CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1299283

Available online at: http://www.iajps.com Review Article

A REVIEW ON KAWASAKI DISEASE

N.Anitha*[1], Adeeba Husna [1], Syed Akbar[2]

*[1] Department of Pharmacology, Sultan-ul-Uloom College of Pharmacy, Road no.3, Banjara Hills, Hyderabad-500 034, Telangana, India.

[2] Department of Pharmaceutical Chemistry, Sultan-ul-Uloom College of pharmacy, Road no.3, Banjara Hills, Hyderabad-500 034, Telangana, India.

Abstract:

Kawasaki disease is defined as an acute systemic vasculitis which majorly causes coronary artery abnormalities in 25% of untreated patients. Diagnosis is done basically in the light of clinical criteria; however, the presentation is roughly incomplete in approximately 25% of patients and this appears to subset at a nearly greater risk of serious complications. The main cause of Kawasaki disease is still unknown, however it is said that there is stimulation in the immune system after the infection in a genetically predisposed person. The infection caused is said to be highly suspected even though there is no specific bacteria or virus detected. Some of the infectious agents are Parvovirus, Staphylococcus aureus, Epstein-Bar virus, Chlamydia and Mycobacterium. This can be further confirmed by the occurrence of this disease in children. The occurrence of this disease is higher in children with affected parents than in all-purpose population. Inflammation of various organs like heart, meninges, lungs, lymph nodes, liver and strawberry tongue is seen during the acute phase. Different treatment methods used includes intravenous immunoglobulin, salicylates, beta blockers, statins and corticosteroids. The treatment is done with high doses of aspirin and immunoglobulin and the fever resolves within 4-5 days and there is a full recovery. Only few drugs are available for the treatment of this disease, and cardiac complications can be minimized only with beta-blockers and statins.

Key words: *Kawasaki disease, vasculitis, aneurysms, intravenous immunoglobulin and beta blockers.*

Corresponding author:

Dr.N.Anitha,

Professor and HOD, Dept. of Pharmacology,
Sultan- ul-Uloom College of Pharmacy, Road no.3,
Banjara Hills, Hyderabad-500 034, Telangana, India.
Email: anirajan_76@yahoo.co.in
Mobile no: 09959971590

QR code

Please cite this article in press N. Anitha et al., ***A Review on Kawasaki Disease,*** *Indo Am. J. P. Sci, 2018; 05(06).*

INTRODUCTION:

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome which mainly affects the infants and children below 5 years. It is an acute systemic vasculitis which majorly causes coronary artery abnormalities in 25% of untreated patients [1]. It is known to surpass rheumatic heart disease as the leading cause of acquired cardiovascular disease in children in the developed world [2].

Tomisaku Kawasaki was the first to report kawasaki disease in the year 1967. The clinical signs and symptoms were described by him in 50 Japanese children with acute mucocutaneous lymph node syndrome [3]. After one year, Yamamoto T published the electro cardiogram abnormalities of KD patients [4]. In 1972 , Japanese physicians finally established the relationship between KD and coronary vasculitis [5]. From that time KD has been described in many countries but mostly in Asia [6].

Diagnosis is done basically in the light of clinical criteria; however, the presentation is roughly incomplete in approximately 25% of patients, and this appears to subset at a nearly greater risk of serious complications [7]. Prevention of coronary artery dilation and aneurysms can be done by timely administration of intravenous immunoglobulin.

HISTORY

Tomisaku Kawasaki was the first to report this disease in a four-year-old child with a rash and fever at the Red Cross Hospital in Tokyo in January 1961 and he published a similar report on 50 other cases [8]. Later, Kawasaki and his colleagues were convinced of positive cardiovascular inclusion when they examined and announced 23 cases, of which 11 (48%) patients had variations from the normal recognized by an electrocardiogram [9]. Melish et al in the year 1976 described the same illness in 16 children in Hawaii [10]. Same diagnostic criteria was established independently for this disorder by Mellish and Kawasaki, which are still used today to make the diagnosis of Kawasaki disease [11].

A question was raised whether the disease just began amid the period in the vicinity of 1960 and 1970, however later a preserved heart of a seven-year-old kid who died in 1870 was analyzed and indicated three aneurysms of the coronary arteries with clots, and also pathologic changes consistent with Kawasaki disease [12].

