Arch Pediatr Infect Dis. 2016 October; 4(4):e27946. doi: 10.5812/pedinfect.27946.

Published online 2016 June 11. **Brief Report**

The Relationship Between Severity of Kawasaki Disease and History of Ischemic Heart Disease in the Parents

Fariba Shirvani,[1,*] Sasan Saket,[2] Abdolah Karimi,[1] Saeed Mojtahedzadeh,[3] Reza Shiari,[3] Kimia Seifi,[1] and Somaye Shamsy[3]

[1]Pediatric Infections Research Center, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Pediatric Neurology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[*]*Corresponding author*: Fariba Shirvani, Pediatric Infections Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel: +98-9123277918, E-mail: shirvanifariba@rocketmail.com

Received 2015 March 07; **Revised** 2016 January 16; **Accepted** 2016 February 09.

Abstract

Background: Kawasaki disease (KD) is the most important cause of ischemic heart disease in children. Its pathogenesis is not well understood, but geographic, ethnic and familial pattern of this syndrome is reported. Ischemic heart disease (IHD) in parents can be the result of KD in their children. This is a study on the prevalence of IHD in parents of children with severe and non-severe Kawasaki disease.

Objectives: The current study aimed to estimate the prevalence of IHD in the families of children with KD.

Patients and Methods: Sixty-one children with Kawasaki disease were admitted from December 21, 2004 to January 21, 2008to Mofid Children Hospital (from one month to thirteen-year old) and 50 patients entered the study. Subjects were divided into the severe (24subjects) and non-severe (26 subjects) groups. All of the parents were called for investigation. Data were analyzed by SPSS ver. 21 software.

Results: Thirty-two (64%) subjects were male and 18(36%) were female.(1.8/1), mean age of children was 43 $\pm$ 33.1 months, and mean age in the severe and non-severe groups were 53.48 $\pm$ 37.26 and 32.19 $\pm$ 25.76 month, respectively (CI = 2-38.2, P = 0.02). History of IHD was more common in fathers of children in the severe Kawasaki disease group (P = 0.001) with no mean age difference between them. History of cardiac drug usage and hypertension was more common in the severe Kawasaki group (P = 0.009 and P = 0.046).

Conclusions: Results of the current study revealed higher incidence of IHD in fathers of the subjects with severe KD. More investigation of genetic predisposition to Kawasaki disease acquisition is recommended.

Keywords: Epidemiology, Family History, Kawasaki Disease, Ischemic Heart Disease

1. Background

Kawasaki disease is an acute vasculitis in children and affects medium sized arteries, especially coronary arteries. In 1970, a nationwide survey of KD in Japan documented 10 autopsies cases of sudden cardiac death after KD (1, 2). Occurrence of cardiac complications was 0.03 in 159 Iranian children (3). Its etiology remains unknown, but in accordance to clinical and epidemiologic features, infectious agents are strongly suspected as etiologic factors. The disease has various incidence rate among ethnic groups, with higher rates in Asians; therefore, genetic predisposition and familial pattern is also likely (2, 4, 5); there are reports of Kawasaki disease in children of parents who had Kawasaki disease in their childhood. In a 10-year study period from 1999 to 2008, 0.43% of the children with Kawasaki disease had a history of the disease in their parents (6). Among 14,163 parental pairs with Kawasaki disease, 33 parents had a history of the disease. The number of parents expected to have a history of Kawasaki disease was less than the observed cases. It was shown that children, whose parents had a history of Kawasaki disease, had a more severe course of their disease with a higher history of coronary abnormalities (2).

2. Objectives

The current study aimed to investigate the prevalence of Ischemic heart disease (IHD) in parents of children with severe and non-severe Kawasaki disease.

3. Patients and Methods

The current retrospective study was conducted on 61 subjects with Kawasaki disease admitted to Mofid Children hospital from December 21, 2004 to January 21, 2008. Inclusion criteria were normal children with no history of diseases such as diabetes, metabolic disorders, cerebral palsy, congenital anomalies, renal and hepatic and congenital heart diseases, with Kawasaki disease in accordance to American heart association (AHA) guideline (7).

