Kawasaki Disease: A Single-Center Study from a Tertiary Care hospital in Dhaka, Bangladesh

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Abstract

Background: *Kawasaki Disease (KD) is recognized as the leading cause of acquired heart disease in children in developed countries. This is a pioneer study from Bangabandhu Sheikh Mujib Medical University (BSMMU), documenting the common epidemiological, clinical, laboratory and echocardiographic findings, including management and immediate outcome of KD children.*

Method: *This retrospective study includes all patients with a diagnosis of KD, who attended the pediatric rheumatology division at BSMMU from January 2015 to December 2019. Data were collected from medical records at diagnosis and immediately after management. Relevant statistical tests were done and a p value < 0.05 was considered as statistically significant.*

Result: *A total of 129 cases were diagnosed with KD, among them complete KD cases were 62% and incomplete KD was 38%. The mean age at onset was significantly higher in incomplete KD than complete KD. The majority of the cases (67%) were between 1 to 5 years of age and male (72%) children were predominant. Fever was the most common presenting feature (100%), followed by bilateral conjunctivitis, mucosal involvement, rash, changes in extremities, cervical lymphadenopathy and others. Coronary artery dilatation was present in 30.5% cases with no significant differences between complete and incomplete KD cases. Aspirin was given to all the cases and IVIG was given to only 46.6% children. Rests of the children were treated with methyl prednisolone. All the cases improved after treatment and there was no immediate mortality.*

Conclusion: *It seems that KD is not an uncommon disease and incomplete KD cases are relatively more prevalent. About 30% KD cases had coronary artery abnormalities. Immediate outcome of management is excellent but needs long term follow-up.*

Keywords: *Kawasaki Disease (KD), complete KD, incomplete KD, Coronary Artery Abnormalities.*

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 etiology[1]. KD is characterized by fever, rash, conjunctival injection, oral mucositis, skin desquamation and cervical lymphadenopathy.

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 [2]. Cardiac lesions are hallmarks of KD and coronary artery aneurism (CAA) develop in about 25% cases if left untreated which can eventually lead to coronary stenosis, myocardial infarction (MI) or sudden death [3] Myocarditis and cardiac tamponade can also occur during the acute phase [2-4].

More than 60 countries in the world have reported KD. Strong epidemiological data are available from

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Japan, Korea, Taiwan, USA and Australia [2,5-7]. 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 [8-14].

Increasing numbers of KD cases are attending the pediatric rheumatology division of Bangabandhu Sheikh Mujib University (BSMMU). However, reports from Bangladesh are very scarce. Only one small study of 27 cases looked at the pattern and outcome of KD[15] and one case report presented a fatal outcome of a young infant.[16]

The present study is a pioneer study from the Department of Pediatrics, BSMMU documenting the common epidemiological, clinical presentation, laboratory and echocardiographic findings, as well as management and immediate outcome of KD children presenting to our center over a period of 5-year. It is very pertinent to note that an established full-fledged Pediatric Rheumatology Division in Bangladesh only exists in this center which is giving service since the year 2001.

Method

This is a retrospective study including all the patients with a diagnosis of KD, who attended the pediatric rheumatology division at the Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from January 2015 to December 2019. Since the year 2015 online records of all the pediatric rheumatology cases are kept in its own website. So, it was possible to collect data from the website.

After taking verbal consent from the parents over telephone, data were collected from medical records by analyzing all the KD patients (both complete and incomplete KD) at diagnosis and immediately after management. The following variables were documented: demography, clinical features, laboratory and echocardiographic findings, treatment received and immediate outcome.

Cases were excluded from the study, if there were any missing information in the medical records.

Definitions

KD case was defined based on the standard diagnostic criteria given by the American Heart Association (AHA) guidelines:[17].

Complete KD: fever for 5 days or more and fulfilled 4 of the 5 clinical features.

Incomplete KD: prolonged unexplained fever, fewer than 4 of the principal clinical findings, and compatible laboratory or echocardiographic findings.

IVIG resistant cases: KD cases with persistence or recrudescence of fever at least 36 hours after completion of 1st IVIG infusion (2gm/kg).

