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Original Article

Paediatrics Section

Demographic Characteristics and Outcome of Children with SARS-CoV-2 Infection Admitted in a Tertiary Care Centre in Central India- A Retrospective Study

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ABSTRACT

Introduction: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is an event of utmost importance in the medical field. It has affected the lives of millions worldwide, affecting adults more than children. But paediatric coronavirus disease is also complicated by its varied clinical presentation, difficulty in diagnosis and non availability of any rational protocol when it comes to the identification and management of cases.

Aim: To assess demographic characteristics and outcome of children with SARS-CoV-2 infection.

Materials and Methods: A single-centre retrospective hospital-based observational study was carried out among 150 children. Nasopharyngeal swabs were taken and tested using real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) for SARS-CoV-2 infection to confirm Coronavirus Disease-2019 (COVID-19). The information was collected from Medical Record Department (MRD) through Case Record Form (CRF). The clinical and laboratory features of all children (age ≥1 months to ≤12 years) were selected between 1st March 2020 to 31st October 2020 were noted and selected. The collected data was tabulated and all statistical analysis was done.

Results: Out of 150 children, 81 (54%) were male and 69 (46%) were female. Only 26 (17.3%) were symptomatic. In these 26, respiratory system involved 12 (46.2%) children, followed by acute febrile illness in 7 (26.9%) and then neurological 3 (11.6%), gastrointestinal 2 (7.7%), haematological 1 (3.8%), and cardiovascular 1 (3.8%). Co-morbidities (thalassaemia, cerebral palsy, seizure disorder and heart disease) were present in 5 (3.3%) children, in which 3 (60%) developed moderate and severe degree of illness. The treatment was given as per the protocol developed at Institutional level from Indian Council of Medical Research (ICMR), and Ministry of Health and Family Welfare (MoHFW) guidelines. One child died and the rest were discharged.

Conclusion: Majority of the children having SARS-CoV-2 infection were asymptomatic, however, few had mild illness. Furthermore, co-morbidities were contributed for severity of illness in the children affected with SARS-CoV-2 infection which leads into more vulnerable outcome.

Keywords: Coronavirus disease 2019, Indian council of medical research, Real-time reverse transcription-polymerase chain reaction

INTRODUCTION

The coronavirus pandemic took the entire world by storm, initially affecting the adult population then started affecting children too. However, there has been a significant increase in the number of paediatric COVID-19 cases, making the awareness of this disease in children of paramount importance. The mid-year 2020, there had been a prominent rise in the number of paediatric COVID-19 cases. The clinical features of COVID-19 in children include respiratory symptoms like fever, cough and cold, whereas the gastrointestinal features include diarrhoea and vomiting. But most of the infected children present to be asymptomatic as compared with adult and may contribute to transmission to other patients [1-3].

The demographic characteristics, clinical features, disease progression and outcome in children and young adults appear significantly milder compared to elderly individuals. Amongst them the percentage of disease in children was only 1-5% [4]. Due to its resemblance to Severe Acute Respiratory Syndrome (SARS), influenza, and other respiratory viruses, children were initially thought to be more susceptible than adults. However, less than 5% of total COVID-19 cases belong to the paediatric age group, and the severity has been milder as compared to adults [5]. Millions of children could be adversely affected by the COVID-19 pandemic, and it is anticipated that the greatest impact could be on those in co-morbidities and poor socio-economic groups [6,7].

Nagpur was one of the adversely affected city in central India. The study centre, being a tertiary care hospital, received many children with SARS-CoV-2 infection from local urban city area and rural area of Chattisgarh and Madhya Pradesh state during March 2020 to October 2020. Thus, the aim of this study was to evaluate the clinical profile, demographic characteristics and outcomes of children with SARS-CoV-2 infection admitted in the study centre.

