Short communication

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An epidemiological study of multisystem inflammatory syndrome in children (MIS-C) and young adults among COVID-19-positive patients – data from National Inpatient Sample database

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Abstract

During the pandemic of COVID-19, a novel atypical set of clinical findings was seen among several children with recent or current exposure to the virus. It was termed the "multisystem inflammatory syndrome in children" (MIS-C). Our study used the 2021 National Inpatient Sample to study the associations of sex, race, and age with the incidence of MIS-C among COVID-19-positive children. Out of 69,440 COVID-19-positive children, 2,790 (4.0%) reported MIS-C. The incidence of MIS-C was highest among those aged 8 years old (17,130 MIS-C cases per 100,000 COVID-19 patients), Asian or Pacific Islanders (API) (5,346 MIS-C per 100,000 COVID-19 cases), and males (4,734 cases per 100,000 COVID-19 cases). Furthermore, 7.9% of MIS-C cases met the classification of Kawasaki disease.

Key words: United States, COVID-19, epidemiology, multisystem inflammatory syndrome in children.

While earlier studies among coronavirus disease 2019 (COVID-19) positive children were linked with lower odds of death, several reports of severe systemic inflammatory disease among children with a close resemblance to features of Kawasaki disease were reported during the pandemic [1, 2]. The term multisystem inflammatory syndrome in children (MIS-C) was coined. While the criteria varied slightly based on different organizations, the presence of fever (≥ 38°C/100.4°F) for 24 hours or more, involvement of several organ systems, and the presence of elevated inflammatory markers with no alternative plausible causes are common among them [2, 3]. The presence of either a recent or current COVID-19 infection or exposure to a closed contact is also one of the criteria listed by the Centers for Disease Control and Prevention (CDC) [3]. Since most studies of MIS-C among COVID-19-positive patients involved smaller samples, we performed a retrospective study using one of the biggest in-patient records from the United States.

Our study followed the age criteria set by the CDC and included patients between 0 and 20 years of age from the 2021 National Inpatient Sample (NIS) [3]. The NIS is part of the Healthcare Cost and Utilization Project (HCUP), which is designed to collect inpatient records in a de-identified fashion. Cases of COVID-19 were

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identified using the ICD-10 code U07.1 and MIS-C via the code M35.81. We estimated the presence of MIS-C in COVID-19 cases per 100,000 COVID cases for age groups, race, and sex using the following formula: MIS-C patients in that group/total COVID-19 cases in that group × 100,000. The number of MIS-C cases meeting the criteria for Kawasaki disease was also estimated. Discharge weights (DISCWT) were used for our analysis, allowing us to confirm national estimates of the condition [4, 5].

Table I. Incidence of MIS-C per 100,000 COVID-19 children aged 0–20 in the United States

Parameter	Incidence of MIS-C per 100,000 COVID-19 cases	*p*-value
Sex		
Male	4,734	< 0.01
Female	3,373	
Race		
White	3,555	< 0.01
Black	4,338	
Hispanic	3,755	
Asian or Pacific Islander	5,346	
Native American	2,581	
Other race	4,875	
Age [years]		
0	832	< 0.01
1	5,496	
2	8,418	
3	9,677	
4	7,787	
5	11,917	
6	12,919	
7	11,528	
8	17,130	
9	13,223	
10	12,734	
11	7,808	
12	7,414	
13	3,656	
14	6,341	
15	3,943	
16	2,392	
17	2,381	
18	741	
19	711	
20	268	

Our study identified 69,440 COVID-19 cases among children aged 0–20 (inclusive) in 2021, with 2,790 patients reporting MIS-C (4,018 MIS-C cases per 100,000 COVID-19 patients, 4.0%; Table I). Multisystem inflammatory syndrome in children incidence followed an incremental pattern with age; the highest incidence was noted in children aged 8 years (17,130 MIS-C cases per 100,000 COVID-19 patients). The incidence then gradually dropped from age 8 years to 20 years (Fig. 1). The median age of MIS-C in COVID-19-positive children was 9 years (interquartile range 4–13 years).

We also noted racial disparities as MIS-C was more common among Asian or Pacific Islanders (API) (5,346 MIS-C per 100,000 COVID-19 cases), with the lowest incidence noted among Native Americans (2,581 MIS-C per 100,000 COVID-19 cases) ($p < 0.01$; Fig. 2). In addition, a sex-based difference was observed as males had a higher rate of MIS-C (4,734 cases per 100,000 COVID-19 cases) than females (3,373 MIS-C cases per 100,000 COVID-19 cases) ($p < 0.01$; Fig. 3).

