RESEARCH

CLINICAL CHARACTERISTICS, RISK FACTORS AND OUTCOME OF PEDIATRIC COVID-19 IN A TERTIARY CARE INSTITUTE, NORTHEAST INDIA

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Abstract

Background: COVID-19 disease in children is generally mild. Data on pediatric COVID-19 are limited. This study aimed to describe the clinical characteristics of COVID-19 disease in children and to identify the outcome of children admitted at a COVID-19 tertiary care institute, Northeast India. **Materials and Methods:** Retrospective observational study on 181 children aged 0 to 14 years admitted in dedicated COVID care center between May 2021 to April 2022 are conducted. All the children with real time polymerase chain reaction SARS-CoV-2 positive children were assess for demographic, clinical characteristics, disease severity and various factors predicting outcome of COVID-19 disease. Variables were compared between children who were symptomatic with SpO2 <94% and asymptomatic/symptomatic with SpO2 ≥94%. **Result:** Mean age was 5.0 years ±4.149SD. Male (64.1%) were affected more than female.17.68% children have comorbidities, 5.52% needed intensive care. Factors that remained associated with symptomatic children having SpO2 <94% were children younger than one year, female, urban region, complication, high mortality, comorbidities with cardiac disease, respiratory disease, hematological and chromosomal disease were significant. Mean duration of hospital stay was 6.9 days ± 2.91SD and 2 (1.10%) children died. **Conclusion:** COVID-19 positive children with SpO2 <94% at hospitalization among symptomatic children has higher mortality than asymptomatic/ symptomatic children with SpO2 ≥94%. Strict triaging for severity of COVID-19 positive children and early protocol-based treatment should be promoted by the health care professionals in all the health centers.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was first reported in Wuhan, China as a cluster of cases of viral pneumonia. COVID-19 infection has spread all over the world irrespective of age and gender, leading to COVID-19 pandemic and become a public health crisis. In United States, children account for approximately 19 % of the cumulative total of COVID-19 cases.[1] In India, <12% of all confirmed cases are in individuals below 20 years.[2] The government has imposed several regulations to contain its spread. Approximately 14% of all cases of COVID-19 reported to the CDC were among children.[3] Family clustering appears to play the major role in disease transmission among children. Health care associated outbreaks and cases of possible transmission from teachers or school staff to students and among students in the school setting have also been reported.[4,5] The most common symptoms include fever, cough, poor appetite, headache and diarrhea especially among children. The severe form of COVID-19 disease among children is less common than adults. International pediatric data suggest lower rates of severe coronavirus disease 2019 in children and higher rates of asymptomatic infection. Risk factors for severe disease in pediatric populations have not been clearly identified. Most of the cases in children are mild and treatment requires only supportive care. Among the recommendation are bed rest and ensuring sufficient calorie and water intake. Oxygen therapy is recommended for patients with hypoxia.[6] Antimicrobials are generally reserved for children with co- infections. COVID-19-related death in children and adolescents is rare.[7] The study on clinical findings associated with COVID-19 disease

in children could help inform clinical practice, infection prevention and control preparedness at hospital setting. Data on COVID-19 infected children in North eastern region of India are limited. Therefore we have taken up this study on clinical profile, associated risk factors and outcomes of COVID-19 infected children admitted in a tertiary care institute.

MATERIALS AND METHODS

The study was taken up in a Dedicated COVID Care Centre at Jawaharlal Nehru Institute of Medical Sciences, Manipur, Northeast India. Dedicated COVID Care Centre is an isolation ward with ICU facility, specially created for admitting COVID-19 confirmed cases as per national guidelines.[8] Medical records for all children with confirmed SARS-CoV-2 infection by reverse transcription polymerase chain reaction test from nasopharyngeal swabs admitted between May 2021 to April 2022 were retrospectively reviewed.

Inclusion Criteria
Children aged between 0 to 14 years with COVID - 19 infection.

Exclusion Criteria
Children who opted for home isolation and children with COVID-19 vaccinated.

