



PREDICTORS OF SEVERE COVID INFECTION IN PEDIATRIC POPULATION IN INDIA

Pediatrics

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ABSTRACT

Background- The study aimed to assess the epidemiological pattern of COVID 19 infection among pediatric population and to assess the risk factors associated with severe disease among this age group.

Methodology- This study was conducted as observational study on COVID 19 positive children presenting at tertiary care centre, Bhopal. Detailed history was obtained and findings of examination were noted. Necessary investigations were done. Children were categorized as having mild, moderate or severe disease based upon guideline of PGIMER, Chandigarh.

Results- A total of 209 children were enrolled. About 19.6% and 5.7% children had moderate and severe illness respectively. Odds of severe illness was significantly higher in children belonging to age >10 years, rural area, lower middle & lower socioeconomic status, comorbid conditions, Leukocytopenia, raised NLR, D-dimer, CRP and serum ferritin.

Conclusion- Identification of factors associated with moderate to severe disease is important in order to reduce the disease progression and improve health outcomes. It might be helpful in resource allocation and preparedness to combat the upcoming third wave of pandemic.

KEYWORDS

Pediatric, COVID, risk factors, severity, CRP

INTRODUCTION

The COVID 19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is infiltrated in all parts of the country, affecting individuals of all age group including neonates.^[1] Currently, India is facing second wave of infection and third wave is expected in September 2021. During the first wave of COVID 19 infection in India, children were spared, however, few cases were reported. During the second wave, children below 12 years of age were affected but as compared to other age groups, fewer children were affected.^[2] Based upon the trend of infection from other countries, third wave is expected to have its effect on pediatric population.^[3]

Approximately 1.7% to 2% of total cases are observed in children.^[4] Children with COVID 19 infection present with varied clinical features. However, approximately 10 to 20% of the symptomatic children may require hospitalization and about 1 to 3% may have severe disease requiring admission in intensive care admission.^[5] According to studies from various parts of India, various risk factors associated with COVID 19 infection include lower socio-economic status and positive household contact.^[6,7]

Though, literature is plenty regarding the epidemiological pattern and risk factors of severity of infection among adults, little is known about the pattern and predictors of infection in pediatric age group.^[8-10] The present study was therefore conducted to assess the epidemiological pattern of COVID 19 infection among pediatric population and to assess the risk factors associated with severe disease among this age group.

METHODOLOGY

The study was conducted as an observational study at COVID screening centre, COVID care centre, HDU and ICU, Chirayu Medical College and associated Hospital, Bhopal, during the study period of 3 months i.e. from 15th February 2021 to 14th May 2021. The study included all COVID 19 positive children identified by RTPCR, belonging to 2 months to 12 years of age, attending screening or admitted in our institution and whose parents or guardians giving consent for the study. However, children whose parents not giving consent for the study were excluded.

After obtaining clearance from Institute's ethical committee, all the children fulfilling inclusion criteria were enrolled. History regarding sociodemographic variables was obtained from the parents/guardians and entered in questionnaire. Detailed clinical history regarding mode of presentation, duration since symptoms, history of contact, presence of any chronic illness, and other relevant history was noted. All the

children were then subjected to detailed clinical and general examination and findings were noted. COVID profile along with routine investigations and Chest Xray were done. Children were categorized as having mild, moderate or severe disease based upon guideline of PGIMER, Chandigarh as.^[11]

STATISTICAL ANALYSIS-

Data was compiled using IBM SPSS software version 20. Univariate and multivariate analysis was done to assess the predicting factors for severe illness. P value less than 0.05 was considered statistically significant.

RESULTS

A total of 209 children fulfilling the inclusion criteria were enrolled. Mean age of children was 7.89±5.87 years.

