

Clinical Profile and Outcome of COVID-19 Among Immunocompromised Children

This retrospective study describes the clinical profile, risk of infection and outcome of coronavirus disease-19 in immunocompromised children. It was found that children on immunosuppressant medication has 2.89 times increased risk of infection ($P=0.01$). Disease manifestation was asymptomatic ($P=0.01$) or mild with predominant gastrointestinal symptoms ($P=0.02$) without alteration in immunosuppressive treatment regime.

Key words: COVID-19, Children, Immunocompromised, Outcome.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children manifests as mild to moderate disease with low fatality [1]. There is limited information about susceptibility to SARS-CoV-2 infection, clinical profile and outcome among immunocompromised children in India. Published literature has revealed milder disease and favorable outcome without discontinuation of immunosuppressive medication in these children [2-6]. We, herein describe the clinical features and outcome of immunocompromised children diagnosed with SARS-CoV-2 infection at our center.

This was a retrospective analysis of data from 1 June to 31 October, 2020 at a tertiary care center of a teaching hospital. The analysis was approved by institutional ethics committee. All children admitted during the study period were screened for SARS-CoV-2 infection and those who were diagnosed with coronavirus disease 19 (COVID-19) were classified into immunocompromised and immunocompetent. All immunocompromised children in the present study were either on anticancer drugs or immunosuppressive therapy for kidney diseases, and fulfilling criteria for immunocompromised state [6]. The variables extracted from the hospital records were age, gender, presenting symptoms, complications, severity of illness, diagnosis, laboratory investigations, imaging findings, treatment and outcome. The diagnosis of COVID-19 was made by positive reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2. The severity of illness was classified as per guidelines given by Ministry of Health and Family Welfare, Government of India [7], and children were treated as per unit protocol without alteration in immunosuppressive treatment regime. Proportions were compared using Fisher exact test.

Data of 409 children were extracted during the study period; 162 (39.6%) of these were immunocompromised. Of the 409 children, 26 (6.3%) were diagnosed with SARS-CoV-2. Data of one child was incomplete and he was excluded from the analysis. The proportion of SARS-CoV-2 positivity in immunocompromised and immunocompetent children was 16 (9.9%) and 9 (3.6%), respectively [OR (95% CI) 2.89 (1.24-6.73); $P=0.01$]. Comorbidities were present in 184 (44.9%) children, mainly malignancy in 78 (18.9%) and nephrotic syndrome (NS)

Table I Clinical Profile and Outcome of Children with SARS-CoV-2 Infection

Variables	Children with COVID-19	
	Immuno-competent (n=9)	Immuno-compromised (n=16)
Comorbidity ^a	5	16
Severity of illness		
Asymptomatic ^b	0	8 (50)
Mild	0	3 (18.7)
Moderate	5 (55.5)	3 (18.7)
Severe (n=6)		
Septic shock	4 (44.4)	2 (12.5)
ARDS	2 (22.2)	1 (5.9)
Clinical features		
Fever	9 (100)	7 (43.7)
Cough and difficulty in breathing	8 (88.8)	3 (18.7)
Diarrhea and vomiting	0	7 (41.1)
Convulsion and altered sensorium	3 (33.3)	0
Abdominal pain	2 (22.2)	5 (29.4)
Treatment ^d		
Hospitalization	9 (100)	8 (50)
Oxygen	4	2
Vasopressor requirement	4	2
Died	2 (20)	2 (12.5)

Data presented as no. or no. (%). ^aImmunocompetent: 1 each with thalassemia, Wilson disease, diabetes, epilepsy and congenital hydrocephalous with shunt; Immunodeficient: 8 children with nephritic syndrome, 2 with Non-Hodgkin lymphoma and 1 each of Hodgkin lymphoma, acute lymphoblastic leukemia, acute myeloid leukemia, myelodysplastic syndrome, aplastic anemia and retinoblastoma, ^dOnly one immunocompetent patient required ventilation.

in 67 (16.3%). The clinical profile and outcome of children with COVID-19 is shown in **Table I**. All children with severe COVID-19 disease had features of sepsis and shock; however, 3 children had acute respiratory distress syndrome (ARDS). Only 12 children with COVID-19 underwent blood biochemistry, and reports revealed anemia ($n=6$), leucopenia ($n=5$), neutrophil-lymphocyte ratio >3 ($n=5$) and thrombocytopenia in 3 children. High resolution computed tomography of chest showed ground glass opacities in two and air-bronchogram in three children. One child presented with severe abdominal pain and computed tomography of abdomen was suggestive of pancreatitis, he also had elevated amylase (217 μ /L) and lipase (365 μ /L).

Immunocompromised children had a significantly higher risk of SARS CoV-2 infection which may be due to the need of frequent hospital visits for their medications (chemotherapy), which exposed them to get infection. However, they had a lower hospitalization rate [8 (50%) vs 9 (100%), $P=0.01$] as compared to immunocompetent children possibly because of day care

treatment protocol. The occurrence of disease was lesser in immunocompromised children, with most being either asymptomatic or with mild disease, and with complete recovery. It is possibly due to weaker immune response under the influence of immunosuppressants. Similar observations were reported in a survey conducted in 25 countries (>200 children tested and 10000 at risk) among children on anticancer treatment [8] and in a systematic review of 16 articles (100 adults, 10 children) by Minotti, et al. [5], which concluded that these children had asymptomatic or mild disease, and had a favorable outcome. Severe disease manifestations and requirement of intensive care, respiratory support, and inotropes were comparable between the two groups. Overall mortality was 16% and this might be a reflection of high incidence of non-COVID sepsis and associated complications in these patients. In a study on 113 children with kidney diseases receiving immunosuppressive medications from 30 countries; authors found that only 9.7% had severe grade of disease [3]. Features of relapse, or new organ involvement (pancreas) or new onset glomerulonephritis have been seen in children with nephrotic syndrome in present study and this might be like other viruses, SARS Co-V-2 infection may also precipitate relapses or infect new organ [9,10].

The present study has few limitations, one being retrospective analysis and small sample size, and short term follow-up. Additionally, admitting policy kept on changing during the study period depending on government guidelines. We conclude that children with immunosuppressant medication are at an increased risk of SARS Co-V-2 infection, and disease manifestations may be asymptomatic or mild with predominantly gastrointestinal symptoms.

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