MATERIALS AND METHODS

This was a single-centre retrospective study conducted to evaluate hospital records of children admitted in a dedicated COVID-19 hospital under Paediatric ward, at Indira Gandhi Government Medical College, Nagpur, Maharashtra, India from 1st March 2020 to 31st October 2020 and analysis of the data was done from January to March 2021. The Institutional Ethical Committee (IEC) approval was obtained. (Reg.No.ECR/485/Inst/MH/2013/RR-20 and IGGMC/Pharmacology/IEC/476/2020 On Dated 20/11/2020).

Inclusion criteria: Data of all children in the age group of age ≥1 months to ≤12 years tested positive for SARS-CoV-2 by RT-PCR were included in the study.

Exclusion criteria: Missing, incomplete data were excluded from the study.

The diagnosis and management of children with or at risk of COVID-19 were in accordance with guidelines provided by World Health Organisation (WHO) [8] and ICMR [9,10]. As per protocol, the children were categorised as per degree of severity [11]. Baseline laboratory parameters (complete haemogram and C-reactive protein) and, chest radiograph findings were recorded.

Data collection: The information of SARS-CoV-2 infected children was retrieved from CRFs taken though the MRD. The data including age and sex, pre-existing co-morbidities (blood disorders, developmental delays, cerebral palsy, nephrotic syndrome, details on immune therapy, malignancy, medical complexity, obesity etc.,). Cases were classified according to their mode of presentation (i.e., asymptomatic and symptomatic including respiratory, gastrointestinal, neurological and haematological). The information on clinical management-nature of respiratory support (mechanical ventilation i.e., invasive ventilation, Non Invasive Ventilation (NIV), nasal prongs, face mask, High-Flow Nasal Cannula (HFNC), oxygen therapy, or none), adjunctive respiratory support (i.e., inhaled nitric oxide and prone ventilation), and additional organ support, including vasoactive medications, plasma exchange was extracted. As per protocol developed in institute from ICMR and MoHFW guidelines included supportive care, pharmacotherapy of Hydroxychloroquine [12] (400 mg BD stat then on 1st day followed 200 mg BD for 4 days after Electrocardiogram (ECG) assessment), oral antibiotics (amoxcillin 50 mg/kg/day, cefixime 10 mg/kg/day), intravenous antibiotics (Inj. ceftriaxone 80 mg/kg/day, Inj. piperacillin 100 mg/kg/dose) and remdesivir [13,14] (body weight >40 kg-200 mg on 1st day then 100 mg once daily for 4 days and body weight 3.5 kg to 4 kg- 5 mg/kg on 1st day, 2.5 mg/kg once daily for 4 days), and life savings devices like Continuous Positive Airway Pressure (CPAP) therapy, HFNC, Bilevel Positive Airway Pressure (BiPAP) and mechanical ventilation. The drugs were used for treatment on basis of severity of the disease.

STATISTICAL ANALYSIS

The data was entered in excel sheet and results were expressed in terms of number and percentage.

RESULTS

During the study period, 704 children were admitted out of which total 150 children were detected to have SARS-CoV-2 infection as detected by RT-PCR. Amongst them one mortality was present, case fatality rate was 0.006 i.e., 0.6%.

Out of the 150 children, 81 (54%) were male and 69 (46%) were female. Total 48 (32%) children were in the age group of 1 month to 3 years [Table/Fig-1].

Age	N (%)
1 month to 3 years	48 (32)
4 to 5 years	23 (15.3)
6 to 8 years	34 (22.7)
9 to 12 years	45 (30)
Gender	
Male	81 (54)
Female	69 (46)

[Table/Fig-1]: Demographic characteristics of the study population, (N=150).

Classification of cases as per severity: Majority of the COVID-19 positive children as classified as per ICMR and MoHFW guidelines, belonged to the mild category 19 (73.07%) [Table/Fig-2].

Symptomatic	26 (17.3%)
Mild (child had fever, myalgia and other system symptoms include vomiting or loose motion)	19 (73.2%)
Moderate [O_2 support through nasal prongs, face mask and Non Rebreathing Mask (NRM)]	5 (19.2%)
Severe (vasoactive support+O_2 support using nasal prongs, face mask and NRM)	1 (3.8%)
Critical (Vasoactive support+Multi Organ Dysfunction Syndrome (MODS)+On Ventilator)	1 (3.8%)

[Table/Fig-2]: Severity of illness of the study population.

