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Original article

Clinical profile and outcome of COVID-19-positive children in a tertiary care centre of North-East India

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Abstract

Introduction: COVID-19 infection is said to be generally a milder disease in children, compared to adults, and is associated with much lower case-fatality rates. Objective of this study was to find out the clinical characteristics and outcome of COVID-19-positive children and also the differences between the first and the second waves, if any.

Methodology: This was a retrospective study done in the Department of Paediatrics of a tertiary care teaching hospital. Departmental and hospital medical records were reviewed to assess the clinical characteristics, disease severity and outcome of all COVID-19-positive admitted children from May 2020 to September 2021 (the first wave from May 2020 to January 2021 and the second wave from April 2021 to September 2021). Data analyses were done in Microsoft® Excel® 2010.

Results: Out of total 560 COVID-19-positive children attending the hospital during the study period, 266 children (76 in the first wave and 190 in the second wave) were admitted. The majority of the children (25%) were in the age group of 1-6 months during the first wave, while in the second wave the majority of the children (27.9%) were in the age group of 5-10 years. The most common presenting complaint was fever (51.1%), followed by cough (13.9%). Co-morbidities were present in 23.3% of cases. Asymptomatic, mild, moderate, severe and critical cases were 16.5%, 51.9%, 18.4%, 6.4% and 6.8%, respectively. The case fatality ratio was 3.75% (21/560) among all positive cases. Ventilator support was required in only 10.1% of cases. There were some significant differences between the 2 waves regarding age

distribution, disease severity, outcome and some presenting complaints.

Conclusions: The majority of the COVID-19 infections were either asymptomatic or of mild variety. Males suffered more than females. The admission rate was higher in the second wave but death was higher in the first wave, indicating higher infectiousness and milder nature of the disease in the second wave. Most of the deaths occurred within 24 hours of admission, indicating that late admission may be an important risk factor for mortality. Except for age distribution, severity and outcome, other parameters were comparable between the first and the second wave.

Keywords

Children, clinical characteristics, disease severity, first and second waves, mortality, SARS-CoV-2 infection.

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Introduction

Coronaviruses (CoVs) are a large family of single-stranded, zoonotic RNA viruses [1]. In humans, CoVs mostly cause respiratory and gastrointestinal symptoms, coagulopathy, multi-organ failure and death [1]. CoVs are capable of rapid mutation and recombination, leading to novel CoVs that can spread from animals to humans [1]. CoVs are novel betacoronaviruses belonging to the lineage B or subgenus sarbecovirus, which includes severe acute respiratory syndrome CoVs (SARS-CoVs) [2].

A novel CoV disease 2019 (COVID-19) emerged in Wuhan, Hubei Province, China in December 2019 and on 12th March 2020, the WHO announced that it had reached Pandemic status. The official names for this novel virus had been announced as severe acute respiratory syndrome CoV 2 (SARS-CoV-2) or CoV disease 2019 (COVID-19) virus on 11th February 2020. In India, the first case was detected on 27th January 2020 who was a student returned from Wuhan, China, to Kerala [3]. The incubation period of SARS-CoV-2 is 1 to 14 days, and most commonly 3 to 7 days [4]. However, Guan et al. described a patient with an incubation period of up to 24 days [5].

COVID-19 is generally a mild disease in children, including infants, causes fewer symptoms and less severe disease compared to adults, and is associated with much lower case-fatality rates. Preliminary evidence suggests that children are just as likely as adults to become infected with SARS-CoV-2, but are less likely to be symptomatic or develop severe symptoms [1].

Various explanations stated about why COVID-19 infection is less severe in children than in adults, are the followings.

i. Angiotensin-converting enzyme 2 (ACE 2) allows SARS-CoV-2 to enter the body's cells. Children have fewer ACE 2 receptors in the lungs than in adults [6, 7].
ii. Adults infected by SARS-CoV-2, especially those with a severe disease, usually have decreased lymphocyte count. Lymphocyte count is very high in the first months of life and decreases in later childhood and in adolescence. Moreover, lymphocytes could be higher in children even due to frequently experienced viral infections in childhood, which results in an everlasting immune system activation in the first few years of life [8].
iii. Milder disease presentation in children might be linked to "trained immunity" [9]. "Trained immunity" represents an innate immune memory and it is formed by innate immunity cells that became "memory cells" after antigen exposure.
iv. Children produce lower levels of inflammatory cytokines and IL-6 production increases with age [10].

