

# Kawasaki Disease in Children: A Brief Update

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## Abstract:

*Kawasaki disease (KD) is a common acute vasculitis of childhood that may lead to coronary artery abnormalities in about 25% of patients if left untreated. KD is reported as the leading cause of acquired heart disease in children replacing rheumatic fever in developed countries. Strong epidemiological data are not available from developing countries, but it is increasingly recognized in rapidly industrializing countries of Asia including India, where it might have replaced rheumatic heart disease as the most common cause of acquired heart disease. This increasing recognition could be due to actual rise in number of KD cases or due to more diagnosis following increased awareness.*

*The status of KD in Bangladesh is not known. But unpublished data from Bangabandhu Sheikh Mujib Medical University (BSMMU) show a sustained and significant increase in the number of KD cases over the years. The reasons for this increase may be similar to our neighbouring country India. Aetiology of KD still remains unknown. But there have been many*

*hypotheses including infection, immune dysregulation, super-antigen and genetic factors.*

*The diagnosis of KD is based on the presence of e" 5 days of fever and the presence of e" 4 of the 5 principal clinical features (1. Extremity Changes, 2. Conjunctival injection, 3. Oral changes 4. Exanthem/Rash, and 5. Lymphadenopathy).*

*The diagnosis of KD may be very challenging for even a very experienced paediatrician. It must be considered in a child with prolonged fever, undue irritability and sequential appearance of principal clinical features.*

*KD patients should be managed timely with intravenous immunoglobulin (IVIG) and aspirin in proper dose. It is to be remembered that KD is no longer considered as a one-time disease of childhood, as it can be associated with significant long term sequelae.*

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## Introduction:

Kawasaki disease (KD) is one of the most common vasculitides of children with predilection for coronary arteries. It is an acute, self-limiting medium vessel vasculitis of unknown aetiology. KD is characterized by fever, rash, conjunctival injection, oral mucositis, extremity changes, cervical lymphadenitis and, in a number of cases dilatation or aneurism of coronary and other arteries<sup>1</sup>.

The first case of KD was diagnosed by Dr. Tomisaku Kawasaki in 1961 and a detailed description of this illness in 50 Japanese children was published in 1967 by him as an acute mucocutaneous lymph node syndrome.<sup>2</sup> Since then the incidence of KD has been consistently increasing in Japan, Taiwan and Korea<sup>3</sup>.

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Kawasaki disease is recognized as the leading cause of acquired heart disease in children in developed countries replacing rheumatic fever as the most common cause<sup>4</sup>. Literature suggests that KD may soon replace or already may have replaced rheumatic heart disease as the most common cause of acquired heart disease in India and other Asian countries<sup>5</sup>.

Cardiac lesions are hallmarks of KD and coronary artery abnormalities (CAA) develop in about 25% cases if left untreated which can eventually lead to coronary stenosis, myocardial infarction (MI) or sudden death<sup>6</sup>. Myocarditis and cardiac tamponade can also occur during the acute phase<sup>4,6,7</sup>. In developing countries like Bangladesh, where incidence of infectious diseases in children is still very high, KD may not be commonly included in the differential diagnosis of fever in children, as awareness about KD is not optimal<sup>8</sup>. So, majority of cases could remain undiagnosed and incidence rates are underestimated.

## Epidemiology:

More than 60 countries in the world have reported KD but most robust epidemiological data are available from

Japan, Korea, Taiwan, USA and Australia<sup>7-10</sup>. Japan reported the highest number of KD cases in the world, with around 12,000 new cases per year<sup>8</sup>. Approximately 85% of KD cases in Japan are younger than 5 years with a male: female ratio of 1.5:1. Incidence rate for KD in Japan is 322/100,000 children in less than 5 years. Epidemiological pattern is different in different regions. For example, incidence rates in Japan, Korea and Taiwan are much above 50/100,000 children <5 years and rates are continuously increasing for last 20 years<sup>5</sup>. But incidence in the US, Canada, Australia and European countries is about 4-25/100,000 children < 5 years and these rates are not increasing in recent years, which means they may have reached a plateau.<sup>5</sup>