Clinical profile: A total of 124 (82.7%) children were asymptomatic and 26 (17.3%) were symptomatic. Among the symptomatics, respiratory involvement was most common 12 (46.2%) followed by acute febrile illness 7 (26.9%). Co-morbidities were present in 5 children, out of which 2 (1.33%) had seizure disorder. Thalassaemia, heart disorder and cerebral palsy were present in one (0.67%) child each [Table/Fig-3-5].

Clinical presentation	N (%)
Asymptomatic	124 (82.7%)
Symptomatic	26 (17.3%)
Respiratory (cough, cold, running nose and difficulty in breathing)	12 (46.2%)
Gastrointestinal (vomiting and loose motion)	2 (7.7%)
Neurological (headache and convulsion)	3 (11.6%)
Haematological (anaemia)	1 (3.8%)
Cardiovascular (cardiogenic shock)	1 (3.8%)
Acute febrile Illness (fever and myalgia)	7 (26.9%)

[Table/Fig-3]: Clinical presentation of the study population.

Co-morbidites	N (%)
Thalassaemia	1 (0.7%)
Cerebral palsy	1 (0.7%)
Seizure disorder	2 (1.4%)
Heart disease	1 (0.7%)
Total (Out of 150 children)	5 (3.3%)

[Table/Fig-4]: Co-morbidities of the study population.

Children with co-morbidities (n)	Severity of illness	Percentage of children with co-morbidities developing moderate or above illness
Seizure disorder (1)	Asymptomatic	3/5 (60%)
Seizure disorder (1)	Moderate	
Thalassaemia major (1)	Asymptomatic	
Cerebral Palsy (1)	Moderate	
Heart disease (1)	Severe	

[Table/Fig-5]: Severity of illness based on the co-morbidities.

The study reported mortality in one child with fever, cough, and abdomen distension, along with respiratory failure and shock since one day. The child was put on ventilator support and treatment included intravenous fluid, intravenous antibiotic, inotropes, vitamin K, Fresh Frozen Plasma (FFP). Only erythroid hypoplasia was a predisposing factor which was already diagnosed using bone marrow examination. There were no adverse outcomes among the rest of the children. These favour towards less severe presentation among children with good clinical outcome.

Clinical management: In the present study, children required oxygen supply via nasal prongs, face mask or Non Rebreathing Mask (NRM) and CPAP. Only one (3.8%) child required mechanical ventilation [Table/Fig-6].

Maximum respiratory support	N (%)
Oxygen support by Nasal prongs, Face mask and NRM	5 (19.2%)
Non Invasion Ventilation (NIV) like High flow nasal canula (HFNC)	0
NIV like Continuous Positive Airway Pressure (CPAP)/Bi-Level Positive Airway Pressure (BiPAP)	1 (3.8%)
Intubation/Ventilation	1 (3.8%)

[Table/Fig-6]: Respiratory support used.

In pharmacotherapy, 15 children received oral antibiotics, 10 received intravenous antibiotics and 1 was on hydroxychloroquine. Remdesivir or other antiviral therapy like flavipiravir and tocilizumab were not required [Table/Fig-7]. Asymptomatic children were given only multivitamin, calcium and zinc as supplement and immune-booster, vasoactive drug was given to 2 (7.7%).

Pharmacotherapy	N (%)
Hydroxychloroquine	1 (3.8%)
Oral antibiotics	15 (57.7%)
Intravenous antibiotics	10 (38.5%)
Remdesivir	0
Tocilizumab	0

[Table/Fig-7]: Pharmacotherapy used.

Outcomes: Out of 150 children, only one child (0.7%) died (cause of death was shock with disseminated intravascular coagulation, with anaemia) during the course of treatment [Table/Fig-8].

