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Comparison of Clinical Outcome between Immunocompetent and Immunocompromised Children Aged 1 to 12 Years Admitted with Acute COVID-19 Infection – A Retrospective Review

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Abstract

The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created havoc in adults and children. Immunocompromised children are considered a high-risk group for the extreme manifestation of coronavirus disease 2019 (COVID-19) infection. There are conflicting reports on the outcome of SARS-CoV-2 disease in immunocompromised children. We aimed to find the difference in clinical outcomes of COVID-19 infection between immunocompetent and immunocompromised children. This includes a retrospective chart review of children admitted with COVID-19 infection in a tertiary care pediatric hospital in Northern India from March 1, 2021, to May 31, 2021. There were 35 COVID-19-positive children aged 1 to 12 years admitted during the study period. The study participants were divided into two groups: immunocompetent and immunocompromised patients. The clinical features, laboratory parameters, treatment needs, and outcomes in both groups were compared. Among 35 patients enrolled, 17 were immunocompromised and 18 were immunocompetent. The median duration of hospital stay, clinical features, laboratory parameters, severity of illness, treatment needs, and outcomes were comparable between the two groups. Immunocompromised children are not at a higher risk of severe COVID-19 manifestation compared to immunocompetent children.

Keywords
- immunocompromised
- immunocompetent
- COVID-19

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is responsible for over 170 million cases and over 3 million deaths.[1] Coronavirus disease 2019 (COVID-19) manifestation ranges from mild to severe symptoms like acute respiratory distress syndrome, septic shock, multiorgan failure, and death.[2] COVID-19 manifests in two phases – the first acute viremic phase followed by a hyperimmune phase.[3,4] Immunosuppression enables uncontrolled viral replication, causing severe disease in patients with a compromised immune response either due to disease or cytotoxic therapy.[5] Severe COVID-19 is also associated with cytokine release syndrome and secondary hemophagocytic lymphohistiocytosis.[6] Since the immune system of immunocompromised patients is suppressed, it is still unclear whether COVID-19 infection is associated with intense cytokine release.[7] It is still unclear whether immunocompromised patients are at higher risk of the disease with

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Table 1 Comparison of socio-demographic characteristics between immunocompromised and immunocompetent groups

Socio-demographic characteristics	Immunocompromised	Immunocompetent	Total	*p*-Value
Age (years)	7.26 ± 3.28	6.06 ± 5.22	6.35 ± 4.84	0.265[a]
Duration (days)	16.25 ± 15.97	10.02 ± 9.26	11.51 ± 11.4	0.056[a]
Gender				
Female	6 (35.29%)	21 (38.89%)	27 (38.03%)	0.79[b]
Male	11 (64.71%)	33 (61.11%)	44 (61.97%)	

[a]Independent *t*-test.
[b]Chi-square test.

increased severity, atypical manifestations, or conversely, whether they are protected from intense cytokine storms.

Immunocompromised patients suffer a greater risk of acquiring severe COVID manifestations than the general population and an overall increase in mortality by 5 to 6%.[8,9] Patients with hematological malignancies have a more significant increase in a fatality rate of 37% amongst them.[10]

With this background, we reviewed all the cases admitted from March 1, 2021, to May 31, 2021, and studied their clinical profiles, manifestations, and outcomes.

Methodology

All the COVID-19-positive children aged 1 to 12 years admitted to a tertiary care super specialty hospital from March 1, 2021, to May 31, 2021, were enrolled. SARS-CoV-2-positive cases were identified using reverse transcription-polymerase chain reaction and they were divided into two groups. The first group included patients who did not have cancer, categorized as immunocompetent children. The other group included those patients who had cancers; such as acute lymphoblastic illness, acute myeloid leukemia, and solid organ cancers. These children were categorized as immunocompromised patients. Their treatment records were studied and compared to evaluate the chief differences in their clinical presentation, course during the disease, duration of positivity, laboratory findings, and clinical outcome.

Inclusion criteria: all children aged between 1 month and 12 years tested COVID positive from March 1, 2021, to May 31, 2021.

