



The high prevalent of the left coronary artery in Kawasaki disease patients referred to Gorgan's Taleghani Hospital: A retrospective study

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Abstract

Background: Kawasaki disease (KD) is a febrile systemic vasculitis that affects children. Further research is required due to the disease's significance, consequences, and increasing prevalence. This study aimed to determine the frequency of coronary artery complications in patients with KD referred to Taleghani Hospital (Gorgan, Iran) from 2007 to 2017.

Methods: Between 2007 and 2017, 108 cases with a definitive diagnosis of KD were studied retrospectively. Data were obtained from medical records and the patients' biographical, clinical, laboratory, radiographic, and echocardiographic data.

Results: A total of 108 patients diagnosed with KD were involved in the study, 21 (19.44%) of whom showed coronary artery-associated complications. There was no significant difference in clinical and laboratory findings and coronary artery involvement between male and female groups (P -value < 0.05). Left coronary artery (LCA) involvement and the pattern of vascular involvement as ectasia and aneurysm were significantly higher in the echocardiography of the studied patients (P -value = 0.0001).

Conclusion: Kawasaki disease-related coronary artery complication is more common in children under the age of 3, particularly males, in Gorgan. The LCA is the most common site of coronary artery complications in KD children. The findings can improve the prognosis of KD patients and their related heart diseases.

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Introduction

Kawasaki disease (KD) is a febrile systemic vasculitis spreading across developing countries, mainly affecting children under 5 years old (1). There are 4 stages of the disease: acute, subacute, collapsing, and chronic. Fevers of 39 °C, distinguishing the acute phase or higher, could be fatal for children (2). Diagnosis is based on clinical (3) and laboratory findings (2). After KD, the most common complication is coronary artery involvement, which can range from no evident involvement in the majority of patients to several large aneurysms (4).

The most severe consequence of KD is coronary artery lesions (CALs) (2,5), which account for around 15-20% of KD sequelae and can develop into significant coronary artery stenosis and ischemic heart disease (6). The first-line treatment of the disease includes intravenous injection (IV) of high doses of immunoglobulin (IVIG), along with aspirin (2). Coronary artery lesions decrease after treatment with IVIG with aspirin (7). However, treatment may be delayed due to different levels of diagnosis and therapeutics, and some patients may not respond to routine treatment regimens (8,9). The disease's management and monitoring depend on the severity and extent of coronary artery involvement. Children with KD-associated coronary artery aneurysms or obstructions require long-term drug treatment and monitoring (10). According to studies, KD has become more prevalent in recent years (11-13).

Given the significance of KD in children, its complications, and its increased incidence, it is critical to examine positive cases of the disease to assess its characteristics, risk factors, and complications, particularly coronary artery disease, which is a significant factor in Kawasaki-related mortality rates in children. According to Cheraghali et al., from 2005 to 2012, the prevalence of KD among children admitted to Gorgan (Iran) hospitals was 37.39% (14). Given the relatively high incidence of KD in children hospitalized at Gorgan's children's hospitals, it is critical to conduct a retrospective analysis to assess the prevalence of coronary artery-related sequelae. As a response, this study sought to investigate the medical histories of children with KD referred to Taleghani Hospital in Gorgan between 2007 and 2017 and emphasize the incidence of coronary artery disease and its contributing aspects.

Methods

In this retrospective study, patients referred to Taleghani Subspecialty Center during 2007-2017 who had clinical symptoms of KD were examined for disease frequency and demographic information.

Patients with symptoms including fever lasting more than 5 days, bilateral nonpurulent conjunctivitis, oral and pharyngeal mucosal changes (redness, dryness, cracked lips, strawberry tongue), limb involvement (swelling of hands and feet, redness of hands and feet, or scaling in the acute stage), skin rash, and unilateral cervical adenopathy larger than 1.5 cm were included in the study.

Also, patients who had similar diseases with infectious causes or incomplete clinical information were excluded from the study.

The census approach was employed for sampling in this study. Thus, all eligible patients admitted to the hospital between 2007 and 2017 who had records in the hospital were chosen at random.

The current investigation was approved by the Ethics Committee, Golestan University of Medical Sciences, under the approval code of IR.GOUMS.REC.1400. As a retrospective study, the patients' parents were requested to provide their informed consent to use their child's medical records. Personal information gathered during the research is kept private.

Retrospective research was conducted on individuals diagnosed with KD by a pediatric cardiologist. A total of 108 patients met the inclusion criteria for the research. The information needed for the investigation was gathered from the patient's medical records. Patients' demographic data, such as age and sex, and paraclinical results, such as examination results, echocardiography and chest radiography reports, and treatments received, were thoroughly examined and extracted.

