



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

VMMC and Safdarjung Hospital  
New Delhi, India

**Nitesh Gupta, DM**

Department of Pulmonary  
Critical Care and Sleep Medicine  
VMMC and Safdarjung Hospital  
New Delhi, India

**Sumita Agrawal, DM**

Department of Pulmonary Medicine  
Medipulse Hospital  
Jodhpur, Rajasthan, India

**Pranav Ish, DM**

Department of Pulmonary  
Critical Care and Sleep Medicine  
VMMC and Safdarjung Hospital  
New Delhi, India

<https://doi.org/10.1016/j.jpeds.2020.04.062>

## References

- Who is at High Risk for Flu Complications? Centers for Disease Control and Prevention (CDC, USA). <https://www.cdc.gov/flu/highrisk/index.htm>. Accessed April 6, 2020.
- Jhung MA, Swerdlow D, Olsen SJ, Jernigan D, Biggerstaff M, Kamimoto L, et al. Epidemiology of 2009 pandemic influenza A (H1N1) in the United States. *Clin Infect Dis* 2011;52(suppl 1):S13-26.
- Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020. <https://doi.org/10.1111/apa.15270> [Epub ahead of print].
- Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19. An overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. *Pediatr Infect Dis J* 2020;39:355-68.
- Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020. <https://doi.org/10.1542/peds.2020-0702> [Epub ahead of print].
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-62.
- Principi N, Bosis S, Esposito S. Effects of coronavirus infections in children. *Emerg Infect Dis* 2010;16:183-8.
- Lau AC-W, Yam LY-C, So LK-Y. Management of critically ill patients with severe acute respiratory syndrome (SARS). *Int J Med Sci* 2004;1:1-10.
- World Health Organization. Epidemiological summary of pandemic influenza A (H1N1) 2009 virus – Ontario, Canada, June 2009. Weekly epidemiological record. 20 November 2009. No. 47, 84. p. 485-92. Available at: <https://www.who.int/wer/2009/wer8447.pdf>. Accessed April 6, 2020.
- Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Hospitalized Patients with 2009 H1N1 Influenza in the United States, April–June 2009. *N Engl J Med* 2009;361:1935-44.
- Skarbinski J, Jain S, Bramley A, Lee EJ, Huang J, Kirschke D, et al. Hospitalized patients with 2009 pandemic influenza A (H1N1) virus infection in the United States—September–October 2009. *Clin Infect Dis* 2011;52(suppl 1):S50-9.
- Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. *N Engl J Med* 2010;362:1708-19.
- Dawood FS, Iuliano AD, Reed C, Meltzer MI, Shay DK, Cheng PY, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. *Lancet Infect Dis* 2012;12:687-95.
- Louie JK, Jean C, Acosta M, Samuel MC, Matyas BT, Schechter R. A review of adult mortality due to 2009 pandemic (H1N1) influenza A in California. *PLoS One* 2011;6:e18221.
- Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). World Health Organization (WHO). <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>. Accessed April 6, 2020.
- Sorbello M, El-Boghdady K, Di Giacinto I, Cataldo R, Esposito C, Falchetta S, et al. The Italian coronavirus disease 2019 outbreak: recommendations from clinical practice. *Anaesthesia* 2020. <https://doi.org/10.1111/anae.15049> [Epub ahead of print].
- CDC COVID-19 Response Team. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19)—United States, February 12–March 16, 2020. <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6912e2-H.pdf>. Accessed April 6, 2020.

