Clinical Profile of Kawasaki Disease (KD) in Children admitted at Dhaka Shishu Hospital

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Abstract

Background : Kawasaki disease (KD) is an acute, febrile, self-limiting vasculitis of the medium-and small-sized arteries of unknown etiology. Recently its incidence is increasing worldwide.

Objective : The aim of this study was to evaluate its presenting symptoms, clinical features and laboratory tests for the diagnosis of complete and incomplete KD in children.

Materials & Methods : Medical records of 20 children with KD admitted in Dhaka Shishu Hospital from January, 2011 to December 2014, were reviewed. Demographic features, diagnostic clinical features of KD, and additional clinical findings including arthritis and/or arthralgia, gastrointestinal symptoms, respiratory symptoms and central nervous system symptoms were recorded for each patient. Besides, available laboratory findings collected on admission before Intravenous Immunoglobulin (IVIG) administration were reviewed. The diagnosis of complete and incomplete KD was made using the American Heart Association (AHA) recommendations.

Results : About two-thirds of the children (65%) were 30 – 60 months, 20% were < 30 months and 15% were 60 or above 60 months old with mean age being 42 months. Over half (55%) of the children were female and 50% affected in summer season. Of the five principal signs, polymorphous skin rash was predominant (90%), followed by changes in oral mucosa or lip (85%), conjunctival hyperemia (75%), cervical lymphadenopathy (70%) and changes in distal extremities and gastrointestinal symptoms (each 65%). Majority of the children had raised WBC (75%), raised ESR (95%), increased platelet count (70%) and elevated CRP (75%). Uveitis was a predominant complication (45%), followed by facial paralysis (30%) and neurosensory hypoacusia (20%). Cardiovascular complications were less commonly found (30%). Neither age nor sex was found to be associated with type of Kawasaki disease (p = 0.450 and p = 0.535 respectively). Sixty percent of the patient fulfilled the criteria of complete KD and the rest incomplete KD. However, cervical lymphadenopathy and changes in distal extremity were significantly common in complete KD than those in incomplete KD (p = 0.019 and p = 0.05 respectively).

Conclusion : In this study 60% of the patient fulfilled the criteria of complete KD and the rest incomplete KD.

Key words : Kawasaki disease, clinical profile, complete and incomplete Kawasaki disease, children and vasculitis etc.

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Introduction

Kawasaki disease (KD) is an acute, febrile, self-limiting vasculitis of the medium-and small-sized arteries of unknown etiology. The disease predominantly affects infants and preschool children.[1] It was first described in Japan, where the incidence is highest (140/100,000 in children below 5 years of age)[2, 3] and further reported worldwide, with variable incidence. Estimated annual incidence in children below 5 years is 17/100,000 in the USA[3] and 3> 100,000 in South America.[4] Clinical and epidemiological patterns suggest that KD follows exposure to infectious agent(s)[5] like human coronaviruses[7]. Other causative agents include bacteria, fungi and house mites.[6]

In the last decades, an increase in the incidence of KD in Japan,[7] the United States,[8] and Europe has been observed.[9] The incidence in European countries ranges from 5–8/100,000 children under the age of 5 years.[10] However, there is still no definitive diagnostic test to confirm KD.

American Heart Association (AHA) in 2004 established a diagnostic guidelines for the patients with KD.[11] Laboratory parameters in KD patients include leukocytosis, thrombocytosis, raised erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), transaminase and hypoalbuminemia.[11] In the untreated children

the disease often leads to the formation of ectasia, dilatation, or aneurysm of the coronary arteries (CA).[12-13] The disease has become the leading cause of acquired heart disease among children in the United States and other developed countries.[12]

By far, no study evaluating the clinical course of KD, its diagnosis, management and complications has yet been done in the context of our population. Therefore the present study was undertaken to determine the annual admission of children with KD in Dhaka Shishu Hospital and to evaluate its presenting symptoms, clinical features and laboratory tests for the diagnosis of complete and incomplete KD in children.

Methodology

Having ethical clearance obtained from the Institutional Review Board, medical records of 20 children with KD admitted in Dhaka Shishu Hospital, Dhaka between January, 2011 to December 2014, were reviewed. Demographic features, diagnostic clinical features of KD, and additional clinical findings including arthritis and/or arthralgia, gastrointestinal symptoms, respiratory symptoms, and central nervous system symptoms were recorded for each patient. Moreover, available laboratory findings collected on admission or during their stay in the hospital prior to IVIG administration were evaluated which included complete blood count (CBC) parameters, ESR, serum CRP, alanine transaminase (ALT), aspartate transaminase (AST), and albumin levels, urine analysis.