Seven subjects because of being unavailable, one because of parents or child death, and three subjects because of refusal to enter the study were excluded, all subjects were contacted to be visited in cardiology clinic, and both of subjects' parents had echocardiographic investigation by an expert cardiologist. Echocardiography was performed with no charge. All children had echocardiography on diagnosis, 2 - 3 and 6 - 8 weeks later by the same cardiologist, who was not aware of clinical and history information of the subjects. History taking and physical examination was performed on all parents.

The variables of epidemiologic, laboratory, clinical and echocardiographic results were transferred into a questionnaire for each subject. The 50 subjects were divided into two groups: severe (group 1) and non-severe (group 2). Subjects were defined as severe if they had at least one of the three following criteria:

1) Cardiac problems compatible with Kawasaki disease including internal coronary artery diameter more than 3 mm in patients under five years or less than 4 mm in older individuals, or diameter of one part of coronary artery $\geq$ 1.5 times larger than the normal width, and obvious irregularity of coronary artery lumen in each echocardiographic results (8).

2) No decrease of erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) after one week of treatment (9, 10).

3) Elevated alanine aminotransferase (ALT) > 80 IU/mL not related to other diseases (11). Therefore, more severe cases might have more cardiac and hepatic complications (12).

Criteria for presence of IHD in parents were one of the following:

1) History of acute myocardial infarction or unstable angina

2) History of abnormal physical stress test or heart scan

3) History of coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA).

Clinical, laboratory and echocardiographic information of children and parents were collected on the questionnaire and analyzed by SPSS ver. 21 using exact and not exact logistic regression test. P value less than 5% was considered significant.

The research was approved by ethical committee of Shahid Beheshti University of Medical Sciences; all aspects of the world medical association declaration of Helsinki were considered.

4. Results

Thirty-two (64%) subjects of the study were male and 18 (36%) were female (male to female ratio about: 1.8/1). Mean age of children was 43 $\pm$ 33.1 months; 53.48 $\pm$ 37.26 months in the severe and 32.19 $\pm$ 25.76 months in the non-severe groups (CI = 2 - 38.2, P = 0.02). Duration of admission was statistically longer in the severe vs. non-severe group (8.27 $\pm$ 3.7 days vs. 2.24 $\pm$ 3, 54) (CI = 0.7 - 4.2, P = 0.006); 30% of the patients were admitted in spring and summer and 28% of them were admitted in fall and winter. Clinical signs such as oral cavity and mucosal changes were more common in non-severe subjects 18 (75%) vs. 23 (88.5%) in the severe ones, but it was not statistically significant (P > 0.05). There was one case of facial palsy in the severe group. Parental consanguinity and other clinical signs in the two groups are shown in Table 1. History of fathers IHD based on the study criteria (P = 0.001), History of cardiac drug usage (P = 0.009), and hypertension (P = 0.046) were more common in the severe Kawasaki disease group (Table 2); no significant difference was observed in the mean age of fathers between the two groups of severe and non-severe Kawasaki disease. The mean age of fathers in the severe and non-severe groups were 37.7 $\pm$ 6.7 years and 37.4 $\pm$ 6, respectively (P = 0.8).

5. Discussion

Incidence of Kawasaki disease is progressively increasing and the epidemics of this syndrome were studied in Japan (13). There was an increasing number of case reports of Kawasaki disease in parents and children in the literature (14, 15). In a study conducted in japan from 1999 - 2000 among 14163 children with Kawasaki, maternal incidence of Kawasaki disease was higher than expected cases in general population. Higher incidence of Kawasaki disease in mothers of children with Kawasaki disease than the statistically expected occurrence in general population shows the possible inherited risk factors in families. Among these children, the prevalence of coronary abnormalities one month after the onset of the disease was reported twice, and prevalence of a recurrence of Kawasaki disease and incidences involving their siblings were five and six times as high as that of all patients, respectively (2);

Table 1. Frequency of Different Clinical and Laboratory Findings and Treatment Options in Severe Kawasaki Disease (n = 24)

