

## SPECIAL ISSUE – KAWASAKI DISEASE

# Diagnosis of Kawasaki disease

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### Abstract

Kawasaki disease (KD) is a medium vessel vasculitis with predilection for coronary arteries. Due to lack of a reliable confirmatory laboratory test, the diagnosis of KD is based on a constellation of clinical findings that appear in a typical temporal sequence. These diagnostic criteria have been modified from time to time and the most recent guidelines have been proposed by the American Heart Association (AHA) in 2017. However, several children may have incomplete or atypical forms of KD and the diagnosis can often be difficult, especially in infants and young children. In this review, we have detailed the steps involved in arriving at a diagnosis of KD and also highlight the important role of echocardiography in diagnosis and management of children with KD.

**Key words:** AHA, diagnosis, echocardiography, Kawasaki disease.

### INTRODUCTION

Kawasaki disease (KD) is a medium vessel vasculitis with predilection for coronary arteries and has been recognized to be the most common cause of acquired heart disease in children.<sup>1</sup> KD is now being increasingly recognized in several developing countries. Even though more than 50 years have passed since the first case of KD was identified by Dr Tomisaku Kawasaki,<sup>2</sup> the diagnosis of KD continues to remain a clinical dilemma and there is no confirmatory laboratory test.

The diagnostic criteria for KD have been modified from time to time. The two sets of diagnostic criteria that have been used most frequently for this condition are as follows (Table 1):

- 1 Kawasaki Disease Research Committee guidelines (Japanese guidelines), 2002<sup>3</sup>
- 2 American Heart Association (AHA) guidelines, 2004.<sup>1</sup>

These criteria are based on clinical findings and do not differ significantly from the original descriptions of

cases of KD given by Dr Kawasaki himself.<sup>2</sup> The major difference between the Japanese and AHA criteria is that while fever for more than 5 days is an essential prerequisite in the AHA criteria,<sup>1</sup> it is not so in the Japanese version.<sup>3</sup> In other words, a diagnosis of KD can be proffered even when there is no fever when one is using the Japanese criteria. Despite several limitations, both these criteria have stood the test of time and have been widely used by clinicians the world over.

In this review, we have provided a critique on the diagnostic criteria for KD including the 2017 guidelines.<sup>4</sup> We have detailed the usefulness and limitations of echocardiography in the diagnosis and management of children with KD. We have also alluded to several clinical and laboratory manifestations that help clinicians in arriving at a diagnosis of KD but do not find a mention in the KD criteria. We highlight the diagnostic challenges faced by pediatricians while managing these patients, especially in resource-constrained settings.

The seven cardinal findings in KD are detailed in Table 2.

### SPECIAL CONSIDERATIONS IN DEVELOPING COUNTRIES

The major limitation in the diagnosis of KD is that this diagnosis is often not considered upfront in

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**Table 1** Kawasaki Disease Research Committee guidelines and AHA guidelines for diagnosis of KD

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 Kawasaki Disease Research Committee guidelines (Japanese guidelines) for diagnosis of KD (2002)<sup>3</sup>

Five of the following six criteria:

- 1 Fever persisting  $\geq$  5 days
- 2 Bilateral conjunctival congestion
- 3 Changes of lips and oral cavity
- 4 Polymorphous exanthema
- 5 Changes of peripheral extremities
- 6 Acute non-purulent cervical lymphadenopathy

AHA guidelines for diagnosis of KD (2004)<sup>1</sup>

- 1 Fever persisting at least 5 days with
  - 2 At least four of the five principal clinical features:
    - i) Changes in extremities
      - Acute: Erythema of palms, soles; edema of hands, feet
      - Subacute: Periungual peeling of fingers and toes in weeks 2 and 3
    - ii) Polymorphous exanthema (diffuse maculopapular, urticarial, erythroderma, erythema-multiforme like, not vesicular or bullous)
    - iii) Bilateral bulbar conjunctival injection without exudates
    - iv) Changes in lips and oral cavity: erythema, lips cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosae
    - v) Cervical lymphadenopathy ( $>$  1.5 cm diameter), usually unilateral
  - 3 Exclusion of other diseases with similar findings (e.g., scarlet fever, viral infections like measles, adenovirus, Stevens-Johnson syndrome, toxic shock syndrome)
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AHA, American Heart Association, KD, Kawasaki disease.