The total number of children admitted during the study period was 38, out of which three children were excluded on account of being less than 1 month of age. Among 35 children, 17 were immunocompromised and 18 were immunocompetent.

Statistical Analysis

The categorical variables were presented in the form of numbers and percentages (%). On the other hand, the quantitative data with normal distribution were presented as the means ± SD. The data normality was checked by using the Kolmogorov-Smirnov test. In cases where the data was not normal, we used non-parametric tests. The data entry was done in the Microsoft EXCEL spreadsheet, and the final analysis was done using Statistical Package for Social Sciences software, IBM manufacturer, Chicago, United States, version 21.0.

A *p*-value of less than 0.05 was considered statistically significant.

Results

The distribution of gender was comparable between the immunocompromised and immunocompetent groups (female: 35.29 vs. 38.89%, respectively, male: 64.71 vs. 61.11%, respectively) ($p = 0.79$). The mean age in the immunocompromised group was 7 years, and in the immunocompetent group was 6 years, with no significant difference between them ($p = 0.265$). The mean ± SD of duration in the immunocompromised group was 16.25 ± 15.97 days and in the immunocompetent group was 10.02 ± 9.26 days with no significant difference between them ($p = 0.056$). It is shown in ►**Table 1**.

The incidence of vomiting was significantly higher in the immunocompetent group (25.93%) than in the immunocompromised group (0%) ($p = 0.016$). The distribution of clinical features was comparable between the two, as shown in ►**Fig. 1**.

A comparison of the differences in the laboratory parameters between immunocompetent and immunocompromised patients is shown in ►**Table 2**.

The need for oxygen via a mask, ventilator requirement, and antibiotic need was comparable between the two groups, as shown in ►**Fig. 2**.

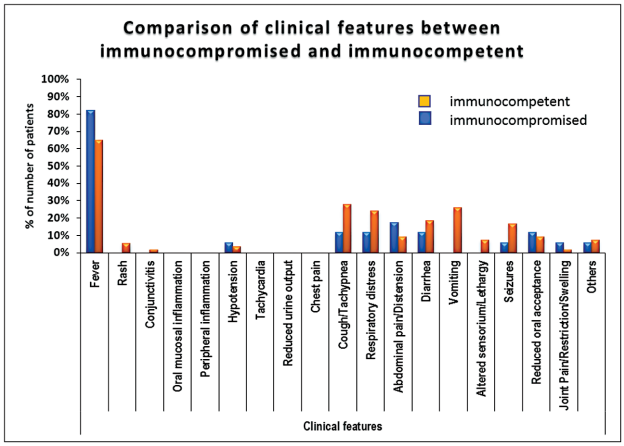

Fig. 1 Comparison of clinical features between immunocompromised and immunocompetent groups.

The distribution of outcomes was comparable between immunocompromised and immunocompetent patients (admitted: 0 vs. 2.27%, respectively, death: 25 versus 13.64%, respectively, discharge: 75 vs. 84%, respectively) ($p = 0.761$).

Discussion

In our study, there are no significant differences between the immunocompetent and immunocompromised children infected with COVID-19 infection in terms of their clinical features, duration of illness, laboratory parameters, and clinical outcomes. We were able to enroll an equal number of immunocompromised and immunocompetent patients. The number of immunocompromised patients with COVID-positive is higher in our center as our center is one of the referral hospitals for northern India and has continued super specialty services during the COVID pandemic.

In our study, the most common symptom with which the patients presented was fever. Fever was present in 82% of immunocompromised and 64% of immunocompetent patients. No significant difference in the comorbidities in either of the groups was present. No significant difference

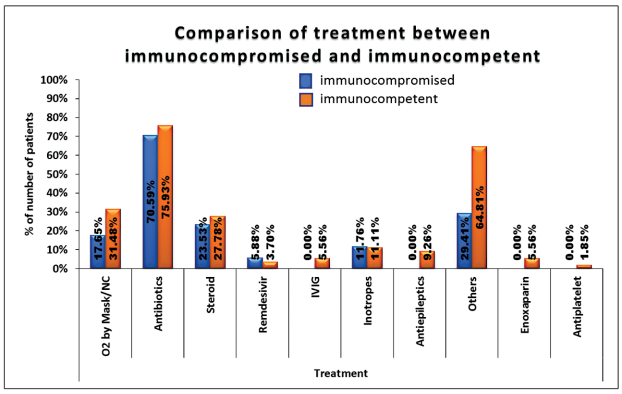

Fig. 2 Comparison of treatment between immunocompromised and immunocompetent groups.