The diagnosis of complete and incomplete KD was made using the AHA recommendations.[11] Accordingly, complete KD was defined by – · fever>5 days and

· more than or equal to four of the five principal clinical features
i. bilateral conjunctival injection
ii. cervical lymphadenopathy
iii. polymorphous skin rash
iv. changes in the lips or oral mucosa and
v. changes in the distal extremities.[11]

In case of a child with fever of unexplained origin, who did not fulfill the classic criteria of KD and any other diseases (with similar clinical features) were excluded then the child could be diagnosed as incomplete KD. This diagnosis was often based on echocardiographic findings of coronary artery abnormalities.

The statistical analysis was performed using computer software SPSS version 17 and test statistics used to analyze the data were descriptive statistics. The data presented on continuous scale was compared between children with complete KD and incomplete KD using Mann Whitney Test and the data presented on categorical scale were compared between groups with the help of Fishers Exact Test. The level of significance was set at 5% and $p < 0.05$ was considered significant.

Result

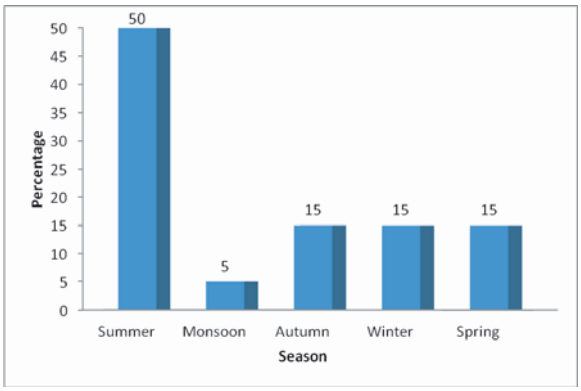
Almost two-thirds (65%) of the patients were 30 – 60 months old, 20% < 30 months and 15% 60 or above 60 months old. Over half (55%) of the children were female (Table I).

Table I : Demographic characteristics of the Patients (n = 20)

Demographic characteristics	Frequency	Percentage
Age* (months)		
< 30	04	20.0
30 – 60	13	65.0
>60	03	15.0
Sex		
Male	09	45.0
Female	11	55.0

*Mean ± SD = (41.75 ± 1.52) months; range = 14 - 71 months

Half of the patients were affected in summer season, 15% in Autumn, 15% in Winter, 15% in Spring and only 5% in Monsoon season (Fig.1).



All the children had fever lasting for ? 5 days. Of the five cardinal signs, polymorphous skin rash was predominant (90%), followed by changes in oral mucosa or lip (85%), conjunctival hyperemia (75%), cervical lymphadenopathy (70%) and changes in distal extremities and gastrointestinal symptoms (each 65%). The second common presentations were sterile pyuria (45%) arthralgia (35%) and hepatic dysfunction and respiratory symptoms (30%) (Table II).

Table II : Distribution of patients presenting with symptoms and signs (n = 20)

Presenting symptoms and signs	Frequency	Percentage
Fever (at for least 5 days)	20	100.0
Polymorphous skin rash	18	90.0
Change in oral mucosa or lip	17	85.0
Conjunctival hyperemia	15	75.0
Cervical lymphadenopathy	14	70.0
Change in distal extremities	13	65.0
Gastrointestinal symptoms	13	65.0
Arthralgia	07	35.0
Hepatic dysfunction	06	30.0
Respiratory symptoms	06	30.0
Sterile pyuria	09	45.0

Majority of the children had raised WBC (75%), raised ESR (95%), increased platelet count (70%) and elevated CRP (75%). Anemia was observed among 45% of the patients and half of the patients (50%) had low albumin. The mean hematocrit, hemoglobin, neutrophil, and S. albumin values are shown in the table III.

Table- III : Distribution of patients by laboratory findings (n = 20)

Laboratory findings	Frequency (%)	Mean ± SD
WBC count (> 15,000/mm^3)	15(75.0)	
Raised ESR (> 40 mm/h)	19(95.0)	
Platelet count(> 500,000/mm^3)	14(70.0)	
CRP (> 3 mg/dL)	15(75.0)	
Hematocrit (%)		36.6 ± 4.4
Hemoglobin (g/dL)		11.1 ± 1.65
Anemia for age	09(45.0)	
Neutrophils (%)		72.2 ± 18.9
S. Albumin (> 3 g/dl)	10 (50.0)	3.2 ± 0.5
S. ALT > 45 U/L	12(60.0)	61.9 ± 28.4
S. AST > 45 U/L	9(45.0)	51.1 ± 20.27

Uveitis was a predominant complication (45%), followed by facial paralysis (30%) and neurosensory hypoacusia (20%). Cardiovascular complications were less commonly found (30%) which included coronary artery aneurism (CAA) (15%), pericarditis (10%) and myocarditis only 5% (Table IV).