febrile children in countries where infectious diseases are still very common, as for example India and China, the two most populous countries in the world.<sup>14</sup> Broad spectrum antimicrobials are commonly prescribed for febrile illnesses in children and are often replaced by second level antimicrobials if fever continues to persist.<sup>15–17</sup> If the child develops rash during the course of illness, it is often taken as a drug rash<sup>8,18</sup> and the diagnosis of KD may get further delayed. As many of the clinical manifestations of KD (such as redness of eyes, redness of lips, tongue and oral cavity, rash and edema of the hands and feet) are commonly seen in childhood infectious diseases as well, the diagnosis of KD is often delayed or missed altogether. Parents often seek multiple consultations from different healthcare facilities. Many of these clinical signs are often not documented and might have disappeared by the time the child is seen by another doctor. Although KD is now being diagnosed frequently in several developing countries, there is no dearth of skeptics who question this diagnosis.<sup>19</sup> In our experience there have been several instances when KD was diagnosed in time by a pediatrician but parents sought multiple consultations and several doctors questioned the

diagnosis and this resulted in avoidable delays in initiation of specific treatment.<sup>20</sup>

### CLINICAL SIGNS WITH DIAGNOSTIC IMPORTANCE BUT NOT INCLUDED IN THE DIAGNOSTIC CRITERIA

Many clinical signs of the disease provide important diagnostic clues; however, they have not been included in the diagnostic criteria. Periungual desquamation is an important clinical sign (Table 3).<sup>7</sup> It usually appears a few days prior to the appearance of periungual desquamation and may provide the initial diagnostic clue. Similarly, reactivation of the bacillus Calmette–Guérin (BCG) injection site is a pathognomonic clinical sign of KD and may be more commonly observed than cervical lymphadenopathy.<sup>21,22</sup> However, this has not been given enough consideration in the diagnostic criteria. Sterile pyuria,<sup>23</sup> peripheral arthritis,<sup>24</sup> hydrops of gall bladder<sup>25</sup> and myocarditis<sup>4,26</sup> are other important indicators of KD. Extreme irritability, out of proportion to the illness, is observed in children with KD, especially in young infants,<sup>27</sup> and may be a prominent clinical finding but this too does not find a mention in the diagnostic criteria.

**Table 2** Cardinal findings in Kawasaki disease (KD)

Clinical manifestation	Characteristics	Remarks
Fever	Fever is typically abrupt onset, high grade, unremitting, without any response to antimicrobials and not accompanied by mucosal inflammation. While majority of children with KD have fever that usually lasts more than 5 days, this figure is rather arbitrary. Children with KD can have short-lasting fever as well	In the Japanese criteria fever is not taken as an essential prerequisite <sup>3</sup> A few cases of KD without fever have also been reported. <sup>5</sup> An experienced physician can diagnose KD on day 3 or day 4 of illness and fever may subside before 5 days if appropriate treatment is instituted <sup>4</sup>
Extremity changes (acute)	Children with KD often have erythema of palms and soles that is usually non-specific. The edema of hands and feet is rather characteristic	However, these clinical features are transient and usually subside within a few days
Extremity changes (subacute)	Periungual peeling of skin is a pathognomonic sign of KD that usually appears in the 2nd to 3rd week of illness. However, in India, periungual desquamation seems to occur early and can often be seen by day 10 of fever <sup>6</sup>	It is often not very useful for early diagnosis. <sup>7</sup> On the other hand, periungual desquamation, often missed, usually appears earlier than periungual peeling and facilitates early diagnosis
Rash	Diffuse erythematous polymorphous rash usually appears in the first few days of illness and may be seen in up to 96% of patients. Bullous, vesicular and petechial lesions are not seen in KD <sup>8</sup>	It is non-specific (mimics many viral or bacterial infections) and it is often transient and hence may be missed, especially in dark-skinned children
Conjunctival involvement†	Bilateral conjunctival injection with sparing of limbus and without exudate is an important and specific clinical sign and often helps in making a clinical diagnosis. It may be seen in up to 89% of patients <sup>8</sup>	There is no conjunctivitis and not associated with any discharge
Lips and oral cavity changes†	Erythema of lips and oral cavity with lip cracking in a febrile child is an important diagnostic clue and is seen in up to 96% of patients <sup>8</sup>	Presence of distinct oral ulcerations make the diagnosis of KD unlikely
Cervical lymphadenopathy	Unilateral cervical lymphadenopathy is a characteristic clinical sign of KD but is seen in only 60% of patients <sup>8-11</sup>	Often mistaken for suppurative lymphadenitis <sup>12,13</sup>
Exclusion of other diseases with similar findings	An important component of the KD definition is exclusion of other illnesses	It is not clear whether the exclusion is clinical or if there is a well-defined panel of laboratory investigations that need to be carried out before satisfying this point

†Conjunctival injection and lip changes are not seen in scarlett fever and are important differentiating points. In addition, KD is predominantly a disease of children < 2 years old, while scarlet fever is always seen beyond 2 years of age.