EPIDEMIOLOGY

In the United States Rheumatology Clinic Population Study, Kawasaki disease appeared to represent 23% of all pediatric vasculitides and is the second most common multi-system vasculitis of infancy and childhood behind Henoch-Schonlein Purpura [13-15]. Although significant differences in epidemiological distribution have been seen worldwide [16], large number of factors appears to be relatively constant. These incorporate a male predominance, with a male-to-female apportion of in the vicinity of 1.5:1 and 2:1 [17-19]; marked seasonality, with increased occurrence in winter and early springs in temperate climates [20] and summer peaks in some Asian countries under 5 years of age [21]. An increased incidence in people of Asian descent, both inside and outside Asia was seen [22-24]. A rising frequency has been observed worldwide over time, may be due to increased incidence in people of Asian plunge, both observed worldwide over time, may be due to increased awareness and acknowledgement of the disease [25, 26].

ETIOLOGY

The main cause of KD is still unknown, however it is said that there is stimulation in the immune system after the infection in a genetically predisposed person [27]. The infection caused is said to be highly suspected even though there is no specific bacteria or virus detected [28], some of the infectious agents given are Parvovirus [29], Staphylococcus aureus [30], Epstein-Bar virus [31], Chlamydia & Mycobacterium [32]. This can be further confirmed by the occurrence of this disease in children. The prevalance of this disease is higher in children with affected parents than in all-purpose population [33]. But with still certain doubt that the mechanism of KD is triggered by immune system related symptoms [34, 35].

Clinical Manifestations

- It is usually accompanied with high fever lasting for more than 5 days
- Rash development takes place with peeling of skin between the chest and legs.
- Unusual swelling in hands and feet
- Redness in the eyes
- Glands gets enlarged especially in neck
- Inner mouth, tongue and throat gets irritated
- Joint pain with stomach ache, diarrhea and vomiting
- Swollen bright and strawberry tongue [36].

Figure no 1 and 2 shows the picture of straberry tongue and enlarged neck which is observed as clinical symptoms in KD.

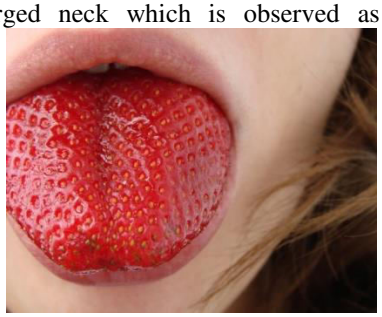

Fig no 1: Strawberry tongue

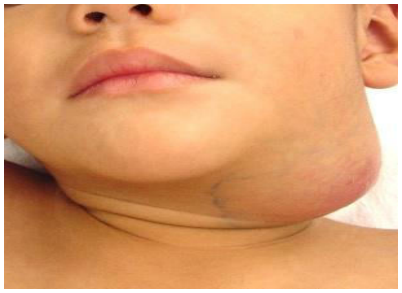

Fig no 2: Enlarged neck

KD has three stages:

1. Stage 1: Acute febrile phase
2. Stage 2: Sub acute phase
3. Stage 3: Convalescent phase

Stage 1 (0-10 days): The acute febrile phase is mainly characterized by fever. The fever in KD is usually higher than 39° C (102° F) and is unresponsive to antipyretics and antibiotic therapy [37]. Untreated children can have fever that lasts typically upto 1 to 2 weeks. Conjunctivitis (non purulent and bulbar), oropharyngeal changes (erythema, cracking of the lips, strawberry tongue, and non-exudative erythema of the oropharynx), polymorphous light eruption are the most common clinical features of KD in its acute phase [38]. Erythema or edema of the palms or soles occurs during the acute phase of KD. Cervical lymphadenopathy is not common in KD, found as a unilateral, firm and non-fluctuant node with a diameter greater than 1.5 cm [39].

Stage 2 (10-28 days): It begins with fever, rash and lymph adenopathy lasts up to one or two weeks after the beginning of the fever with persistent irritability. Anorexia, conjunctival infection, skin peeling of fingers, toes and thrombocytosis is seen which lasts for weeks. Risk of sudden death is high during this stage [40].

Stage 3: This stage begins after the disappearance of all clinical signs of illness usually 6 to 8 weeks after the onset of the illness and continues until the sedimentation rateis back to normal, at six to eight weeks after the onset of illness. Changes of the lips and oral cavity include erythema and cracking of the lips, strawberry tongue, and erythema of the oropharyngeal mucosa were seen. Adults and children have different intensity of symptoms. Adults' neck lymph nodes are affected more, 93% of adult's vs 15% of children, hepatitis 65% adult vs 10% in children and arthralgia 61% adult vs 24–38% in children [41].