## Severe neutropenia in infants with severe acute respiratory syndrome caused by the novel coronavirus 2019 infection

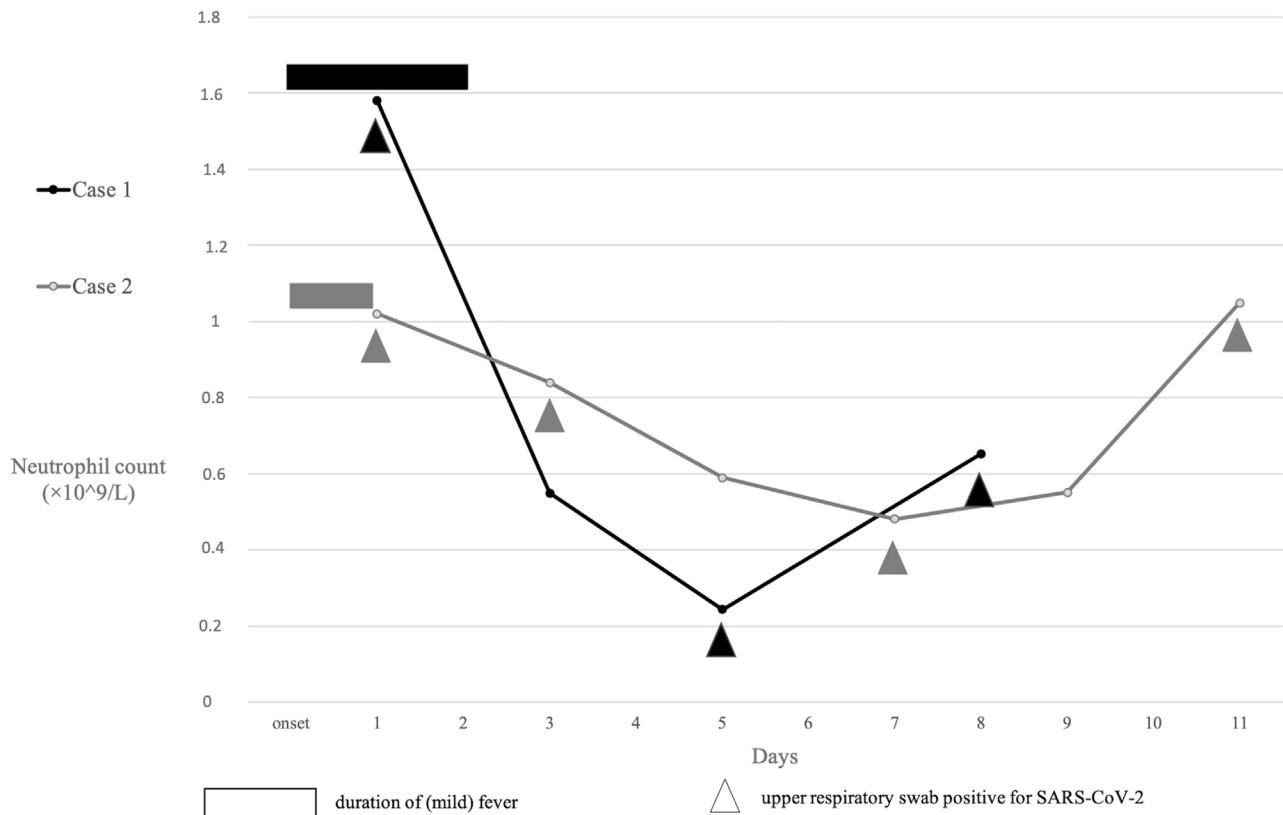


### To the Editor:

Infection with severe acute respiratory syndrome caused by the novel coronavirus 2019 (SARS-CoV-2) and resulting coronavirus disease 2019 (COVID-19) is a global pandemic.<sup>1</sup> Pediatric cases have some peculiarities, such as milder clinical manifestations and different laboratory abnormalities.<sup>2</sup> A systematic review on laboratory data identified 12 articles, with a total of 66 pediatric patients.<sup>3-15</sup> Lymphopenia was found in only 3% of children, whereas lymphopenia often is described in adult patients.<sup>16,17</sup> Neutropenia was recorded in 6% of cases, but it was never less than  $0.500 \times 10^9/L$  in this population.<sup>3</sup>

