

# Frequency of heart involvement in Kawasaki disease during a decade in Iran

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## Abstract

**Background:** Kawasaki disease (KD) is an acute febrile illness of unknown etiology that is also associated with cardiovascular complications, making it the most common manifestation. It primarily occurs in children under the age of 5.

**Objectives:** This study aimed to investigate the clinical and preclinical findings of Kawasaki disease and determine heart involvement in Iranian child patients with Kawasaki disease.

**Methods:** In this retrospective study, medical records of all hospitalized child patients with Kawasaki disease in four hospitals in TEHRAN during the years 2011 to 2021 were examined. Patients with cardiac involvement were identified according to specific criteria. Demographic data, clinical and pre-clinical symptoms, the type and severity of cardiovascular disease, the type of complications, and mortality were recorded.

**Results:** Out of 108 child patients with Kawasaki disease, 36 patients (33.3%) had heart involvement. Among these patients with heart involvement, 63.2% were male, and 72.2% were aged less than 5 years old. Echocardiography results showed that 66.7% of patients had pericardial effusion as evidence of cardiac involvement. No mortality was recorded.

**Conclusions:** Heart involvement in Iranian children with Kawasaki disease was found to be 33.3% and was more common in boys. The most common type of heart involvement was pericardial effusion.

**Keywords:** Kawasaki, Heart involvement, Children, Iran.

## Introduction

Dr. Tomisaku Kawasaki originally characterized Kawasaki disease, an acute febrile vasculitis of kids, in Japan in 1967. The incidence of Kawasaki disease in Asian children is statistically higher than in other ethnic groups, but the disease occurs worldwide. It mainly affects children, with 80% of patients being younger than 5 years old, although it can also affect teenagers and adults.<sup>1,2</sup>

Diagnosis is based on clinical symptoms. Fever for more than 5 days and at least four of the following five symptoms are required to diagnose Kawasaki disease: bilateral non-purulent conjunctivitis, swelling and redness of the hands and feet in the acute phase and desquamation in the subacute phase, inflammation and redness of the mouth and pharynx, rash, and cervical lymphadenopathy greater

than 1.5 cm.<sup>2,3</sup>

According to the American Heart Association (AHA), patients with fever for more than 5 days, even with less than 4 clinical signs, should be considered to have Kawasaki disease if they have abnormal echocardiography.<sup>4</sup> Although there is no definitive laboratory test for Kawasaki disease, several laboratory abnormalities such as normocytic anemia, leukocytosis, thrombocytosis, elevated ESR, positive CRP, sterile pyuria, and moderate elevations in liver enzymes might be useful.<sup>5,6</sup>

The most important complications of this disease are coronary artery involvement in the form of aneurysms and myocardial infarction. About 20% of untreated patients develop coronary artery abnormalities such as aneurysms, which make them susceptible to arterial thrombosis or

stenosis, myocardial infarction, ruptured aneurysms, and sudden death.<sup>7</sup> Intravenous immunoglobulin injection and aspirin prescription, which have been found to lower the incidence of coronary artery disease to less than 5%, are the ideal treatments to reduce cardiac problems, particularly coronary artery involvement.<sup>8</sup> It has been illustrated that the long-term prescription of low molecular weight heparin in 100 patients with severe coronary artery anomalies has been more effective than warfarin.<sup>9</sup>

Today, in many countries, Kawasaki disease is a major cause of acquired heart diseases and has replaced acute rheumatic fever in children. Cardiac involvement is the most important manifestation of Kawasaki disease. At least 50% of patients will present with myocarditis, and pericarditis is a common occurrence in these patients. Coronary artery aneurysms are typically seen during the second and third weeks of the disease.<sup>8,9</sup>

According to a study by Nakamura et al., heart disease in infants, particularly those younger than 6 months of age, is more common than in older children (64 vs. 9%).<sup>10</sup> Several studies from developed countries, such as Japan, America, Canada, and Australia, as well as Iran, have identified Kawasaki disease (KD) as an alternative for acute rheumatic fever and as the most common acquired heart disease.<sup>10-12</sup> In developing countries, there are fewer organized reports, but studies have shown that KD is increasingly being recognized in many developed and developing countries.<sup>5,13-15</sup>

## Objectives

The study aimed to evaluate the prevalence of cardiac involvement in child patients with Kawasaki disease in Iran over a period of ten years.

## Methods

This cross-sectional study was conducted in four hospitals in Tehran, Iran. By coordinating with the hospitals' management and obtaining the necessary permits, the researcher gained access to the patients' medical files. All data were recorded in the preliminary checklist, and incomplete files were excluded from the study.

Demographic and clinical data, including age, sex,

clinical symptoms, cardiac involvement at the time of hospitalization, and mortality, were recorded in a checklist.

## Statistical analysis

The continuous variables were expressed as the mean $\pm$ SD, and the categorical variables were presented as a percentage. All statistical analyses were performed with SPSS (version 16.0, SPSS Inc, Chicago, IL, USA). A "P value" less than 0.05 was considered significant.

## Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki, and Institutional Review Board approval was obtained. The present study did not interfere with the process of diagnosis and treatment of patients. All data were extracted from the patients' medical records. By not gathering any personally identifiable information, such as names, phone numbers, email addresses, IP addresses, physical attributes, photographs, or videos, anonymity was ensured.

## Results

The study included 108 child patients with Kawasaki disease, of whom 67 (62%) were female and 41 (38%) were male, resulting in a male-to-female ratio of almost 1.6. A total of 83 patients (76.9%) were in the age group of less than or equal to 5 years, with the minimum and maximum ages recorded as 8 months and 13 years, respectively [Table 1].