Outcome	N (%)
Discharged	149 (99.3%)
Death	1 (0.7%)

[Table/Fig-8]: Outcome of the study population.

DISCUSSION

There has been increase in number of COVID-19 disease cases in children after the onset of the same in India. According to the study done by Dong Y et al., in China, Shekerdemian LS et al., in United states (US) and Fakiri KE et al., in Morocco most of the children were asymptomatic [11,15,16]. Previously, reports from India describing the clinical profile of disease amongst children, showed that children were asymptomatic and mortality amongst them was very less [Table/Fig-9] [11,15-20].

This might be probably the largest set of data reported from central India. The study primarily emphasised on clinical profile of 150 SARS-CoV-2 infected children. The study reported male preponderance similar to those reported by others [11,15,17-20]. However, the results were in contrast with studies done by Fakiri KE et al., and Tagarro A et al., where female preponderance was seen [16,21]. This study revealed that children younger than three-year-old and 9-12 years were most commonly afflicted with the infection which was similar to other studies [15-17,22,23]. This was however, contrary to Tagarro A et al., who reported that most affected children were of a younger age group (age 1 year) [21].

In the present study, only 17.3% were symptomatic, in which respiratory system infection was most common. Neurological, haematological and cardiovascular system involvement was also seen but was smaller in number. Studies done by Shekerdemian LS et al., Rao S et al., Ramteke S et al., and Banerjee S et al., noticed findings similar to the above study [15,17,18,20]. At the same time, the study done by Sarangi B et al., found fever was the most common symptom [19], and Fakiri KE et al., noticed that respiratory symptoms and fever most commonly occurred [16].

In the present study, it was found that 5 (3.3%) children, had co-morbidities out of which seizure was the most common. Similar findings were observed by others [15-17,19,20]. The cases of co-morbidities were classified according to severity of illness as 'Mild', 'Moderate' and 'Severe'. Of which mild cases were observed in the studies by Fakiri KE et al., Ramteke S et al., and Banerjee S et al., [16,18,20]; case with moderate illness was seen in the study by Sarangi B et

Parameters	Rao S et al., [17] (n=123)	Ramteke S et al., [18] (n=30)	Sarangi B et al., [19] (n=50)	Banerjee S et al., [20] (n=41)	Fakiri KE et al., [16] (n=74)	Dong Y et al., [11] (n=731)	Shekerdemian LS et al., [15] (n=48)	Present study (n=150)
Age	<1 m age=16 (13%) 1 m-1 y=31 (25.2%) 1 y-5 y=39 (31.7%) 5 y-10 y=26 (31.7%) >10 y=11 (8.9%)	<1 y=4 (13%) 1y-4 y=3 (10%) 5y-9y=5 (17%) 9y-12y=12 (40%) >12y=6 (20%)	1 m to 1y=9 (18%) >1y-5y=15 (30%) >5y-10y=12 (24%) >10y-15y=11 (22%) >15y to 18 y=3 (6%)	<28 d=6 (14.6%) 28 d-<1 y=12 (29.3%) 1-5 y=15 (36.6%) 6-10 y=6 (14.6%) >10 y=2 (4.9%)	Median age 7 y (range, 2 m -17 y)	<1 y=86 (11.8%) 1y-5y=137 (18.7%) 6y-10y=171 (23.4%) 11y-15y=180 (24.6%) >15y=157 (21.5%)	<1y=8 (17%) 1-5 y=6 (13%) 6-10 y=7 (15%) 11-21 y= 27 (56%)	1 m-3y=48 (32%) 4-5 y=23 (15.3%) 6-8 y=34 (22.7%) 9-12 y=45 (30%)
Sex	Male- 71 (57.7%)	Male- 18 (60%)	Male- 28 (56%)	Male- 24 (58.53%)	Male- 34 (45.94%)	Male- 420 (57.5%)	Male- 25 (52%)	Male- 81 (54%)
Clinical presentation	Asymptomatic- 27 (21.9%) Symptomatic- 96 (78.1%) Respiratory upper and lower- 30 (32.5%) Fever- 24 (19.5%) Gastrointestinal- 15 (12.2%) Neurological- 13 (10.6%) others- 14 (11.4%)	Asymptomatic- 21 (70%) Symptomatic- 9 (30%) Respiratory- 11 (37%) Fever- 9 (30%) Headache- 1 (3%)	Asymptomatic- 29 (58%) Symptomatic- 21 (42%) Fever- 17 (34%) Myalgia- 4 (8%) Respiratory- 15 (30%) Gastrointestinal- 2 (4%) Headache- 2 (4%)	Asymptomatic- 11 (26.8%) Symptomatic- 30 (73.2%) Respiratory- 13 (31.7%) Fever- 9 (21.0%) cough- 5 (12.1%) Gastrointestinal- 3 (7.3%)	Asymptomatic- 54 (72.80%) Symptomatic- 20 (27.20%) Fever- 8 (10.8%) Respiratory- 8 (10.8%) Gastrointestinal- 4 (5.4%)	Asymptomatic- 94 (12.55%) Symptomatic- 637 (87.45%) -	Asymptomatic- 1 (2%) Symptomatic- 47 (98%) Respiratory- 35 (73%) Gastrointestinal- 1 (2%) Neurological- 2 (4%) Circulatory- 2 (4%) Others- 7 (15%)	Asymptomatic- 124 (82.7%) Symptomatic- 26 (17.3%) Respiratory- 12 (46.5%) Gastrointestinal- 2 (7.7%) Neurological- 3 (11.6%) Cardiovascular- 1 (3.8%) Haematological- 1 (3.8%) Fever- 7 (26.9%)