Table IV : Distribution of patients by complications (n = 20)

Complications	Frequency	Percentage
Uveitis	09	45.0
Hepatitis	06	30.0
Facial paralysis	05	25.0
Neurosensory hypoacusia	05	25.0
Cardiovascular complications	06	30.0

Sixty percent of the patients fulfilled the criteria of complete KD and the rest incomplete KD.

Age and sex distribution were almost identical between complete and incomplete KD (p = 0.450 and p = 0.535 respectively) (Table V).

Table V : Association between demographic characteristics and type of KD

Demographic characteristics	Group		Total
	Complete KD	Incomplete KD	
Total number	12 (60%)	8 (40%)	
Age (yrs)	3.6 ± 1.3	3.2 ± 1.1	0.450*
Sex			
Male	5(41.7)	4(50.0)	0.535**
Female	7(58.3)	4(50.0)	

*Data were analyzed using Mann Whitney Test and were presented as mean ± SD

**Data were analyzed using Fisher's Exact Test and were presented as requency (%)

However, cervical lymphadenopathy and changes in distal extremity were significantly common in complete KD than those in incomplete KD (91.7% vs. 35.5%, p = 0.019 and 83.3% vs. 25%, p = 0.05 respectively) (Table VI).

Table VI : Association between clinical characteristics and type of KD

Clinical characteristics	Group		p-value
	Complete KD (n = 12)	Incomplete KD (n = 8)	
Conjunctival hyperemia	10 (83.3)	5 (62.5)	0.296*
Cervical lymphadenopathy	11 (91.7)	3 (37.5)	0.018*
Polymorphous skin rash	11 (91.7)	7 (87.5)	0.653*
Changes in oral mucosa or lip	11 (91.7)	6 (75.0)	0.344*
Changes in distal extremities	10 (83.3)	2 (25.0)	0.015*

*Data were analyzed using Fisher's Exact Test and were presented as frequency (%)

Discussion

Epidemiological data on KD suggest that its incidence is increasing worldwide.[14] but there is no study on the incidence of KD in Bangladeshi children has yet been published. In the present study, out of 20 children hospitalized with KD, incomplete KD was diagnosed in 40% of cases, which is consistent with other studies.[15] However, this proportion is higher compared to the incidence (20%) reported by several other studies.[16] Published AHA guidelines, including supplementary laboratory criteria as well as the use of echocardiography, result in better recognition of KD.[17] Regarding patients' age and sex, our study showed the similar complete and incomplete KD groups (p = 0.450 and 0.535 respectively) as compared to that with the findings of Gorczyca et al. (2014).[15] However, this finding is not consistent with other previous data that suggest that incomplete KD is more common in children younger than 1 year and older than 8 years.[18,19]

In our study, we analyzed the frequency of the five cardinal signs, polymorphous skin rash was predominant (90%), followed by changes in oral mucosa or lip (85%). Several studies also found mucosal changes and polymorphous skin rash as the most frequently occurring signs.[15,20] Gorczyca et al[15] reported that number of patients with incomplete KD presented with conjunctival injection, changes in extremities and cervical lymphadenopathy significantly less. This distribution of clinical signs was reported that in the previous studies.[16,21] In our study as well, these changes were also less commonly observed in incomplete KD. In the present study gastrointestinal symptoms, sterile pyuria and arthralgia were found as non-classical signs which are consistent with the findings of Yun et al and Manlhiot et al who demonstrated abdominal pain, vomiting, diarrhea, and

arthralgia, to be the common non-classical signs.[16,22]

Published studies have shown that incomplete KD is associated with higher risk of developing coronary abnormalities.[23] In the present study out of 6 (30%) patients with cardiovascular complications, 3 had complete and 3 incomplete KD. All the 6 children with cardiovascular complications were treated with IVIG. Gorczyca and associates (2014)[15] reported that they did not find coronary artery aneurysm (CAA) in incomplete KD children on echocardiography. On investigation we found leucocytosis (75%), thrombocytosis (70%), raised ESR (95%), hypoalbuminemia (50%), elevated serum ALT and AST (50% and 45% respectively) and elevated CRP (75%). All these may reflect severity of the disease. Printz et al.[24] reported the relationship between elevated WBC count and coronary cardiac abnormalities. Furthermore, Falcini et al.[20] suggested that unexplained febrile child with elevated acute-phase reactants and platelet count requires echocardiography assessment.

Conclusion

In case of a child with fever of unexplained origin, who did not fulfill the classic criteria of KD and any other diseases (with similar clinical features) were excluded in them then the child could be diagnosed as incomplete KD. This diagnosis was often based on echocardiographic findings of coronary artery abnormalities. In this study 60% of the patient fulfilled the criteria of complete KD and the rest were incomplete KD.Cervical lymphadenopathy and changes in distal extremity were significantly common in complete KD than those in incomplete KD. The present study was conducted on a very small sample and as such the findings should be considered non-conclusive.

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