PATHOPHYSIOLOGY

Kawasaki disease involves systemic inflammation of medium sized blood vessels, mainly coronary arteries. Inflammation of various organs like heart, meninges, lungs, lymph nodes and liver is seen during the acute phase. Initially, polymorph nuclear invasion is found in vessel walls and mononuclear cells soon replace this [42]. Inflammation subsides during recovery but leaves behind fibrous connective tissue in the vessel wall along with proliferation of intima. This fibrin makes the vessels less elastic, stiffer and unable to generally stretch with higher arterial pressure but instead the arteries develop permanent bulging called aneurysms [43]. Aneurysms 8mm larger are at the most risk of rupturing, which reduces blood flow to the heart causing ischemia and potentially myocardial infarction. In some cases fibrosis doesn't lead to aneurysms but instead it makes the vessel walls thicker reducing the lumen diameter restricting blood flow which again leads to myocardial infarction or heart attack [44].

DIAGNOSIS

Kawasaki disease can be diagnosed only by clinical manifestation i.e, by managing medical signs and symptoms. No specific laboratory investigations are available for this condition. Establishment of diagnosis is difficult especially in the early course of the illness and mostly children are not diagnosed until they have visited to many health care providers.

The criteria for establishing the diagnosis classically include fever for 5 consecutive days and additionally four of the five diagnostic criteria which include the following [45].

1. Lips or oral cavity shows erythema or lips cracking is seen
2. A rash on the trunk can be seen
3. Hands or feet experiences swelling and erythema

4. Eyes are red (conjunctival infection)
5. At least 15 mm of swollen lymph node is seen at neck area

Blood tests

- Complete blood count can diagnose normocytic anemia and later thrombocytosis.
- Evaluation of the Erythrocyte sedimentation rate can be done.
- C-reactive protein can be estimated.
- Liver function tests may reveal evidence of hepatic inflammation and low serum albumin levels in this condition.

Other optional tests include:

- Electrocardiogram may reveal evidence of ventricular dysfunction or, rarely, arrhythmia occurs due to myocarditis.
- Subtle coronary artery changes or later true aneurysms can be established by Echocardiogram.
- Hydrops (enlargement) of the gallbladder can be revealed by Ultrasound or computerized tomography scan.
- White blood cells and protein in the urine (pyuria and proteinuria) without evidence of bacterial growth can be established by Urinalysis [46].

TREATMENT

- IVIG (Intravenous immunoglobulin)

  For the treatment of Kawasaki disease the IVIG intravenous immunoglobulins are considered as standard treatment [47], provided in high doses which produces marked improvement usually observed within 24 hours. If the fever does not respond, further an additional dose may have to be given. In some of the rare cases, a third dose may be given to the child. IVIG is useful within the first seven days of onset of fever, in terms of preventing coronary artery aneurysm [48].

  Mechanism of action: The efficacy of IVIG administered in the acute phase of KD is well established to reduce the prevalence of coronary artery abnormalities. Their exact mechanism of action is unknown [49]. They act by either suppressing the over active immune response or inhibiting the binding of WBC to damaging antibodies or removes all the antibodies from the body [50, 51].

  Side effects: Headache, fever, fatigue, chills, flushing, urticaria, dizziness [52].

- **SALICYLATES (Aspirin)**

  Salicylates therapy is an important part of the treatment. However salicylates are not more effective than IVIG. Aspirin therapy is provided in high doses until fever gets reduces, followed by low dose until the patient went to home [53-56]. This is continued normally for two months which prevents the blood clotting. Aspirin therapy is not preferred for the children due to the association with the Reye's syndrome. The reason behind this is children with Kawasaki disease are given the aspirin for several months [57], these children should be regularly given vaccination for the varicella and influenza because these infections are likely to cause the Reye's syndrome. Sometimes the high doses of the aspirin cause the anemia [58].

  Mechanism of action: They work by inhibiting the cycloxygenase which reduces the chances of thrombus formation. They reduce the inflammation and inhibit the platelet aggregation thereby responsible for ischemia leading to MI.

  Side effects: Upset of stomach, heartburn, dark urine, difficulty in hearing.