## KD IN SPECIAL SITUATIONS

### KD in infants

Kawasaki disease in infants is always a diagnostic challenge as infants often may not manifest the complete form of disease (incomplete KD).<sup>27</sup> Incomplete forms of KD should not be assumed to be milder forms of KD. As children with incomplete KD often remain undiagnosed for several days, there are greater chances of development of coronary artery abnormalities (CAAs).<sup>28</sup> Infants with KD can also present with pyuria (as a result of the associated urethritis) and this may be

erroneously thought to be due to a urinary tract infection. This can result in further delays in arriving at a diagnosis.

### KD in older children

Kawasaki disease in a child who is more than 10 years old is relatively difficult to diagnose and is often more severe.<sup>29,30</sup> As the diagnosis usually gets delayed in these children, there is higher risk of CAAs. Another problem faced by clinicians while managing such patients is difficulty in the assessment of CAAs using echocardiography because of their thick chest wall.

**Table 3** Critique of 2004 American Heart Association criteria for diagnosis of Kawasaki disease (KD)

- 1 There is sequential appearance of clinical signs and symptoms and many of them disappear by the time the child reaches a healthcare facility. Hence, appropriate parental history has important contributions in reaching a diagnosis
- 2 Incomplete KD is often believed to be a mild form; however, because of delay in diagnosis there are often higher risks of coronary artery abnormalities. KD in infants is almost always incomplete. The diagnostic algorithm for incomplete KD is complicated and not very helpful in clinical decision making
- 3 There have been no standard recommendations for grading the severity of coronary artery abnormalities on echocardiography
- 4 The limitation of echocardiography and other diagnostic modalities have not been highlighted

### KD associated with infection

Infections are often considered triggers for KD<sup>31–33</sup> and clinical manifestations of many viral illnesses can mimic KD.<sup>34</sup> However, if there are typical clinical features of the disease, the diagnosis of KD cannot be excluded even in the presence of a documented infection. Adenovirus,<sup>35</sup> measles virus,<sup>36</sup> coronavirus<sup>34,37</sup> respiratory syncytial virus,<sup>34</sup> dengue virus,<sup>38,39</sup> enteroviruses, have been reported to trigger KD in children. Staphylococcal<sup>40</sup> and streptococcal toxin-mediated diseases<sup>41–43</sup> are also closely associated with the pathogenesis of KD.

### KD myocarditis

It is not often recognized that myocarditis is an integral part of KD and can, at times, be severe and symptomatic.<sup>4,26</sup> Whenever a young child presents with fever, myocardial dysfunction and shock, KD should also be included in the differential diagnosis of viral myocarditis/ septic shock.

### Atypical KD

The term 'Atypical KD' is used when there are one or more atypical features of KD such as pulmonary involvement (e.g., pneumonia),<sup>44,45</sup> arthritis,<sup>24</sup> nephritis,<sup>23,46,47</sup> myositis, uveitis,<sup>48,49</sup> retinal vasculitis<sup>50</sup> and central nervous system involvement (e.g., facial palsy and meningoencephalitis).<sup>51–54</sup> The diagnosis of KD is more challenging in the presence of one or more atypical manifestations. Pulmonary presentation of KD can be very challenging for even astute clinicians.<sup>44,45</sup>

## THE 2017 GUIDELINES OF THE AHA FOR DIAGNOSIS OF KD

The AHA has recently published revised criteria for diagnosis of KD<sup>4</sup>. While fever for at least 5 days remains an essential criterion and there is no change in the five principal clinical manifestations of the disease, the drafting committee has suggested several changes.