Echocardiography Findings:

Cardiovascular complications at first presentation, including coronary artery lesions, myocarditis, pericarditis, valvular regurgitations and heart failure were assessed using Vivid E-95 echocardiogram machine (made in Norway) with 4s and 6s transducers.

The coronary artery abnormalities (CAA) were classified according to AHA 2017 recommendation as followsb:[17]

1. No involvement: Z score < 2
2. Dilatation: Z score 2 to < 2.5
3. Small aneurysm: Z score ≥2.5 to < 5
4. Medium aneurysm: Z score ≥5 to < 10
5. Giant aneurysm: Z score ≥10

Statistical Analysis:

Quantitative variables were expressed as mean, SD and range, and qualitative data as percentage. Pearson's chi-square test was used to compare distribution between groups of qualitative data. Student's t test was used to find the significance between two groups for normally distributed continuous variables. A p value < 0.05 was considered as statistically significant.

Results:

A total of 129 cases of KD were diagnosed at BSMMU during the five years study period. Eleven cases were excluded because of incomplete data in their records.

Demographic and clinical feature including the diagnostic criteria are summarized in Table I. Complete KD cases were 62% and rests were incomplete KD cases. The mean age at onset was significantly higher (p<0.01) in incomplete KD (5.4± 1.2 years), than complete KD (3.4±0.78 years).

Gender ratio was 2.57: 1 with 72% male children. Among the 118 cases, the majority (n= 79, 67%) were between 1 to 5 years of age, followed by below 1 year (n= 25, 21%) of age (Fig 1).

Majority of patients (n=81, 68.7%) were admitted during the winter and early spring season. Disease duration was also significantly higher (p< 0.01) among incomplete KD and though not significant, hospital stay was higher in incomplete KD cases.

Fever was the most common presenting features (100%), followed by bilateral injection of conjunctiva, changes in lips and oral cavity (mucosal involvement), rash, changes in extremities (erythema and oedema of the dorsum of the hands and feet followed by desquamation which starts from the periungual regions of hands and feet), cervical lymphadenopathy and others (Table I).

Laboratory results and echocardiographic findings are described in Table II, showing high ESR, CRP and mean total white cell count in all the cases. ESR and mean white cell count was significantly higher in complete KD. Mean neutrophil counts were also higher in both the groups but there was no significant difference. Mean platelet counts were higher in complete KD cases and serum albumin level was low in both the groups with no significant differences.

Coronary artery dilatation was present in 36 (30.5%) cases with no significant differences between complete and incomplete KD cases. Though not significant, medium and large aneurysms were more common in incomplete KD cases (Table II). Most commonly affected coronary vessels were the left main coronary artery in 32 (27%) cases followed by left anterior descending (n=19, 16%) and right coronary artery (n= 9, 7.6%). Trivial valvular regurgitation was found in 12 (10%) children involving mitral (n=5, 4%) and aortic (n=7, 6 %) valves. No evidence of myocarditis was found and ejection fractions were normal.

Figure 2 shows that there was a gradual increase in diagnosis of KD cases over the 5 years period from 14 in 2015 to 34 in 2019 (p= 0.0017)

Table I

Demography and Clinical Characteristic of the Patients with Kawasaki Disease (n=118)

| Variables	Complete KD	Incomplete KD
	(n= 73, 62%)	(n=45, 38%)
Age (years)	3.4 ± 0.78	$5.4\pm1.2^*$
Mean ±SD	(0.5 – 8.0)	(4.0 – 9)
Gender	M 52	M 33
	F 21	F 12
Admitted during winter and Spring n (%)	49 (67%)	32 (71%)
Disease duration in days, mean± SD (range)	$8 \pm 3.5(6–14)$	$14 \pm 3.0 (7–19)$
Hospital stay in days, mean± SD (range)	$3\pm1.2(3–6)$	$3.5\pm1.8^{**} (4–6)$
Clinical Characteristics		
Fever for at least 5 days, n (%)	73 (100)	45 (100)
Conjunctival injections, n (%)	66 (90.4)	38 (84.4)
Changes in lips & oral Mucosa, n (%)	66 (90.4)	37 (82.2)
Rash n (%)	62 (85.0)	32 (71.0)
Changes in extremities , n (%)	59 (81.0)	26 (57.8)
Cervical lymphadenopathy, n (%)	55 (75.3)	26 (57.8)
Arthralgia/arthritis, n (%)	37 (50.6)	18 (40.0)
Sterile pyuria, n (%)	19 (26.0)	18 (40.0)
GIT symptoms. n (%)	6(8.21)	4 (8.8)
Respiratory symptoms, n (%)	5 (6.84)	2 (4.4)

$^*p < 0.01$, #p < 0.01, $^{**} p < 0.07$.