Clinical Findings	Severe Kawasaki		OR	Lower Limit of 95%CI	Upper Limit of 95%CI	P Value
	Yes	No				
Parent consanguinity	2 (20.00)	22 (55.00)	0.21	0.02	1.24	0.10
Oral and mucosal abnormality	18 (43.90)	6 (66.67)	0.40	0.06	2.18	0.39
Conjunctival injection	20 (51.28)	4 (36.36)	1.84[a]	0.46	7.32	0.38
Rash	18 (62.07)	6 (28.57)	4.09[a]	1.22	13.69	0.02
Adenopathy	12 (60.00)	12 (40.00)	2.25[a]	0.71	7.14	0.17
Irritability	3 (25.00)	21 (55.26)	0.27[a]	0.06	1.16	0.07
Finger desquamation	10 (58.82)	14 (42.42)	1.94[a]	0.59	6.36	0.27
Anal desquamation	7 (46.67)	17 (48.57)	0.93[a]	0.28	3.11	0.90
Erythema at BCG	1 (20.00)	23 (51.11)	0.25	0.005	2.74	0.40
Vomiting and diarrhea	5 (71.43)	19 (44.19)	3.09	0.44	35.83	0.35
Gallbladder hydrops	1 (100)	23 (46.94)	1.08[b]	0.03	Infinity	0.96
Sterile pyuria	7 (63.64)	17 (43.59)	2.26	0.57	9.02	0.24
Arthritis	2 (40.00)	22 (48.89)	0.70	0.05	6.75	> 0.99
Convulsion	1 (33.33)	23 (48.94)	0.53	0.008	10.80	> 0.99
Facial palsy	0	24 (48.98)	1.08	0	42.25	> 0.99
Otitis media	2 (40.00)	22 (48.89)	0.70	0.05	6.75	> 0.99
Pericardial effusion	6 (31.58)	18 (58.06)	0.33[a]	0.10	1.11	0.07
(Coronary) aneurism	-	24 (48.00)	-	-	-	-
(Other) Echo findings	4 (57.14)	20 (46.51)	1.52	0.23	11.65	0.91
Two times IVIG	6 (100)	18 (40.91)	10.91[a]	1.46	+Infinity	0.02

Abbreviations: BCG, bacilli Calmette-Guerin; IVIG, intravenous immunoglobulin; OR, odd ratios.
[a] Logistic regression (not exact).
[b] Median unbiased estimates.

data from 16th to 20th nationwide survey on patients with Kawasaki from 1999 to 2008 in Japan shows that history of Kawasaki disease in parents increased from 0.15% to 0.7%, the increasing pattern may be due to more concern on diagnosis (6). Although in North America, 0.7% of 424 subjects with Kawasaki syndrome (KS) had sibling cases and nine families were identified with KS in two generations (16). These results strengthen the genetic predisposition to cardiac sequel of KD in families.

Racial difference in incidence of KD, that is higher in Japanese (17), and higher occurrence of KD in siblings and parents than the general population (18) promoted investigators to find a specific locus of human leukocyte antigen (HLA) in children with Kawasaki or clarifying a genetic susceptibility to KD in children and their parents with a history of KD (19). Based on genetic predisposition, possible exposure to a common infectious agent (20) can be the proposed factors of KD occurrence in twins at the same time (21). The same genetic factors play the role of disease occurrence in two generations (18, 22). In this study more severe Kawasaki cases had higher incidence of fathers with IHD that may be related to previous history of Kawasaki in them, history of drug consumption and hypertension may be related to other cardiac conditions; accordingly, the significant difference between severe and non-severe subjects in the history of cardiac drug usage in fathers of the current study subjects may be unreliable; association between hypertension and coronary artery disease (CAD) is stated in epidemiologic studies but higher incidence of hypertension in fathers of children with severe KD is a matter of debate. This finding neither shows a causative relationship between hypertension and Kawasaki disease nor predicts more incidence of IHD in patients' parents; further investigations are recommended (23). Koren et al. showed that duration of fever, as a factor to predict severity of ongoing vasculitis (24), was not different in the two groups of the current study. In a study by Sano T, patients who were non-responsive to intravenous immunoglobu-

Table 2. Risk Factor in the Parents of Subjects With Severe Kawasaki Disease (n = 24) Group in Comparison With Those of the Non-severe Subjects