- 1 The controversy regarding duration of fever has been addressed and it has been recommended that in the presence of  $\geq 4$  principal clinical features, particularly when redness and swelling of the hands and feet are present, KD can be diagnosed even with 4 days of fever. Experienced physicians who have treated many patients with KD may be able to arrive at a diagnosis within 3 days of fever.
- 2 Presence of one or more principal clinical manifestations of disease that can be revealed on history but have disappeared by the time of presentation to the hospital, have been considered important for diagnosis. This has been a major change in the present guidelines as many physicians, especially in developing countries, have faced this problem due to late referrals. Because of multiple consultations in a febrile child, the acute stage clinical manifestations are often missed and not documented. By the time the diagnosis of KD is considered, many of the salient clinical manifestations would have already disappeared.
- 3 Shock has been mentioned as an important cardiovascular manifestation of KD. KD shock syndrome (KDSS) has been given special consideration in the 2017 revised guidelines because in the presence of shock the diagnosis is often considered as bacterial sepsis. These patients are also at higher risk of developing coronary artery abnormalities, intravenous immunoglobulin (IVIg) resistance and myocardial dysfunction.
- 4 KD in infants has been given special consideration. It has been suggested that clinicians should have a lower threshold for diagnosis of KD in this age group. As per the recent guidelines, the diagnosis of KD in infants may be considered in the following situations:
  - infants < 6 months old with prolonged fever and irritability
  - infants with prolonged fever and unexplained aseptic meningitis
  - infants or children with prolonged fever and unexplained or culture-negative shock

- infants or children with prolonged fever and cervical lymphadenitis unresponsive to antibiotic therapy
  - infants or children with prolonged fever and retropharyngeal or parapharyngeal phlegmon unresponsive to antibiotic therapy.
- 5 The issue of infections and KD has been detailed at length. It has been emphasized that the diagnosis of KD must not be excluded even in the presence of a documented infection when typical clinical features of KD are present. In the presence of some features of KD and when bacterial cultures are sterile or if there is response to antimicrobials, a possibility of KD must be considered.
- 6 Bacterial lymphadenitis is often confused with the lymphadenitis of KD. The recent guidelines have emphasized the important ultrasonography and computed tomography (CT) findings in differentiating the two conditions: bacterial lymphadenitis is often single and has a hypoechoic core on ultrasonography, while lymphadenopathy in KD is usually multiple and is associated with retropharyngeal edema or phlegmon.

## DIAGNOSTIC ALGORITHM FOR INCOMPLETE KD

The diagnostic algorithm for evaluation of incomplete KD proposed by the AHA in 2004 had several limitations and was difficult to use in clinical practice.<sup>1</sup> The 2017 guidelines have proposed a modified algorithm that is relatively easy to use and is more likely to be clinically meaningful.<sup>4</sup> However, as there are no specific laboratory investigations, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) remain the most important laboratory investigations for deciding the therapy. ESR and CRP are non-specific laboratory markers for inflammation. Most other laboratory investigations (anemia, thrombocytosis, leukocytosis, hypoalbuminemia, high alanine aminotransferase and pyuria) have only supportive roles in the diagnosis. There is an urgent need to have a laboratory gold standard for KD.

## BIOMARKERS IN KD

Role of several biomarkers has been evaluated for the diagnosis of KD.<sup>55,56</sup> Th1 and Th2 cytokines (interleukin 6 [IL-6], IL-20, tumor necrosis factor- $\alpha$  [TNF- $\alpha$ ] and interferon- $\gamma$ ) have been found to be elevated

during the acute phase of KD and decline promptly following IVIg administration. Furthermore, levels of TNF- $\alpha$  continued to remain elevated in patients with IVIg resistance or with coronary artery abnormalities. Th17 cytokine (IL-17) has also been found to be elevated in the acute phase of KD. Wu *et al.*<sup>57</sup> evaluated the diagnostic utility of NT-proBNP (N-terminal pro-brain natriuretic peptide) and IL-17 to differentiate incomplete KD from other febrile infectious illnesses of childhood and found that when the cut-offs for IL-17 and NT-proBNP were set at 11.55 pg/mL and 225.5 pg/dL, respectively, the sensitivity and specificity of differentiating incomplete KD from infectious illnesses reached as high as 86.5% and 94.8%, respectively. NT-pro-BNP estimation (a marker of myocardial damage) has recently been evaluated for inclusion in the diagnostic criteria of KD.<sup>58,59</sup> Although NT-pro-BNP is not specific for KD and may be elevated in any disease that leads to myocardial damage, NT-pro-BNP-based diagnostic algorithm has been proposed that scores better than the AHA diagnostic algorithm for incomplete KD. In addition, proteomic studies have identified biomarkers for the diagnosis of KD. However, none of them has been validated for clinical use.<sup>60,61</sup> Thus, more research is needed to identify a potential biomarker for KD that can be used in clinical practice.