There are few published data on COVID-19-positive children from India and, to our knowledge, this is the first study on COVID-19-positive children from the North-East region of our country. Aim of this study was to analyse the clinical characteristics and outcome of the admitted COVID-19-positive children in this tertiary care hospital in 2020 (first wave) and 2021 (second wave), and also to determine whether there was any dissimilarity between the characteristics of the first and the second waves.

Methodology

This was a hospital-based retrospective study done in the Department of Paediatrics of Assam

Medical College Hospital (AMCH), Dibrugarh, Assam. The study period was from May 2020 to September 2021 (the first wave continued from May 2020 to January 2021 and the second wave from April 2021 to September 2021). The study population was COVID-19-positive children (tested either by rapid antigen test from nasopharyngeal swab or reverse transcriptase polymerase chain reaction from nasopharyngeal and oropharyngeal swab) admitted during the study period. Information regarding the study population was taken from both the departmental and hospital records. The study population also included those children who were already admitted for other clinical illnesses in the Department of Paediatrics and subsequently tested positive for COVID-19 while inpatients.

A total of 560 COVID-19-positive children (232 in the first wave and 328 in the second wave) attended our hospital during the study period. Out of them, 266 children were admitted into the COVID-19 Ward and Intensive Care Unit (ICU) (76 cases during the first wave and 190 cases during the second wave). The remaining children were either sent for home isolation or sent to COVID-19 Care Centres (CCCs) as per protocol laid down by the Government of Assam at that time. Some children opted for home isolation after an undertaking was given by the parents/guardians. These children were either asymptomatic or had very mild symptoms.

All the admitted children were treated and discharged as per protocol laid down by the Government of Assam or the Indian Academy of Paediatrics.

Ethical clearance from the Institutional Ethics Committee was obtained before conducting this study.

Statistical analysis

Data was saved in Microsoft® Excel® 2010. Percentages and means were calculated for the variables. Chi-Square test was performed to find out the significant differences between first and second wave data. P-value of < 0.05 was taken as significant.

Results

A total of 266 children (76 in the first wave and 190 in the second wave) were admitted into the COVID-19 Ward and ICU, out of a total of 560 COVID-19-positive children (232 in the first wave and 328 in the second wave) attending our hospital from May 2020 to September 2021 (no COVID-19-positive children were admitted from February 2021 to March 2021). After that, 1 or 2 sporadic cases were admitted, but there was no third wave till now (December 2021). The admission rate was 32.8% (76/232) in the first wave and 57.9% (190/328) in the second wave. Total admission of COVID-19-positive cases, including adults, during that period was 9,900. Hence, children constituted 2.7% (266/9,900) of all COVID-19 patients admitted to our hospital.

The majority of the children (25%) were in the age group of 1-6 months followed by neonates (21.1%) during the first wave, but in the second wave the majority of the children (27.9%) were in the age group of 5-10 years. Average age was 2.8 years ranging from 1 day to 12 years and 3.9 years ranging from 4 days to 12 years, in the first and the second wave, respectively. The male:female ratio was 1.6:1 in the first wave and 2.1:1 in the second wave (**Tab. 1**).

Being a tertiary care teaching hospital, it caters patients from whole upper Assam. In our study, 44.7% and 41% of cases (in the first wave and the second wave, respectively) were from the Dibrugarh district and the remaining cases were from neighbouring districts. Few patients were from neighbouring states like Arunachal Pradesh and Manipur. Most of the cases came during the month of August 2020 (31.6%) followed by September 2020 (26.3%) during the first wave and in the month of July 2021 (62%) followed by August 2021 (42%) in the second wave (**Fig. 1**).

Contact history was present in 11 (14.5%) cases in the first wave and in 144 (75.8%) cases in the second wave. Co-morbidities were present in 17 (22.4%) children in the first wave; in the second wave, 46 (24.2%) cases had co-morbidities. Co-morbidities were congenital anomalies, prematurity, malignancy, nephrotic syndrome, thalassemia, Japanese encephalitis, post-operative condition, severe malnutrition, intestinal obstruction, septic arthritis, fracture, neonatal jaundice, congenital heart disease, chronic kidney disease, cerebral palsy, seizure disorder and culture-proven sepsis. There were 2 (2.6%) cases of multisystemic inflammatory syndrome (MIS) in the first wave and 10 (5.3%) cases in the second wave.