We describe a 23-day-old and a 39-day-old infant with mild COVID-19 and severe neutropenia who were cared for at our tertiary care referral pediatric hospital. They both came to medical attention with low-grade fever and mild respiratory symptoms with a history of contact with an infected person or persons. At admission, leukocyte and neutrophil counts were normal, nasopharyngeal swab tested positive for COVID-19, and co-infection with influenza-like viruses was excluded. On the fifth day and days after the beginning of symptoms, the 39-day-old girl and the 23-day-old girl developed severe neutropenia, with a nadir of  $0.244 \times 10^9/L$  neutrophils and  $0.482 \times 10^9/L$  neutrophils, respectively (Figure). No other alterations on routine examinations were recorded and the neutrophil values improved without clinical complications.

The presence of isolated severe neutropenia has not been described in children with COVID-19. This finding is noteworthy, because postinfectious transient neutropenia has been associated with many other viral infections in infancy, which might share pathogenic mechanisms.<sup>18,19</sup> Moreover, the evidence of neutropenia in neonates and infants could be another manifestation



**Figure.** Absolute neutrophil counts in two infants with SARS-CoV-2 infection.

of the age-related different immunologic response to SARS-CoV-2 infection.

Complete blood counts might be indicated 5-7 days after illness onset to detect neutropenia. We hope to alert providers to evaluate children, especially the youngest, with evidence of new symptoms during the second week after onset of illness to exclude severe neutropenia and possible secondary infection.

**Elisabetta Venturini, MD, PhD**  
Pediatric Infectious Disease Unit  
Meyer Children University Hospital

**Giordano Palmas, MD**  
Department of Health Sciences  
University of Florence

**Carlotta Montagnani, MD, PhD**  
Pediatric Infectious Disease Unit  
Meyer Children University Hospital

**Elena Chiappini, MD, PhD**  
Pediatric Infectious Disease Unit  
Meyer Children University Hospital  
Department of Health Sciences  
University of Florence

**Francesco Citera, Bs**  
**Valeria Astorino, Bs**  
**Sandra Trapani, MD**  
Department of Health Sciences  
University of Florence

**Luisa Galli, MD**  
Pediatric Infectious Disease Unit  
Meyer Children University Hospital  
Department of Health Sciences  
University of Florence  
Florence, Italy

<https://doi.org/10.1016/j.jpeds.2020.04.051>

## References

1. World Health Organization. Novel coronavirus (COVID-19) situation. <https://who.sprinklr.com>. Accessed March 27, 2020.
2. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020 [Epub ahead of print].
3. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *Clin Chem Lab Med* 2020 [Epub ahead of print].

4. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci* 2020;63:364-74.
5. Chan JF, Yuan S, Kok K-H, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514-23.
6. Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin Infect Dis* 2020 [Epub ahead of print].
7. Cai JH, Wang XS, Ge YL, Xia AM, Chang HL, Tian H, et al. [First case of 2019 novel coronavirus infection in children in Shanghai]. *Zhonghua Er Ke Za Zhi* 2020;58:86-7.
8. Chen F, Liu Z, Zhang F, Xiong RH, Chen Y, Cheng XF, et al. [First case of severe childhood novel coronavirus pneumonia in China]. *Chin J Pediatr* 2020;58:179-82.
9. Feng K, Yun YX, Wang XF, Yang GD, Zheng YJ, Lin CM, et al. Analysis of CT features of 15 children with 2019 novel coronavirus infection. *Zhonghua Er Ke Za Zhi* 2020;58:007.
10. Kam K, Yung CF, Cui L, Lin Tzer Pin R, Mak TM, Maiwald M, et al. A well infant with coronavirus disease 2019 (COVID-19) with high viral load. *Clin Infect Dis* 2020 [Epub ahead of print].
11. Wang D, Ju XL, Xie F, Lu Y, Li FY, Huang HH, et al. Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China. *Zhonghua Er Ke Za Zhi* 2020;58:011.
12. Zhang YH, Lin DJ, Xiao MF, Wang JC, Wei Y, Lei ZX, et al. 2019 Novel coronavirus infection in a three-month-old baby. *Zhonghua Er Ke Za Zhi* 2020;58:182-4.
13. Zeng L, Tao X, Yuan W, Wang J, Liu X, Liu Z. China's first neonatal coronavirus pneumonia. *Chin J Pediatr* 2020;58.
14. Zhang G, Zjang A, Huang L, Cheng LY, Liu ZX, Peng XL, et al. Twin girls infected with SARS-CoV-2. *Chin J Contemp Pediatr* 2020;22:221-5.
15. Zhao R, Shen X, Yu K, Sheng. A case of children with 2019 novel Coronavirus Infection. *Zhejiang Med J*; 2020 [Epub ahead of print].
16. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. Chinese Pediatric Novel Coronavirus Study Team. SARS-CoV-2 infection in children. *N Engl J Med* 2020 [Epub ahead of print].
17. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 [Epub ahead of print].
18. Husain EH, Mullah-Ali A, Al-Sharidah S, Azab AF, Adekile A. Infectious etiologies of transient neutropenia in previously healthy children. *Pediatr Infect Dis J* 2012;31:575-7.
19. Karavanaki K, Polychronopoulou S, Giannaki M, Haliotis F, Sider B, Brisimitzi M, et al. Transient and chronic neutropenias detected in children with different viral and bacterial infections. *Acta Paediatr* 2006;95:565-72.

