Decreased Severity and Incidence of SARS-CoV-2 infection in younger patients with bone marrow failure: Description of 4 clinical cases.

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Abstract

The Coronavirus Disease 2019 pandemic, caused by the severe acute respiratory syndrome-associated coronavirus (SARS-CoV-2), is having devastating effects on every country around the world. SARS-CoV-2 can be fatal in patients with described risk factors. A question remains as to whether other immunosuppressed populations are at risk for severe complications. There is limited data on the impact of COVID-19 in young patients with bone marrow failure syndromes (BMFs). 29 institutions, from the NAPAAC consortium, reported 4 with BMFs diagnosed with SARS-CoV-2. These patients presented with relatively mild clinical courses, raising questions as to why this apparently low morbidity and mortality

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Abbreviation	**Full term**
COVID-19	Coronavirus Disease 2019
SARS-CoV-2	Severe acute respiratory syndrome-associated coronavirus-2
BMF	Bone marrow failure
NAPAAC	North American Pediatric Aplastic Anemia Consortium

While younger patients generally appear to experience fewer severe manifestations of the active Coronavirus Disease 2019 (COVID-19) infection, caused by the novel severe acute respiratory syndrome-associated coronavirus (SARS-CoV-2), it is not known whether pediatric and young adult patients with bone marrow failure (BMF), while intuitively vulnerable, are in fact susceptible to its severe manifestations. A multi-center collective cohort study from Hubei Province, China reported that patients with hematological malignancies were especially susceptible to severe complications associated with SARS-CoV-2 infection.[1] There are only scarce data reported on the impact of COVID-19 in children and young adult patients with BMF. We carried out a survey of 38 pediatric institutions, constituting the North American Pediatric Aplastic Anemia Consortium (NAPAAC). Twenty-nine institutions reported only 4 of 1205 active patients with bone marrow failure who were diagnosed with COVID-19. These four patients presented with relatively mild clinical courses.

We identified two children and two young adult patients with BMF who tested positive for SARS-CoV-2. Three of these patients were reported from New York and one patient from Georgia. The patients reported in this study represent approximately 0.3% of 1205 active patients with BMF followed at 29 NAPAAC institutions; a prevalence lower than for the population at large (˜2-22%) (www.cdc.gov).

The relatively low number of patients, all of whom presented with mild-to-moderate clinical features, raises the question of why there have been so few confirmed COVID-19 affected patients in the BMF population. Infections might have been reduced by better adherence to recommendations for social distancing in patients and their families who were concerned about heightened risk due to their underlying disease. The immunosuppressed status of this patient population may also have reduced the SARS-CoV-2 pro-inflammatory features and even prevented enough symptomatology to be tested for SARS-CoV-2. As well, these four patients did not have any other comorbidities described as risk factors for poor outcomes.[2]

The commonalities in our patient population were: 1) non-Caucasians; 2) lack of comorbidities other than BMF syndromes; 3) worsening blood counts of at least one blood cell lineage in 3 out of 4 patients; 4) absence of multi system inflammatory syndrome; and 5) three of four patients became SARS-CoV-2 PCR negative. In this survey, we observed decreased morbidity and mortality in comparison to the published BMF adult cases with COVID-19.[3]

NAPAAC recognizes that data from a larger number of patients with BMF during all phases of treatment will be necessary to determine appropriate management changes for severely cytopenic patients. Although the small number of patients precludes conclusions as to why these younger patients seems to have better outcomes than their older counterparts these cases appear to offer some reassurance to younger patients with BMF.

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References:

1. Dai M, Liu D, Liu M, et al. Patients with Cancer Appear More Vulnerable to SARS-COV-2: A Multicenter Study during the COVID-19 Outbreak. *Cancer Discov.* Apr 2020.

2. Boulad F, Kamboj M, Bouvier N, Mauguen A, Kung AL. COVID-19 in Children With Cancer in New York City. *JAMA Oncol.* May 2020.

3. Lu X, Zhang L, Du H, et al. SARS-CoV-2 Infection in Children. *N Engl J Med.* 04 2020;382(17):1663-1665.

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