Over the last few decades, KD has been increasingly reported from other countries in Asia: China, Philippines, Singapore and our neighboring countries including India, Nepal, Srilanka, and Pakistan<sup>9, 11-16</sup>. KD has replaced rheumatic fever as the commonest cause of acquired heart disease in developed countries<sup>13</sup>. As strong epidemiological data are not available from developing countries, conclusion cannot be drawn, but it is increasingly recognized in rapidly industrializing countries of Asia including India and China, where it may have replaced rheumatic heart disease as the most common cause of acquired heart disease<sup>5</sup>. This increasing recognition could be due to actual rise in number of KD cases or due to higher rate of diagnosis because of increasing awareness<sup>17</sup>. At the same time incidence of rheumatic fever in a country like India has been showing a gradually decreasing trend. So, it may be extrapolated that KD may have already replaced rheumatic fever as the commonest acquired cardiac disorder in India<sup>6,18</sup>.

Exact status of KD in Bangladesh is not known. But data from the Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) shows that there is a sustained increase in the number of KD cases over the 5 years of a study period, which was highly significant (from 14 in 2015 to 34 in 2019,  $p=0.001$ , unpublished data from BSMMU). Same as in India or China, it is not known, whether this increase in number could be due to actual rise of KD cases or due to increased awareness among pediatricians. However, it may be speculated that most of the KD cases are still remaining undiagnosed. Like any other developing countries, the burden of infectious diseases is still high

in Bangladesh. And so, may be, KD is very often not considered in the differential diagnosis of persisting fever in children.

The peak mortality occurs 15 to 45 days after the onset of fever, when there is presence of well-established coronary artery vasculitis. However, sudden death due to myocardial infarction can occur many years later in children and adults with coronary artery aneurysms and stenosis. Causes of many cases of MI in young adults (fatal and non-fatal) are now being considered to 'undiagnosed and untreated KD in childhood'<sup>19</sup>.

### **Aetiology**

Aetiology of KD still remains unknown. But there have been several hypotheses and postulations.

### **Infections:**

Some of its epidemiological and clinical features suggest an infectious origin<sup>1</sup>. Childhood onset of the disease and virtual absence in adulthood is suggestive of infection. It could be due to, childhood exposures providing protective immunity. Very rare incidence in early infancy could be due to maternally derived immunity<sup>20</sup>. Additionally, seasonality, geographical clustering and occasional occurrence in families may also suggest infectious and environmental origin. Rowley et al suggested a previously unidentified RNA virus which enters the body through mucosal surfaces as causative agents for KD<sup>21</sup>. But no single pathogen is regularly identified, though Epstein- Barr virus, rotavirus, other viruses and some bacteria have been reported<sup>1</sup>.

### **Immune Factors:**

KD may be caused by activation of innate immunity, with high number of activated neutrophils in the circulation resulting in release of several pro-inflammatory cytokines including IL-1, IL-6, IL-18, TNF- $\alpha$ , and IL-8.<sup>22,23</sup> Humoral factors including anti-endothelial cell antibodies, circulating immune complexes and anti-neutrophil cytoplasmic antibodies (ANCA), are reported by researchers in a number of patients<sup>1</sup>. There is also presence of excess T-lymphocytes with V $\alpha$ 2 in the coronary arteries, intestine and blood. A theory also exists of an unknown stimulus triggering an inflammatory cascade with activation of both the innate and adaptive immune system, suggesting the disease to be super antigen mediated disorder<sup>20,24</sup>.

**Genetic:**

The importance of genetic predisposition of KD is reported in recent genome wide association studies<sup>25</sup>. The hypothesis is further supported by higher risk of KD among Japanese, and other Asian children regardless of where they live. For example the incidence of KD is much higher among Japanese ancestral children living in Hawaii than other ethnic children living there. In addition there is higher frequency of history of KD in the parents and siblings of the newly diagnosed KD cases in Japan<sup>1</sup>.

