



Letters to the Editor

Clinical Manifestation of Children with Kawasaki Disease during the COVID-19 Pandemic in Iran: A Case Series

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To the editor.

Kawasaki disease is a rare disease, but it is one of the most common childhood vasculitis,^{1,2} with approximately 85% of affected children being under 5 years of age and the most common age of onset being 18 to 24 months.¹ The diagnostic criteria for Kawasaki disease established by the American Heart Association include ≥ 5 days of fever, oral mucosal changes, bilateral no exudative conjunctivitis, eczematous rash, peeling of the hands and feet, and cervical lymphadenopathy. Apart from hyperthermia, at least four of the five main clinical features are required for a complete form of Kawasaki disease and fewer than four for an incomplete form of Kawasaki disease.²⁻⁴ Coronavirus infection in children and rarely in infants is associated with acute respiratory syndrome.¹⁻³ The COVID-19 pandemic has brought Kawasaki disease into the spotlight in both overt and covert forms. The overt form is the most common primary vasculitis in children,⁴ primarily affecting medium-sized and small arteries. The covert form, on the other hand, is multisystem inflammatory syndrome in children (MIS-C), a rare but severe disease that affects children 2 to 6 weeks after infection with SARS-CoV-19 and was initially mistaken for Kawasaki disease.^{4,5} However, there has been an increase in the incidence of Kawasaki-like disease among children with COVID-19, either concomitantly or after resolution of symptoms.⁷ Although the etiology of Kawasaki is unclear, a role for a viral and infectious agent has been suggested.¹⁻³ In a systematic review by Mardi et al. (2021) in Iran, the incidence of Kawasaki-like syndrome increased significantly during the COVID-19 pandemic.⁸ Other studies have also shown that the COVID-19 pandemic has increased the incidence of Kawasaki-like syndrome.³⁻⁴ Given that the manifestations of Kawasaki disease overlap with acute infectious diseases such as COVID-19, timely recognition of clinical manifestations and timely treatment in children with Kawasaki manifestations are essential to prevent acute and chronic complications in

children such as cardiac, pulmonary, and renal complications. We conducted a retrospective study to evaluate the demographic, clinical, and laboratory characteristics of 10 children with Kawasaki disease during the COVID-19 pandemic in a government hospital in Mazandaran province (northern Iran) from February 2020 to May 2023. We collected medical records of all children with Kawasaki disease or Kawasaki-like disease admitted to the hospital using the Kawasaki-specific code in the discharge records in the Health Information System (HIS). We also collected information on demographic characteristics, clinical symptoms, laboratory findings, radiological findings, cardiac examination results, and disease diagnosis (initial, in-hospital, and final). The inclusion criteria for the study included children aged 0-16 years who had typical and atypical symptoms of Kawasaki disease. Half of the children (50%) were boys (**Table 1**). Fever was observed in all patients; 1 (10%) patient required intensive care and gastrointestinal symptoms were observed in more than three-quarters of patients (**Table 2**). Pericarditis was observed in only 1 (10%) patients. X-ray, CT-scan, and LP results were positive in only 1 (10%) patient. The duration of hospitalization was 3.8 days (**Table 1**).

Complete Kawasaki disease was diagnosed in 6 patients (60%) and its incomplete form in 4 patients (40%) by the opinion of pediatric and cardiovascular specialists (**Table 2**).

None of the patients developed coronary aneurysms, dilatations, or myocarditis. Pericardial effusion was seen in one patient (10%). Kawasaki disease has a wide range of clinical signs and symptoms.⁶⁻⁹ The most common presenting symptoms are high fever, rash, conjunctivitis, lymphadenopathy, and strawberry tongue.^{7,10} In addition, gastrointestinal manifestations of fever lasting more than 5 days have been suggested as a predictor of coronary artery involvement. In a study by Jafari et al. (2023) in Iran, the results of multivariate regression analysis showed that the duration of fever until

Table 1. Characteristics of patients with Kawasaki disease or Kawasaki-like disease.