The information was imported into the SPSS v. 16 statistical software (SPSS Inc., Chicago, IL, USA). The chi-square test was performed to compare qualitative variables between groups. The student t test or one-way analysis of variance (ANOVA) was used to evaluate quantitative variables between groups. P -values of less than 0.05 with a 95% confidence level (CI) were considered significant.

Results

A total of 108 patients with a definitive diagnosis of KD, hospitalized in Gorgan Children's Hospital, were involved in this study from 2007-2007. Sixty-three patients (58.3%) were male, and 45 patients (41.7%) were female. The mean age of the subjects was 20.83 ± 26.87 months. The demographic information of the patients is shown in Table 1. The patients were evaluated for body temperature and duration of fever at admission. At the time of admission, the mean body temperature was 38.5 °C (38.5 °C and 39 °C in the boys and girls, respectively). However, female patients showed higher mean body temperature.

Clinical manifestations of patients at the time of admission, including conjunctivitis, mucosal involvement, skin involvement, organ involvement, and lymphadenopathy, were obtained from their records (Figure 1). No significant differences were observed between the two sexes based on clinical manifestations (P -value < 0.05).

Laboratory radiological records of the patients at admission were extracted and analyzed. The results showed that the mean hemoglobin levels, white blood cell count, and platelet count were 1.33 ± 9.89 , 5.35 ± 13.04 , and 19.88 ± 426.61 , respectively (Table 1). In addition, the results indicated higher erythrocyte sedimentation rate (ESR) levels in female patients. (P -value = 0.008).

Table 1. The demographical and fever information of patients with Kawasaki disease and the differences between the two sexes

Variables	Sex		Sig.€	
	Male (Mean±Std.dev)	Female ((Mean±Std.dev))		
Age (Month)	24.70±18.06	29.91±24.07	0.20	
Weight (Kg)	11.98±3.88	11.60±34.31	0.60	
Body temperature ‡ (°C)	38.5	39	0.062	
Duration of fever	6.52±5.28	6.62±4.17	0.92	
Laboratory findings				
WBC count ×109/L	12.51±5.50	13.77±5.11	0.23	
Hemoglobin/L	9.96±1.52	9.79±1.03	0.51	
Platelet count ×109/L	397.48±14.97	467.40±24.82	0.07	
CRP‡	+1 (%)	11/63 (17.5)	7/45 (15.6)	0.40
	+2 (%)	18/63 (28.6)	18/45 (40.0)	
	+3 (%)	13/63 (20.6)	11/45 (24.4)	
ESR	61.98±30.22	78.42±32.79	0.01	
Albumin (g/dL)	3.72±0.53	3.77±0.52	0.63	
AST (U/L)	43.81±35.90	51.24±53.54	0.75	
ALT (U/L)	51.83±74.71	55.80±80.36	0.79	

‡ The results are reported based on mean IQR.

‡ CRP is reported based on the number of patients (%).

€ Student's t-test and One-way ANOVA were used to assess the significance level between the laboratory findings of the two groups.

WBC: White Blood Cell; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase

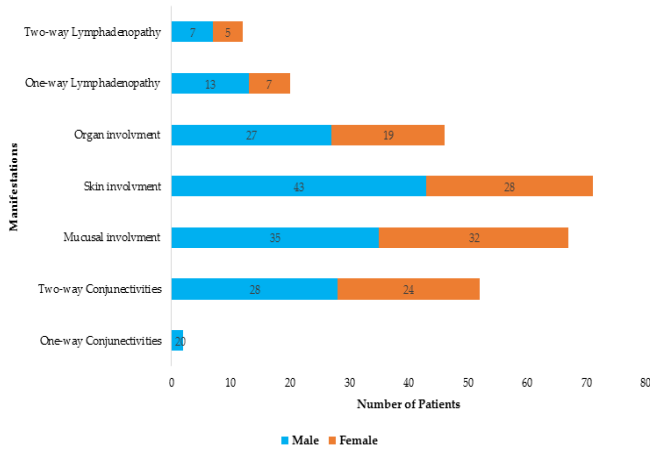


Figure 1. Clinical manifestations of patients with Kawasaki disease. No significant differences in manifestations were observed between male and female patients.

Out of 108 patients, 21 (19.4%) had abnormal echocardiography, of whom 11/108 patients (17.5%) were male and 10/108 patients (22.2%) were female. The patterns of coronary artery involvement were also determined in the patients; 14/108 patients (13%) had involvement of the left coronary artery, 4/108 patients (3.7%) had involvement of 2 coronary arteries, 1/108 patient (0.9%) showed involvement of all 3 coronary arteries, and 1/108 patient (0.9%) had valvular dysfunction. The patients showed different patterns of involvement in echocardiography (Table 2).

