EDITORIAL

Should Coronavirus Disease 2019–Associated Inflammatory Syndromes in Children Affect Social Reintegration?

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Recent reports in several medical journals, including *JAMA*, and the general media have highlighted the emergence of coronavirus disease 2019 (COVID-19)–associated inflammatory syndromes in children.[1-3] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appears to induce this new condition, which has been called *pediatric multisystem inflammatory syndrome* (PIMS) or *pediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2* (PIMS-TS) and described in detail by investigators in Europe and New York, New York.[1-4] Additionally, investigators in Italy have reported[5] a dramatic surge in Kawasaki disease (KD), often associated with positive serological test results for COVID-19. As of May 31, 2020, the New York State Department of Health is investigating 188 reported hospitalized cases and 3 deaths of children, predominantly school-aged, who experienced symptoms similar to KD and toxic shock-like syndrome that were possibly linked to COVID-19.[6] Similarly, more than 200 cases have been reported to the European Centre for Disease Prevention and Control. The US Centers for Disease Control and Prevention has also issued a statement and case reports for the emerging condition, now also termed *multisystem inflammatory syndrome of childhood* (MIS-C), which is currently under investigation.[7] Simultaneously, sporadic cases of MIS-C, KD, and/or Kawasaki shock syndrome have appeared in public health reports and the media, particularly in Washington and other West Coast states.

Investigators in Bergamo, Italy, recently reported[3] 10 patients, most with positive serology results for SARS-CoV-2, who presented with KD-like symptoms between February 18 and April 20, 2020. They compared the number of affected individuals with the 19 KD admissions over the previous 5 years and estimated a 30-fold increase in KD or KD-like cases associated with COVID-19. However, taking into account their data and comparing the previous seasonal peak incidence in 2017 with the current level suggests that an increase of 3-fold to 5-fold occurred. Moreover, they also stated that the current patients differed from the historical cohort from clinical and biochemical perspectives. Additionally, a recent report in *JAMA*[1] compared clinical and laboratory parameters for patients with PIMS with those from historical KD and Kawasaki shock syndrome cohorts. Data used for these comparisons were derived from 2 distinct geographic regions (the UK and San Diego, California) and exhibited very different racial/ethnic compositions.[8] This also represents a concern in defining this potential new syndrome as a separate entity from KD, in that substantial racial/ethnic disparity has been reported for COVID-19–associated illnesses as well as KD itself.[8]

Additional caution in defining epidemiology and determining overall outcomes for these pediatric inflammatory syndromes should be taken because of the lack of a common case definition. On May 15, 2020, the European Centre for Disease Prevention and Control released a rapid risk assessment concerning PIMS-TS.[9] The statement explicitly expresses that the overall risk in the European Union/European Economic Area and the UK is considered low and based on a very low probability of PIMS-TS in children and a moderate or high effect of such disease. The article, which includes the Italian and UK reports as well as data from other European countries, also states that accurate KD incidence comparisons before and during COVID-19 cannot be made with certainty.

The UK and Italian reports each show that children with these inflammatory syndromes began appearing in emergency departments weeks after peak presentation for COVID-19–associated respiratory symptoms in adults.[3,5] The data obtained to date therefore imply that PIMS represents delayed postviral inflammatory responses that are likely linked to adaptive immunity rather than a direct viral insult. However, the Italian authors[5] used their estimate to suggest that these findings should have important implications for public health. Although acknowledging the rarity of these syndromes, they wrote, "The association between SARS-CoV-2 and Kawasaki-like disease should be taken into account when it comes to considering social reintegration policies for the paediatric population."[5(p1777)] Because social integration for children predominantly occurs in schools, this statement may be interpreted as if the increase in these inflammatory syndromes should be used to address dates for school reopenings.

Unfortunately, commentators for media outlets in the US have used these estimates, however accurate, along with the new appearance of MIS-C and sporadic reports of SARS-CoV-2–associated KD, to create some concern among parents and advocate for delays in the reopening of schools in the US.[10] In context, pediatric admissions for COVID-19–associated illnesses represent less than 1% of the total in New York, the most severely stricken state in the US. Regional variations also exist with Western states, so far showing substantially lower numbers of MIS-C.[11] General estimates for KD incidence in the US are about 20 per 100 000 children, with about 5000 new cases per year.[12] Published incidence estimates for Europe are lower, ranging between 4 and 15 per 100 000 children, depending on the country.[13,14] Giant coronary artery aneurysms, the most severe manifestation of the disease, occur variably between 3% and 7% of the population treated for KD and would result in less than 1 in 100 000 children per year in the US. We do not know the prolonged morbidity associated with MIS-C or PIMS-TS, although less than 10 deaths in patients younger than 21 years have been reported nationwide in the US to date. Obvi-

ously, these inflammatory syndromes can cause critical and life-altering illness in individuals. Yet these severe outcomes remain rare and lead to questions on whether they should affect public health decisions for millions of schoolchildren. Prominent opinion pieces have outlined the negative outcomes of delaying school reopenings. These include adverse outcomes on child mental health and learning. Additionally, school delays will produce further societal inequities, as described recently by Esposito et al,[15] who are also from Italy, in *JAMA Pediatrics*.

In summary, the pediatric inflammatory syndromes presumably triggered by SARS-CoV-2 exposure deserve heightened awareness because they have critical and potentially life-altering outcomes on affected children. Substantial research in this area is also absolutely necessary, as are well-defined and uniform case definitions. However, unless a substantial increase in case numbers occurs over the coming months, these syndromes remain rare and should not be used to substantially change decisions affecting millions of schoolchildren.

ARTICLE INFORMATION

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Published Online: July 20, 2020. doi:10.1001/jamapediatrics.2020.2810

Conflict of Interest Disclosures: None reported.

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