The most common presenting complaint was fever (51.1%), followed by cough (13.9%). Asymptomatic cases were 16.5%. Most of the complaints in the 2 waves were comparable, except for loose motion and runny nose, which were significantly lower in the second wave. Mild cases

Table 1. Baseline characteristics, clinical picture and outcome of the children.

Variable		All children (n = 266)	First wave (n = 76)	Second wave (n = 190)	p-value
Age-wise distribution	Neonate	52 (19.5%)	16 (21.1%)	36 (18.9%)	NS
	1-6 months	39 (14.7%)	19 (25%)	20 (10.5%)	**0.00257**
	6-12 months	24 (9%)	4 (5.3%)	20 (10.5%)	NS
	1-2 years	30 (11.3%)	6 (7.9%)	24 (12.6%)	NS
	2-5 years	39 (14.7%)	15 (19.7%)	24 (12.6%)	NS
	5-10 years	66 (24.8%)	13 (17.1%)	53 (27.9%)	NS
	> 10 years	16 (6%)	3 (3.9%)	13 (6.8%)	NS
Sex	Male	174 (65.4%)	47 (61.8%)	127 (66.8%)	NS
	Female	92 (34.6%)	29 (38.2%)	63 (33.2%)	NS
Signs and/or symptoms at the time of admission	Fever	136 (51.1%)	37 (48.7%)	99 (52.1%)	NS
	Skin rash	5 (1.8%)	2 (2.6%)	3 (1.6%)	NS
	Seizure	28 (10.5%)	10 (13.2%)	18 (9.5%)	NS
	Altered sensorium	6 (2.3%)	2 (2.6%)	4 (2.1%)	NS
	Loose motion	21 (7.9%)	10 (13.2%)	11 (5.8%)	**0.04408**
	Abdominal distension	12 (4.5%)	3 (3.9%)	9 (4.7%)	NS
	Difficulty in breathing	33 (12.4%)	10 (13.2%)	23 (12.1%)	NS
	Vomiting	27 (10.2%)	12 (15.8%)	15 (7.9%)	NS
	Runny nose	28 (10.5%)	13 (17.1%)	15 (7.9%)	**0.02701**
	Cough	37 (13.9%)	8 (10.5%)	29 (15.3%)	NS
	Loss of taste and/or smell	3 (1.1%)	1 (1.3%)	2 (1.1%)	NS
Severity of disease	Asymptomatic	44 (16.5%)	15 (19.7%)	29 (15.3%)	NS
	Mild	138 (51.9%)	26 (34.2%)	112 (58.9%)	**0.00026**
	Moderate	49 (18.4%)	19 (25%)	30 (15.8%)	NS
	Severe	17 (6.4%)	7 (9.2%)	10 (5.3%)	NS
	Critical	18 (6.8%)	9 (11.8%)	9 (4.7%)	**0.03714**
Outcome of patients	Discharged	197 (74.1%)	41 (53.9%)	156 (82.1%)	**0.000002**
	DAMA/CCC	48 (18%)	25 (32.9%)	23 (12.1%)	**0.0002**
	Death	21 (7.9%)	10 (13.2%)	11 (5.8%)	**0.04408**
	Still admitted	1 (0.4%)	0	1 (0.5%)	NA
Respiratory support	Not required	199 (74.8%)	56 (73.7%)	143 (75.3%)	NS
	Only oxygen	40 (15%)	12 (15.8%)	28 (14.7%)	NS
	Non-invasive ventilation	16 (6%)	5 (6.6%)	11 (5.8%)	NS
	Invasive ventilation	11 (4.1%)	3 (3.9%)	8 (4.2%)	NS

CCC: COVID-19 Care Centre; DAMA: discharge against medical advice; NS: not significant.