Table II

Laboratory Parameters and Cardiovascular Findings of KD Patients (n=118)

Variables	Complete KD (n= 73)	Incomplete KD (n=45)	p value
ESR (mm/hr)	95±16.5(85–110)	80±14.9 (67–112)	0.001#
CRP (mg/l)	22.4 ± 17.4(16.7–75.3)	27.8 ± 19.6 (13.9–79.9)	0.1215#
TC of WBC (th/cmm)	24.6 ± 12.0 (11–42)	14.6 ± 8.3(6.5–23.4)	0.001#
Neutrophil (%)	82 ±21.3(45–86.7)	79.4 ±22.5 (47–86)	0.5297#
TC of Platelets (lac/cmm)	6.53 ± 2.11(2.25–10.00)	4.30 ± 3.21 (2.29–12.10)	0.0611#
ALT (U/L)	30 ± 8.2(10–66)	38.5 ± 5.4(36–46)	0.001#
S. Albumin (g/L)	3.2 ± 1.7(2.2–4.3)	2.7 ± 0.9 (2.1–3.8)	0.0713#
Echocardiographic Findings			
No involvement (Z score < 2)	51 (69.8 %)	31 (68.9%)	0.573552*
Dilation only (Z score 2 to <2.5)	8 (10.9%)	2 (4.44%)	
Small aneurysm(Z score ≥2.5 to <5)	7 (9.6%)	4 (8.9)	
Medium aneurysm(Z score ≥5 to <10)	5 (6.8%)	6 (13.3)	
Large or giant aneurysm(Z score ≥10)	2 (2.70)	2 (4.44)	
Total dilation	22/73(30.13%)	14/45(31.11%)	

\# Students t test, *Chi Square test
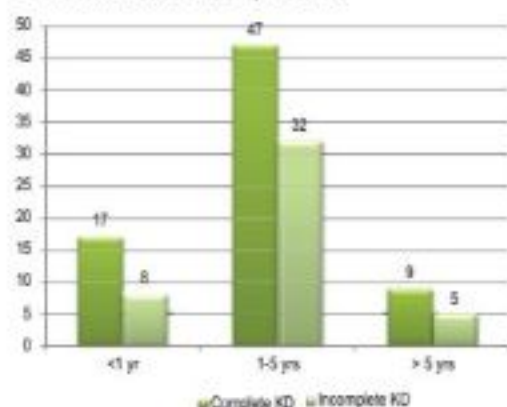
Figure 1: *Number of KD Cases by Age at Admission (in year)*
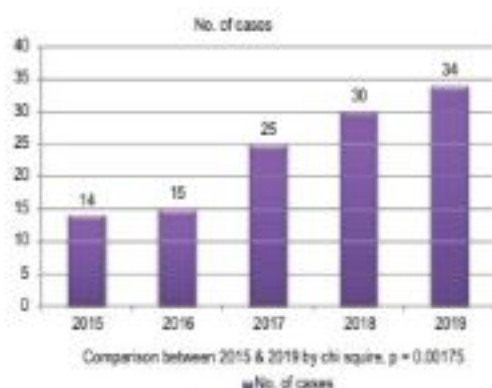
Figure 2: *Year-wise Distribution of Newly Diagnosed Cases of KD*

Comparison of important findings between KD children with coronary artery abnormalities (CAA) and without CAA shows that there was significantly higher frequency of young infants. Conjunctivitis, oral mucosal involvement and extremity changes were more in KD children without CAA. On the other hand, presence of rash and lymphadenopathy was significantly higher in KD with CAA group. Mean ESR, CRP and platelet counts were significantly higher in KD children with CAA (Table III).