Table 2 Comparison of laboratory parameters between immunocompetent and immunocompromised groups

Laboratory parameters	Immunocompromised	Immunocompetent	Total	*p*-Value
Troponin T				
Negative	1 (100%)	0 (0%)	1 (33.33%)	0.333[b]
Positive	0 (0%)	2 (100%)	2 (66.67%)	
Anemia				
No	8 (47.06%)	14 (34.15%)	22 (37.93%)	0.356[c]
Yes	9 (52.94%)	27 (65.85%)	36 (62.07%)	
ESR (mm/h)	51.5 ± 12.02	52.29 ± 20.89	52.11 ± 18.58	0.962[a]
CRP (mg/L)	11.6 ± 12.62	7.6 ± 12.34	8.6 ± 12.3	0.467[a]
IL6 (pg/mL)	191.21 ± 82.2	130.87 ± 55.33	158.52 ± 74.02	0.044[a]
NT-proBNP (pg/mL)	1,810.1 ± 3,332.97	2,652 ± 3,397.15	2,231.05 ± 3,303.81	0.583[a]
Ferritin (ng/mL)	460.82 ± 190.76	265.14 ± 166.27	351.24 ± 199.91	0.012[a]
Fibrinogen (mg/mL)	352.23 ± 69.78	434.91 ± 239.53	390.12 ± 171.04	0.247[a]
Procalcitonin (ng/mL)	1.49 ± 3.12	6.31 ± 14.9	3.9 ± 10.79	0.306[a]
LDH (U/L)	1,309.67 ± 1,405.55	330.75 ± 49	750.29 ± 966.19	0.351[a]
D-dimer (ng/mL)	1,402.57 ± 1,873.55	1,013.96 ± 881.39	1,223.21 ± 1,485.31	0.517[a]
Hemoglobin (g/dL)	9.83 ± 2.16	10.93 ± 3.33	10.62 ± 3.07	0.212[a]
Total leucocyte count (cells/mm^3)	55,998.24 ± 123,641.03	10,100.45 ± 8,999.97	22,891.64 ± 67,565.83	0.146[a]
Platelet count (cells/mm^3)	112,764.71 ± 103,963.65	236,363.64 ± 137,186.87	201,918.03 ± 139,614.5	0.001[a]
Serum sodium (mEq/L)	136.38 ± 3.74	135.09 ± 6.87	135.44 ± 6.17	0.483[a]
Serum potassium (mEq/L)	3.94 ± 0.48	4.11 ± 0.5	4.06 ± 0.5	0.239[a]
Urea (mg/dL)	31.44 ± 28.03	28.63 ± 21.61	29.39 ± 23.3	0.684[a]
Creatinine (mg/dL)	0.59 ± 1.13	0.39 ± 0.36	0.44 ± 0.66	0.29[a]
SHOT (IU/L)	96.19 ± 116.82	66.28 ± 111.9	74.39 ± 113.04	0.371[a]
SGPT (IU/L)	70.25 ± 62.31	114.26 ± 274.12	102.32 ± 236.24	0.529[a]
ALP (IU/L)	168.12 ± 86.16	162.55 ± 176.09	164.09 ± 155.77	0.904[a]
Total serum bilirubin (mg/dL)	1.07 ± 1.59	0.54 ± 0.96	0.68 ± 1.17	0.242[a]

Abbreviations: ALP, alkaline phosphatase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactic dehydrogenase; SGPT, serum glutamic pyruvic transaminase.
[a]Independent *t*-test.
[b]Fisher's exact test.
[c]Chi-square test.

was present in either group regarding their hematological parameters and inflammatory markers, except for the more significant presence of thrombocytopenia in the immunocompromised group. The more significant presence of thrombocytopenia in the immunocompromised group could be due to their primary disease or cytotoxic drug therapy.

