Assessment of Coronary Artery Involvement and its Relevant Factors in Children with Kawasaki Disease

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Abstract

Background: Kawasaki Disease (KD) is a multisystem inflammatory disease of unknown origin that presents with high fever, followed by skin rash, conjunctival hyperemia, oral mucosal hyperemia, fissured and reddened lips, strawberry-like tongue, non-purulent cervical lymphadenopathy, and erythema and edema of the hands and feet. Cardiac involvement is its most important complication that usually presents after the second week. It presents itself in the form of myocarditis, pericarditis, pericardial effusion, valvular involvement, and most importantly, coronary artery involvement and aneurysm formation. Given the significance of cardiac involvement, here we have investigated the relevant factors of coronary artery involvement in patients with KD.

Materials and Methods: One-hundred and twenty (120) KD patients attending Qom's Hazrat Fatemeh Masoumeh Hospital (referral center) from 2010 – 2016 were studied. Using a questionnaire, data were collected from the patients and their medical records. This study was cross-sectional. Random sampling was done. Data were analyzed using SPSS software.

Results: Of the 120 patients examined, 57.5% had mild coronary artery involvement, among whom 54.2% had mild coronary artery dilatation; 7.5% had coronary artery aneurysm, and 59.2% had mitral insufficiency. 39.2% had certain degrees of pericardial effusion. Examination of demographics (age, sex & weight) and laboratory data indicated significant associations between cardiovascular involvement and neutrophil count (p=0.003), CRP (p<0.001), and ESR (p<0.001).

Conclusions: There are significant associations between active phase reactant (ESR, CRP, Neutrophil count) and cardiac complications in Kawasaki disease patients.

Key words: Kawasaki disease, coronary artery involvement, clinical signs, lab findings

Introduction

Kawasaki Disease (KD) is a multisystem inflammatory disease of unknown origin that presents with high fever, followed by skin rash, conjunctival hyperemia, oral mucosal hyperemia, fissured and reddened lips, strawberry-like tongue, non-purulent cervical lymphadenopathy, and erythema and edema of the hands and feet. It was first detected and introduced by Tomisaku Kawasaki in Japan [1], however, it is now observed among all races across the world [2].

The disease is diagnosed based on clinical symptoms. Fever persisting for at least 5 days and four of the following symptoms can establish the diagnosis of KD: 1- bilateral bulbar conjunctivitis; 2- hyperemia of the oropharyngeal mucosa, strawberry-like tongue and fissured red lips; 3- erythema and edema of the hands and feet during the acute phase and desquamation during the subacute phase; 4- unilateral cervical lymphadenopathy exceeding 1.5 cm; 5- rash (macular, hives, erythema multiforme) [3]. A hallmark of this disease is vasculitis of small and medium –sized vessels of different organs, with an inclination toward the involvement of coronary vessels. During the acute phase, all vessels are affected with vasculitis; later on only medium and large –sized vessels may remain affected [4]. This syndrome is observed all over the world, however, it is most prevalent in Asia. The annual attack rate in Asian Americans is greater than in non-Asians [5]. KD is now the most important cause of acquired cardiac disease among children in many countries across the world .Cardiac involvement is the most significant complication of the disease which often presents after the second week [6]. It includes myocarditis, pericarditis, pericardial effusion, valvular involvement and most importantly, coronary artery involvement and aneurysm formation [3,6,7]. The use of aspirin and intravenous gamma globulin (IVIG) considerably reduces the probability of developing cardiac complications. Given the low prevalence of rheumatic heart disease in developed countries, this disease is the most common cause of acquired cardiac disease in children [8].

Thus, bearing in mind the prevalence of KD and the development of cardiac complications in developing countries, this research was conducted with the goal of determining the relevant factors of coronary involvement in KD patients attending Qom's Hazrat Fatemeh Masoumeh Hospital (referral center) from 2010 – 2016 (over a 5-year-period).

Materials and methods

Study design and subjects
A descriptive – analytic cross-sectional study was conducted. The samples were selected on a census basis, from KD patients attending Qom's Hazrat Fatemeh Masoumeh Hospital (referral center) from 2010 – 2016. The research population consisted of all KD patients who had attended the hospital from March 2010 to February 2016.

Data collection
A patient questionnaire was used to collect data. All KD patients' records were extracted from the archives and their demographic data as well as their blood test results were registered. In addition to the background data collected, information related to the patients' assessment in terms of cardiac complications, such as, myocarditis, pericarditis, pericardial effusion, valvular involvement and most importantly, coronary artery involvement and aneurysm formation were also collected; clinical and echocardiographic assessment results were also registered.