Table IV shows the management and immediate outcome of the admitted KD cases. Aspirin was given to all the cases (both complete and incomplete KD). IVIG infusion was given to only 55 children (46.6%). Rests of the children were treated with methyl prednisolone pulse therapy for 3 consecutive days (30 mg/kg/day over 4 hours). Additionally three IVIG resistant KD cases were also treated with methyl prednisolone pulse therapy. All the cases improved after treatment and there was no immediate mortality among the 118 KD cases in this cohort.

Table III
Comparison of Clinical Features and Laboratory Parameters in Kawasaki Disease Children with and without CAA (n=118)

Variables	With CAA(n=36)	Without CAA (n=82)	p value
Age < 1 year (n=34)	9 (25%)	25 (30.4%)	0.17573
Eye signs (n=104)	31/36 (86.1%)	73/82 (89%)	0.97832
Lips and oral mucosa involvement (n=103)	26/36 (72.2%)	77/82 (93.9%)	0.031
Extremity changes (n=85)	11/36 (30.5%)	74/82 (90.2%)	<0.00001
Rash (n=94)	31/36 (86.1%)	63/82 (76.8%)	0.58126
Lymphadenopathy (n= 81)	33/36 (91.6 %)	48/82 (58.5%)	<0.001
Mean febrile days	11.1 ± 2.8	8.7 ± 4.1	0.03#
Mean ESR (mm/hr)	84.7 ± 12.3	56.2 ± 11.7	0.01#
Mean CRP (mg/L)	35.6 ± 9.6	21.3 ± 8.2	0.01 #
Mean PC (lacs/cmm)	6.5 ± 3.4	4.4 ± 1.2	0.045#

*Chi Square test, #unpaired student t test

Table IV
Management and Immediate Outcome of KD Patients (n=118)

Variables	Complete KD(n= 73)	Incomplete KD(n=45)
Management		
Aspirin (n= 118)	73 (100%)	45 (100%)
IVIG (n=55), 46.6%	32 (43.8%)	23 (51.1%)
Before 10 days of illness	6/73 (8.2%)	5/45 (11.1%)
After 10 days of illness	26/73 (35.6%)	18/45 (40.0%)
Methyl prednisolone (n= 66)	43/73(59.0%)	23/45 (51%)
Immediate outcome		
Improved	73 (100%)	45 (100%)
IVIG resistant KD (n=3)	2/73 (2.7%)	1/45 (2.22%)
KDSS*	0	0
Death	0	0

#KDSS - KD Shuck syndrome

Discussion:

Kawasaki disease (KD) is one of the most common vasulitidis in children. It bears the name Kawasaki disease because of the initial description of the disease by Dr. Tomisaku Kawasaki in Japanese children in 1967[1]. Recent reports from India suggest that KD might very soon replace rheumatic fever as the commonest cause of acquired heart disease [5,18].

The epidemiological features, with a male predominance and a majority of patients <5 years of age, were similar to those reported in other studies [19-21].

More than 68% of our KD cases were admitted during winter and early spring, which is reported from many other centers [22].

In this study, incomplete cases were higher than other reports, with 38% of cases compared to about 20% reported in other studies [23-24]. The difference may be explained by a high index of suspicion in our center. Mean duration of fever was also higher in incomplete cases.

The present study found significant number of higher age group; disease duration and hospital stay among

incomplete KD. But studies from neighboring countries including India and Pakistan reported that younger age group was more likely to develop incomplete KD [11,14]. Likely explanation of this difference could be due to the facts that, many of the young infants and children with incomplete presentation were not suspected as KD and treated outside as infection, and not brought to our hospital. This explanation can be further supported by the finding of higher disease duration at presentation in incomplete KD patients, which means those who had unremitting fever even after 1 to 2 weeks were brought to the hospital. Natural history of KD suggests that this is a self-limiting disease and fever usually subsides by 2nd week[1].