No significant increase in intensive care requirements was found in the immunocompromised group. Belsky et al found that, although adult patients with immunosuppression have higher comorbidities, greater levels of inflammatory markers at the time of diagnosis, and a higher rate of admission to an intensive care unit with more significant mortality, no such difference in clinical presentations, outcome, and mortality was found in children who have immunosuppression as compared to children who do not have immunosuppression.[11] Simioli et al found that immunocompromised adult patients are at risk of adverse outcomes from COVID-19, with a higher risk in patients having hematological malignancies.[12] Like our study, Fung and Babik reported similar manifestations of COVID-19 in immunocompromised and immunocompetent patients.[13]

In our study, 25% of immunocompromised patients died compared to 13% of immunocompetent patients, which was not statistically significant. A study conducted in the United States, Canada, and Spain on 928 patients enrolled in COVID-19 and Cancer Consortium found no increased risk of death in patients with cancer.[14]

Another analysis in New York of 423 patients with symptomatic COVID-19 found no increase in the risk of complications in cancer patients who have recently received chemotherapy or have metastasis.[15]

The outcomes in either group in our study in terms of discharge or death were comparable. A study of COVID-19 patients with cancers who were matched 1:4 to individuals without cancer in terms of age, sex, and other health conditions again found similar outcomes for both groups.[16]

Contrary to our finding, Belsky et al reported that immunocompromised patients have a higher need for intensive care support and mortality than their immunocompetent counterparts.[11]

It is essential to acknowledge the limitations of this study. Since the research on COVID-19 is rapidly growing, it is difficult to draw firm and durable conclusions since data will accumulate and change over time. COVID-19 infection, due to routine screening in immunocompromised children, is likely to be picked up early.

Conflict of Interest

None declared.

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References

1 World Health Organization WHO coronavirus (COVID-19) Dashboard
2 Zhou Y, Yang Q, Chi J, et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: a systematic review and meta-analysis. Int J Infect Dis 2020;99:47–56
3 Vabret N, Britton GJ, Gruber C, et al; Sinai Immunology Review Project. Immunology of COVID-19: current state of the science. Immunity 2020;52(06):910–941
4 Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis 2020;71(15):762–768
5 Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020;20(05): 533–534
6 Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science 2020;368(6490):473–474
7 Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJHLH Across Specialty Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395(10229):1033–1034
8 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323(13):1239–1242
9 Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21 (03):335–337
10 Mehta V, Goel S, Kabarriti R, et al. Case fatality rate of cancer patients with COVID-19 in a New York Hospital System. Cancer Discov 2020;10(07):935–941
11 Belsky JA, Tullius BP, Lamb MG, Sayegh R, Stanek JR, Auletta JJ. COVID-19 in immunocompromised patients: a systematic review of cancer, hematopoietic cell and solid organ transplant patients. J Infect 2021;82(03):329–338
12 Simioli F, Martino M, Annunziata A, Carannante N, Fiorentino G. Therapeutic approach for severe COVID-19 and immunocompromised patients. A case series. Respir Med Case Rep 2021; 33:101397
13 Fung M, Babik JM. COVID-19 in immunocompromised hosts: what we know so far. Clin Infect Dis 2021;72(02):340–350
14 Kuderer NM, Choueiri TK, Shah DP, et al; COVID-19 and Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020;395(10241):1907–1918
15 Robilotti EV, Babady NE, Mead PA, et al. Determinants of COVID-19 disease severity in patients with cancer. Nat Med 2020;26(08): 1218–1223
16 Brar G, Pinheiro LC, Shusterman M, et al. COVID-19 severity and outcomes in patients with cancer: a matched cohort study. J Clin Oncol 2020;38(33):3914–3924