Co-morbidities	Seizure- 13 (10.6%)	-	Seizure- 1 (2%) Diabetes mellitus- 1 (2%)	Malignancy- 8 (19.5%) Haematological- 5 (2.2%) Congenital heart disease- 4 (9.7%) Neurological abnormalities- 4 (9.7%) Chronic lung disease- 2 (4.9%) Multiple congenital anomalies- 2 (4.9%)	Asthma- 2 (2.70%) Seizure- 1 (1.35%) Diabetes 1 (1.35%) Down syndrome- 1 (1.35%)	-	Diabetes- 4 (8%) Seizure- 3 (6%) Obesity- 7 (15%) Congenital heart disease- 3 (6%) Sickle cell disease- 2 (4%) Chronic lung disease- 2 (4%) Malignancy- 11 (23%) Other congenital malformations- 2 (4%)	Seizure- 2 (1.3%) Thalassaemia- 1 (0.7%) Cerebral palsy- 1 (0.7%) Heart disease- 1 (0.7%)
Severity of illness a-mild b-moderate c-severe d-critical	54 (43.9%) 26 (21.1%) 32 (26.0%) -	9 (30%) - -	20 (40%) 1 (2%) - -	14 (34.1%)	20 (27.20%) - -	315 (43.1%) 300 (41.05%) 18 (2.5%) 3 (0.4%)	14 (29%) 1 (2%) 16 (33%) 17 (35%)	19 (73.2%) 5 (19.2%) 1 (3.8%) 1 (3.8%)
Treatment given 1. Pharmacotherapy	Supportive	Supportive	Supportive	Supportive	Supportive	Supportive	Hydroxychloroquine- 21 (44%) Azithromycin- 8 (17%) Remdisivir- 8 (17%) Toclizumab- 5 (10%)	Hydroxychloroquine- 1 (3.8%) Oral antibiotic- 15 (57.7%) Intravenous antibiotic- 10 (38.7%) Remdisivir- 0 Toclizumab- 0
2. Respiratory support a-only oxygen b- NIV c-Invasion ventilation (Mechanical ventilator)	20 (16.3%) 6 (4.9%) 13 (10.6%)	- - -	- - -	10 (24.4%) HFNC-2 (4.9%) 2 (4.9%)	- - -	- - -	6 (13%) HFNC-11 (23%) CPAP/BiPAP- 4 (8%) 18 (38%)	5 (19.23%) HFNC-0 CPAP/BiPAP- 1 (3.8%) 1 (3.8%)
3. Vasoactive support	17 (13.8%)	-	-	-	-	-	12 (25%)	2 (7.69%)
Outcome a- Death b- Discharge c- Still admitted	14 (11.4%) 105 (85.4%) 4 (3.2%)	0 30 (100%) -	0 50 (100%) -	1 (2.4%) 40 (97.65)	0 74 (100%) -	1 (0.13%) 730 (99.87%) -	2 (4.16%) 31 (64.59%) 15 (31.25%)	1 (0.7%) 149 (99.3%) -