Methodology
Approval from institutional ethics committee was obtained. After getting permission from Medical superintendent patient's information was collected from the hospital medical record consisting of demographic details, month of admission, presenting symptoms, presence of comorbidity, laboratory parameters, radiological findings, clinical course during hospitalization, and treatment provided during hospitalization etc. Categorization of COVID-19 disease severity was done as per Guidelines on Operationalization of COVID Care Services for Children & Adolescents, Government of India, Ministry of Health and Family Welfare.[9] Children with mild disease may present with sore throat, rhinorrhea, cough but no fast breathing, Moderate disease represents age appropriate rapid respiration, oxygen saturation (SpO2) between 90 % to <94%.and may have pneumonia. Severe disease represents children with SpO2 level < 90%, may have severe pneumonia/ acute respiratory distress syndrome/ septic shock/ multiple organ dysfunction syndrome/ Pneumonia with cyanosis, grunting, severe retraction of chest, lethargy, somnolence or seizure. There was record for measurement of oxygen saturation (Spo2) for every case at the time of admission using standardizes electronic Pulse oxymeter. Laboratory investigations and imaging studies were recorded. Therapeutic principles were mainly general supportive care, control of fever, oxygen support and/or mechanical ventilation, early initiation of antimicrobials as indicated and treatment of associated comorbid conditions. Monitoring of cases and discharge criteria were followed as per guidelines.[10]

Statistical Analysis
Data was entered in MS Excel, All statistical analysis were performed using SPSS version 21. Descriptic analysis were done to calculate frequency, percentage and mean ± standard deviation for continuous variables. Categorical variables were reported as proportions. The study outcomes were compared among symptomatic children with SpO2 <94% and asymptomatic/symptomatic children with SpO2 ≥ 94%. Logistic regression was applied to obtain a propensity score for the study patients. The adjusted odds ratio with 95% confidence intervals was analyzed. and p value less than 0.05 using chi square test was considered statistically significant.

RESULTS

The present study included 181 children aged between 0 to 14 years infected with real time polymerase chain reaction confirmed SARS-CoV-2. Baseline characteristics of the study population were detailed in [Table 1]. The mean (SD) age of presentation was 5.0 ±4.15 years. Majority (32.04%) of children were in the age group between 1 to 5 years. Children below1 year comprises 21.55%, of which children less than 1 month (neonates) was only 9 (4.97%). Male (116) were more affected than females (65) with a ratio of 1.8:1. More than half (55.80%) of children belongs to urban region. The most common source of infection was from one of family members 78(42.81%). Of the total study children 17.68% had comorbid conditions. The most common comorbidity was severely underweight (n=10,5.52%) followed by cardiovascular disease (n=5, 2.76%). Other comorbidity includes 4 (2.21%) neurological disease (2 cerebral palsy, 2 seizure disorder), 3 (1.66%) chronic respiratory disease (asthma), 2 (1.10%) chromosomal disease (Down syndrome), one each (0.55%) gastrointestinal (chronic liver disease with portal hypertension) and hematological disease (Aplastic anemia). 5(2.76%) patients had neonatal jaundice. Among the study children, 10 (5.52%) patients presented as surgical case (7 appendicitis, 3 abscess). More than 80 % of children at admission had oxygen saturation (SpO2) 94% and above. 26 children had SpO2 between 90% to <94 % and only 9 (4.97%) children had SpO2 below 90%. The mean SpO2 were 95.7% ± 5.03 SD. Categorization of disease severity shows 146 (80.66%) children with asymptomatic or mild disease and 4.97% had severe form of illnesses. [Figure 1]
The most common symptom present at hospitalization was fever (60.22%) followed by

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cough (32.04%). Detailed symptoms presentation is shown in [Figure 2]. Majority of the children (89.50%) presented with combination of more than one symptom. The investigation record shows 17(9.39%) children having abnormal chest x ray findings and 35 (19.34%) patients with abnormal blood findings.12 (6.63%) study children had bacterial co-infection. 40 (22.10%) children required respiratory support of which 39 (21.55%) needed oxygen therapy and one child received mechanical ventilation. 10 (5.52%) children needed intensive treatment. Maximum children were admitted during the month of January 2022. [Figure 3]. A total of 100 (55.25%) children needed hospital stay for 7 or more days. Mean duration of hospital stay was 6.9 days ±2.91SD (range 2 to14 days). 37(20.44%) children developed medical complications. Only 2 children died (1encephalitis with shock and1 Down syndrome with multiorgan failure.) and case fatality rate was 1.10%. 98.90 % children were discharge with full recovery.

