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Clinical profile of patients with Kawasaki disease from a tertiary care hospital of western region of Assam

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Abstract

Kawasaki disease (KD) is a common vasculitic disease occurring predominantly in children. Early diagnosis of this condition is very important because if untreated or not instituted the treatment with intravenous immunoglobulin (IVIg) before 10 days of illness, 25% of children can develop coronary artery aneurysm. After timely treatment this figure comes down to 3-4%. KD is reported from all regions of the world and from almost all states of India. Annual incidence is highest in Japan followed by Korea and Taiwan. There is paucity of reports on KD from Assam. In this study we report our experience of managing 11 children with KD at our centre. In this study five patients with KD were complete KD and six patients were incomplete KD. There were several unusual findings in our study like presentation with acute arthritis and fever in one patient, gastrointestinal complaints (e.g., diarrhea, vomiting and pain abdomen) in four patients, hydrops of gallbladder in one patient, BCG inoculation site reactivation in one patient and pericardial effusion in one patient. Cardiovascular complications like left ventricular dysfunction was observed during acute phase in one patient and mild dilatation of left main coronary artery was observed in one patient. Nine out of 11 patients had responded promptly to IVIg infusion at the dose of 2 g/kg over 12-15 hours. Two children were resistant to IVIg and one of these patients had developed polyserositis after four days post-IVIg. However, parents refused further treatment of these children. There was no death in our cohort and nine patients who responded well to IVIg had completed a median of 0.3 year (Range, 0.1 -1 year) follow-up.

Key words: Kawasaki disease, arthritis, hydrops

INTRODUCTION

Kawasaki disease (KD) is an acute vasculitis commonly occurring in children. It involves the medium vessels. It has a predilection to involve coronary arteries[1]. If not diagnosed and treated on time, it can lead to coronary artery aneurysm in 25% of cases[1]. Though KD is common in children under 5 years of age it also can occur in older children adolescents, and adults[1, 2]. The incidence of KD is highest in Japan (322 per 100,000 children under 5 per year) followed by Korea (134.4 per 100,000 children under 5 per year) and Taiwan (82.8 per 100,000 children under 5 per year)[3, 4, 5]. In India, the exact incidence of KD is still unknown. In a study from Chandigarh reported an incidence of 5.35 per 100,000 children under 5 per year during 2009-2014[6]. There is paucity of report on KD from Assam. In this study, we report our experience of managing KD in 11 patients at our centre over a period of one year.

PATIENTS AND METHOD

This was a prospective study with limited follow-up. This study was carried out in the Department of Pediatrics, Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH), Barpeta, Assam. Our hospital is situated in the Western part of Assam. The study period was from 1st June 2024 to 31st May 2025. Data were collected in a pretested proforma from all patients with KD admitted in pediatric ward of our hospital during the period of the study. The diagnosis of complete KD was made according to the diagnostic criteria developed by American Heart Association in 2017 (AHA-2017) (Table 1). Incomplete KD was defined in any infant or child with prolonged unexplained fever documented to have less than 4 principal features of complete KD, and/or presence of coronary artery abnormalities on transthoracic 2-dimensional echocardiography (2D Echocardiography), and/or presence of periungual peeling of the skin. Resistant KD was defined in patients with persistent or recrudescent fever after at least 36 hours and less than 7 days after completion of IVIg infusion[1].

Demographic characteristics like (age, sex) clinical (symptoms and clinical signs), laboratory investigations, echocardiography findings and follow-up data of each patient in our cohort were recorded in the study proforma. Patients

were treated with intravenous immunoglobulin (IVIg) at the dose of 2 g/kg infused over 12-15 hours and aspirin at the dose of 30-50 mg/kg/day in four divided doses till 48 hours of defervescence followed by 3-5 mg/kg/day for 4-6 weeks in patients without coronary artery abnormalities (CAAs) or continued in patients with CAAs. In patients with severe presentation, oral prednisolone was used as an adjunctive treatment at the dose of 2 mg/kg/day in single or divided doses for 2 weeks followed by tapering. 2D Echocardiography was done in all patients during admission and subsequently on follow-up after 2 weeks and six weeks after initial treatment. We calculated the z- scores of the internal diameters of the coronary arteries using the online equation developed by Dallaire and Dahdah in 2010[7]. The z-score of a coronary artery ≥2.5 - <5 is labeled as mild aneurysm, z-score ≥5 - <10 is moderate aneurysm and z-score of ≥ 10 is labeled as severe or giant aneurysm. The ethics committee of our institute had approved the study.