Table 1- Distribution of children according to baseline variables

Baseline variables	No. of cases (n=209)	Percentage
Age (years)	<1	9.1
	1-5	18.2
	5-10	45.4
	>10	27.3
Sex	Boy	56.5
	Girl	43.5
Residence	Rural	59.3
	Urban	40.7
SES	Upper Middle	5.7
	Middle	16.7
	Lower middle	31.1
	Lower	46.4
Severity	Asymptomatic/ mild	74.7
	Moderate	19.6
	Severe	5.7
Comorbidities (n=72)	Present	34.4
	Hematological disorders	44.4
	CHD	11.1
	Malignancy	6.9
	Neurological abnormalities	16.7
	Multiple congenital anomalies	5.6
	Renal disorders	4.2

Endocrinological disorder	5	6.9
Chronic lung disease	3	4.2

Majority of children belonged to age range of 5 to 10 years (45.4%) and 56.5% cases were boys. Maximum children were either asymptomatic or suffered from mild infection (74.7%). About 19.6% and 5.7% children had moderate and severe illness respectively. Comorbidities were present in 34.4% children with COVID 19 infection, of them, most common comorbidities were hematological disorders (44.4%), followed by neurological abnormalities (16.7%).

Table 2- Univariate And Multivariate Analysis For Predicting Moderate To Severe Disease

Variables		Univariate analysis		Multivariate analysis	
		OR (95% CI)	P value	OR (95% CI)	P value
Age (years)	<1	Ref			
	1-5	1.02 (0.56-1.35)	0.67	1.15 (0.72-1.69)	0.54
	5-10	1.19 (0.44-2.46)	0.41	1.25 (0.69-2.29)	0.46
	>10	1.31 (0.96-2.59)	0.03	2.28 (1.18-5.38)	0.001
Sex	Boy	0.84 (0.54-1.64)	0.39	1.35 (0.62-2.94)	0.45
	Girl	Ref			
Residence	Rural	1.73 (0.6-3.5)	0.75	1.59 (1.06-3.55)	0.03
	Urban	Ref			
SES	Upper Middle	Ref			
	Middle	0.56 (0.0-9.3)	0.878	1.60 (0.7-3.76)	0.10
	Lower middle	1.37 (0.2-5.4)	0.03	2.1 (0.90-3.91)	0.02
	Lower	1.75 (0.7-2.2)	0.01	2.23 (1.3-3.28)	0.002
Comorbidities	Present	2.12 (1.10-4.6)	0.001	5.7 (1.15-17.9)	0.001
	Absent	Ref			

Univariate and multivariate analysis was conducted for predicting moderate to severe disease. Odds of severe illness was significantly higher in children belonging to age range of more than 10 years on both univariate and multivariate analysis (OR-1.31, 95% CI-0.96-2.59 and 2.28, 95% CI-1.18-5.38; $p<0.05$). However, risk of severe illness was 1.59 times higher in children residing in rural areas as compared to urban area on multivariate analysis ($p<0.05$). Lower middle and lower socioeconomic status was significantly associated with higher risk of severe illness ($p<0.05$). Presence of comorbidities were associated with higher odds of severe illness i.e. 2.12 (95% CI-1.10-4.6; $p<0.05$) on univariate analysis and 5.7 (95% CI- 1.15-17.9; $p<0.05$) on multivariate analysis.

Table 3- Univariate And Multivariate Analysis Of Laboratory Parameters Among Children With Severe Illness

Lab parameters		Univariate analysis		Multivariate analysis	
		OR (95% CI)	P value	OR (95% CI)	P value
Hemoglobin (gm/dl)	<10	0.8 (0.5-1.3)	0.51	0.63 (0.03-1.13)	0.56
	>10	Ref			
TLC (cells/cumm)	<4	1.39 (0.81-2.7)	0.006	1.91 (0.96-3.44)	0.001
	4-11	Ref			
	>11	0.88 (0.39-1.65)	0.76	1.2 (0.69-2.1)	0.38
NLR	<1	Ref			
	>1	1.44 (1.09-3.01)	0.001	2.54 (1.08-3.88)	0.001
Platelet ($\times 10^9/L$)	<1.5	0.56 (0.27-1.16)	0.57	0.93 (0.66-1.51)	0.35
	>4	0.54 (0.22-1.03)	0.54	0.69 (0.26-1.71)	0.32
	1.5-4	Ref			
ESR (mm/h)	<50	Ref			
	>50	0.76 (0.25-1.9)	0.26	0.89 (0.46-1.31)	0.15
D Dimer ($\mu g/mL$)	<10	Ref			
	>10	2.92 (1.44-3.23)	0.001	4.15 (1.6-15.8)	0.001
CRP (mg/dl)	<10	Ref			
	>10	1.67 (1.05-2.29)	0.001	3.16 (1.01-5.12)	0.001

Ferritin (ng/ml)	<500	Ref			
	>500	1.33 (1.0-3.91)	0.027	2.1 (1.2-4.1)	0.018

In present study, odds of severe illness was significantly higher in children with leukocytopenia, raised NLR, raised D-dimer, CRP and serum ferritin level on both univariate and multivariate analysis ($p<0.05$), as depicted in table 3.