Table 1: Baseline characteristics of study participants

Variables	Frequency (N=181)	Percentage (%)
Age in years		
0 - < 1	39	21.55
1 - <5	58	32.04
5 - <10	52	28.73
10 – 14	32	17.68
Gender		
Male	116	64.09
Female	65	35.91
Region:		
Urban	101	55.80
Rural	80	44.20
Source of Infection		
Family members	78	43.09
Parents	64	35.36
Unknown	39	21.55
Comorbidity	32	17.68
Surgical case	10	5.52
Disease severity		
Asymptomatic	40	22.10
Mild	106	58.56
Moderate	26	14.36
Severe	9	4.97
Abnormal X-ray chest	17	9.39
Abnormal blood findings		
Low hemoglobin	10	5.52
Leucocytosis	21	11.60
Leucopenia	10	5.52
Thrombocytopenia	4	2.21
Co-infection	12	6.63
Treatment		
Intensive care needed	10	5.52
Respiratory support needed	40	22.10
Only Oxygen therapy	39	21.55
Ventilator support	1	0.55
Blood transfusion	1	0.55
Steroid	5	2.76
Vasopressor drug	1	0.55
Season of admission		
May to August 2021	38	20.99
September to December 2021	70	38.67
January to April 2022	73	40.33
Duration of hospital stay		
<7 days	81	44.75
≥7days	100	55.25
Outcome		
Death	2	1.10
Discharge	179	98.90

Table 2: Multivariate analysis for determining risk factor among symptomatic study population presented with SPo2 <94% at admission

Variable	Total N = 181 (%)	Symtomatic with SpO2<94% (n = 35)	Asymtomatic /Symptomatic with SpO2 ≥94% (n= 146)	AOR (95% CI)	P value
Age years					
0 - < 1	39 (21.55)	10 (25.65)	29 (74.36)	1.6 (0.8 – 3.0)	0.153
1 - <5	58 (32.04)	13 (22.41%	45 (77.59)	1.3 (0.7 – 2.4)	0.382
5 - <10	52 (28.73)	5 (9.62)	47 (90.38))	0.4 (0.2 – o.7)	0.004

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10 - 14	32 (17.68)	7 (21.88))	25 (78.13)	1.2 (0.6 – 2.4)	0.695
Gender					
Male	116 (64.09)	22 (18.97)	94 (81.03)	0.9 (0.5 – 1.7)	0.920
Female	65 (35.91)	13 (20.00)	52 (80.00)	1.0 (0.6 – 1.9)	0.920
Region					
Urban	101 (55.80)	21 (60.00)	80 (79.21)	1.2 (0.7 – 2.1)	0.514
Rural	80 (44.20)	14 (17.50)	66 (82.50)	0.8 (0.5 – 1.4)	0.515
Comorbidity					
Cardiac disease	5 (2.76)	3 (60.00)	2 (40.00)	6.6 (1.5 – 32.8)	0.003
Respiratory	3 (1.66%)	2 (66.67)	1 (33.33)	8.6 (1.2 – 96.9)	0.015
Neurological	4 (2.21)	2 (50.00)	2 (50.00)	4.3 (0.7 – 23.7)	0.077
Gastrointestinal	2 (1.10)	1(50.00)	1(50.00)	4.2 (0.3 – 58.8)	0.356
Hematological	1 (0.55)	1 (100.00)	0	-	0.046
Severe Underweight	10 (5.52)	3 (30.00)	7 (70.00)	1.9 (0.6 – 5.4)	0.342
Neonatal jaundice	5 (2.76)	1 (20.00)	4 (80.00)	1.0 (0.1 – 5.3)	0.725
Genetic disease	2 (1.10)	2 (100.00)	0	-	0.0005
Surgical Case	10 (5.52)	2 (20.00)	8 (80.00)	1.0 (0.2 – 3.3)	0.830
Hospital stay					
<7 days	81 (44.75)	16 (19.75)	65 (80.25)	(0.6 – 1.8)	0.962
≥7 days	100 (55.25)	19 (19.00)	81 (81.00)	0.9 (0.5 – 1.6)	0.962
Complications	22 (12.15)	15 (68.18)	7 (31.82)	14.5 (6.8 – 32.3)	0.000
Death	2 (1.10)	2 (100.00)	0	-	0.0005