Fever was the most consistent finding (100%) in this study followed by bilateral conjunctivitis (88%), lips and oral mucosa involvement (87%), rash, extremity changes and cervical lymphadenopathy. These findings were almost consistent with other reports[14, 25-27]. Rash was not very common in the present study, may be due to late reporting of cases. Most of the patients came to us by the end of 1st or in the 2nd week (mean duration of complete KD was 8 days and incomplete KD 14 days), when rash disappeared in many cases. Rash in KD usually appears within 5 days of fever onset and persists only for few days[17]. Moreover because of dark complexion in our country, rash may not be clearly visible and might have been missed. Cervical lymphadenopathy was the least common of the major criteria in the present study which is also consistent with documented findings [14, 17, 25-27].

Laboratory features were also consistent with reported documents showing raised ESR, raised CRP, leukocytosis, thrombocytosis and low albumin level[1,26].

In this cohort 30.5% KD cases had coronary artery abnormalities at admission, which is slightly higher than reported incidence of CAA (about 25% if left untreated)[1,28].

In a recent study, Sakina et al in their cohort in Pakistan found 32% CAA at diagnosis and also at two weeks which is almost similar to our finding[14]. On the other hand Bhattad et al from Indian study found CAA in 43.6% of their KD children[26]. The previous study from our country conducted by Fatema et al found about 88% coronary abnormalities in their KD cohort which appears unusually high[15]. All these three studies had very small sample size (n=25, 32

and 27). Additionally, the KD cases in the Fatema et al study were collected from the echocardiography facilities. May be there could be some sample bias.

In the present study, KD cases were admitted having fever for a minimum of 6 day and maximum of 19 day duration. So, at presentation, 1st echocardiogram was done at 2nd to 3rd week. Coronary artery abnormalities were almost equally found in complete and incomplete KD cases but though not significant, medium size and large/ giant aneurysm were more common in incomplete KD. This finding may be explained by longer duration of illness of KD cases at admission.

While comparison was done in between KD with CAA and without CAA cases, significantly higher number of young infants (<1 year), bilateral eye injections, mucosal involvement and extremity changes were found in without CAA group. It is reported that young infants are more likely to develop coronary artery abnormalities as they often have incomplete forms of KD and are misdiagnosed or late diagnosed. Moreover, some of the diagnostic criteria of KD including: rash, lymphadenitis is also present in many pediatric infectious diseases. So, it is very likely to miss the cases if KD is not thought of in the differential diagnoses. As the features of KD are transient and usually change from day to day, criteria of diagnosis might easily be missed as well. As sequelae, they may have coronary artery disease[6].

Unlike many other reports our cohort found higher prevalence of young infants (<1 year) in KD without coronary dilatation group. May be because of the facts mentioned earlier, our cohort missed majority of infants with incomplete KD and CAA. It is not unlikely that, ethnic and genetic variation may play a role. But from this single center study and without a nationwide survey, it cannot be argued as such.

It is shown in the present study that there was a sustained increase in the number of KD cases in our center over the 5 years study period, which was highly significant (from 14 in 2015 to 34 in 2019, p=0.001745). India had also significant rise in the overall incidence of the disease over the years[29,30]. But 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.

In the present study, all the patients were managed with adequate doses of aspirin. But IVIG was infused only in 46.6% cases as others could not afford the cost of IVIG. So, as an alternative, Intravenous methyl prednisolone was given to other patients. Additionally, three resistant cases were also treated with I/V methyl prednisolone. Immediate mortality was absent in the present cohort. This may be due to absent cases of Kawasaki Disease Shock Syndrome (KDSS) or cardiac tamponade in this series. It may be presumed that these complicated KD cases are still missed out by paediatricians in our country. It may be noted here that documentation of long term outcome of our KD cases was not the objective of this study. A follow up study in next few years' time hopefully would clearly identify that. Since most of our patients were treated with methylprednisolone in place of recommended IVIG infusion, their long term sequelae in comparison to IVIG group deserves to be documented.

Conclusion

Diagnoses of KD cases are significantly increasing. Incomplete KD cases are relatively more prevalent in Bangladesh. It could be due to a true increase in number or late diagnosis for late referral. But still lot of cases must have been missed out. About 30% KD cases had coronary artery abnormalities and incomplete KD cases had more medium and large coronary aneurysm. KD is no longer to be diagnosed when there is no other cause of persisting fever in a child is found. Rather KD must be considered in the differential diagnosis of any child with fever for 5 days, so that diagnosis can be done early and treated timely to prevent cardiac complications. KD is a challenge for all the paediatricians in our country.

