

Epidemiologic trends in Kawasaki disease during coronavirus disease-19 in Singapore



To the Editor:

We read with interest the clinical profile of 33 children with multisystem inflammatory syndrome in children by Kaushik et al from 3 New York City tertiary care children's hospitals.¹ There have been similar reports of a surge in children presenting with systemic inflammation, including Kawasaki-like disease from Europe and other parts of the US but not from Asia to date.²⁻⁵ We compared the epidemiologic trends in Kawasaki disease at the only public specialist children's hospital in Singapore before coronavirus disease-19 (COVID-19) (January 1, 2017, to December 31, 2019) and during COVID-19 (January 1, 2020, to April 30, 2020).

Since the emergence of severe acute respiratory syndrome coronavirus disease-2 (SARS-CoV-2) in Singapore, the number of cases of Kawasaki disease was lower ($n = 41$) compared with the average for the same period before COVID-19 ($n = 56$). Although cases in children 4 years of age and younger mirrored the overall lower trend, cases in children 5-9 years of age seem to be higher during COVID-19 (Figure). In the ≥ 10 -year-old category, there were no major variations with 1 case in 2020 vs 2 each in 2019 and 2018 and none in 2017. Comparing 2017-2019 with 2020, the mean age of patients with Kawasaki disease increased from

2.53 years to 2.80 years of age and the proportion of female cases increased from 43.9% to 51.2%. There was no significant change in average duration of hospitalization (4.9 days to 5.6 days), which may be a proxy measure of no change in Kawasaki disease case severity.

Pediatric COVID-19 cases in our hospital have been mild to moderate with no cases requiring oxygen or ventilatory support and no mortality. We have not detected a surge in Kawasaki disease cases during COVID-19 in Singapore, but noted a possible increase in age and shift in sex distribution. Close monitoring and analysis of children with systemic inflammation, especially their exposure to SARS-CoV-2 through serologic testing is warranted to evaluate whether children in Asia are at similar risk to the phenomenon reported in Europe and the US.

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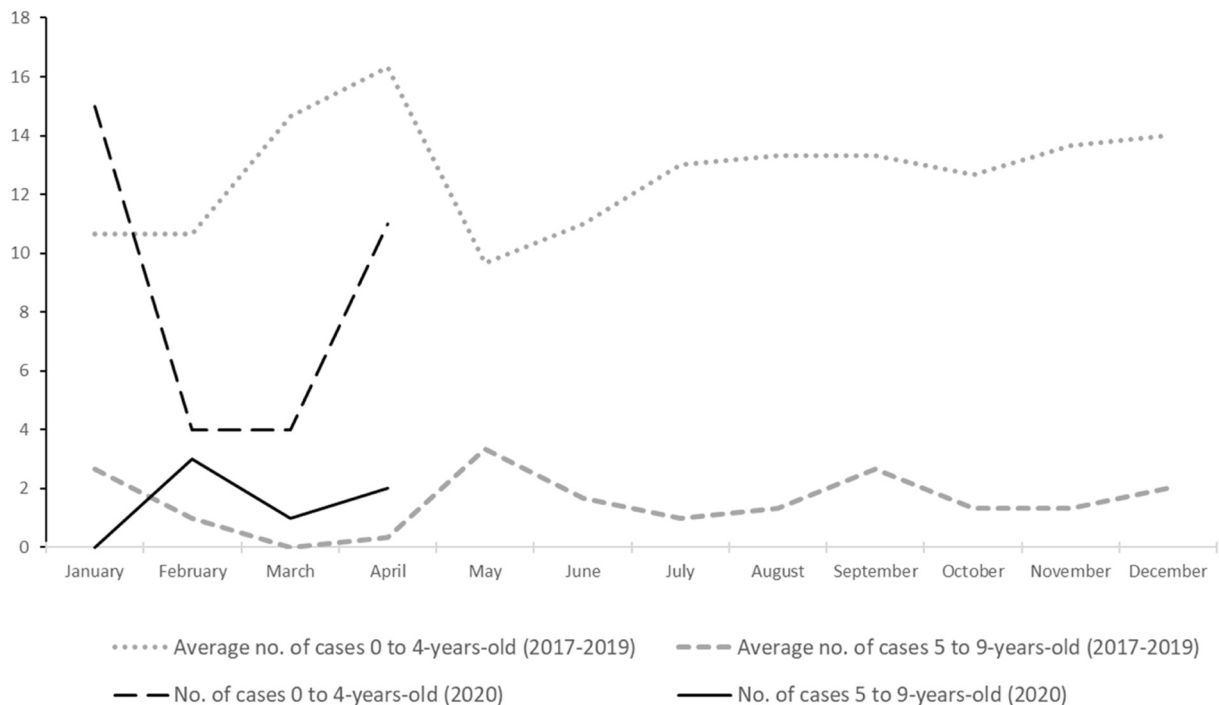


Figure. Temporal and age distribution of Kawasaki disease in 2020 compared with 2017-2019.

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Reply



To the Editor:

We read with interest the well-founded observation made by Yung et al regarding no change in epidemiology or cases of Kawasaki disease in Singapore amid the current ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. When it was initially recognized, there was uncertainty whether the SARS-CoV-2 associated multisystem inflammatory syndrome in children (MIS-C) represented Kawasaki disease. Evidence and evolving understanding suggest it to be a separate clinical entity.

A recent large multicenter case series from the US and Europe show that 22%-40% of MIS-C cases met either complete or incomplete Kawasaki disease criteria and were either classified as Kawasaki disease or Kawasaki disease shock syndrome.¹⁻³ The diagnostic criteria for Kawasaki disease and MIS-C are broad because both Kawasaki disease and MIS-C are inflammation-associated syndromes, and there is overlap.

Accumulating literature highlights the similarities and differences between MIS-C and Kawasaki disease.⁴ Although a case definition for MIS-C was released by the US Centers for Disease Control and Prevention, vastly differing treatment modalities ranging from supportive care to immunomodulating agents and plasma infusion have been implemented with a lack of consensus on how to best treat this condition. Reassuringly, MIS-C thus far has been associated with low mortality.

Our study was designed to include critically ill children and adolescents who met criteria for SARS-CoV-2 associated MIS-C. Some patients in our series also may have met Kawasaki disease criteria. Whether “overlap” patients have Kawasaki disease, atypical Kawasaki disease, Kawasaki disease with macrophage activation syndrome, or represent a spectrum of MIS-C requires ongoing surveillance and longer term follow-up.

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Association of early antibiotic exposure and necrotizing enterocolitis: causality or confounding bias?



To the Editor:

We read with great interest the report by Li et al that compared the incidence of necrotizing enterocolitis (NEC) in infants with very low birth weight according to early antibiotic treatment.¹ We would like to raise the question: association of early antibiotic exposure and NEC: causality or confounding bias?

Antibiotic use was different from one neonatal intensive care unit to another, resulting in a small and highly selected nonexposed group. Indeed, the 2 groups displayed different baseline characteristics (gestational age, proportions of small for gestational age, and cesarean delivery), which suggest that the causes of preterm birth (not analyzed and potentially a confounding factor, ie, a pre-exposure covariate independently associated with both the exposure and the outcome) differ between the groups. Moreover, small for gestational age status is not equal to fetal growth restriction. Although a crude positive association between no early antibiotics and NEC was found, adjusting for relevant confounders such as fetal growth restriction or causes of preterm birth may decrease the OR and support the concept of confounding by indication. We suggest that indication bias would have been handled better using appropriate statistical