Table 2. Echocardiographic findings of patients with Kawasaki disease based on sex

Findings		Sex		Total (%)	Sig.
		Male (%)	Female (%)		
Echocardiographic imaging	Normal	52 (82.5)	35 (77.8)	87 (80.6)	0.54
	Abnormal	11 (17.5)	10 (22.2)	21 (19.4)	
Grand total (%)		63 (100)	45 (100)	108 (100)	
Coronary artery involvement	Normal	52 (82.5)	35 (77.8)	87 (80.6)	0.64
	LCA	7 (11.1)	7 (15.6)	14 (13.0)	
	2 Vessels	2 (3.2)	2 (4.4)	4 (3.7)	
	3 Vessels	1 (1.6)	0 (0.0)	1 (0.9)	
	Valvopathy	0 (0.0)	1 (2.2)	1 (0.9)	
	Other	1 (1.6)	0 (0.0)	1 (0.9)	
Grand total (%)		63 (100)	45 (100)	108 (100)	
Pattern of coronary artery involvement	Normal	52 (82.5)	35 (77.8)	87 (80.6)	0.72
	Brightness	0 (0.0)	1 (2.2)	1 (0.9)	
	Lack of tapering	1 (1.6)	1 (2.2)	2 (1.9)	
	Shining	1 (1.6)	1 (2.2)	2 (1.9)	
	Ectasia	3 (4.8)	1 (2.2)	4 (3.7)	
	Dilated	2 (3.2)	1 (2.2)	3 (2.8)	
	Aneurism	1 (1.6)	3 (6.7)	4 (3.7)	
	ASD	1 (1.6)	0 (0.0)	1 (0.9)	
	MR	0 (0.0)	1 (2.2)	1 (0.9)	
	Multiple findings	2 (3.2)	1 (2.2)	3 (2.8)	
Grand total (%)		63 (100)	45 (100)	108 (100)	

LCA: Left Coronary Artery; MR: Mitral Regurgitation

The relationship between variables was measured to assess the risk factors for coronary artery involvement and abnormal echocardiographic findings. The results showed no significant relationship between clinical manifestations and abnormal echocardiographic findings (Table 3).

Table 3. Association of clinical manifestations of patients with Kawasaki disease with echocardiography findings

Clinical manifestations	Echocardiography		Spearman Corr.	Sig.	
	Normal (%)	Abnormal (%)			
Conjunctivitis	1-way	1 (1.1)	1 (4.8)	0.29	0.31
	2-way	40 (46.0)	12 (57.1)		
Mucosal involvement	52 (59.8)	15 (71.4)	0.23	0.45	
Skin involvement	57 (65.7)	14 (66.7)	0.92	0.92	
Organ involvement	38 (43.7)	8 (38.1)	0.65	0.64	
Lymphadenopathy	1-way	16 (18.4)	4 (19.0)	0.11	0.21
	2-way	6 (6.9)	4 (19.0)		

The relationship between laboratory findings at the time of admission and abnormal findings in echocardiography was examined. The results showed no significant relationship between the studied variables and abnormal findings in echocardiography (Table 4).

Table 4. Laboratory findings associated with echocardiographic findings

Laboratory findings	Mean differences	Std. Error differences	Confidence interval of the difference		Sig.‡
			Lower	Upper	
WBC count ×109/L	0.99	1.30	-1.59	3.58	0.45
Hemoglobin/L	-0.16	0.33	-0.80	0.49	0.63
Platelet count ×109/L	-58650.25	48224.18	-154259	36958.88	0.23
CRP‡	-0.15	0.27	-0.69	0.39	0.59
ESR	-6.83	7.84	-22.37	8.72	0.39
Albumin (g/dl)	-0.07	0.13	-0.18	0.32	0.58
AST (U/L)	5.32	10.74	-15.98	26.62	0.62
ALT (U/L)	4.56	18.75	-32.70	41.72	0.81

‡ Independent samples t-test was used for statistical analysis. WBC: White Blood Cell; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase.

The highest incidence of coronary artery disease, with 14/21 cases (66.67%), was related to the left main coronary artery, followed by 4/21 cases (19.05%) related to simultaneous involvement of the left and right coronary arteries (P-value = 0.000). Also, the results demonstrated that ectasia pattern, aneurysm, and dilation had the highest frequency in the vascular involvement pattern in echocardiography (P-value = 0.000) (Figure 2).