- **BETA BLOCKERS**

  They act by reducing cardiac work and oxygen consumption as a consequence of decreased heart rate, ionotropic state and mean BP. Carvedilol, metoprolol succinate or bisoprolol are the β-blocking agents that have been shown to reduce the risk of death. The consideration of β-blocking agents has been incorporated into the long-term management algorithm for KD patients with large or giant aneurysms that persist.

  Side effects: Dizziness, weakness, fatigue, headache, dry mouth, skin or eyes.

- **STATINS**

  Mechanism of action: Hydroxy methyl glutaryl coenzyme-A reductase inhibitors (statins) are a cornerstone of therapy for the primary and secondary prevention of atherosclerotic cardiovascular events in adults. They inhibit the conversion of HMG CoA to mevalonate which decreases cholesterol production. In addition to lowering low-density lipoprotein cholesterol, statins have potentially beneficial pleiotropic effects on inflammation, endothelial function, oxidative stress, platelet aggregation, coagulation and fibrinolysis.

  Side effects: Rabhdomyolysis, liver damage, increased blood sugar.

- **CORTICOSTEROIDS**

  Corticosteroids are utilized when the other drugs for treatment does not works. However addition of corticosteroids to aspirin and globulin did not prove good outcome. Use of corticosteroid in the Kawasaki disease causes increased risk of coronary artery aneurysm, so its use is generally contraindicated.

CONCLUSION:

Kawasaki disease is a mucocutaneous lymph node syndrome in which blood vessels throughout the body become inflamed. The most common symptoms include a fever that lasts for more than five days, large lymph nodes in the neck, a rash in the genital area, redness of eyes, lips, palms or soles of the feet and strawberry tongue. The treatment is done with high doses of aspirin and intra venous immunoglobulin. Fever resolves within 4-5 days and there is a full recovery. The cardiac complications can be minimized with beta-blockers and statins.

Conflicts of Interests

The authors are not having any conflicts of interest.

REFERENCES:

1. Kato H, Sugimura T, Akagi T, Sato N, Hashino K, Maeno Y, Kazue T, Eto G, Yamakawa R. Long-term consequences of Kawasaki disease: a 10-to 21-year follow-up study of 594 patients. Circulation. 1996; 94(6):1379-85.
2. Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2004; 110(17):2747-71.
3. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Arerugi. 1967; 16:178-222.
4. Yamamoto T, Kimura J. Acute febrile mucocutaneous lymph node syndrome (Kawasaki): subtype of mucocutaneous ocular syndrome of erythema multiforme complicated with carditis. Jpn J Pediatr. 1968; 21:336-9.
5. Shigematsu I. Epidemiology of mucocutaneous lymph node syndrome. J Jpn Pediatr Soc. 1972; 76:695-6.
6. Nakamura Y, Yanagawa H. The worldwide epidemiology of Kawasaki disease. Progress in Pediatric cardiology. 2004;19(2):99-108.
7. Manlhiot C, Christie E, McCrindle BW, Rosenberg H, Chahal N, Yeung RS. Complete and incomplete Kawasaki disease: two sides of the same coin. European journal of pediatrics. 2012; 171(4):657-62.
8. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. Arerugi. 1967; 16:178-222.
9. Yamamoto T, Oya T, Watanabe A. Clinical features of Kawasaki disease. Jpn J Pediatr. 1968;21:291-7
10. Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. Pediatrics. 1974; 54(3):271-6.
11. Melish ME, Hicks RM, Larson EJ. Mucocutaneous lymph node syndrome in the United States. American journal of diseases of children. 1976; 130(6):599-607.
12. Gee SJ. Cases of morbid anatomy: aneurysms of coronary arteries in a boy. St Bartholomew's Hosp Rep. 1871; 7.
13. Tullus K, Marks SD. Vacuities in children and adolescents. Pediatric Drugs. 2009; 11(6):375-80.
14. Galeotti C, Bayry J, Kone-Paut I, Kaveri SV. Kawasaki disease: aetiopathogenesis and therapeutic utility of intravenous immunoglobulin. Autoimmunity reviews. 2010; 9(6):441-8.
15. Bowyer S, Poettcher P. the Pediatric Rheumatiology Database Research Group. Pediatric rheumatology clinic populations in the United States: results of a 3 year survey. J Rheumatol 1996; 23:1968-74
16. Luca NJ, Yeung RS. Epidemiology and management of Kawasaki disease. Drugs. 2012; 72(8):1029-38.
17. Singh GD, Wong M, Isaacs D. Diagnosis, treatment and outcome of Kawasaki disease in an Australian tertiary setting: A review of three years experience. J Pediatr Child Health. Cardiol. 1997; 6:181-5.
18. Lin YT, Manlhiot C, Ching JC, Han RK, Nield LE, Dillenburg R, et al. Repeated systematic surveillance of Kawasaki disease in Ontario from 1995 to 2006. Pediatr Int. 2010; 52:699–706.
19. Gerding R. Kawasaki disease: a review. Journal of Pediatric Health Care. 2011; 25(6):379-87.
20. Chang RK. Hospitalizations for Kawasaki disease among children in the United States, 1988–1997. Pediatrics. 2002; 109(6):e87.
21. Burgner D, Harnden A. Kawasaki disease: what is the epidemiology telling us about the etiology?. International journal of infectious diseases. 2005; 9(4):185-94.
22. Uehara R, Belay ED. Epidemiology of Kawasaki disease in Asia, Europe, and the United States. Journal of epidemiology. 2012; 22(2):79-85.
23. Nakamura Y, Yashiro M, Uehara R, Sadakane A, Tsuboi S, Aoyama Y, et al. Epidemiologic features of Kawasaki disease in Japan: results of