Table 1: Diagnostic criteria for complete Kawasaki disease[1]

A complete case of KD is diagnosed in a child with fever for at least 5 days (the day of fever onset is taken as day 1 of illness) in presence of at least 4 out of 5 following principal features. In the presence of ≥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. Experienced clinicians who have treated many patients with KD may establish the diagnosis with 3 days of fever in rare cases.

1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal 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 subacute phase
5. Cervical lymphadenopathy (≥1.5 cm), usually unilateral

KD- Kawasaki disease

Statistical analysis:

Continuous variables were analyzed using median with interquartile range and mean with standard deviation (mean ± SD).

RESULTS

A total of 11 patients were diagnosed with KD during the period of study. Out of these, five patients were complete KD, and six were incomplete KD. The median age at presentation was four years (Range, 0.5-11 years). Six patients in our cohort were male and five patients were female. The mean duration of fever at presentation in our cohort was 6.4±1.8 days. The diagnosis of KD was established within 10 days of onset of symptoms in 10 patients. The clinical profile of the patients in our cohort is shown in Table 2.

Table 2: Clinical profile of patients with Kawasaki disease

Sl. No.	Age/sex	Duration of symptoms	Presenting symptoms and signs	Laboratory investigations	2D-Echo	Treatment and response	Follow-up
1, SM	6 Mo/F	7 days	Loose motion, vomiting, fever, cough, irritability, red and cracked lips, perianal and periungual desquamation	Hb-9.2 g/dL, TLC-20,810/mm3, DLC-N38, L56, PC-4,00,000/mm3, ESR-15 at 1st hr, CRP-119 mg/L	Minimal pericardial effusion, no CAAs	IVIg on day 8 of fever, aspirin Dramatic response	Completed one year Asymptomatic
2, DK	11yr/M	10 days	Fever, pain abdomen, vomiting, cervical LAP, strawberry tongue, periungual desquamation	Hb-11.3 g/dL, TLC-23,600/mm3, DLC-N93, L4, PC-1,50,000/mm3, ESR-105 at 1st hr, CRP-96 mg/L	Decreased left ventricular wall motion, EF: 45%, no CAAs	IVIg on day 11 of fever, aspirin Oral prednisolone Dramatic response	Completed four months Asymptomatic