However, till date no single gene is implicated and KD is not considered as an inherited disorder.

Most likely KD is triggered by some infections or environmental factors in genetically susceptible children<sup>20</sup>.

**Clinical Features and Diagnosis**

The onset of fever is typically abrupt. Sometimes preceding history of upper respiratory tract or gastrointestinal illness may be present. Irritability may also be present in some patients prior to fever. Over the next few day features of KD including cervical adenitis, conjunctival injection, erythema of buccal mucosa, pleomorphic rash, oedema of hands and feet develops. Clinical manifestations of KD comes sequentially but

there is no particular order and can fluctuate in the first 7 to 10 days of illness<sup>1</sup>.

There is no diagnostic test for KD, rather the diagnosis is based on recognition of a constellation of clinical features appearing in a temporal sequence and excluding other similar clinical conditions (Table 1).

**Five Principal Clinical Findings:**

## 1. Fever

Fever is usually high grade, may exceed 40<sup>0</sup> C and last for more than 5 days and usually associated with extreme irritability<sup>20</sup>. The fever typically does not respond to antibiotics. In the absence of appropriate therapy, fever continues for 1 to 3 weeks<sup>26</sup>.

## 2. Extremity Changes:

Distinctive erythema and oedema of palms and soles and induration of dorsum of hands and feet are seen in early stages which at times are painful. These changes follow desquamation starting from periungual regions. Desquamation begins usually within 2 to 3 weeks after the onset of fever. These findings are present in about 90% of children with KD. At 1 to 2 months after the onset of fever, deep transverse grooves across the nails (Beau's lines) may be noticed<sup>26</sup>

**Table-I**

*Diagnosis of Classic KD (Adopted from the Guideline given by American Heart Association)<sup>26</sup>*

The diagnosis of classic KD is based on the presence of  $\geq 5$  days fever and the presence of  $\geq 4$  of the 5 principal clinical features. In the presence of  $\geq 4$  principal clinical features, particularly when redness and swelling of the hands and feet are present, the diagnosis of KD can be made with 4 days of fever, although experienced clinicians who have treated many patients with KD may establish the diagnosis with 3 d of fever in rare cases.

1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and phalangeal mucosa.
2. Bilateral bulbar conjunctival injection without exudates.
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like.
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in sub-acute phase.
5. Cervical lymphadenopathy ( $\geq 1.5$  cm diameter), usually unilateral.

A careful may reveal that  $\geq 1$  principal clinical features were present during the illness but resolved by the time of presentation.

Patients who lack full clinical features of classic KD are often evaluated for incomplete KD. If coronary artery abnormalities are detected, the diagnosis is considered confirmed in most cases.

### 3. Conjunctival injection

Non-purulent bilateral conjunctival injection often sparing the limbus is present in about 93% of children with KD<sup>20</sup>. It usually begins shortly after the onset of fever<sup>26</sup>. Watering from the eyes is unusual in KD and if it is present, other causes should be ruled out.

### 4. Oral changes

Changes include: (1) erythema, dryness, fissuring and cracking, peeling and bleeding of lips. (2) "Strawberry tongue" with erythema and prominent fungiform papillae; and (3) diffuse erythema of the oropharyngeal mucosa. Follicular tonsillitis, oral ulcers and exudates point against the diagnosis of KD<sup>20, 26</sup>.

### 5. Exanthem/Rash

The cutaneous manifestations of KD are protean. Although the rash usually appears first in the body, there is often perineal involvement. The rash is erythematous, morbilliform and non-pruritic. Vesicular or bullous lesions are rare. Rash is present in more than 90% KD patients. But it is transient and fades away itself by within few days. Perineal rash is followed by desquamation in the diaper area<sup>1,20</sup>.

### 6. Lymphadenopathy

Unilateral anterior cervical lymphadenopathy is the least common feature of KD, occurring in about 50%-60% patients. Children with KD initially present with fever and unilateral cervical lymphadenopathy, sometimes make it difficult to differentiate from bacterial adenitis until other features of KD appear<sup>1,20</sup>.