the 2009–2010 nationwide survey. Journal of Epidemiology. 2012; 22(3):216-21.
24. Burns JC, Newburger JW. Genetics insights into the pathogenesis of Kawasaki disease. Circ Cardiovasc Genet. 2012; 5:277-278.
25. Burns JC, Glode MP. Kawasaki syndrome. The Lancet. 2004; 364(9433):533-44.
26. Harnden A, Takahashi M, Burgner D. Kawasaki disease. BMJ. 2009; 338:b1514.
27. Yeung RS. Kawasaki disease: update on pathogenesis. Current opinion in Rheumatology. 2010; 22(5):551-60.
28. Kawasaki disease. National Heart Lung and Blood Institute Web site. September 20, 2011; http://www.nhlbi.nih.gov/health/health-topics/topics/kd/.
29. Nigro G, Krzysztofiak A, Porcaro MA, Mango T, Zerbini M, Gentilomi G, et al. Active or recent parvovirus B19 infection in children with Kawasaki disease. The Lancet. 1994; 343(8908):1260-1.
30. Leung DY, Kotzin BL, Meissner HC, Fulton RD, Murray DL, Schlievert PM. Toxic shock syndrome toxin-secreting Staphylococcus aureus in Kawasaki syndrome. The Lancet. 1993; 342(8884):1385-8.
31. Kikuta H, Sakiyama Y, Matsumoto S, Hamada I, Yazaki M, Iwaki T, et al. Detection of Epstein-Barr virus DNA in cardiac and aortic tissues from chronic, active Epstein-Barr virus infection associated with Kawasaki disease-like coronary artery aneurysms. J Pediatr. 1993; 123(1):90-2.
32. Normann E, Naas J, Gnarpe J, Backman H, Gnarpe H. Demonstration of Chlamydia pneumonia in cardiovascular tissues from children with Kawasaki disease. Pediatr Infect Dis J. 1999; 18(1):72-3.
33. Hsu YH, Wang YH, Hsu WY, Lee YP. Kawasaki disease characterized by erythema and indurations at the Bacillus Calmette-Guerin and purified protein derivative inoculation sites. Pediatr Infect Dis J. 1987; 6(6):576-8.
34. Uehara R, Yashiro M, Nakamura Y, Yanagawa H. Kawasaki disease in parents and children. Acta Paediatr. 2003; 92(6):694-7.
35. Mojtahedzadeh S, Saket S, Shiari R, Shirvani F, Karimi A. The relationship between history of ischemic heart disease in parents of children with Kawasaki Disease with severity of heart complications and disease recurrence in these children. Yafte. 2011; 12(4):61-6.
36. Janelle RC, Robert ES. Recognition of Kawasaki Disease. Perm J. 2009; 13(1): 57-61.
37. Kim DS. Kawasaki Disease. Yonsei Med J. 2006; 47(6): 759-72.
38. Lang B. Recognizing Kawasaki disease. Paediatr Child Health. 2001; 6(9):638-43.
39. Friter BS, Lucky AW. The perineal eruption of Kawasaki syndrome. Arch Dermatol.1988; 124(12):1805-10.
40. Hirose O, Misawa H, Kijima Y, Yamada O, Arakaki Y, Kajino Y, et al. Two-dimensional echocardiography of coronary artery in Kawasaki disease (MCLS): detection, changes in acute phase, and follow-up observation of the aneurysm. Journal of Cardiography. 1981; 11(1):89-104.
41. Castro PA, Urbano LM, Costa IM. "Kawasaki disease". Anais Brasileiros De Dermatologia. 2009; 84 (4): 317–29.
42. Matsubara T, Ichiyama T, Furukawa S. Immunological profile of peripheral blood lymphocytes and monocytes/macrophages in Kawasaki disease. Clin Exp Immunol. 2005; 141(3):381–387.
43. Franco A, Touma R, Song Y, Shimizu C, Tremoulet AH, Kanegaye JT, et al. Specificity of regulatory T cells that modulate vascular inflammation, Autoimmunity. 2014; 47(2):95–104.
44. Amano S, Hazama F, Kubagawa H, Tasaka K, Haebara H, Hamashima Y. General pathology of Kawasaki disease: on the morphological alterations corresponding to the clinical manifestations. Acta Pathol Jpn. 1980; 30(5):681–694.
45. Taubert KA, Shulman ST. "Kawasaki Disease. Am Fam Physician. 1999; 59(11):3093-102.
46. Yellen ES, Gauvreau K, Takahashi M, Burns JC, Shulman S, Baker AL, et al. Performance of 2004 American Heart Association recommendations for treatment of Kawasaki disease. Pediatrics. 2010; 125 (2): e234–241.
47. Heuclin T, Dubos F, Hue V, Godart F, Francart C, Vincent P, et al. Hospital Network for Evaluating the Management of Common Childhood Diseases. Increased detection rate of Kawasaki disease using new diagnostic algorithm, including early use of echocardiography. J Pediatr. 2009; 155:695–699.
48. Muniz JC, Dummer K, Gauvreau K, Colan SD, Fulton DR, New burger JW. Coronary artery dimensions in febrile children without Kawasaki disease. Circ Cardiovasc Imaging. 2013; 6(2)239–244.
49. Bratincsak A, Reddy VD, Purohit PJ, Tremoulet AH, Molkara DP, Frazer JR, et al. Coronary artery dilation in acute Kawasaki disease and acute illnesses associated with fever. Pediatr Infect Dis J. 2012; 31 (9):924–926..