[Table/Fig-9]: Comparision of various studies demographic characteristics and outcome [11,16-20].
m: Month; y: Year; HFNC: High-flow nasal cannula

al., and severe illness were reported by others [11,15,17,19]. This shows that patients with co-morbidities had a high risk of developing moderate and severe degree of illness by COVID-19 disease.

In the present study, five (19.23%) children required oxygen by nasal prongs, face mask or NRM. However, one child (3.8%) was treated using NIV like HFNC or CPAP/BiPAP and invasion ventilation (mechanical ventilation). Similar findings were reported in a study done by Rao S et al., wherein 20 (16%) children required oxygen, 6 (4.9%) NIV like HFNC or CPAP/BiPAP and 13 (10.6%) mechanical ventilation [15,17,20].

In the current study, majority of the cases were treated with oral antibiotics 15 (57.7%), intravenous antibiotics were given in 10 cases (38.7%) and only one case was given hydroxychloroquine {1(3.8%)}. Highest percentage of usage of hydroxychloroquine {21(44%)} were noticed in the study done by Shekerdemian LS et al., [15]. Further the current study reported that vasopressor support was required for 2 (7.69%) children. However, the study by Shekerdemian LS et al., and Rao S et al., reported a higher percentage of vasopressor support usage [15,17]. Shekerdemian LS et al., used remdisivir and toclizumab for treatment in 8 cases (17%) and 5 cases (10%), respectively [15]. Drugs like remdisivir and toclizumab were not used for treatment in the present study.

Out of 150 children in this study, 1 (0.7%) child died. Studies done by others [11,15,17,20] found 1 (0.13%) died and 730 (99.87%) children were discharged, 14 (11.4%) died, 105 (85.4%) discharged and 4 (3.2%) still admitted, 1 (2.4%) died and 40 (97.6%) discharged and 2 (4.16%) died, 31 (64.59%) discharged and 15 (31.25%) still admitted respectively. From above mention studies done by others and present study showed that mortality were very little in children and some other studies showed that zero mortality in children likes Fakiri KE et al., Ramteke S et al., and Sarangi B et al., [16,18,19].

A study conducted by the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, China in 2020 [22] showed that, mortalities were more in adult, predominantly age group 50-59 years, 60-69 years, 70-79 years and >80-year-old. Similarly studies conducted by Livingston E and Bucher K in Italy, also found that mortalities were high, in the adult age groups of 70-79 years and 80-89 years and zero mortality was seen in children [23]. A study conducted by CDC COVID-19 Response Team, USA in March 2020, revealed that mortalities were higher in the adult age groups of 65-74 years and >85 years and no death were reported in children [24]. From the above mentioned studies conducted across various countries, it can be concluded that, mortality due to COVID-19 disease is higher in adults, as compared to children.

Limitation(s)

With this the limitations of this study are; firstly, it was a retrospective study. Secondly, the sample size could have been larger to draw a firm conclusion.

CONCLUSION(S)

Majority of children with SARS-CoV-2 infection remain asymptomatic having mild illness and thus have a better prognosis. Furthermore, the result of this study shows a strong relation of co-morbidities with severity of illness in the children affected with SARS-CoV-2 infection which results into more vulnerable and leads to severe or critical disease and hence special attention should be initiated in those children.

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