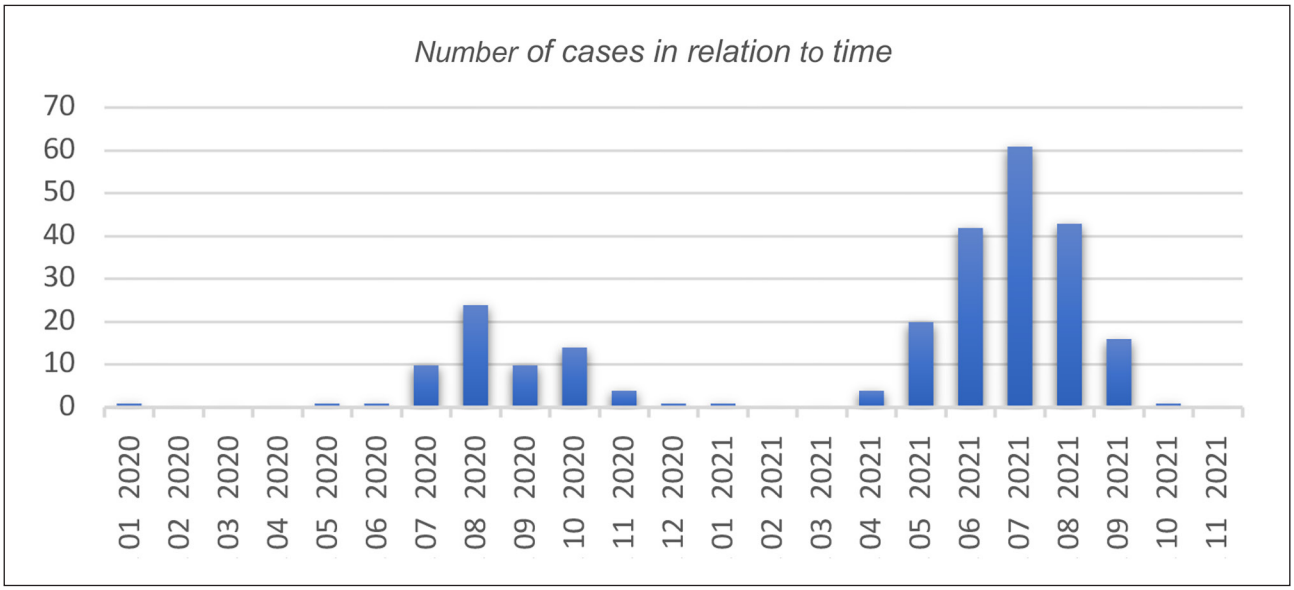

Figure 1. Number of cases from January 2020 to November 2021.

were more in the second wave (34.2% vs 58.9%, p = 0.00026) and critical cases were more in the first wave (11.8% vs 4.8%, p = 0.03714). 53.9% and 82.1% of children were discharged after the COVID-19 test became negative in the first and the second wave, respectively (p = 0.000002), excluding the cases who went for discharge against medical advice (DAMA) or to CCC. 74.8% of children did not require any oxygen support. Non-invasive ventilation was required in 6% and invasive ventilation in 4.1% of cases. There was not much difference in the requirement of oxygen support between the 2 waves. The mortality rate among admitted children was higher in the first wave than in the second wave, i.e. 13.1% vs 5.8% (p = 0.04408) (**Tab. 1**). The case fatality ratio among all positive children was 4.3% (10/232) and 3.4% (11/328) in the first and the second wave, respectively.

Three (30%) expired children had co-morbidities (1 post-VP shunt, 1 kwashiorkor, and 1 cerebral palsy) in the first wave; in the second wave, 5 (45.5%) expired children were with co-morbidities (1 Japanese encephalitis, 2 bacterial meningitis, 1 culture-proven sepsis, and 1 post-operative transverse colostomy). Death in the neonatal period was 12.5% (2/16) and 8.3% (3/36) in the first and the second wave, respectively. Most of the deaths occurred within 24 hours of admission, 90% (9/10) in the first wave and 72.7% (8/11) in the second wave. Death was more frequent in males than females in both the waves, i.e. 60% vs 40% in the first wave and 54.5% vs 36.4% in the second wave.

Discussion

In this hospital-based retrospective study, we described the clinical characteristics and outcome of 266 COVID-19-positive admitted children from March 2020 to September 2021.

The first COVID-19-positive case in our state was reported on 31st March 2020 and the first positive child was detected on 25th May 2020, in our hospital. In India, the first wave started in March 2020, achieved its peak in September and gradually decreased in intensity in February 2021, while the second wave started appearing at the end of March 2021, reached its peak in May 2021 and then gradually decreased [11]. But in Dibrugarh the first wave started from May 2020 and the second wave started from April 2021. The first wave reached its peak in August 2020 and the second wave reached its peak in July 2021 (**Fig. 1**)