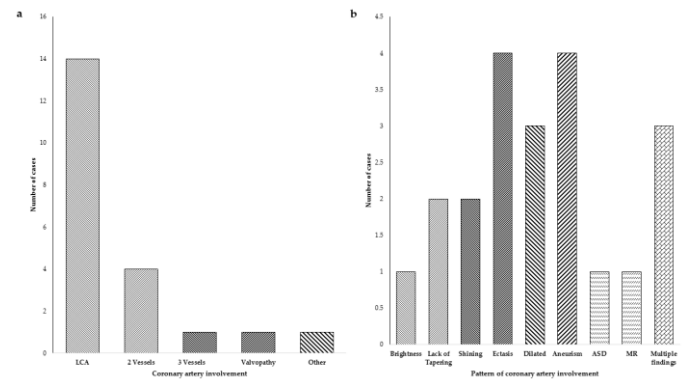


Figure 2. Abnormal echocardiography and coronary artery involvement pattern. a) shows the number of cases with coronary artery involvement. a) illustrates the number of cases with different patterns of coronary artery involvement with abnormal echocardiography findings. b) shows the number of patterns of coronary artery involvement in patients with KD.

Discussion

The first case of KD was described in the 1960s by Tomisaku Kawasaki (15). The severity of coronary artery lesions measures prolonged prognosis. Therefore, KD is currently the leading cause of acquired heart disease in developed countries (9,16). This retrospective study aimed to evaluate the frequency of coronary artery lesions in Golestan Province and study the clinical factors observed in patients referred to Taleghani Hospital during 2007-2017.

The coronary artery is the most common site of KD (17). Narrowing or obstructing the lumen most likely involves the LCA following the right coronary artery (18). The findings of the present study support the highly prevalent involvement of LCA. Additionally, it was observed that > 19% of the cases were related to simultaneous involvement of the left and right main coronary arteries. On the other hand, the pattern of vascular involvement in echocardiography showed ectasia, aneurysm, and dilation with the highest frequency, respectively.

Most of the current study records comprised children < 3 years old. This was

consistent with a retrospective study in northern Iran, showing that most patients with KD in northern Iran are between 1 and 3 years old and are mostly boys (19). In addition, all patients were treated with a single dose of intravenous immunoglobulin along with a high-dose salicylic acid, as was reported before (8,9,17,18,20).

Different geographical regions may affect the incidence of KD-associated coronary artery lesions. From 2004 to 2014 in Canada, KD-related coronary artery lesions affected 3.5% of all patients (21). In the United States, 3.20-2.25% of patients with KD suffered from coronary artery aneurysms (22,23). In addition, a study in Australia found that the incidence of coronary artery dilatation was 16.7% (24). The range of KD-associated coronary artery complications in Asian countries is around 3% to 30% (18,25-28). Further studies have been conducted in Iran. In a study of Mazandaran Province, 25% of cases with KD had heart disorders (19). In studies conducted in Yazd (29), Urmia (30), and Ilam (31), 39.5%, 12%, and 32.9% of cases had KD-coronary artery diseases, respectively. The present study's findings demonstrated KD-associated coronary artery in 19.4% of patients. Differences in reported coronary artery symptoms could be due to different diagnostic levels, differences in treatment protocols, or delays in diagnosis and

Coronary artery lesions vary with sex and age, and boys and infants are more prone to KD-associated coronary artery lesions (28). However, pathological factors have not yet been identified. It was found that at the start of KD, there was an increase in ESR, C-reactive protein (CRP), white blood cell (WBC) count, liver enzymes, and a drop in hemoglobin and albumin levels (32). However, we found no association between the laboratory findings, including WBC count, hemoglobin, platelet, CPR, ESR, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and coronary artery; similar results were reported Rahbarimanesh et al. (32).

The development of Kawasaki-associated coronary artery lesions is a chronic process that requires close monitoring of patients, as some vascular problems can develop later, even after the coronary aneurysm has disappeared. In some cases, no coronary artery lesions are found in the acute phase, which is generally a good prognosis. However, long-term cardiovascular risk is still possible. It is challenging to know and justify the processes of coronary artery involvement over a long period because follow-up data have so far been limited to monitoring middle-aged and elderly patients with a high prevalence of cardiovascular disease (33).

Conclusion

Kawasaki disease-associated coronary artery complications are more frequent in children under 3 years old, especially boys, in Gorgan. The left coronary artery is the most common site of coronary artery complication in KD children in Gorgan. The physicians can use the findings for a better prognosis of patients with KD.

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Ethical statement

The Ethics Committee at Golestan University of Medical Sciences has approved the study under the approval code of IR.GOUMS.REC.1400.

Conflicts of interest

The authors declare that they have no competing interests.

Author contributions

All the authors have participated in one or more parts of the present study, including data gathering, data entry, data analysis, writing the first draft of the manuscript, and editing the manuscript.

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