## ECHOCARDIOGRAPHY IN KD

Echocardiography is mandatory in the acute phase of disease to monitor cardiac complications. Two-dimensional (2-D) echocardiography has been considered to be the imaging modality of choice in evaluation of children with KD. However, it is important to understand that a normal echocardiography examination can never rule out a diagnosis of KD. On the other hand, if there are echocardiography changes, the diagnosis is more secure. Similarly, a normal baseline echocardiogram in the first 7 days does not exclude the possibility of later development of coronary artery aneurysms.<sup>4</sup> Experienced clinicians now recommend frequent echocardiography examinations during the first few days of the disease. This should be repeated at time of discharge and at 2 weeks.<sup>62</sup> In developing countries, where trained pediatric cardiologists may not be easily accessible, echocardiography is often performed by cardiologists who deal with adults and may not have the expertise, experience and patience to perform detailed echocardiography examination of coronary artery abnormalities in small children.<sup>14,63</sup> As a result, the echocardiographic examination in these circumstances

may not pick up these abnormalities that are often very subtle. In our experience, it is not uncommon to find gross coronary artery abnormalities getting missed on echocardiographic examination.

There is little or no consensus on reporting of echocardiography findings in children with KD in developing countries. Many centers are still using Japanese criteria for grading the coronary artery involvement.<sup>64</sup> It is mandatory that body surface area-adjusted Z-scores be used to grade the severity of coronary artery involvement so that objectivity can be maintained and results can be compared with other studies.<sup>4</sup>

### ECHOCARDIOGRAPHY CRITERIA FOR CORONARY ARTERY ABNORMALITIES

The initial criteria for CAAs in KD were proposed by the Japanese Ministry of Health (Table 4).<sup>65</sup> The classification was later modified (in 2008).<sup>64</sup> This definition partially accounts for the body size, but fails to distinguish between different degrees of coronary artery aneurysms at different age groups. Hence this classification is likely to result in diagnostic confusion.

The AHA 2004 classification<sup>1</sup> was a major advance as it proposed the use of Z-scores for defining CAAs. The most widely accepted classification scheme for CAA is the one proposed by Manlhiot *et al.*<sup>66</sup> (based on body surface area-adjusted Z-scores).

### PROBLEMS WITH STANDARDIZATION OF ECHOCARDIOGRAPHY, INCLUDING BODY SURFACE AREA

Use of body surface-adjusted Z-scores has improved the uniformity of reporting of coronary artery abnormality and is more meaningful for treatment decisions. However, there are still several limitations that need to be addressed, as follows.

- 1 An inter-individual variation in measurement of coronary artery diameter can change the Z-scores and subsequently the risk category. This can impact both acute and long-term management.
- 2 There are various standards that have been used for calculation of body surface area (the most recent has been proposed by Dallaire *et al.*, 2011).<sup>67</sup> Also, a small difference in measurement of height (especially in infants and young children) can significantly impact the body surface area and subsequently the coronary artery Z-scores
- 3 The Z-scores for left circumflex coronary artery has not been uniformly standardized. Manlhiot *et al.* has derived the left circumflex coronary artery Z-scores based on regression formulas for left anterior descending artery (LAD). However, Kobayashi *et al.*<sup>68</sup> and Dallaire *et al.*<sup>67</sup> have provided the normative data for left circumflex coronary artery as well.

**Table 4** The Japanese Ministry of Health and the American Heart Association (AHA) criteria for diagnosis of Kawasaki disease (KD)