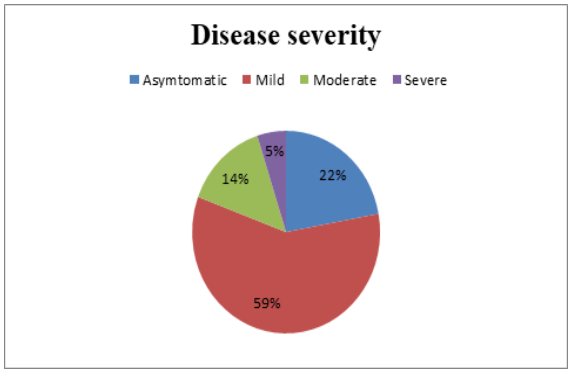

Figure 1: Categorization of disease severity among study patient at admission

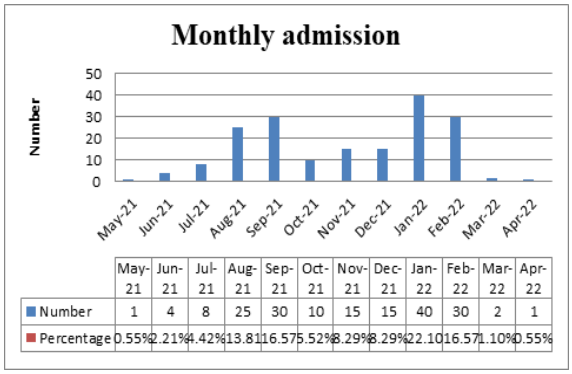

Figure 3: Monthly number of COVID-19 children admitted during the study period

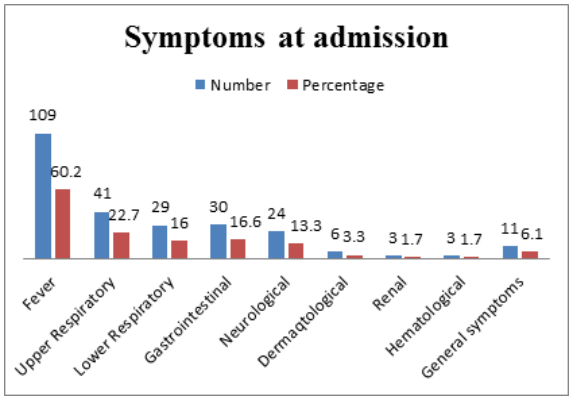

Figure 2: Distribution of symptom presentation at admission

In multivariate logistic regression analysis, the factors that remained associated with symptomatic children having SpO2 less than 94% were children younger than one year old (AOR 1.6, 95% CI0.8 – 3.0), female (AOR1.0, 95% CI 0.6-1.9), urban region (AOR 1.2, 95% CI 0.7-2.1), complications (AOR 14, 95% CI 6.8-32.3) and all the comorbidities. Table 2 Among the comorbidities, association with cardiac disease, respiratory disease, hematological and chromosomal disease are statistically significant (p-value <0.05).

DISCUSSION

Many previous studies on COVID-19 disease among adult were reported in India. However clinical data on SARS-CoV-2 infection in children are limited. Present study is the first of its kind in Manipur, Northeast India. In the present study, most commonly affected children were in the age group between 1 to 5 years. This finding is similar with a study done by Sudha Rao et al. [11] which showed the most common age group affected by COVID-19 disease was between 1 to 5 years (31.7%). In our study, male were affected more than female children. This observation is near to similar with a study done by Florian G et al.[12] Family clustering appears to play a major role in COVID-19 disease transmission Based on limited data, no confirmed cases of vertical mother to fetus intrauterine transmission of the virus have been reported thus far. Most of the children in the US data also had exposer to a patient with COVIV-19 in the household or community.[13] In the present study, the most common source of infection was from one of the family members. Poor clinical outcomes among COVID-19 infected adults are associated with a higher comorbidity burden. In US study on

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COVID -19 infected children common comorbidities defined chronic lung disease, cardiovascular disease and immune suppression.[14] Malnourished children have increase susceptibility to infection compare with normally nourish children due to immune system deficiency. The common comorbidities observed in our study were severely underweight children, cardiovascular disease and chronic lung disease which is similar with previous studies. COVID-19 symptoms in children are generally less severe than for adults with variable symptoms like fever, dry cough and gastrointestinal symptoms such as diarrhea or vomiting.[15] Majority of children in our study does not have typical COVID-19 symptoms. However, more than half of study children presented with fever at admission. Previous studies in different population in diverse settings and with varying age distribution reported that 40-70% of pediatric patient may present with fever and respiratory symptoms. In our data record respiratory symptoms represent 38.67% among the study children. This finding is similar with a study done earlier where fever (41.49%) as the most observe symptom followed by respiratory symptoms (cough) 37- 46.[16,17]

