

Coronavirus disease 2019, Kawasaki disease, and multisystem inflammatory syndrome in children



To the Editor:

There has been a rise in the number of critically ill patients presenting with an unusual clinical picture; all have in common features of Kawasaki disease and a confirmed or suspected coronavirus disease 2019 (COVID-19) infection. According to Harahsheh et al, the diagnosis/treatment of Kawasaki disease was missed or delayed owing to the forced lockdown and doctors being focused on treating patients with COVID-19.¹ A similar concern was shared by adult cardiologists, who observed a significant drop of admissions to coronary intensive care units because patients with acute myocardial infarction were afraid to risk infection should they need to come to the hospitals.²

Reports from Italy and the United Kingdom have highlighted a significant increase of Kawasaki disease cases in children positive for COVID-19 or even negative, but with a likely exposure to the infection. The number of admissions due to Kawasaki disease was reported to be a 30-fold increase compared with previous years during the same season.^{3,4} We agree with the conclusions by Harahsheh et al and emphasize a “call for action” for a prompt diagnosis and treatment as needed, with the aim of preventing Kawasaki-induced coronary artery aneurysms and related late complications.

Pier Paolo Bassareo, MD, PhD, MSc, FESC
University College of Dublin
Mater Misericordiae University Hospital
Our Lady's Children's Hospital Crumlin
Dublin, Ireland

Giuseppe Calcaterra, MD
University of Palermo (Postgraduate Medical School)
Palermo, Italy

Vassilios Fanos, MD
Neonatal Intensive Care Unit
University of Cagliari
Cagliari, Italy

<https://doi.org/10.1016/j.jpeds.2020.06.033>

References

1. Harahsheh AS, Dahdah N, Newburger JW, Portman MA, Piram M, Tulloh R, et al. Missed or delayed diagnosis of Kawasaki disease during the 2019 novel coronavirus disease (COVID-19) pandemic. *J Pediatr* 2020;222:261-2.
2. De Filippo O, D'Ascenzo F, Angelini F, Bocchino PP, Conrotto F, Saglietto A, et al. Reduced rate of hospital admissions for ACS during Covid-19 outbreak in Northern Italy. *N Engl J Med* 2020;383:88-9.
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.

Reply



To the Editor:

We thank Bassareo et al for their comments and agree that our community needs to come together to improve timely diagnosis and treatment of children with Kawasaki disease and Kawasaki disease-like illnesses during the 2019 novel coronavirus disease (COVID-19) pandemic to prevent the development of coronary artery aneurysms.

We would like to use this opportunity to provide context for writing our original letter and what we have learned in the interim. Between January 1, 2020, and April 1, 2020, we noted a decrease in the number of children presenting to large academic centers with Kawasaki disease. Several children at different centers presented late with Kawasaki disease; one of them was diagnosed with giant aneurysm. We were concerned that the “health care providers have focused on [the 2019 novel coronavirus disease] management during the pandemic” and that patients with Kawasaki disease were underdiagnosed or underwent delayed treatment. Our letter was submitted on April 10, 2020, revised on April 20, 2020, and accepted 1 day later. On April 26, 2020—5 days after the letter's acceptance—cases of severe inflammatory syndrome were reported in the UK with some patients having features of Kawasaki disease.^{1,2} Shortly after, cases were reported first throughout Europe and then in the eastern US.^{3,4} However, we believe that the estimated 30-fold increase in Kawasaki disease is inaccurate because the investigators did not account for typical seasonal variations.⁵ Multiple different case definitions have been developed so far by various societies and public health agencies in response to the rapidly emerging syndrome^{1,6-9} (Figure; available at www.jpeds.com). With the emergence of the multisystem inflammatory syndrome in children (also referred to as the pediatric multisystemic inflammatory syndrome), awareness about Kawasaki disease has increased. We should now focus not only on early treatment of classic Kawasaki disease to prevent coronary artery aneurysm but also on investigating the immunobiology and developing treatment to prevent heart disease in multisystem inflammatory syndrome in children/pediatric multisystemic inflammatory syndrome.

We thank Angela J. Doty, MD, for her editorial assistance.

Ashraf S. Harahsheh, MD, FACC, FAAP
Division of Cardiology
Department of Pediatrics
Children's National Hospital
The George Washington University School of Medicine
Washington, DC

Nagib Dahdah, MD
Division of Cardiology
Department of Pediatrics
CHU Ste-Justine
University of Montreal
Montreal, Quebec, Canada

Jane W. Newburger, MD, MPH
Department of Cardiology
Boston Children's Hospital
Department of Pediatrics
Harvard Medical School
Boston, Massachusetts

Michael A. Portman, MD
Division of Cardiology
Department of Pediatrics
Seattle Children's Hospital
University of Washington
Seattle, Washington

Robert Tulloh, DM, FRCPC
Department of Congenital Heart Disease
Bristol Heart Institute
University of Bristol
Bristol, UK

Brian W. McCrindle, MD, MPH
Division of Cardiology
Department of Pediatrics
University of Toronto
The Hospital for Sick Children
Toronto, Ontario, Canada

Rolando Cimaz, MD
Department of Clinical Sciences and Community Health
University of Milan
Milan, Italy

Jane C. Burns, MD
Department of Pediatrics
Rady Children's Hospital
University of California San Diego
San Diego, California

<https://doi.org/10.1016/j.jpeds.2020.06.072>

The authors declare no conflict of interest.