Criteria	Description
Japanese Ministry of Health criteria	Aneurysm defined as internal diameter > 3 mm in children < 5 years and > 4 mm in children ≥ 5 years
Japanese Ministry of Health criteria modified in 2008	Small aneurysm (dilation with internal diameter < 4 mm or if child is ≥ 5 years of age, internal diameter ≤ 1.5 times that of an adjacent segment) Medium aneurysm (dilation with internal diameter > 4 mm but ≤ 8 mm or if child is ≥ 5 years of age, internal diameter 1.5–4 times that of an adjacent segment) Large aneurysm (dilation with internal diameter > 8 mm or if child is ≥ 5 years of age, internal diameter > 4 times that of an adjacent segment)
AHA 2004 criteria	Aneurysm defined as internal diameter Z-score > 2.5 (as per body surface area adjusted Z-scores) Small, medium and giant aneurysm defined based on absolute diameter, i.e., < 5 mm, 5–8 mm and > 8 mm respectively
AHA 2017 criteria (Manlhiot <i>et al.</i> )	No involvement (Z-score always < 2) Dilation only (Z-score 2 to < 2.5; or if initially < 2, a decrease in Z-score during follow-up ≥ 1 thereby suggesting that coronary artery was dilated during acute stage although diameter was within normal standards and the diameter has regressed on follow-up) Small aneurysm (Z-score ≥ 2.5 to < 5) Medium aneurysm (Z-score ≥ 5 to < 10, and absolute dimension < 8 mm) Large or giant aneurysm (≥ 10, or absolute dimension ≥ 8 mm)

**Table 5** Echocardiography in Kawasaki disease (KD): revision in the 2017 American Heart Association guidelines

- 1 It has been stressed that initial echocardiogram in the 1st week of illness is usually normal and doesn't rule out the diagnosis of KD
- 2 Echocardiography has high sensitivity and specificity for detection of abnormalities in proximal segment of coronary arteries. It has been observed that absence of proximal coronary artery abnormality virtually rules out a significant distal coronary artery involvement
- 3 It has been emphasized to measure aortic root diameter as a routine and to use Z-scores for the same
- 4 As per the recent guidelines, use of Z-scores adjusted for body surface area to grade the severity of coronary artery abnormality is essential to maintain the uniformity and for treatment decisions
- 5 Limitations of echocardiography and indications of higher imaging modalities has been more clearly highlighted (e.g., limitation of evaluation of distal coronaries in older children, long-term assessment of aneurysm in presence of dystrophic calcification that can obscure the visualization of luminal diameter)
- 6 Assessment of ventricular systolic and diastolic function should be a part of routine echocardiographic examination in KD
- 7 It has been emphasized that in patients with evolving or significant coronary artery abnormalities, a more frequent echocardiographic assessment should be done during acute stage till the changes stabilize
- 8 An important observation that most of the patients with KD having coronary artery abnormalities are having dilation or normal diameter only, but demonstration of reduction in luminal diameter in serial measurements of coronary artery diameter may suggest that coronary artery was actually dilated

- 4 Normative data are available only for proximal coronary arteries and it has been proposed that a definition of > 1.5 times the size of adjacent segment for a distal coronary artery may still be more reliable.<sup>4</sup>
- 5 The other limitations of echocardiography include frequent non-visualization of distal coronaries,<sup>69</sup> difficulty in visualization of left circumflex coronary artery, difficult to comment on stenosis or thrombosis and limited field of visualization in older children.

### ECHOCARDIOGRAPHY FINDINGS IN KD OTHER THAN CAA (SOFT SIGNS OF ECHOCARDIOGRAPHY)

Echocardiography findings in KD, other than coronary artery ectasia, dilation and aneurysm, include lack of tapering of coronary arteries, myocardial dysfunction, pericardial effusion, aortic root dilatation and valvular regurgitation.<sup>4</sup> It is important to identify and document these findings. Myocardial involvement with left ventricular dysfunction may be seen in up to 20% of patients and is usually associated with CAAs. The 2017 AHA guidelines have highlighted certain important points related to echocardiography in KD as given in Table 5.

### CONCLUDING REMARKS

KD is the most common vasculitis in children.<sup>70</sup> More than 50 years have elapsed since the first description of this disease, the diagnosis of KD is still based on few clinical manifestations and there is no laboratory gold standard test. Although the AHA 2017 criteria have

been able to clarify a few issues related to the diagnosis of KD (such as the algorithm for evaluation of incomplete KD, including a special emphasis in infants, fulfillment of diagnostic criteria based on history alone and uniformity in use of Z-scores for echocardiography evaluation of CAA), there still remain several challenges that need to be addressed. A few important and specific clinical manifestations (such as BCG site reactivation and perineal desquamation) that have not been included in the diagnostic criteria, must be actively looked for while evaluating these children. Echocardiography findings must be interpreted carefully and treatment should not be delayed if facilities for echocardiography are not easily available (as may often be the case in developing countries).

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