Data analysis
Data were analyzed using SPSS version 20, and were described using descriptive statistical indices. Chi square and Fischer's exact test were used to compare the percentage affected with cardiac complications among the groups. T-test was used to compare ESR and WBC with cardiac involvement between the two groups, and level of significance (p-value) was set at 0.05.

Results

As seen in the table, among those affected with cardiovascular disease (CVD), 58% were boys and 42% were girls. No significant association was observed between gender and cardiac complications (p value=0.447) [Table 1].

Another feature examined was coronary artery aneurysm; out of 111 cases, 6 (5%) had left coronary aneurysm. One person (0.8%) had right coronary aneurysm , and 2 (1.7%) had aneurysms on both sides. These 111 persons (92.5%) had no evidence of aneurysm on echocardiography. Moreover, 59.2% had mild mitral valve insufficiency and the remaining 40.8% had none. 39.2% of the patients had mild pleural effusion and 60.8% did not have pericardial effusion. There were no abnormal findings in most of the patients' ECGs; only 10% had abnormal ECGs. Ejection fraction (EF) was also investigated; 95.8% had normal, and the remaining had reduced, EF.

Table 2 shows the demographic variables and lab findings based on coronary artery complication. Among these variables, neutrophil count, ESR & CRP were significantly associated with coronary artery complications.

The mean neutrophil count in patients with cardiac complications was 10,277.54, and in patients without complications it was 7,657.06, indicating a significant difference (p value=0.003). Patients with cardiac complication had a higher neutrophil count as opposed to patients who did not [Table 2].

The mean ESR level in patients with cardiac complications was 100.6957 and in patients without complication it was 76.2157, which was significant (p value=0.000) [Table 2].

In patients with cardiac complications, the mean CRP was 45.5826, and in those without complications it was 26.9039; with a p value of 0.000 a significant association

Table 1: Gender distribution among Kawasaki Disease patients in Hazrat Fatemeh Masoumeh Hospital from 2010 to 2016

Disease	Boy		Girl		P value	OR	Confidence interval
	Number	Percent	Number	Percent			
Present	40	58	29	42	0.447	0.754	1.561-0.364
Absent	26	51	25	49			

Table 2: Distribution of demographic variables and lab findings based on coronary artery complication in patients with Kawasaki Disease

	Coronary artery complication	Number	Mean	Standard deviation	P value
Age	Present	51	3.4167	2.09575	0.705
	Absent	69	3.5978	2.88684	
Weight	Present	51	15.5961	5.77401	0.355
	Absent	69	16.9348	9.01588	
WBC	Present	51	13839.22	5823.026	0.067
	Absent	69	15811.59	5746.650	
Neutrophil count	Present	51	7657.06	4769.214	0.003
	Absent	69	10277.54	4497.883	
Albumin	Present	51	3.6837	0.46882	0.121
	Absent	69	3.5401	0.51822	
ESR	Present	51	76.2157	34.58515	<0.001
	Absent	69	100.6957	31.27266	
CRP	Present	51	26.9039	20.83623	<0.001
	Absent	69	45.5826	24.17445	
Hemoglobin	Present	51	10.500	1.6659	0.620
	Absent	69	46.06	53.423	
SGOT	Present	51	46.06	53.423	0.271
	Absent	69	146.41	646.020	
SGPT	Present	51	44.61	77.731	0.230
	Absent	69	116.88	422.328	
Platelets	Present	51	417254.90	186857.576	0.906
	Absent	69	413449.28	164645.210	

Table 3: The duration of fever and coronary artery involvement in patients with Kawasaki Disease

		Coronary artery involvement		P	OR	Confidence interval
		Absent	Present			
Duration of fever	Less than 5 days	10	8	0.244	1.86	0.677 – 5.108
	More than 5 days	41	61			
Number of diagnostic criteria	Fewer than 5	22	33	0.610	0.828	0.4 – 1.714
	More than 5	29	36			

was observed between CRP and cardiac complications [Table 2].

We also studied the duration of fever and the incidence of coronary artery involvement, where we observed no significant association between the two [Table 3].

Discussion

In the current study, 120 patients with Kawasaki Disease who included 66 boys and 54 girls were examined. Here, we investigated the cardiac complications created as a result of Kawasaki Disease and examined through echocardiography. Then, these patients were classified into two groups with cardiac complications and without complications. The demographic variables and lab findings were reviewed in both groups, upon which we learned that there were no significant differences. No significant differences were observed between the groups with and without cardiac complications in terms of age, weight, fever duration, number of diagnostic criteria, Platelets, Hb, WBC, Albumin, SGOT and SGPT.