Upon clinical examination, 8 out of 108 child patients with Kawasaki disease (7.4%) had a heart murmur, and 36 patients (31.5%) had abnormal echocardiography. Fever was recorded as the main symptom in 104 patients (96.3%) [Table 1].

The demographic and clinical findings of the 36 Kawasaki child patients with cardiac involvement are presented in Table 2. Of these patients, 23 (63.9%) were male and 13 (36.1%) were female, resulting in a male-to-female ratio of approximately 1.7 to 1. Most of the patients (26, 72.2%) were in the age group of less than or equal to 5 years.

Echocardiography revealed various forms of cardiac

involvement, with 24 patients (66.7%) displaying pericardial effusion, 11 patients (30.6%) exhibiting mitral regurgitation, and 10 patients (27.8%) exhibiting tricuspid regurgitation. There was no death reported.

**Table 1.** Demographic and clinical findings of 108 Kawasaki child patients

		N (%)
<b>Sex</b>	Girl	67 (62.0%)
	Boy	41 (38.0%)
<b>Age</b> (years old)	≤ 5	83 (76.9%)
	6-10	17 (15.7%)
	>10	8 (7.4%)
<b>Clinical examination</b>	Murmurs	8 (7.4%)
	Normal auscultation	100 (92.6%)
<b>Echocardiography</b>	Normal	72 (66.7%)
	Abnormal	36 (33.3%)
<b>Symptoms *</b>	Fever	104 (96.3%)
	Skin rashes	69 (63.9%)
	Limb Edema	13 (12.0%)
	bilateral non-purulent Conjunctivitis	57 (52.8%)
	Lymphadenopathy	50 (46.3%)
	High ESR	87 (80.6%)
	CRP+	63(58.3%)

\* Some symptom is reported in most patients

**Table 2.** Demographic and clinical findings of 36 Kawasaki child patients with heart involvement

		N (%)
<b>Sex</b>	Girl	23 (63.9%)
	Boy	13 (36.1%)
<b>Age</b> (years old)	≤ 5	26 (72.2%)
	6-10	7 (19.4%)
	>10	3 (8.3%)
<b>Echocardiography</b>	Pericardial effusion	24 (66.7%)
	Mitral regurgitation	11 (30.6%)
	Tricuspid regurgitation	10 (27.8%)
	Coronary artery dilation	3 (8.3%)
	Arrhythmia	1 (2.8%)
	Left ventricular dilatation	1 (2.8%)

## Discussion

Kawasaki disease is an acute vascular inflammation condition with an unclear etiology, primarily affecting infants and young children. In the present study, 76.9% of Kawasaki disease cases were observed in children under 5 years old, with patients ranging in age from 8 months to 13 years old. In a study by Kordi et al.,<sup>16</sup> the age range of patients with Kawasaki disease was found to be between 15 months and 13 years old, while another study reported an age range of 10 months to 7 years old.<sup>17</sup> Martinez et al.,<sup>18</sup> included 45 children with Kawasaki disease ranging in age from 4 months to 13 years in their research. In the present study, in contrast to some previous studies,<sup>19,20</sup> the frequency of Kawasaki disease is higher in females than in males. In Japan, a country with the highest reported incidence, the frequency of Kawasaki disease was higher in males than in females.<sup>10</sup> In the current study, fever symptoms were recorded in 96.3% of child patients with Kawasaki disease. A study conducted by Martinez et al. found that fever was the most prevalent symptom, affecting 98% of the patients, which is consistent with the present findings.<sup>18</sup>

In the present study, bilateral conjunctivitis was observed in 52.8% of the cases, which is higher than previous studies. Additionally, skin rash was reported in 63.9%, a figure that aligns with previous reports.<sup>17,19</sup> In the current study, 80.6% of the cases reported an abnormal ESR, while Gheini et al.,<sup>21</sup> found this figure to be 95.7% in their study.

Cardiac involvement is the most significant complication of Kawasaki disease. In the current study, 33.3% of Iranian child patients with Kawasaki disease had cardiac involvement, while the frequency was 44%, 27.3%, and 18% in the USA, Australia, and Spain, respectively.<sup>21,15,22</sup>

In this study, the most common type of heart involvement was pericardial effusion, affecting 66.7% of the cases. This rate is higher than the 35% reported in a study in Poland.<sup>23</sup> Following pericardial effusion, coronary artery dilatation was the next most reported cardiac involvement, with a rate of 8.3%.

In this study, 63.9% of the patients with cardiac involvement were male. Sadeghi et al. found that cardiac involvement was greater in males than in girls in comparable research.<sup>24</sup> No mortality was observed in the

current study, which may be related to early diagnosis, adequate treatment, or insufficient follow-up. In previous studies, the mortality rate was 2.3%.<sup>1,8,14,15</sup>

The study had several limitations that should be noted. The retrospective nature of the data gathering exposes the data to sampling bias and does not allow the establishment of any causal relationship. Additionally, after discharge, the researchers did not have access to some patients and encountered missing data. Furthermore, the sample size was relatively small. To overcome these limitations, prospective studies of these populations are needed.

## Conclusions

The current findings revealed that 33.3% of Iranian children with Kawasaki disease had heart involvement, which was more common in boys. The most prevalent type of heart involvement was found in children under 5 years old, with pericardial effusion being the most common type of involvement.

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## Competing interests

The author declare that she has no competing interests.

## Abbreviations

American Heart Association: AHA;  
Erythrocyte sedimentation rate: ESR

## Authors' contributions

Author read and approved the final manuscript. She take responsibility for the integrity of the data and the accuracy of the data analysis.

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## Availability of data and materials

The data used in this study are available from the corresponding author on request.

## Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Institutional Review Board approval was obtained. The present study did not interfere with the process of diagnosis and treatment of patients.

## Consent for publication

By submitting this document, the author declare her consent for the final accepted version of the manuscript to be considered for publication.

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