3, MR	1 yr 2Mo/M	7 days	Fever, conjunctival injection, oral ulcer, polymorphous rash, strawberry tongue, tachypnea	Hb-9 g/dL, TLC-18,100/mm3, DLC-N58, L34, PC-4,50,000/mm3, ESR-120 at 1st hr, CRP-93 mg/L	Normal ventricular function, no CAAs	IVIg on day 8 of fever, aspirin Dramatic response	Completed six months Asymptomatic
4, RA	2 yr/F	7 days	Fever, vomiting, loose motion, abdominal distension, polymorphous rash, perineal desquamation, lip cracking, irritability	Hb-8.4 g/dL, TLC-27,070/mm3, DLC-N76, L15, PC-2,40,000/mm3, ESR-130 at 1st hr, CRP-415 mg/L	Normal ventricular function, no CAAs	IVIg on day 10 of fever, aspirin Dramatic response	Completed seven months Asymptomatic
5, HK	4 yr/F	7 days	Fever, cough difficulty in breathing, polymorphous rash, swelling of extremities, irritability, tender hepatomegaly, muffled heat sounds	Hb-9.4 g/dL, TLC-22,430/mm3, DLC-N72, L25, PC-40,000/mm3, ESR-90 at 1st hr, CRP-90 mg/L, Alb-2.6 mg/dL, AST-61, ALT-19	Not done	IVIg on day 8 of fever, aspirin No response, planned for second dose of IVIg, however, parents refused treatment and had taken away the child from hospital against medical advice	Could not be communicated with parents
6, AN	8.5 yr/F	6 days	Fever, cough, polymorphous rash, cervical LAP, strawberry tongue, periungual desquamation	Hb-13 g/dL, TLC-11,500/mm3, DLC-N66, L22, PC-3,20,000/mm3, ESR-40 at 1st hr, CRP-6.7 mg/L	Good ventricular function, no CAAS	IVIg on day 8 of fever, aspirin Dramatic response	Completed 9 months Asymptomatic
7, YA	1.5 yr/M	4 days	Fever, difficulty in breathing, extremity edema, irritability, periungual desquamation at fingers and toes, gallop rhythm	Hb-6.5 g/dL, TLC-18,040/mm3, DLC-N65, L24, PC-2,80,000/mm3, ESR-100 at 1st hr, CRP-96 mg/L	Minimal pericardial effusion, no CAAs	IVIg of day 5 of fever, aspirin Had response initially, however, the patient relapsed after 4 days with polyserositis and edema. Referred to another tertiary care hospital equipped with cardiology services	Lost to follow-up
8, MP	5 yr/F	3 days	Fever, maculopapular rash, oral ulcer,	Hb-10.3 g/dL, TLC-11,240/mm3, DLC-N84,	**LMCA-z-score 2.96**, LAD-z-	IVIg on day 6 of fever, aspirin	Completed two months LMCA diameter normalized

			irritability, perineal desquamation, BCG site reactivation	L12, PC-4,30,000/mm3, ESR-110 at 1st hr, CRP-27 mg/L	score 1.08, RCA-z-score 1.6		
9, CD	10 yr/M	7 days	Fever, limping withsevere pain and immobility of right hip joint, mid-inguinal point tenderness, periungual desquamation	Hb-10 g/dL, TLC-23,230/mm3, DLC-N78, L18, PC-6,40,000/mm3, ESR-106 at 1st hr, CRP-123 mg/L, blood culture- sterile, USG hip joint: synovial thickening, USG abdomen: hydrops GB	Good ventricular function No CAAs	IVIg on day 9 of fever, aspirin, oral prednisolone Rapid defervescence, Rt. Hip pain reduced with persistence of some limping at discharge, GB hydrops reduced to half after 5 days and disappeared after 2 weeks	Some limping persisted on Rt. LL after 6 weeks, initiated on oral Mtx 10 mg/week, asymptomatic after 3 months
10, R	11 Mo/M	6 days	Fever, macular rash, cracked lips, strawberry tongue, perineal erythema, periungual desquamation, swelling of extremities, irritability	Hb- 8.4 g/dL, TLC-18,430/mm3, DLC-N73, L25, PC-4,40,000/mm3, ESR-105 at 1st hr, CRP-90 mg/L	Good ventricular function, no CAAs	IVIg on day seven of fever, aspirin Dramatic response	Completed 1 month, asymptomatic
11, AI	8 yr/M	7 days	Fever, irritability, cracked lips, conjunctival injection, strawberry tongue	Hb-10.4 g/dL, TLC-6,940/mm3, DLC-N46, L42, PC-100,000/mm3, ESR-90 at 1st hr, CRP-10 mg/L, Alb-2.6 mg/dL, AST-61, ALT-19	Good ventricular function, no CAAs	IVIg on day 9 of fever, aspirin Dramatic response	Completed 1 month, asymptomatic

The unusual features noted in our patients were, vomiting in one patient (Patient 2, Table 2), both loose motion and vomiting in two patients (Patient 1 and 4, Table 2), respiratory distress in two patients (Patient 5 and 7, Table 2), pain abdomen in one patient, mono-arthritis of right hip joint in one patient (Patient 9, Table 2), BCG site reactivation in one patient (Patient 8, Table 2) and hydrops of the gallbladder in one patient (Patient 9, Table 2). Laboratory investigations are shown in Table 3.