References

1. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). <https://emergency.cdc.gov/han/2020/han00432.asp>. Accessed May 16, 2020.
2. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020;395:1607-8.
3. DeBiasi RL, Song X, Delaney M, Bell M, Smith K, Pershad J, et al. Severe COVID-19 in children and young adults in the Washington, DC Metropolitan Region. *J Pediatr* 2020;223:199-203.e1.
4. Assistance publique-Hôpitaux de Paris. <https://www.aphp.fr/espace-presse>. Accessed May 27, 2020.
5. 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.
6. Multisystem inflammatory syndrome in children and adolescents with COVID-19. <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>. Accessed May 16, 2020.
7. Pediatric multi-system inflammatory syndrome temporally associated with COVID-19 Interim case definition in New York state. https://health.ny.gov/press/releases/2020/docs/2020-05-13_health_advisory.pdf. Accessed May 17, 2020.
8. Paediatric multisystem inflammatory syndrome temporally associated with COVID-19. <https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatricmultisystem-%20inflammatory%20syndrome-20200501.pdf>. Accessed May 10, 2020.
9. European Centre for Disease Prevention and Control. Paediatric inflammatory multisystem syndrome and SARS-CoV-2 infection in children – 15 May 2020. Stockholm: ECDC. <https://www.ecdc.europa.eu/en/publications-data/paediatric-inflammatory-multisystem-syndrome-and-sars-cov-2-rapid-risk-assessment>. Accessed May 28, 2020.

Resistin/uric acid index for weight loss prediction?



To the Editor:

I read with interest the report by Zurita-Cruz concerning the utilization of a resistin/uric acid index as a prognostic marker for body mass index (BMI) reduction.¹

It is intriguing that both uric acid alone and the resistin/uric acid index provided significantly different values for those with vs those without BMI z-score reduction with metabolite scores of 6.3 ± 1.7 vs 5.3 ± 0.7 ($P \leq .001$) and 2.7 ± 0.6 vs 2.2 ± 0.9 ($P = .02$). It has previously been noted that uric acid alone can predict weight loss in those undergoing weight loss surgery.² Could uric acid, as a more commonly tested (and thus less expensive) metabolite, prove just as useful as the suggested index in weight loss prediction within this tested cohort?

It would be of interest to know how the composite indices were formed. It is surprising that the leptin/uric acid index performs so poorly when one would suspect an additive or multiplicative composite index to maintain a higher score (even if not significant) in those with a BMI z-score reduction than those without.

Comorbidities associated with obesity were recorded, but were not reported or included as controlled covariates within the analysis. Knowing these may provide interesting insights to ensure that confounding aspects of a metabolic syndrome are not contributory to the results.

Finally, it is increasingly recognised that BMI may not be the most accurate method for determining adiposity

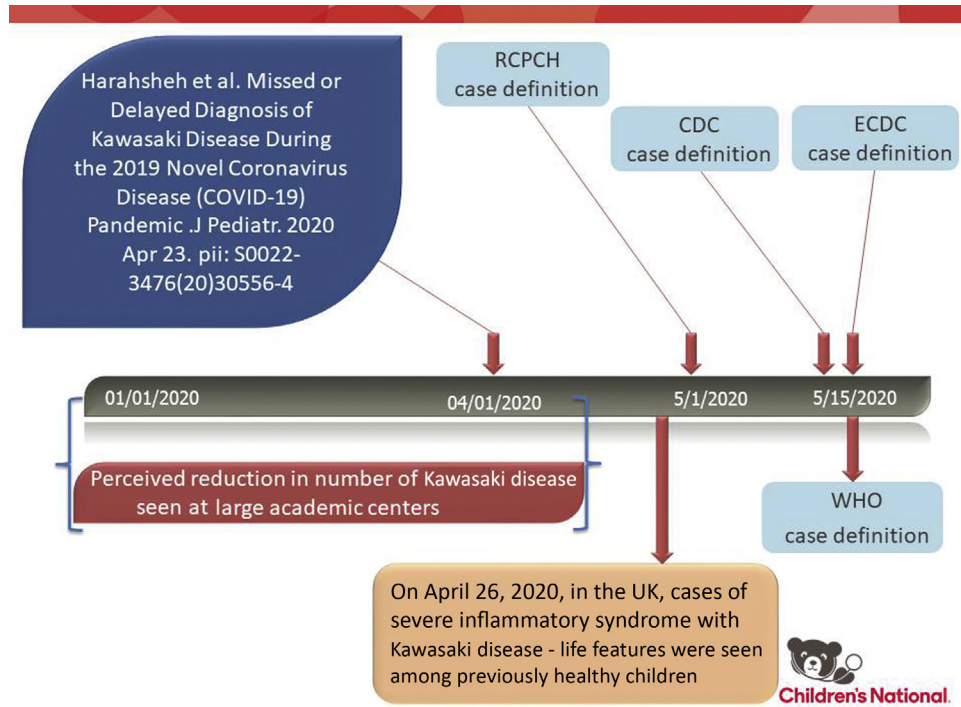


Figure. Timeline of Kawasaki disease through the 2019 novel coronavirus disease (COVID-2019) pandemic. *CDC*, Centers for Disease Control and Prevention; *ECDC*, European Centre for Disease Prevention and Control; *RCPCH*, Royal College of Paediatrics and Child Health; *UK*, United Kingdom; *WHO*, World Health Organization.