## Disease course

Clinical course of KD is divided into 3 phases: acute, sub-acute, and convalescence phase<sup>27</sup>.

- i. Acute febrile phase is characterized by high-spiking fevers (typically > 39.0<sup>0</sup> C, irritability, rash, oral changes (strawberry tongue, red cracked lips) and extremities changes. It last anywhere from 7 to 14 days. Signs of myocarditis may also appear in the acute phase evidenced by tachycardia, gallop rhythm and congestive cardiac failure.
- ii. Sub-acute phase is often an asymptomatic period after the febrile episode and lasts up to 4 to 6 weeks.

But patients may still have desquamation of the digits and arthralgia. Sub-acute phase ends with return of acute phase reactants to normal. This is the most vulnerable period when coronary artery abnormalities develop<sup>20,27</sup>.

- iii. Convalescent phase is typically an asymptomatic period; lasting from months to years during which healing of the arteries occur which may be associated with remodeling and scarring. There is still (though significantly low) a risk of development of aneurysm<sup>20,27</sup>.

The recurrence rate of KD in Japan is less than 3% and in the US it is about 1.7%. But in US it is about 3.5 % in Asian and Pacific Islander descent<sup>28</sup>. It is reported that there is a higher risk of coronary artery involvements with recurrence<sup>29,30</sup>.

## Other Clinical Features of Kawasaki Disease

Although important long-term sequelae are confined to principally coronary arteries, many other organs and tissues are usually inflamed during the acute phase and can cause symptoms.

Re-activation of BCG scar with induration and erythema is common in KD children<sup>31</sup>.

Common neurological findings include extreme irritability and aseptic meningitis (AHA).

Other neurological manifestations include: transient unilateral and less commonly bilateral facial nerve palsy<sup>32</sup>, and profound sensori-neural hearing loss<sup>33</sup>.

Genitourinary findings may include urethritis, phimosis and hydrocele.

Gastrointestinal findings may include diarrhea, hepatitis, vomiting, pain abdomen and cholecystitis<sup>26</sup>.

Involvement of joints is common during the first week extending to 2<sup>nd</sup> and 3<sup>rd</sup> week having arthralgia and arthritis of multiple small inter-phalangeal joints and also large weight bearing joints<sup>34</sup>.

## Incomplete KD

Patients who do not fulfill the complete diagnostic criteria for KD are preferably diagnosed as incomplete KD. Incomplete KD is more common in infants and they are the patients who are at highest risk of developing coronary artery aneurysm (CAA). But in presence of coronary artery abnormalities in a child with unexplained

fever associated with any of the principal clinical features, the diagnosis of KD can be confirmed<sup>26</sup>.

### Atypical KD

When KD patients present with clinical features which are not common in this illness, the diagnosis may be preferred as atypical KD, e.g. nephritis, hepatitis, seizures or hypertension<sup>35</sup>.

### Kawasaki Disease Shock Syndrome (KDSS)

Some of the KD patients may present with features of warm shock associated with peripheral vascular dilation and depressed ejection fraction. KDSS can be defined as the presence of hypotension and shock requiring the initiation of volume expanders, the infusion of vasoactive agents, or transfer to intensive care units<sup>36</sup>. The causes of KDSS may involve the release of endogenous molecules that mediate a decrease in peripheral vascular resistance, myocardial dysfunction from myocarditis with or without myocardial ischemia, and capillary leakage, KDSS is often associated with more severe laboratory markers of inflammation and higher risk of coronary arterial dilation<sup>37, 38</sup>.

### Cardiovascular Findings

Cardiovascular manifestations and complications are the major contributors to morbidity and mortality, both during acute illness and in the long-term<sup>26</sup>. All the 3 layers of heart including valves and coronary arteries may be inflamed.

During acute phase clinical findings may include a hyperdynamic precordium and gallop rhythm. Rarely pericardial rub or tamponade may be found. About 5% of children with KD in the United States present with cardiovascular collapse<sup>26</sup>.