Table 3: Laboratory investigations in the patients in the cohort.

Parameters	Results
Hemoglobin (g/dL)	Mean 9.6±1.7
Total leucocyte count (/mm3)	Mean 18308±6147
Platelet count (/mm3)	Mean 3,34,000±1,77,963
Erythrocyte sedimentation rate (at 1st hr)	Mean 92±34
C reactive protein (mg/L)	Median 93 (Range, 7 - 415)

Cardiovascular complications observed in our cohort were, minimal pericardial effusion in two patients (Patient 1 and 7, Table 2), CAA in one patient who had dilatation of left main coronary artery (LMCA) with a Z score of 2.96 (Patient 8, Table 2), left ventricular (LV) dysfunction in one patient (Patient 2, Table 2).

All patients with KD in our cohort had received IVIg and aspirin. Prednisolone as an adjunctive therapeutic agent was used in one patient (Patient 9, Table 2) who had severe presentation. Nine out of 11 patients had dramatic response to the treatment with rapid defervescence and reductions in inflammatory parameters. Post-IVIg, the patients with cardiovascular complications had also showed improvement in left ventricular dysfunction, resolution of pericardial effusion and normalization of coronary artery diameter (revealed on 2nd and 3rd 2D Echo). In the patient with gallbladder hydrops, hydrops size was reduced to half on repeat ultrasonography (USG) done after 5 days post-IVIg followed by absence of hydrops detected on 3rdUSG after 2 weeks post-IVIg. The severe joint pain and limitation of movement in the patient with right hip mono-arthritis was improved rapidly post-IVIg and some limping persisted at the time of discharge and on follow-up after 6 weeks. In this patient oral methotrexate 10 mg/week was initiated at 6 weeks post-IVIg and on follow-up after 3 months on methotrexate revealed completely normal joint movements and gait. Two patients in our cohort were resistant to IVIg. However, parents of one had not given consent for its treatment and took the child away from the hospital against medical advice (Patient 5, Table 2). The other patient with resistant-KD was referred to higher facility with cardiovascular services for worsening of clinical condition post-IVIg in the form of polyserositis and edema (Patient 7, Table 2). Only three patients in our cohort had fever and chill, and rigor immediately following initiation of IVIg. No patient had any serious reaction to IVIg like anaphylaxis. There was no death in our cohort during admission or follow-up.

Nine out of 11 patients in our cohort had completed a median follow-up of 0.3 years (Range, 0.1-1 year). On follow-up, there was no new problem or recurrence of clinical symptoms.

DISCUSSION

Currently KD has been diagnosed, treated and reported from all countries. To the best of our knowledge, so far, from Assam, only one case series has been published in literature[8]. This is a report stating the experience of managing children with KD from a still unreported part of Assam. Being a tertiary care hospital, we were able to diagnose and treat KD in 11 patients over a period of 1 year. The comparisons of our study with other recent Indian studies are mentioned in Table 4.

Table 4: Comparison of the present study with other recently reported studies form India.

Parameters	Present study N=11	Sharma et al (8) N=73	Bhattad et al (10) N=39	Banoo et al (9) N=31
Age	Median 4 yr(Range 0.5 – 11yr)	Median 3 yr (IQR 4.25)	Mean 42±38.5 months	<10 yr
Sex (M/F)	6/5	49/24	27/12	23/8
Complete KD	4	53	18	19
Incomplete KD	6	20	14	12
Resistant KD	2	10	7	2
BCG site reactivation	1	0	1	0
Hydrops of gallbladder	1	0	0	0
Arthralgia/arthritis	1	3	0	9
Pericardial effusion	2	11	1	0
LV-dysfunction	1	0	0	0
CAAs	1	15	17	17
GI involvement	4	3	3	13

IQR interquartile range, M- male, F- female, KD- Kawasaki disease, LV- left ventricle, CAAs- coronary artery abnormalities, GI- gastrointestinal.