Risk Factor	Severe Kawasaki		OR	Lower Limit of 95%CI	Upper Limit of 95%CI	P Value
	Yes	No				
Mothers' Risk Factors						
History of cardiac drugs usage	3 (75.00)	21 (45.65)	3.49	0.26	194.84	0.34
History of MIa and unstable angina	-	24 (48.00)	-	-	-	-
HTNb	1 (50.00)	23 (47.92)	1.09	0.01	88.69	1
Chest pain	2 (100)	22 (45.83)	2.70[a]	0.21	+Infinity	0.23
Exercise test abnormality	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
Ischemic heart disease	3 (75.00)	21 (45.65)	3.49	0.26	194.84	0.34
MRc	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
TRd	-	24 (48.00)	-	-	-	-
MVPe	9 (69.23)	15 (40.54)	3.22	0.73	17.06	0.11
PSf	0	24 (48.98)	1.08[a]	0	42.25	1
HCMg	0	24 (48.98)	1.08	0	42.25	1
Rheumatic fever	0	24 (48.98)	1.08	0	42.25	1
Fathers' Risk Factors						
History of cardiac drugs usage	6 (100)	18 (40.91)	10.91[a]	1.46	+Infinity	0.009
History of MI and unstable angina	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
HTN	4 (100)	20 (43.48)	6.42[a]	0.76	+Infinity	0.046
Chest pain	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
Exercise test abnormality	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
Ischemic heart disease	8 (100)	16 (38.10)	16.46[a]	2.32	+Infinity	0.001
MR	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48
TR	2 (100)	22 (45.83)	2.70[a]	0.21	+Infinity	0.23
MVP	3 (50.00)	21 (47.73)	1.09	0.13	9.09	1
PS	-	24 (48.00)	-	-	-	-
HCM	-	24 (48.00)	-	-	-	-
Rheumatic fever	1 (100)	23 (46.94)	1.08[a]	0.03	+Infinity	0.48

Abbreviations: HCMg, hypertrophic cardiomyopathy; HTNb, hypertension; MIa, myocardial infarction; MRc, mitral regurgitation; MVPe, mitral valve prolapse; OR, odd ratios; PSf, pulmonary stenosis; TRd, tricuspid regurgitation.
[a]Median unbiased estimates.

lin (IVIG) had higher CRP and aspartate aminotransferase (AST). Total bilirubin and Body surface area adjusted coronary dimensions were statistically more in diameter in non-responsive group (25). Kubayashi et al. proved that sodium $\leq$ 133 mM/L, neutrophils > 80%, days of illness at initial treatment $\leq$ four days, AST, age in months $\leq$ two, platelet count < 300,000/μL and CRP $\geq$ 10 mg/dL were independent predictors of non-responsive-IVIG, but not for coronary complications (26). The retrospective study which looked at risk factors for refractory KD in Japan resulted that in 20% of cases who did not respond to initial IVIG therapy, risk factors associated with the need for retreatment were initial treatment on/before the fifth day of illness, recurrent episodes of KD and male gender) (25). A scoring system by Nakano H. et al. used age, CRP and platelet count to predict and determine the patients with higher chance for coronary problems (27). In a study by sleeper LA et al. in eight centers in North America the most consistent variables as independent risk factors for IVIG retreatment model included male gender, lower albumin, and higher AST (c-statistic 0.83). However, the associations between Kubayashi score and coronary artery dimension were relatively weak (the largest Spearman correlation coefficient was 0.29) (12).

Therefore, the current study had a special focus on using the severity factors to investigate the parental ischemic heart disease. Choosing coronary artery lesion as a criterion of severity can select the genetically susceptible cases to tissue damage; other criteria of the study, such as no decrease of ESR and CRP after one week and elevation of ALT, are in accordance with further cardiac damage occurred in the current study patents. Higher CRP after one week is a factor of severity and ESR can be an additional helping indicator, although it may rise after IVIG treatment (9). Tremoulet et al. measured the laboratory values of 312 subjects with KD, which was statistically different between IVIG resistant and IVIG responsive subjects either in the subacute or convalescent phase. This is thought to occur as a consequence of the net positive charge of IgG molecule that neutralizes the net negative charge of the red blood cell (RBC) surface (zeta potential), leading enhanced rouleaux formation and accelerated RBC sedimentation. Tremoulet et al. stated no difference in comparison of convalescent ESR in IVIG-resistant vs. - subjects responsive to KD; in subjects with aneurysms suggested that the higher ESR was due to more inflammation rather than an effect of a second dose of IVIG (10). It is important to note that both groups of the current study used IVIG; therefore, the effect of IVIG on ESR rise affected both groups.