### Myocardial Dysfunction

Myocardial involvement is frequent in KD. It is reported that myocardial inflammation in KD occurs before coronary artery abnormalities<sup>39</sup>. Myocarditis in KD improves rapidly with the exception of the more typical short-term impact of mild myocarditis in KD leading to KD shock syndrome<sup>26</sup>.

### Coronary Artery Abnormalities

A coronary artery abnormality in KD is the most frequent sequelae of KD range from mild dilatation to aneurysms of various numbers and sizes. Initially proximal segments are involved and then extend distally. The majority of patients with CAA have dilatation only.

### Other Arterial Abnormalities

Patients with severe coronary artery involvement may also develop other medium sized arteries including axillary, subclavian, brachial, femoral, iliac, splanchnic, and mesenteric arteries, usually near or at branching points<sup>26</sup>.

**Table-II**

Risk Factors for the development of CAA <sup>20,26</sup>	
Gender	Male
Age	Early infancy
Lab Findings	Thrombocytopenia at presentation Nutropenia Hyponatraemia and Hypoalbuminaemia
Course of disease	Prolonged fever or Recrudescence of fever
Response to treatment	Failure to respond to IVIG

### Laboratory Investigations

Kawasaki Disease is a clinical diagnosis based on set of criteria (Table 1). However there are certain investigations which may support the clinical diagnosis, especially when the clinical manifestations are incomplete or atypical.

Most of the KD patients typically present in the acute phase with normocytic normochromic anaemia, leukocytosis with a shift to the left and elevated acute phase reactants including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)<sup>1</sup>. Platelet counts may be normal at the onset but thrombocytosis is typically seen by the second week and they may reach 1,000, 000 /mm<sup>3</sup> in most severe cases<sup>1,20</sup>. Thrombocytopenia, anaemia and only a modest elevation or normal ESR may indicate accompanying macrophage activation syndrome<sup>1</sup>. Sterile pyuria is common which is of urethral origin<sup>40</sup>.

Liver enzymes are often mildly raised or there may be raised bilirubin, which results from intra-hepatic inflammation. Serum lipid profiles may show abnormalities with elevated level of triglycerides and low density lipoprotein and low levels of high-density lipoproteins<sup>1</sup>. Cerebrospinal fluid analysis would be consistent with aseptic meningitis, though it is not indicated in KD.

## Evaluation of Cardiovascular System

### Electrocardiography (ECG)

During acute phase, if there is myocardial or pericardial involvement, ECG may show arrhythmia, including sinus node and atrio-ventricular node functional abnormalities with prolonged PR interval and nonspecific ST and T wave changes. If there is myocardial or pericardial involvement, there may be low voltage association<sup>41</sup>.

### Echocardiography

2D echocardiography is the imaging modality for cardiac assessment because it is non-invasive and is highly sensitive and specific for detecting the abnormalities of proximal coronary artery segments in KD patients<sup>20,26</sup>. Echocardiography should be performed at diagnosis as soon as possible. But it should be remembered that initiation of treatment should not be differed for echocardiography<sup>27</sup>.

As mentioned in the previous section, CAAs include ectasia (mild dilatation) and/or aneurysms in proximal left main coronary artery, left anterior descending artery, left circumflex artery and/or right coronary artery<sup>20</sup>. Echocardiography should be carried out by a paediatric cardiologist having requisite training and experience in evaluating coronary arteries. Equipment and transducers should also be age-appropriate<sup>26</sup>.

### Classification of Coronary Artery Abnormalities

According to American heart association (AHA) guideline, it is always preferable to use z-scores for evaluation of coronary arteries<sup>26</sup>.

#### Z-Score Classification

1. No involvement : always  $< 2$
2. Dilatation only:  $2$  to  $< 2.5$ ; or if initially  $< 2$ , a decrease in Z score during follow up  $e^{> 1}$
3. Small aneurysm:  $e^{> 2.5}$  to  $< 5$
4. Medium aneurysm:  $e^{> 5}$  to  $< 10$ , and absolute dimension  $< 8$
5. Large or giant aneurysm:  $e^{> 10}$  or absolute dimension  $e^{> 8}$

When using z scores, a very small error in measuring coronary artery diameter can lead into a large difference in z scores, and the child's risk category might change<sup>26</sup>.

