References

1. Kaushik S, Aydin SI, Derespina KR, Bansal PB, Kowalsky S, Trachtman R, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2 infection (MIS-C): a multi-institutional study from New York City. J Pediatr 2020;224:24-9.
2. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic. Circulation 2020 [Epub ahead of print].
3. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 2020;395:1771-8.
4. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet 2020;395:1607-8.
5. Chiotos K, Bassiri H, Behrens EM, Blatz AM, Chang J, Diorio C, et al. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: a case series. J Pediatric Infect Dis Soc 2020;9:393-8.

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.

Shubhi Kaushik, MBBS
Pediatric Critical Care Medicine
Children's Hospital at Montefiore
Bronx, New York
Kravis Children's Hospital
Mount Sinai Health System
New York

Kim R. Derespina, MD
Shivanand S. Medar, MD
Pediatric Critical Care Medicine
Children's Hospital at Montefiore
Bronx, New York

https://doi.org/10.1016/j.jpeds.2020.07.064

The authors declare no conflicts of interest.

References

1. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 2020;324:259-69.
2. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med 2020;383:334-6.
3. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem inflammatory syndrome in children in New York State. N Engl J Med 2020;383:347-58.
4. Rowley AH. Multisystem inflammatory syndrome in children and Kawasaki disease: two different illnesses with overlapping clinical features. J Pediatr 2020;224:129-32.

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