Although investigation of IHD on parents of the children with Kawasaki disease is prone to observation and recall bias, no other information about possible relationship with parents offered in the current study. Parents of the severe and non-severe groups were also in the same age range. With regard to the same results in other studies further studies on this important clinical issue are recommended.

5.1. Conclusions

Kawasaki disease is an important disease with unknown etiology and as described earlier, genetic factors may be related to its occurrence. The current study showed higher incidence of IHD in fathers of children with severe KD, which may be correlated with Kawasaki disease in their childhood; therefore, it is essential to take a careful family history from parents of the children with KD. Conducting a follow-up study on the children with this disease up to their adulthood and investigation of their children in prospective studies can provide more valuable information.

Acknowledgments

Authors wish to thank all the staff and associated workers of pediatric infections research center in Mofid Children hospital for their co-operation. Authors specially thank Ahmadreza Shamshiri for his patience and scientific statistical revision.

References

1. Kosaki F, Kawasaki T, Okawa S, Sonobe T, Tanaka N, Shigematsu I, et al. Clinicopathological conference on 10 fatal cases with acute febrile mucocutaneous lymph node syndrome. *Shonika Rinsho Jpn J Pediatr.* 1971;**24**:2545–59.
2. Yanagawa H, Nakamura Y, Yashiro M, Ojima T, Tanihara S, Oki I, et al. Results of the nationwide epidemiologic survey of Kawasaki disease in 1995 and 1996 in Japan. *Pediatrics.* 1998;**102**(6):E65. [PubMed: 9832593].
3. Moradinejad MH, Kiani A. Kawasaki disease in 159 iranian children. *Iran J Pediatr.* 2007;**17**(3):241–6.
4. Freeman AF, Shulman ST. Kawasaki disease: summary of the American Heart Association guidelines. *Am Fam Physician.* 2006;**74**(7):1141–8. [PubMed: 17039750].
5. Uehara R, Yashiro M, Nakamura Y, Yanagawa H. Clinical features of patients with Kawasaki disease whose parents had the same disease. *Arch Pediatr Adolesc Med.* 2004;**158**(12):1166–9. doi: 10.1001/archpedi.158.12.1166. [PubMed: 15583102].
6. Uehara R, Yashiro M, Nakamura Y, Yanagawa H. Parents with a history of Kawasaki disease whose child also had the same disease. *Pediatr Int.* 2011;**53**(4):511–4. doi: 10.1111/j.1442-200X.2010.03267.x. [PubMed: 21040190].
7. Newburger JW, Taubert KA, Shulman ST, Rowley AH, Gewitz MH, Takahashi M, et al. Summary and abstracts of the Seventh International Kawasaki Disease Symposium: December 4-7, 2001, Hakone, Japan. *Pediatr Res.* 2003;**53**(1):153–7. doi: 10.1203/00006450-200301000-00026. [PubMed: 12508096].
8. Research Committee on Kawasaki disease . Report of subcommittee on standardization of diagnostic criteria and reporting of coronary artery lesions in Kawasaki disease. Japan: Ministry of Health and Welfare; 1984.
9. Feigin RD, Cherry J. Textbook of pediatric infectious diseases: Volume 1. WB saunders; 1998.
10. Tremoulet AH, Jain S, Chandrasekar D, Sun X, Sato Y, Burns JC. Evolution of laboratory values in patients with Kawasaki disease. *Pediatr Infect Dis J.* 2011;**30**(12):1022–6. doi: 10.1097/INF.0b013e31822d4f56. [PubMed: 21817952].
11. Sundel R, klien-Gitelman M, Kaplan S. Refractory Kawasaki disease 2014. Available from: http://www.uptodate.com/contents/refractory-kawasaki-disease.
12. Sleeper LA, Minich LL, McCrindle BM, Li JS, Mason W, Colan SD, et al. Evaluation of Kawasaki disease risk-scoring systems for intravenous immunoglobulin resistance. *J Pediatr.* 2011;**158**(5):831–835 e3. doi: 10.1016/j.jpeds.2010.10.031. [PubMed: 21168857].
13. Nakamura Y, Yashiro M, Uehara R, Sadakane A, Chihara I, Aoyama Y, et al. Epidemiologic features of Kawasaki disease in Japan: results of the 2007-2008 nationwide survey. *J Epidemiol.* 2010;**20**(4):302–7. [PubMed: 20530917].
14. Iwata F, Hanawa Y, Takashima H, Shimoura K, Nishibayashi Y. Kawasaki disease in a father and son. *Acta Paediatr Jpn.* 1992;**34**(1):84–6. [PubMed: 1580158].
15. Segawa M, Saji T, Ozawa Y, Oaki Y, Matsuo N. Familial Kawasaki disease in mother and son: occurrence in two generations. ; 1995.
16. Dergun M, Kao A, Hauger SB, Newburger JW, Burns JC. Familial occurrence of Kawasaki syndrome in North America. *Arch Pediatr Adolesc Med.* 2005;**159**(9):876–81. doi: 10.1001/archpedi.159.9.876. [PubMed: 16143748].

