



Original Research Article

Clinical profile and outcome of COVID-19 in children with comorbidity in a tertiary care teaching hospital: An observational study

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in majority of children manifests as mild to moderate illness and low rate of severe/critical illness/fatality. There is limited information about the SARS-CoV-2 infection, clinical profile and outcome in children with comorbid conditions.

Objective: To analyze the clinical profile, severity and outcome of COVID-19 in children with and without comorbidity.

Study design: An observational study was conducted in the pediatric unit of tertiary care hospital. Children between 1-12 years with positive RT PCR report for COVID-19 were included. All admitted children were classified into comorbidity and without comorbidity groups. They were assessed clinically, categorized as mild, moderate and severe based on Ministry Of Health and Family Welfare (MOHFW) guidelines and Outcomes were measured.

Categorical variables were compared using Chi-square test and Proportions were compared using Fisher's Exact test. Probability (p) value less than 0.05 was taken as significant.

Result: Fever (100%) was the most common presentation, followed by cough (61.8%). Respiratory distress (41.6%) and hypoxia (37.5%) were the significant (p value <0.05) respiratory manifestations in children with comorbidity. Mean duration of hospital stay was longer for children with comorbidities (10.25days) compared to those without comorbidities (7.93days). Children with comorbidity, 50 % of them required respiratory support and 41.6% had severe COVID-19. Children without comorbidity, 19.35% needed respiratory support and same had severe COVID-19. Our study shows mortality of 0.5% in COVID-19 children.

Conclusion: COVID-19 in comorbid children had a statistically significant impact on clinical presentation but no impact on outcomes of disease.

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1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents causes mild symptoms and fewer deaths than adults.¹ The World Health Organization [WHO] scientific brief on coronavirus disease (COVID-19) in children and adolescence stated that children less than 5 years old and children between

5 to 14 years accounted for 1.8% & 6.3% of global cases respectively and 0.1% of global deaths.² Children of all ages are susceptible to COVID-19 and clinical presentation varies from asymptomatic to critical illness like shock, multiorgan dysfunction.³ The biological mechanisms for the age-related differences in severity are still under investigation but hypotheses include differences in the functioning and maturity of immune systems in young children compared with adults.⁴

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Severe illness risk from COVID-19 increases in adults of any age with certain underlying medical conditions.⁵ A systematic review and meta-analysis of 42 studies containing 275661 of comorbid children and 9353 of children without comorbidities concluded that children with comorbidities have a higher risk of severe COVID-19 and associated mortality than children without underlying disease.⁶ There have been only few studies available in India on the impact of pediatric comorbidities on the severity of COVID-19 in children. Dipti Kapoor et al study concluded that there is no impact on outcome of COVID-19 in children with comorbidity.⁷ A retrospective study conducted in Northern India among 2919 children with suspected SARS- CoV-2 illness concluded that COVID-19 was asymptomatic / mild in two-third of infected children and the adverse outcomes were more commonly seen in infants and children > 10 years of age with malnutrition and comorbid illness.⁸ Our knowledge about COVID-19 Clinical manifestations and Severity in children with comorbidities is limited. Hence a study was proposed to analyze the Clinical profile and Outcome of COVID-19 in children, with comorbidity and without comorbidity.

2. Materials and Methods

A prospective observational study was conducted during the second wave of SARS-COV-2 illness in the pediatric department of Gandhi hospital for a period of 4 months from April 2021 to July 2021. Institutional Ethical committee approval was taken. All admitted children between 1 month to 12 years of age with positive RT PCR (Real time reverse transcription-polymerase chain reaction) for SARS-COV-2 illness were included in the study and detailed history, examination were done, after obtaining oral consent from the parents. Children with Asymptomatic/ Mild COVID- 19 disease were not included in this study.

Children who were RT PCR negative for SARS-COV-2 illness, Children who succumbed to death in less than 6 hours of admission were excluded from the study. Comorbidity was defined as any distinct additional, acute or chronic condition that has existed or may occur during the clinical course of a patient who has the index disease under study, and might alter the course of disease or the outcome.⁴ Children were categorized as Mild, Moderate and Severe COVID-19 disease based on clinical presentation as per MOHFW (Ministry of Health and Family welfare), Government of India.⁹ Hematological investigations including complete blood picture, inflammatory markers for COVID-19, Liver function test, kidney function test and serum electrolytes were done for all children. CT chest and cardiac workup were done, when needed. Children were categorized into two groups; one group was children with comorbidities and another group was children without comorbidities. Clinical features, laboratory parameters were compared in both the

groups. All children were treated for COVID-19 disease as per the MOHFW guidelines and as per unit protocol for existing comorbidity. COVID-19 outcomes measured in terms of disease severity, duration of hospital stay, need of respiratory support and mortality.

2.1. Statistical analysis

Categorical variables were compared using Chi-square test and Fisher's Exact test. Probability(p) value less than 0.05 was taken as significant.