On the other hand, significant differences were observed between the two groups in terms of raised neutrophils, ESR and CRP, such that these lab findings were considerably elevated in patients with cardiac complications.

Upon comparing the current study with Arabi et al, we made the following observations: the sample size of this study was greater, and 86.7% of our patients had abnormal echos, whereas, in Arabi's study, 69% had no signs of cardiac involvement. One reason behind these differences may be the difference in number of patients studied. Moreover, in our study, 59.2% had mitral insufficiency, as opposed to Arabi's study wherein only 10% had this complication. This difference can explain the high percentage of patients with cardiac complications in our study. Mitral insufficiency is a common finding during the acute phase of the disease and usually requires no special intervention, which was taken into consideration in our study. However, in Arabi's study, mitral changes have been examined over a period of 7 years, i.e. progressive mitral insufficiency has been taken into account, thus explaining how the percentage of patients with this complication have reduced in percentage. Our study examined the patients in the acute phase of the disease, while Arabi's study reported the echo results 7 years after treatment. We may thus infer from these findings that timely and appropriate treatment can reduce cardiac complications. Aneurysm was seen in 13% of patients, while in our study 7.5% had developed aneurysms; given the sample size of the two studies, no significant difference was observed between them. Pleural effusion was investigated in both studies; we reported 39.2% and Arabi reported 11%. This statistical difference may be explained by the type and duration of the studies. Our study was a cross-sectional study wherein the echo had been performed during the acute phase of the disease. Conversely, Arabi's study was conducted serially, and the echo results of 7 consecutive years of treatment and follow-up were analyzed.

Eventually, A'rabi Moghadam et al concluded that appropriate treatment with IVIG and aspirin reduces the prevalence of cardiac complications in comparison to treatment with aspirin alone. We could not investigate this issue in our study, as, firstly, it was cross-sectional, and secondly, most of the patients (84.2%) had received this treatment already [9].

Elsewhere, in another study, Karbasi et al examined patients who had fever for more than five days; 39.5% of them had developed cardiac complications, while this figure was 57.5% in our study. This difference may be attributed to the greater sample size of our study, or, that our population had attended the hospital later and had been diagnosed later. In both studies, the percentage of boys affected with KD was higher than the girls [10].

Ram Krishna et al studied the risk factors for cardiac involvement in KD patients and found 21% affected. Since the sample size was much smaller than ours we cannot compare and assess the results with our own. Eventually, lengthy fever and pyuria were known to raise the risk of cardiac disease in KD patients; neither of these two factors have been examined in our study [11]. Akhtar et al \ investigated the cardiac complications of KD, and observed that 41% of the study population had coronary artery involvement. In the current study, this figure was 57.5%, indicating the consistency of results of both studies. In their study, the patients were again assessed after being treated, where coronary artery involvement had fallen to 8% [12]. Such a comparison was not done in our study. Another study conducted by Gowin et al found that 60% of patients had cardiac complications, and 13.3% had developed coronary artery aneurysms. This study was statistically similar to ours [13]. Narayanan et al studied cardiac involvement in KD patients; 18.5% had coronary artery involvement, whereas, our finding was 42.5%, the difference of which may be attributed to the greater sample size of our study [14].

Conclusion

As stated earlier, Kawasaki Disease is a multi-system inflammatory disease of unknown origin. It is most common in Asia. One of the characteristics of this disease is vasculitis of small and medium –sized vessels in various organs, with an inclination toward involving coronary vessels. This disease is the most important cause of acquired cardiac disease in children in many countries, including developing countries. Thus, this study was conducted to determine the relevant factors of coronary artery complications in patients with KD over a five-year-period. Subsequently, 120 KD patients were assessed. Significant associations were observed between raised neutrophils, CRP and ESR and cardiac complications in KD. However, no significant associations were observed between gender, age, weight, fever duration, number of diagnostic criteria, Platelets, Hb, WBC, Albumin, SGPT, SGOT, and cardiac complications. The higher the neutrophil count, CRP and ESR levels, the more likely cardiac complications occur. Given the findings of this study, we may conclude that the timely and

accurate examination of laboratory criteria can be a relative predictor of cardiac complications, which, if diagnosed on time and treated appropriately, can be controlled and improved.

Limitations

There were certain limitations in this study, namely, the use of patients' archived records, which is not devoid of error. The advantage of this study over its similar counterparts is that it covers a 5-year-period and the sample size is greater than most other studies.

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