17. Yashiro M, Nakamura Y, Hirose K, Yanagawa H. Surveillance of Kawasaki disease in Japan, 1984-1994. Proceedings of the Fifth International Symposium on Kawasaki disease. Amsterdam. Elsevier Science; .
18. Fujita Y, Nakamura Y, Sakata K, Hara N, Kobayashi M, Nagai M, et al. Kawasaki disease in families. *Pediatrics.* 1989;**84**(4):666–9. [PubMed: 2780128].
19. Kaneko K, Obinata K, Katsumata K, Tawa T, Hosaka A, Yamashiro Y. Kawasaki disease in a father and daughter. *Acta Paediatr.* 1999;**88**(7):791–2. [PubMed: 10447146].
20. Leen C, Ling S. Mycoplasma infection and Kawasaki disease. *Arch Dis Child.* 1996;**75**(3):266–7. [PubMed: 8976676].
21. Turel O, Bornaun H, Hatipoglu N, Oztarhan K. Kawasaki disease in dizygotic twins in Turkey. *J Rheumatol.* 2011;**38**(8):1812–3. doi: 10.3899/jrheum.110286. [PubMed: 21807808].
22. Kato S, Kimura M, Tsuji K, Kusakawa S, Asai T, Juji T, et al. HLA antigens in Kawasaki disease. *Pediatrics.* 1978;**61**(2):252–5. [PubMed: 634680].
23. Rosendorff C, Black HR, Cannon CP, Gersh BJ, Gore J, Izzo JJ, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. *Circulation.* 2007;**115**(21):2761–88. doi: 10.1161/CIRCULATIONAHA.107.183885. [PubMed: 17502569].
24. Koren G, Lavi S, Rose V, Rowe R. Kawasaki disease: review of risk factors for coronary aneurysms. *J Pediatr.* 1986;**108**(3):388–92.
25. Sano T, Kurotobi S, Matsuzaki K, Yamamoto T, Maki I, Miki K, et al. Prediction of non-responsiveness to standard high-dose gamma-globulin therapy in patients with acute Kawasaki disease before starting initial treatment. *Eur J Pediatr.* 2007;**166**(2):131–7. doi: 10.1007/s00431-006-0223-z. [PubMed: 16896641].
26. Kobayashi T, Inoue Y, Takeuchi K, Okada Y, Tamura K, Tomomasa T, et al. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. *Circulation.* 2006;**113**(22):2606–12. doi: 10.1161/CIRCULATIONAHA.105.592865. [PubMed: 16735679].
27. Nakano H, Ueda K, Saito A, Tsuchitani Y, Kawamori J, Miyake T, et al. Scoring method for identifying patients with Kawasaki disease at high risk of coronary artery aneurysms. *Am J Cardiol.* 1986;**58**(9):739–42. [PubMed: 3766414].