50. Cai Z, Zuo R, Liu Y. Characteristics of Kawasaki disease in older children. Clin Pediatr. 2011; 50(10):952–956.
51. Dengler LD, Capparelli EV, Bastian JF, Bradley DJ, Glode MP, Santa S, et al. Cerebrospinal fluid profile in patients with acute Kawasaki disease. Pediatr Infect Dis J. 1998; 17(6):478–481.
52. Duhem C, Dicato MA, Ries F. Side effects of intravenous immune globulins. Clin Exp Immunol. 1994 Jul; 97(Suppl 1): 79-83.
53. Oates-Whitehead RM, Baumer JH, Haines L, Love S, Maconochie IK et al. Intravenous immunoglobulin for the treatment of Kawasaki disease in children. The Cochrane Database of Systematic Reviews. 2003; 4: CD004000.
54. Hsieh KS, Weng KP, Lin CC, Lee CC, Huang SM. Treatment of acute Kawasaki disease: aspirin's role in the febrile stage revisited. Pediatrics. 2005; 114 (6): e689–93.
55. Mindy SL and Jane WN. Role of intravenous immunoglobulin in the treatment of Kawasaki disease. International Journal of Rheumatic Diseases. 2018; 21: 64-69.
56. Kuo H-C, Lo M-H, Hsieh K-S, Guo MM-H, Huang Y-H. High-Dose Aspirin Is Associated with Anemia and Does Not Confer Benefit to Disease Outcomes in Kawasaki Disease. PLoS ONE 2015; 10(12): e0144603.
57. Sundel RP, Baker AL, Fulton DR, Newburger JW. Corticosteroids in the initial treatment of Kawasaki disease: report of a randomized trial. The Journal of pediatrics. 2003; 142(6):611-6.
58. Newburger JW, Sleeper LA, McCrindle BW, Minich LL, Gersony W, Vetter VL, et al., Randomized trial of pulsed corticosteroid therapy for primary treatment of Kawasaki disease, N Engl J Med. 2007; 356(7):663-75.