DISCUSSIONS

SARS-CoV is one of the dreadful pandemic, affecting all the sections of society in every corner of the world. However, in the presence of this highly infectious illness, identification of epidemiological pattern and assessing laboratory characteristics especially in pediatric population is essential to predict the severe illness and determine the prognosis. In present study, a total of 209 children were included with mean age of 7.89 ± 5.87 years. Children with infection presented with varied clinical manifestation, predominantly involving respiratory system similar to adults. Based upon mode of presentation, children categorized as having asymptomatic / mild infection, moderate illness and severe illness.^[11] About 74.7% children had mild or no symptoms whereas 19.6% children had moderate and only 5.7% children had severe illness. However, Zhou et al, documented severe infection in 75% children.^[12] MoHFW also stated that approximately 1 to 3% children may present with severe illness and require admission in ICU.^[5]

We observed that children belonging to more than 10 years of age had higher risk of moderate to severe illness, as compared to younger children. The higher risk of infection among older children could be attributed to the transition into adolescence during which nutritional demand increases. Younger children usually play at home, where chances of infection may be low. However, older children tend to play with their peer group and infection rate may be high as well as chances of infection varied strain may lead to severe disease among them. Whittaker et al also documented higher risk of severe illness among children of older age as compared to younger age.^[13]

In present study, children residing in rural area presented with severe illness as compared to children residing in urban area. Health care services are sub-optimal in rural areas and amidst lockdown, transportation facilities are affected and parents or guardians had to look for alternate option to reach the health care facilities. This led to delay in reaching the health care facilities and getting appropriate treatment. Also, patients prefer to seek medical care from traditional healers, this further contribute to delay in seeking appropriate health care. Lower and lower middle socioeconomic status was associated with severe illness in our study. Our study findings were concordant with findings of previous studies, in which incidence of COVID 19 infection was higher in lower-income individuals. As COVID 19 infection spread mainly via respiratory route, lower socioeconomic status is associated with ill-ventilation, overcrowding; which further contribute to spread of COVID 19 infection. Also, poverty is associated with poor health outcomes and greater rates of pediatric ICU admissions in general.^[14,15]

About 34.4% children presented with comorbidities in our study irrespective of severity of infection. Our study documented that pediatric comorbidities were significantly associated with higher odds of severe illness among pediatric age group of population. Previous literature suggest that comorbidities in children such as cardiovascular disease, chronic lung diseases, chronic kidney disease, immunosuppression, obesity, and sickle cell disease are predisposing factors associated with unfavorable clinical outcome and increased risk of death.^[16,17]

Hematological parameters may help in predicting the severity of disease among pediatric population. In our study, lower WBC count, raised NLR, D-dimer, CRP and serum ferritin level levels were associated with severe illness in children. These findings were supported by findings of Fernandes et al in which raised ferritin, D dimer, CRP and LDH levels were associated with severe infection.^[18] Raised D-dimer reflects hypercoagulability, which could be due to increase in systemic pro-inflammatory cytokine responses which further contribute to atherosclerosis, plaque rupture. These activities has been associated with local inflammation and lead to induction of procoagulant factors.^[19] However, CRP levels indicates inflammatory activity and may enhance phagocytosis by activating complement system.^[20] Serum ferritin levels may suggest immune dysregulation and hyperferritinemia has direct immunosuppressive and pro inflammatory effects. All these factors lead to cytokine storm, the

underlying pathology of severe illness.^[21]

Our study has certain limitations, all the investigations such as LDH, BNP, IL-6 could not be done due to resource constraints. Outcome of children could not be assessed due to its cross sectional nature.

CONCLUSION

Children are susceptible to COVID infection and may present with varied clinical symptoms. Various factors such as older age, residence, socioeconomic status, comorbidities, and laboratory markers are helpful in predicting the severity of infection. Identification of factors associated with moderate to severe disease is important in order to reduce the disease progression and improve health outcomes. Also, it might be helpful in resource allocation and preparedness to combat the upcoming third wave of pandemic.

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