References:

1. Son MBF, Burns JC, Newburger JW. Kawasaki Disease. In: Petty RE, Laxer RM, Lindsley CB, Weddenburn L, Mellins ED , Fuhlbrigge RC. editors. Textbook of Pediatric Rheumatology. 8th ed. Philadelphia: Elsevier Saunders; 2021. P.473-483.

2. Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, Burns JC 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: 2747-71.

3. Singh S, Bhattad S, Gupta A, Suri D, Rawat A, Rohit M.

Mortality in Children with Kawasaki Disease. 20 years of Experience from a Tertiary Hospital in North India. Cli Exp Rheumatol 2016; 34 (supple. 97): S129-S133.

4. Burns JC, Glode MP. Kawasaki Syndrome. Lancet 2004; 364: 533-44.

5. Singh S, Vignesh P, Burgner D. The Epidemiology of Kawasaki Disease: A Global Update. Arch Dis Child 2015; 100 (11): 1084-88.

6. Makino N, Nakamura Y, Yashiro M, Ryusuke N, Tsuboi S, Aoyama Y et al. Descriptive Epidemiology of Kawasaki Disease in Japan, 2011-2012: From the Results of the 22nd Nationwide Survey. J Epidemiol 2015; 25 (3) 239-45.

7. Kim GB, Han JW, Park YW, Song MS, Hong YM, Cha SH. Epidemiological Features of Kawasaki Disease in South Korea: Data from Nationwide Survey. 2009-2011. Pediatr Infect Dis J 2014; 33: 24-27.

8. Jiao F, Jindal AK, Pandiarajan V, Khubchandani R, Kamnath N, Sabui T, Mondal R, Pai P, Singh S. The Emergence of Kawasaki disease in India and China. Global Cardiology Science and Practice 2017: 21 http://dx.doi.org/10.21542/gcsp.2017.21.

9. Chua D, Cueto-Velasco M, Galvez E. A Ten Year Review of Kawasaki Disease: The Chinese Generao Hospital Experience. Pediatric Infectious Disease Society of the Philippines Journal 1999; 3: 6-15 Chong CY, Tan NWH, Yung CF, Nadua K, Kam KQ, Li J et alPediatric Kawasaki Disease Trends Prior to and During COVID-19 Outbreak in Singapore. Journal of the Pediatric Infectious Disease Society 2021; 10 (11) 1029-32.

10. Chong CY, Tan NWH, Yung CF, Nadua K, Kam KQ, Li J et al. Pediatric Kawasaki Disease Trends Prior to and During COVID-19 Outbreak in Singapore. Journal of the Pediatric Infectious Disease Society 2021; 10 (11) 1029-32.

11. Singh S, Kawasaki T. Kawasaki Disease in India-Lessons Learnt over the Last 20 years. Indian Peditr 2016; 53: 119-124.

12. Rajak K, Twayana AR, Shreshta R, Amatya P, Ghimire C. Prevalence of Kawasaki Disease in a Tertiary Care Hospital : A Descriptive Cross-sectional Study. J Nepal Med Assoc 2019; 57 (220): 408-411. Open Access. doi: 10.31729/Jnma.4746

13. Rodrigo PTM. Utilization of Clinical Criteria and Laboratory Investigations to Identify High Risk Children for Coronary involvement in Kawasaki Disease Presenting to Lady Ridgway Hospital, Colombo, Sri Lanka. Archivos de Medicina 2020: 16 (5) 7-8.

14. Sakina S, Owais SS, Khan EA, Sheikh AM. Kawasaki Disease: Clinico-laboratory Spectrum and Outcome in a Cohort of Children Treated at a Tertiary Care Hospital in Islamabad, Pakistan. Pak J Med Sci 2020; 36 (2): 260- 264. doi:// doi.org/10.12669/pjms.36.2.910.

15. Begum NNF, Mia AA, Mostafi M, Akhter K, Sultana M, Sarker FR. Kawasaki Disease Hospitalization: Outcomes in Two Tertiary Care Hospitals I Bangladesh. Bangladesh Medical Research Council Bulletin 2017; 43 (3): 143-148.