The admission rate was higher in the second wave, i.e. 32.8% vs 57.9%, as the infection rate was higher in the second wave because of the high infectivity of Delta variant. The national figure also showed a sharp rise of cases towards the end of May 2021 [11]. Most of the children were in the age group of 1-6 months in the first wave and in the age group of 5-10 years in the second wave. In a study from Europe, most of the children (40%) were below 2 years [12] and another study from UK showed maximum number of children (26.4%) in the age group of 1 month-1 year [13]. Two studies from India showed maximum number, i.e. 36.6% and 31.7%, in the age group of 1-5 years [14, 15]. Neonates constituted between 7-8.1% in Western countries [12, 13], while 13-14.6% in Indian studies [14, 15], like our study, where we found 19.5% neonatal cases. Hence, it has been seen that, in the Indian scenario, neonatal involvement was higher in comparison to Western countries. We saw a shifting of age structure, i.e. from 1-6 months age group in the first wave to 5-10 years age group in the second wave. In all the above-mentioned studies, which were done during the first wave, most of the cases were seen in the younger age groups. Males constituted more than females in both the waves in our study, which was the same as in other studies [12, 14-17]. Death was also more frequent in male children than female children. The exact cause of this male preponderance is not yet known. CDC COVID-19 Response Team stated that the predominance of males in pediatric cases suggests that biologic factors might play a role in any differences in COVID-19 susceptibility by sex [2]. Patel et al. stated in their study that circulating ACE 2 levels are higher in men than in women [18].

Fever was the most common symptom, like in other studies done all over the world. In our study, fever was present in 51.1% of children. Other studies showed fever in 64%, 34%, 50% and 70% of children [12, 16, 17, 19]. Cough was seen in 38% of children in one Indian study [16] and 56% in the European study [12], but in our study cough was seen in only 13.9% of children. Loose motion was seen in 7.9% of cases in our study, whereas it was seen in 4% and 5% of cases in two other studies [19, 20].

We had seen that most of the cases were of mild nature, followed by moderate severity. This finding was similar to other studies [15, 16]. Asymptomatic cases were 16.5%, which was similar to another study [12]. But Sarangi et al. showed 58% of children as asymptomatic [16].

The majority of children in both the waves did not require any oxygen support and only 10.1% of children required ventilator support. This finding was in accordance with one study from India [14]. Death was significantly lower in the second wave in comparison to the first wave; that can be attributed to a better understanding of the disease and the availability of better ICU facilities in the second wave.

The proportion of deaths among all admitted children was lower in the second wave. This result resembles the data shown in an Indian study, where it was stated that the death rate was lower in the second wave in comparison to the first wave [21]. Neonatal mortality rates among non-COVID-19 babies were between 11-14% in pre-COVID-19 times and between 9-13% during the COVID-19 pandemic, though the number of newborn babies attending our hospital, both inborn and outborn, were increased by being a tertiary care government hospital. This slight decrease in mortality may be due to the availability of better treatment facilities as a whole and decrease in the infection rate due to the maintenance of COVID-19 protocol. If we consider non-COVID-19 mortality of children (excluding newborns), it was 6.4% in the pre-COVID-19 period and 7.7% during the COVID-19 pandemic. This increase in the death rate was due to the admission of more sick children during COVID-19 times due to lockdown. Death from COVID-19 constituted 3.5% (21/595) of all child deaths (both newborn and children) in our Department during the study period. A higher number of cases were discharged in the second wave in comparison to the first wave and the difference was statistically significant, which proved the milder nature of the disease in the second wave. We observed no association between the presence of co-morbidity and death in our study, as showed in another study [22].

Conclusions

To conclude, the first wave of COVID-19 infection started 2 months later than in other Indian states, but the second wave started almost at the same time. The majority of the children suffering from COVID-19 infection were of mild severity (more in the second wave). Males were more prone to suffer from the disease and also to develop a severe disease. Sex distribution, presenting complaints (except for loose motion and runny nose), oxygen requirement and presence of co-morbidities were comparable between the first and the second waves. There were significant differences in age distribution and outcome of COVID-19 children between the first and the second waves. The percentage of death among all admitted children was lower in the second wave, though the admission rate was higher in the second wave. Early treatment seeking behaviour will decrease the duration of morbidity and also death, as most of the death occurred within 24 hours of admission. People should be made aware of the actual nature of the disease and not to believe unscientific faiths and superstitions, which are rampant in this part of the country. Mortality depends on the virulence and infectivity of the subtype of the virus, along with the availability of treatment facilities, including ICUs.

Some important parameters could not be gathered in our study, like the source of infection and incubation period, as this was a retrospective study. Duration of hospital stay and exact duration of COVID-19 positivity in all children could not be analysed, as a large number of patients had DAMA or were sent to CCC. Being a hospital-based study, it may not reflect the exact incidence and mortality rate of children in the community.

Declaration of interest

The Authors declare that there is no conflict of interest.

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