.

Authors' Contributions MJ had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. All authors participated in the study concept and design. MJ, KN and SKA had collected, analysed and interpreted study data. KN and SKA drafted the manuscript. MPS and IB helped in laboratory confirmation of COVID-19 through RT-PCR. PVML helped in epidemiological data and contact tracing. AB, JM, and SV gave critical inputs during revision of the manuscript. MJ, NS, RRG and GDP provided administrative, technical, or material support. All authors read and approved the final manuscript.

Data Availability The data analyzed in this study is available from the corresponding author on reasonable request.

Compliance with Ethical Standards

Conflict of Interest None.

Ethics Approval The study protocol was approved by the Institute Ethics Committee (Ref. No. NK/6533/Study/276) and Departmental Review Board (Ref. No. DRB-149-20).

Consent to Participate This was a retrospective study with de-identified data and waiver of consent was approved by the Institute Ethics Committee.

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