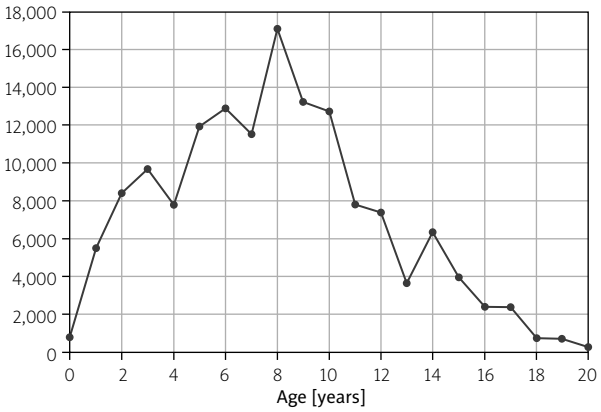

Fig. 1. Incidence of MIS-C per 100,000 COVID-19 cases based on age.

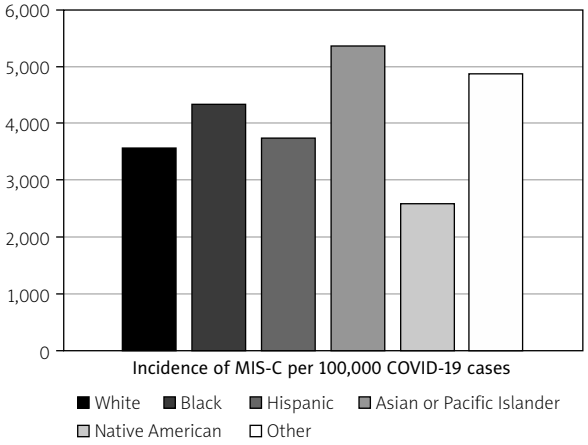

Fig. 2. Incidence of MIS-C based on race among COVID-19 positive patients aged 0–20 years.

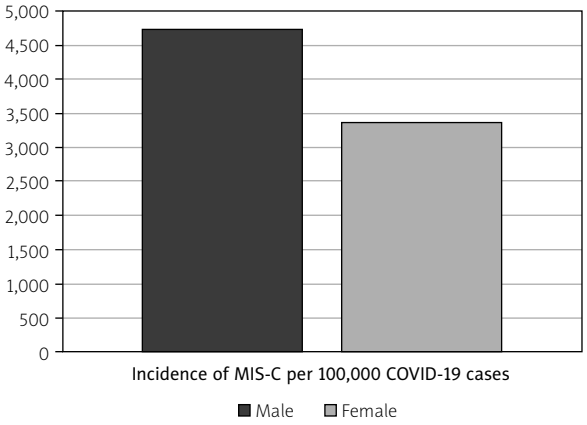

Fig. 3. Sex-based incidence of MIS-C among COVID-19 patients.

Around 220 MIS-C cases met the criteria for Kawasaki disease (7.9%) and they were younger (mean age 5.18 years vs. 9.07 years in other MIS-C cases, $p < 0.01$).

To date, this is the biggest retrospective study investigating events of MIS-C among COVID-19-positive children from the United States. Among the 131 MIS-C cases with a positive COVID-19 test in a study conducted by Feldstein et al. [6], the majority were Hispanics (or Latino) (40%), which was different from our study. However, the overall median age of 9.1 years of MIS-C COVID-19 cases was similar to our study (9.1 years vs. 9.0 years) [6]. Various studies with smaller samples of MIS-C cases in COVID-19 patients included more males than females; for example, in their study of 268 cases, Flood et al. [7] had 60.1% classified as males. Studies investigating only MIS-C cases (irrespective of COVID-19 status) also found a higher proportion of males (54% in the study by Dufort et al. [8]). As there is a lack of additional data on the prevalence of MIS-C among COVID-19 children from different countries, we encourage physicians across different countries to pursue a similar investigation. Furthermore, the higher incidence among Asian/Pacific Islanders in our study also corresponds to the racial disparities previously seen in that particular group for Kawasaki disease [9]. We also noted a high incidence among Black people and agree with Middelburg et al. [10] that additional studies are necessary and awareness should be increased among physicians of such racially associated risk factors [9, 10].

To conclude, our study of MIS-C among COVID-19-positive children found the highest incidence in those aged 8, along with a higher incidence among males and APIs, and the lowest incidence among Native Americans. As MIS-C is a new condition and has a close resemblance to Kawasaki disease, it is vital for the affected children to have a close follow-up, and any presence of short-term and long-term cardiac anomalies should be treated early [11]. Similar studies across different countries with diverse backgrounds should be encouraged.

Disclosures

Conflict of interest: The authors declare no conflict of interest.
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Data availability: Not applicable. Our coauthors handling the database have all signed the DUA from HCUP for its use and publication.

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