In a study done by Lu X et al,[18] 171 children with COVID-19 disease were evaluated at Wuhan Children's Hospital in China, they reported that diarrhea accounts 8.85% of patients as one of the common symptoms. In our study, the common gastrointestinal symptoms presented at admission was diarrhea (7.73%), this is similar with previous findings. In another study done by Moradveisi B et al,[19] diarrhea was the presenting symptom of COVID-19 disease in children. Among the gastrointestinal symptoms 1 case of pancreatitis was observed in our study population. NL Samies et al,[20] also observe pancreatitis as one of gastrointestinal symptoms present in COVID-19 infected children. In an international cross-sectional study on neurological symptom, 40% of 1278 children hospitalized with acute SARS-CoV-2 presented with at least one neurological manifestation and 8% presented as seizure case with encephalitis.[21] The present study showed 12.71% children presented with seizure and one of them manifest as encephalitis. Dermatological finding has been reported infrequently among children with COVID-19 infection. In our study few children presented with skin rashes including one urticarial rash. The clinical presentation of COVID-19 disease in children overlaps with other clinical symptoms in the present study only 1.7 % children presented with urinary tract symptoms and 3 children with hematological symptoms like epistaxis, vomiting blood and blood in stool. 6.10% children had nonspecific symptoms which includes malaise, weakness myalgia and fatigue. In a registry study of 176 neonates with SARS-CoV-2 infection 19 patients presented with tachypnea, 2% with rashes, 26 % feeding intolerance and 7% with irritability.[22] Among the nine neonates in our study, symptoms at presentation were tachypnea (3), rashes (1), irritability (1) and feeding intolerance (4). Though the number of neonates are small the clinical presentation is similar with the previous studies.

The most commonly reported chest-x-ray findings of COVID-19 are bilateral lung consolidation and ground glass opacity. However nonspecific findings on chest-x-ray includes unilateral ground glass opacities and consolidation, bilateral peribronchial thickening and opacities.[23] In previous multicentric study of COVID-19 infected children, 19.44% had abnormalities on chest radiograph or computed tomography.[24] Our present study observed that 9.39% children have abnormal findings as bilateral basal lung consolidation with ground glass opacities. According to previous studies, in general, 19% leucopenia, 31% lymphopenia and thrombocytopenia are noted in both adults and children.[25] In the present study abnormal blood examination findings includes 5.52% leucopenia,3.31% lymphopenia, and 4.21% thrombocytopenia. Which shows lower percentage than the previous studies as the clinical spectrum may be different in different places. Data on co-infection with bacterial pathogens among COVID-19 infected children are scarce. Our study observed that 6.63% children was associated with bacterial co-infection (2staphylococcus aureus, 3 Escherachia coli and 8 others).

Treatment of SARS-CoV-2 infection consist mainly of supportive care including respiratory support as oxygen therapy and mechanical ventilation. In the present study 31.55% required oxygen support and only one patient needed mechanical ventilator support.77.90% study children did not required respiratory support at any stage of their illness during the hospital stay. This finding is similar with the prior study done by Florian G at al.[12] More than half of study children require hospital stay for ≥7 days and majority of them were discharge without any complications. In pooled analysis from seven develop countries, the COVID-19 related death rate among children (9-19 years) was 0.17 per 100,000 population as of February 2021.[26] Our case fatality rate was 0.01% which is consistent with the previously reported (<2%) in other studies.[27]

CONCLUSION

SARS-CoV-2 infection in children posses challenges different from adults. More than two third of children included in the present study was symptomatic though disease severity is mainly of mild form. The present retrospective analysis showed higher mortality with symptomatic children having hypoxia (SpO2 <94%) at admission. Pediatric patient with COVID-19 infection come to the hospital with varied clinical symptoms. The entire health-care professional should triage patients characterizing the severity of disease spectrum and provide protocol-based management. Initiating

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prompt treatment can improved the disease outcome and reduces mortality.

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