3. Results

Total 597 RT PCR positive children were evaluated during the study period. Out of 597, 72 children were admitted and 525 (87.93%) children were treated in home isolation. Among 72 children, 55 children fulfilled the inclusion criteria and 17 children were excluded from study. All age groups were equally affected with COVID-19 disease in this study, 75 % of children with comorbidity were found in the age group of 6-9 years and the difference was statistically significant ($p < 0.05$) compared to children without comorbidity as shown in Table 1. The mean age in the study was 5.3 years with male preponderance (64.9%). The percentage of comorbid children in the study group was 43.63% (24) and the most common comorbidities were central nervous system abnormality (20.8%) and coinfections (20.8%). Next common comorbidity was malignancy (16.6%) followed by renal (12.5%) and hematological (12.5%) diseases.

Fever was the most common clinical symptom (100%) at presentation, followed by cough (61.8%). Respiratory distress (41.6%) and hypoxic (37.5%) were the significant (p value- < 0.05) respiratory manifestations observed in children with comorbidity. Gastrointestinal symptoms were more common in children without comorbidity but the difference was not statistically significant. Children with comorbidity had a statistically significant difference in proportions of Anemia ($p = 0.0147$), thrombocytopenia ($p = 0.01$), abnormal Chest x-ray ($p = 0.0410$) and Hyponatremia ($p = 0.0461$) as shown in Table 2.

Mean duration of hospital stay was longer for children with comorbidities (10.25days) compared to those without comorbidities (7.93days). Severe COVID-19 disease was seen in 41.6% of children with comorbidity and 19.35% of children without comorbidities. Respiratory support in the form of low flow O₂ requirement was seen in 37.5% children in the comorbid group and 16.12% of children in the non-comorbid group. HHFNC (Heated, Humidified High-flow Nasal Cannula) and invasive ventilation required for 12.5% and 8.3% of children in the comorbid group when compared to 3.2 % of children in the non-comorbid group. Out of 24 children with comorbidity, 3 children (12.5%) succumbed and mortality was not seen in the non-comorbid

Table 1: Age wise distribution of Children with COVID-19.

Age group in years	Total No. of children N=55 (%)	No. of children with comorbidity. N=24(%)	No. of children without comorbidity. N=31(%)	P-Value
<1	14 (25.45)	2 (14.2)	12 (85.7)	0.0069
1-5	15 (27.27)	7 (46.66)	8 (53.33)	0.715
6-9	12 (21.81)	9 (75)	3 (25)	0.0371 (<.05)
10-12	14 (25.45)	6 (42.8)	8 (57.14)	0.45

Table 2: Comparison of clinical presentation and laboratory manifestations of COVID-19 in children with and without comorbidities.

Parameter		No of children with comorbidity N=24(%)	No of children without comorbidity N=31(%)	p-value
Mean Age in years	5.3	6.6	4.2	
No of male children (%)		14 (58.3)	23 (74.19)	0.308
Symptoms admission	Fever	24(100)	31 (100)	
Respiratory manifestations	Cold	6 (25)	12 (38.7)	0.297
	Cough	16 (66.6)	20 (64.51)	0.86
	Respiratory Distress	10 (41.6)	5 (16.12)	0.0459(<0.05)
	Hypoxia (Spo2 <94)	9 (37.5)	2 (6.45)	0.016(<0.05)
	Altered sensorium	3 (12.5)	2 (6.45)	0.43
Centra Nervous System	Seizures	4 (16.6)	5 (16.12)	0.95
Centra Nervous System	Vomiting	4 (16.6)	7 (22.58)	0.59
	Diarrhea	1 (4.16)	5 (16.12)	0.202
	Pain abdomen	0 (0)	2 (6.45)	
Laboratory parameters				
Anemia (Hb ^a < 2SD for age in g/dl)	16 (16.6)	10 (32.25)	0.0147(<0.05)	Anemia (Hb ^a < 2SD for age in g/dl)
Leucopenia (< 4.0 ×10 ⁹ /L)	9 (37.5)	5 (16.12)	0.0832	Leucopenia (< 4.0 ×10 ⁹ /L)
NLR ^b >3	6 (25)	4 (12.90)	0.258	NLR ^b >3
Thrombocytopenia (<1.5 lakh / μL)	10 (41.6)	2 (6.45)	0.01(<0.05)	Thrombocytopenia (<1.5 lakh / μL)
Elevated CRP ^c > 5 mg /L	8 (33.3)	5 (16.12)	0.147	Elevated CRP ^c > 5 mg /L
Abnormal Chest X-ray	8 (33.3)	3 (9.67)	0.04(<0.05)	Abnormal Chest X-ray
Hyponatremia (serum Sodium < 135 mEq/L)	12 (50)	7 (22.58)	0.04(<0.05)	Hyponatremia (serum Sodium < 135 mEq/L)

^aHB-Hemoglobin, ^bNLR- Neutrophil lymphocyte ratio, ^cCRP- C-reactive protein.

Table 3: Comparison of COVID-19 outcome between children with and without comorbidities.