## Missed or delayed diagnosis of Kawasaki disease during the 2019 novel coronavirus disease (COVID-19) pandemic



### To the Editor:

Due to “stay-at-home” orders and the risk of novel coronavirus disease 2019 (COVID-19), many parents now hesitate or fear seeking in-person consultations for their children. This has led to reductions in emergency department visits and hospital admissions for other critical illnesses. In addition, healthcare providers have focused on COVID-19 management during the pandemic. Because of Bayesian

thinking, other diseases may be underdiagnosed or undergo delayed treatment.

Because COVID-19 now leads as the probable diagnosis for first-line providers encountering febrile patients, the potential for missed or late diagnosis and treatment of Kawasaki disease in children is particularly concerning.<sup>1</sup> Prompt diagnosis of Kawasaki disease and treatment with intravenous immunoglobulin (IVIG) prevents coronary artery aneurysms (CAA).<sup>2,3</sup> Without timely treatment, CAAs could occur in up to 25% of children with Kawasaki disease.<sup>3</sup>

We respectfully remind caregivers of the following principles for the care of children with suspected or definite Kawasaki disease: (1) Keep a high suspicion for Kawasaki disease in all children with prolonged fever, but especially in those younger than 1 year of age. (2) Administer IVIG within 10 days, and ideally within 7 days, from onset of fever. (3) In the presence of ongoing systemic inflammation, children with Kawasaki disease presenting with greater than 10 days of fever and/or CAA may warrant IVIG treatment. (4) Continue to obtain recommended echocardiograms according to published guidelines.<sup>3</sup> (5) Watch for late manifestations of Kawasaki disease, review the clinical history, and seek pediatric cardiology consultation.<sup>4,5</sup> (6) In the case of delayed diagnosis, refer to the American Heart Association management guidelines or contact an expert in Kawasaki disease.<sup>3</sup> (7) Offer telemedicine services, remote echocardiogram, and direct-to-consumer visits that allow for nonverbal communication when evaluating children with confirmed or suspected Kawasaki disease.<sup>6-8</sup>

With this, we hope to avoid a future surge in the prevalence of CAAs in patients due to missed or delayed diagnosis of Kawasaki disease.

*We thank Angela J Doty, MD, and Maryam Harahsheh for their editorial assistance.*

**Ashraf S. Harahsheh, MD, FACC, FAAP**

Division of Pediatric Cardiology

Department of Pediatrics

Children's National Hospital

The George Washington University School of Medicine

Washington, District of Columbia

**Nagib Dahdah, MD**

Division of Pediatric Cardiology

Department of Pediatrics

CHU Sainte 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