Age & Gender	Rash	Conjunctivitis	Fever with duration	Complete presentation (fever >4 days and ≥4 principal criteria)	Hospitalization period	SARS-CoV-2 PCR positive	ECG	Chest X-ray	CT-scan	LP Result
7-month-old girl	Yes	Yes	5>days	Yes	5 days	Yes	NL	NL	Not done	Not done
2-year-old girl	Yes	Yes	5>days	Yes	5 days	Yes	Tachycardia TWI +STD +	NL	Not done	Not done
1-year-old girl	Yes	No	10 days	Yes	2 days	NO	Tachycardia TWI +STD +	Not done	Not done	Not done
8-year-old boy	Yes	Yes	10 days	Yes	2 days	Yes	No	Not done	Not done	Not done
8-year-old boy	Yes	No	3>days	Yes	5days	Yes	NL	Not done	Not done	Not done
3-year-old boy	No	No	3>days	Yes	5days	Yes	TWI +	NL	Not done	Not done
11-month-old girl	Yes	No	5 days	Yes	5days	Yes	No	NL	A slight increase in the extra-axial fluid can be in the context of meningitis.	Yes (STAFF>100000)
1-year-old boy	No	No	5 days	Yes	5days	Yes	No	Yes, (hyperpara cardiac damage) of the lungs results from infectious damage.	Not done	Not done
6-year-old boy	Yes	Yes	3>days	Yes	5days	Yes	No	NL	Not done	Not done
1-year-old girl	Yes	No	3>days	Yes	5days	Yes	Tachycardia	NL	A slight increase in the extra-axial fluid can be in the context of meningitis.	Yes negative

Table 2. Diagnosis strategies.

Diagnosis	Patient 1	Patient2	Patient 3	Patient4	Patient 5	Patient6	Patient 7	Patient8	Patient9	Patient10
Initial diagnosis	FWLS (Fever of undetermined origin)	Kawasaki	Kawasaki	Kawasaki	Kawasaki	Influenza	Fever (Sepsis)	MISC	Kawasaki	Kawasaki
Diagnosis during treatment	Kawasaki	Kawasaki	Kawasaki	Kawasaki	Kawasaki	COVID-19	COVID-19	MISC	Kawasaki	Meningitis
Final Diagnosis	Kawasaki	Kawasaki	Semi Kawasaki	Kawasaki	Kawasaki and Herpes	Kawasaki	Semi Kawasaki	Semi Kawasaki	Kawasaki	Semi Kawasaki

diagnosis (fever more than 5 days) was a predictor of coronary artery involvement.¹⁰ In the present study, more than three-quarters of children had a fever for more than 5 days, and coronary artery involvement was observed in one-quarter of children. Seven children (70%) had positive CRP. The study conducted by Li et al. (2024) also confirmed that a nomogram can effectively predict the risk of coronary artery lesions using CRP, IL-6, ESR, HDL, ox-HDL, etc. These findings suggest that when hospital laboratory resources are limited, standard detection indices such as HDL, ox-HDL, and ESR can be used to forecast the level of oxidative stress and inflammation-associated targets in coronary artery lesions associated with Kawasaki disease.¹¹ Although cardiac manifestations were less observed in the present study, gastrointestinal symptoms were reported in almost 100% of children. Early diagnosis and timely treatment when gastrointestinal symptoms are observed are recommended.⁴

Kawasaki disease lacks a definitive association with any single agent, and several infectious triggers, such as rhinovirus, Para influenza virus, respiratory syncytial virus, adenovirus,¹⁰ human coronavirus,⁶ and novel coronavirus, are known. However, some studies have ruled out the association of human coronavirus with

Kawasaki disease.¹⁰ At the same time, a study by Feldstein et al. (2020) in the U.S. reported Kawasaki-like disease during the COVID-19 epidemic.² Therefore, it is still unclear whether the diagnosis of COVID-19 in children with Kawasaki-related symptoms should be treated with a diagnosis of Kawasaki disease or whether a new separate diagnosis of COVID-19 infection is required. There is a need to differentiate coincidental COVID-19 infection with Kawasaki disease from Kawasaki disease caused by COVID-19. This article will help to understand and address the Kawasaki-like manifestations of pediatric COVID-19 infection, especially in intensive care units, and its possible complications. It will also help to make timely and appropriate decisions about its treatment and management. Based on the results of the present study, the manifestations of Kawasaki disease overlap with acute infectious diseases such as COVID-19, so timely identification and treatment of children with Kawasaki manifestations is essential to prevent acute and chronic cardiac, pulmonary, and renal complications. Therefore, the preparation of standard guidelines for screening and early identification of children with symptoms of acute inflammatory diseases (MISC, COVID-19, and KD) seems necessary.

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Competing interests: The authors declare no conflict of Interest.

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