Outcome	No. of children with comorbidity. N=24(%)	No. of children without comorbidity. N=31(%)	P-value
Duration of hospital stay	10.25 days	7.93 days	0.103
Severe COVID-19 disease	10 (41.6%)	6 (19.35%)	0.372
Low flow O2 requirement	9 (37.5%)	5(16.12%)	0.07
Humidified High flow nasal cannula support (HHFNC)	3 (12.5%)	1(3.2%)	0.18
Invasive ventilation	2 (8.3%)	1(3.2%)	0.42
Death	3 (12.5%)	0 (0)	0.073

group in the present study. But these findings were not statistically significant ($p < 0.05$) as shown in Table 3. The overall mortality was 0.5% (3 out of 597) for total COVID-19 positive children with and without admission.

4. Discussion

Study was conducted during the second wave of SARS-CoV-2 illness in a designated COVID center for all age groups in the state of Telangana. India witnessed a sharp increase in the number of cases in the second wave with the peak being over 4 lakh new cases a day of SARS-CoV-2 illness. The number of Children and adolescents with COVID-19 have also increased.¹⁰ As per available literature, most of the infected children were asymptomatic or had mild symptoms and COVID-19 was severe or critical in 4% of children.¹¹ However some children are at risk of developing severe disease including hospitalization, requiring invasive ventilation and death.³ In our study 87.93% of children were asymptomatic / had mild symptoms and 12.07% of children admitted in hospital (72 out of 597) because of their symptoms and underlying comorbidity. Studies have found that risk of severe disease outcomes were seen in individuals with some underlying medical complexity^{12,13} and having more than one pre-existing comorbidity is associated with an increased risk of disease.^{13,14}

In the present study, all age groups were almost equally affected with COVID-19 and the mean age was 5.3 years. A systematic review and Meta-analysis of children with COVID-19 from 31 countries conducted between 1 December 2019 to 8 January, concluded that the mean age was 7 years.¹⁵ The difference in mean age is probably due to changing admission criteria as per MOHFW in the first and second wave of SARS-CoV-2 infection. The male predominance in the present study was consistent with other studies.¹¹ The comorbidity was 43.6%, which was similar to a study conducted by Dipti Kapoor et al⁷ and the most common comorbidities found in this study were CNS abnormality and coinfections.

The most prevalent symptom in the present study is fever followed by cough. Clinical presentation of COVID-19 in this study was not different from other studies and a systematic review of 38 studies containing 1124 cases.^{7,11,16} However, children with comorbidity were presented with Respiratory distress and hypoxia and need of respiratory support was more than children without comorbidity. Retrospective review of case records of 50 admitted children from New-York city showed obesity (22%) was the most common comorbidity and 32% of children required respiratory support.¹⁷ A study on the effect of COVID-19 in five children with comorbidity showed that fever and tachypnea (60%) was the most common symptom on admission and 60% of patients required respiratory support.¹⁸

Anemia and thrombocytopenia were significantly higher in children with comorbidity. The results were in contrast to study by Dipti Kapoor et al,⁷ the reason being proportion of malignancies and hematological abnormalities cases on variables noted in present study. Children with comorbidity were also found to have dyselektrolytemia (serum Sodium < 135 mEq/L) similar to study done by Gheorghe Gina et al¹⁹ in adults and data not available in children for comparison. Hence, further studies are needed to validate this finding of our study.

Outcome of COVID-19 disease measured in the form of duration of stay, severity of disease and requirement of Oxygen, have not shown any statistical difference in between children with and without comorbidity.

Mortality rate of COVID-19 disease varies from country to country and also with underlying comorbidity status.^{20,21} A systematic review and metaanalysis concluded that children with pre-existing conditions are at a greater risk of severe COVID-19 and associated mortality.⁶ The mortality rate was 0.03% (77 children) across 8 studies out of 19 studies, of the 274,647 children with COVID-19 and 1.5% (134 children) died of the 8960 children with pre-existing comorbidity across 15 studies.⁶

Three deaths were reported during the study period so that no analysis could not be done for this outcome. The overall mortality in this study was 0.05%, comparable to the reported mortality rate globally. All three deaths were seen in comorbid children in the age group of 6-9 years with mean age of 7.6 years. Among them two were males and one female. The comorbidities were global developmental delay with seizures for two cases and Thalassemia in one case. All three cases were admitted with respiratory distress and hypoxia and succumbed to death with acute respiratory distress syndrome and shock. Similar to the present study as a cause of death, Dewi and her colleagues reported that two of the most common causes of death were acute respiratory distress and septic shock in a study of COVID-19 deaths in children at a hospital in Indonesia.²²

Limitations of the present study include having small sample size, done in hospital setting and diversity in comorbidities of children. As a result, finding of the study may not be applicable to the general population.

5. Conclusion

Our study concluded that COVID-19 in comorbid children had a statistically significant impact on clinical presentation but no impact on outcomes of disease. Early intervention may improve outcomes. Hence these children should be considered as high risk and COVID etiquettes to be emphasized to their guardians and parents.

6. Conflict of Interest

None.

7. Source of Funding

None.

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