Echocardiography can also detect decreased ejection fraction (due to myocarditis), mild valvular regurgitation,

higher brightness of coronary vessels and pericardial effusion, which are all indicators of ongoing inflammation. It is very important that a normal echocardiography in the first week of illness does not rule out CAA in any KD patients.

### Non-Invasive Coronary Angiogram

Newer imaging modalities including magnetic resonance coronary angiography and dual source computed tomography (DSCT) have been found to be extremely useful in the diagnosis and follow-up of KD patients if facilities are available. Abnormalities in distal segments of coronary arteries and circumflex coronary arteries may be very difficult to pick up by echocardiogram or may be missed up. However, proper training and expertise to carry out the procedures and interpretation of the findings is very important, which could be a barrier in developing countries like ours<sup>9,42</sup>.

### Management of KD

The child should be hospitalized for evaluation of cardiac status and management of acute manifestations. The goal of therapy is to control acute inflammation, prevent long-term sequelae like coronary artery abnormalities, arterial damage and to prevent thrombosis if there is CAA. Treatment with acetyl salicylic acid (Aspirin/ASA) and Intravenous Immunoglobulin (IVIG) should be initiated as soon as the diagnosis is established<sup>1,26</sup>.

#### Acetylsalicylic Acid (ASA/Aspirin)

ASA has important anti-inflammatory activity at medium dose (30-50 mg/kg/day) and high doses (50-80 mg/kg/day) and antiplatelet activity at low doses (3-5 mg/kg/day)<sup>45</sup>. ASA dose should be reduced from moderate/high dose to low dose when the child has been afebrile for 48 to 72 hours. Low dose ASA should be continued until the patient has no evidence of coronary changes by 6 to 8 weeks after onset of illness. If there is coronary abnormality, ASA may be continued indefinitely<sup>26</sup>.

#### Intravenous Immunoglobulin (IVIG)

The efficacy of single dose IVIG administration in the acute phase of KD is well established for reducing the incidence of CAA<sup>44</sup>. Mainstay of initial treatment for both complete and incomplete KD is infusion of high dose of IVIG (2gm/kg), along with ASA. IVIG should be administered as early as possible, preferably within first 10 days of onset of fever over a period of 10 to 12 hours.

IVIG should also be administered to children presenting after the tenth day of illness if they have ongoing systemic inflammation as manifested by persistent fever, coronary artery aneurysms or elevation of ESR or CRP<sup>26</sup>.

The exact mechanism of action of IVIG in treatment of KD is unknown. Most likely it has a generalized anti-inflammatory effect. Possible mechanisms of actions include modulation of cytokine production, neutralization of toxins or other pathogenic agents, augmentation of regulatory T-cell activity and suppression of antibody synthesis<sup>45</sup>.

Live vaccines including measles, mumps, and varicella immunizations should be deferred for 11 months after receiving high dose IVIG<sup>46</sup>. ESR is accelerated by IVIG therapy and therefore should not be used to assess response to IVIG therapy. Infusion reactions (fever and hypotension) occasionally accompany IVIG administration. It should be managed by slowing the infusion rate and treating with diphenhydramine. Headache is a very common complaint and may occur up to 72 hours after the IVIG infusion<sup>1</sup>.

#### **IVIG Resistance**

Approximately 10% to 20% of KD patients develop recrudescence or persistent fever at least 36 hours after the end of their IVIG infusion and are termed IVIG resistant<sup>47,48</sup>. There is no strict guideline of therapeutic agents for IVIG resistance. Hence, there are three recommended treatment protocols, i.e., retreatment with a second dose of IVIG (2 g/kg) 36 hours after completion of the first dose, or, the use of corticosteroids including IVMP (30 mg/kg/day for 1 to 3 days, maximum of 1 g) or prednisone at 2 mg/kg/day or, infliximab as a single dose (5 to 10 mg/kg). Regardless of which approach is selected, treatment should be continued until fever resolves, and frequent monitoring of the coronary arteries is recommended to follow for worsening dilation<sup>1</sup>.