Gastrointestinal involvement in the form of vomiting, diarrhea and pain abdomen was observed in four patients in our cohort. In a study from Srinagar, India, had reported similar gastrointestinal involvement in 13 patients and in another studies form Bangalore and Assam reported gastrointestinal involvement in 3 and 9 patients with KD respectively[8, 9, 10]. In all these studies including the index study, patients had prompt recovery form gastrointestinal symptoms following treatment with IVIg. The associated gastrointestinal vasculitis and mucosal involvement is the pathogenic mechanism of such manifestations[2]. We could diagnose KD in one patient after detection of hydrops gallbladder on abdominal ultrasonography. Though it is a rare presentation, KD is the commonest cause of hydrops gallbladder. Other common causes of this manifestation are Epstein-Barr virus infection, leptospirosis, IgA vasculitis, systemic sclerosis, Sjogren's syndrome and Familial Mediterranian Fever[11, 12]. The immunological basis of hydrops

gallbladder in KD is not clearly known[2]. This is self-limiting in nature and also responds well to the treatment with IVIg like in the index case. (Patient 9, Table 2).

Mono-arthritis of right hip joint with severe pain and limping was the presenting feature in one child in our cohort (Patient 9, Table 2). Arthritis in KD was also reported by Sharma et al[8], and Banoo et all[9] in their case series. Gong et al reported arthritis in KD in 7.5% of cases with oligo-articular presentation in 55% and poly-articular presentation in 45% [13]. Arthritis in KD usually resolves completely after treatment with IVIg. However, our patient with arthritis was not completely resolved even after treatment with IVIg and prednisolone and it resolved completely after 3 months treatment with weekly oral methotrexate.

BCG injection site reactivation was observed in one five year old patient in our cohort. This was also reported by Bhattad et al[10] and Kumar et al[14] from India. This is commonly observed in infants with KD and is a pathognomonic sign of KD.

The cardiovascular involvement in our cohort was transient in nature with mild dilatation of LMCA in one patient, LV dysfunction in one patient and minima pericardial effusion in two patients. All these manifestations responded promptly to IVIg with absence of LV dysfunction, and pericardial effusion and normalization of LMCA diameter on follow-up examinations. Myocarditis with ventricular dysfunction is common in the acute phase of KD[1,2]. It can also occur in patients without CAAs[15]. The index patient in our cohort also did not have CAAs (Patient 2, Table 2). Pericardial effusion and sometimes cardiac tamponade is a known manifestation in KD, especially in Indian case series[9, 16, 17].

All patients in our cohort had receive IV Ig as initial treatment which is the gold standard of treatment for KD. Only two patients were resistant to it. One patient with resistant KD had developed polyserositis along with edema and fever after 4 days post-IV Ig. Polyserositis in KD is anecdotally reported in literature. It was first reported from Amsterdam by Dahlem et al in an 8 year old boy after eight days of treatment with IVIg[18]. Though several options like repeat IV Ig, pulse methyl prednisolone were available with us, we could not treat the patients with resistant KD for parental unwillingness.

The limitations of our study are- this is a single-center prospective cohort of only 11 patients with KD with limited follow-up and the study population in our cohort is not a true representative of this region of the country. Some issues like assessment of cardiovascular function, dyslipidemia and assay of pro-inflammatory cytokine levels were not carried out. There is a need to increase the awareness among the doctors, nurses and other health care workers in our center about Kawasaki disease. Also, a long term prospective study is needed in a large cohort of patients for detailed description of these issues in this part of the state.

CONCLUSION

KD has been increasingly reported from most states. Though the duration of the study is short and numbers of patients is less, in a centre from where this disease is not previously reported, 11 numbers of cases in the context of KD is an accountable number. This is a second case series from Assam reported so far. Patients in our cohort had diverse presentations including arthritis, BCG site reactivation, gallbladder hydrops, LV-dysfunction and polyserositis in resistant KD. The majority of patients had prompt response to IVIg without any severe treatment related site effects.

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