16. Akhter S, Islam SMS, Islam N, Baki A, Ahmed A, Nahar J et al. Kawasaki Disease-A rare Presentation in a Bangladeshi Infant: A Case Report. BIRDEM Medical Journal 2012; 1(1): 43-45. https:// doi.org/10.3329/birdem.vii.12392.

17. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M et al. Diagnosis, Treatment, and Long-term Management of Kawasaki Disease: A Scientific Statement for Health Professionals from the American Heart Association. Circulation 2017; 135: e927-e999.

18. Kumar RK, Tandon R. Rheumatic Fever and Rheumatic Heart Disease: The Last 50 Years. Indian J Med Res 2013; 37: 643-58.

19. Harnden A, Mayon-White R, Perrera R, Yeates D, Goldacre M, Burgner D. Kawasaki Disease in England: Ethnicity, Deprivation, and Respiratory Pathogens. Pediatr Infect Dis J 2009; 28: 21-4. doi: 10.1097/INF. 0b013e3181812ca4.

20. Giannouli G, Tzoumaka-Bakoula C, Kopsidas I, Papadogeorgou P, Chrousos GP, Michos A. Epidemiology and Risk Factors for Coronary Artery Abnormalities in Children with Complete and Incomplete Kawasaki Disease During a 10-Year Period. Pediatr Cardiol 2013; 34:1476-81. Doi: 10.1007/s00246-013-0673.9.

21. Tacke CE, Breunis WB, Pereira RR, Breur JM, Kuipers IM, Kuijpers TW. Five Years of Kawasaki Disease in the Netherlands: a National Surveillance Study. Pediatr Infect Dis J 2014; 33: 793-97.

22. Burns JC, Herzog L, Fabri O, Tremoulet AH, Rodo X, Uehara R et al. Seasonality of Kawasaki Disease: A Global Perspective. PLoS One 2013; 8: e 74529. doi: 10.1371/journal.pone.0074529.

23. Nakamura Y, Yashiro M, Uehara R, Sadakane A, Tsuboi S, Aoyama Y et al. Epidemiologic Features of Kawasaki Diseasein Japan: Results of the 2009-2010 Nationwide Survey. J Epidemiol 2012; 22: 216-21. doi: 10.2188/jea.JF.20110126.

24. Lin YT, Manlhiot C, Ching JCY, Han RK, Nield LE, Dillenburg R et al. Repeated Systemic Surveillance of Kawasaki Disease in Ontario from 1995 to 2006. Pediatr Int 2010; 52: 699-706. doi: 10. 1111/j.1442-200X.2010.03092x.

25. Belay ED, Maddox RA, Holman RC, Curns AT, Ballah K, Sconberger IB. Kawasaki Syndrome and Risk Factors for Coronary Artery Abnormalities: United States, 1994-2003. Pediatr Infect Dis J 2006; 25: 245-49.

26. Bhattad S, Gupta S, Israni N, Mohanty S. Profile of Kawasaki Disease at a Tertiary Care Center in India. Ann Pediatr Card 2021; 14: 187-91.

27. de la Harpe M, di Bernado S, Hofer M, Sekarski N. Thirty Years of Kawasaki Disease: A Single- center Study at the University Hospital of Lausanne. Front Pediatr 2019; 7: 1-8. doi: 10.3389/fped.2019.00011.

28. Newburger JW, Takahashi M, Burns JC. Kawasaki Disease. J Am Coll Cardiol 2016; 67 (14): 1738-49.

29. Singh S, Aulakh R, Bhalla AK, Suri D, Manojkumar R, Narula N, et al. Is Kawasaki disease incidence rising in Chandigarh, North India? Arch Dis Child 2011; 96: 137-140. doi: 10.1136/adc.2010.194001.

30. Halder A, Pal P, Ahmed N, Roy M, Sarkar SD. The Changing Epidemiology of Kawasaki Disease in Eastern India. Arch Dis Child 2021; 106 (Suppl 1) A1-A514. doi: 10.1136archdischild-2021-rcpch.388.