#### **Corticosteroids**

Addition of corticosteroid to the primary therapy of KD lowers the prevalence of coronary artery abnormalities, duration of fever and inflammation. Dose of corticosteroids have ranged from pulse doses of 20-30 mg/kg (maximum of 1 g) to conventional anti-inflammatory doses (2 mg/kg/day). Administration of a longer course of corticosteroids (e.g, tapering over 2–3

weeks), together with IVIG and ASA, may be considered for treatment of high-risk KD patients<sup>26,49</sup>.

#### **Infliximab**

Numerous case reports and small series described successful use of infliximab (5 mg/kg intravenous over 2 hours) to halt inflammation in highly resistant KD<sup>50,51</sup>.

#### **Refractory KD**

Administration of cyclosporine may be considered in patients with refractory KD in whom a second IVIG infusion, infliximab, or a course of steroids has failed. Administration of immune-modulatory monoclonal antibody therapy (except TNF- $\alpha$  blockers), cytotoxic agents, or (rarely) plasma exchange may be considered in highly refractory patients who have failed to respond to a second infusion of IVIG, an extended course of steroids, or infliximab<sup>26</sup>.

#### **Kawasaki Disease Shock Syndrome (KDSS)**

Rapid initiation of volume expanders, the infusion of vasoactive agents, and IVIG therapy is needed. Inotropic agents and medications to increase peripheral vascular resistance may be needed to support the blood pressure<sup>1</sup>. Quite often KDSS patients require transfer to intensive care units<sup>36</sup>.

#### **Recurrent KD**

Patients with recurrent KD, defined as a repeat episode of complete or incomplete KD after complete resolution of the previous episode, should receive standard therapy with IVIG and Aspirin<sup>26</sup>.

#### **Monitoring Cardiac Status**

Children with Kawasaki disease should get an echocardiogram at the time of diagnosis. AHA recommends repeating an echocardiogram 10 to 14 days after the initial one and 4 to 6 weeks after all laboratory data have normalized. Further follow-up should be individualized depending on presence or absence of CAA<sup>26</sup>.

#### **Prognosis**

KD is a self-limiting disease. The mortality rate has dropped steadily as the diagnosis and treatment have improved<sup>1</sup>. Children receiving standard therapy with IVIG and aspirin given within the first 10 days of illness have an excellent prognosis. However, even when treated with high-dose IVIG regimens within the first 10 days of illness, 20% of children may develop transient coronary

artery dilation, 5% may develop coronary artery aneurysms, and 1% may develop giant aneurysms<sup>26,52</sup>. Deaths in KD can occur in acute stage due to myocardial infarction, myocarditis and coronary thrombosis<sup>6</sup>.

A well-established study in Japan reported that up to 50% of small and medium sized aneurysms resolved on follow up. However, giant aneurysms usually do not resolve and are associated with significant long-term morbidity<sup>53</sup>. Even if they are resolved anatomically, physiological abnormalities of the vessel wall may persist and known to cause myocardial infarction later in adulthood<sup>20</sup>. Mortality in acute KD in the developed countries varied from 1 to 2% in the pre-IVIG era to 0.014% now<sup>6</sup>.

### Conclusion:

Diagnosing and managing Kawasaki disease is a challenge for all the paediatricians of developing countries including Bangladesh and risk of developing coronary artery abnormality is about 25% if not diagnosed and treated timely. Mortality in acute stage is much lower if IVIG infusion and aspirin could be provided within first 10 days of onset of fever.

Missed KD in childhood can also result in coronary problems and present with ischaemia, myocarditis, infarction or sudden death in young adults. Very high cost of treatment (IVIG therapy) is also a major challenge in our country. Therefore, KD needs to be considered as a disease of public health importance. Policy should be taken to create awareness and the availability of IVIG at a subsidized cost must be ensured.

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