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A comparison of the clinical profile of Kawasaki disease in children from Northern India above and below 5 years of age

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ABSTRACT

Objective. *Clinical experience collated over the last 11 years at our center suggests that Kawasaki disease (KD) affects older children more frequently as compared to the Western literature. In this study we have compared the clinical profile of KD in children above 5 years of age (Group I) with those below 5 years (Group II).*

Design. *Chart review of children with KD during the period January 1994-April 2006.*

Results. *Of the 97 children, 38 (39.2%) were in Group I and 59 (60.8%) were in Group II. Mean age at presentation of children in Group I was 8.12 ± 2.0 years while that in Group II was 2.83 ± 1.50 years. Mean time interval to make the diagnosis was 11.2 ± 6.4 days in Group I as compared to 10.8 ± 6.03 days Group II but the difference was not significant ($p > 0.05$). Non-purulent conjunctivitis, mucosal changes in oropharynx, cervical lymphadenopathy and hepatomegaly were seen more frequently in Group II than in Group I, but this difference was also not statistically significant. Desquamation at presentation and arthralgia/arthritis were significantly more common in Group I, while edema over hands and feet was significantly more frequent in Group II ($p < 0.05$). Among laboratory parameters, hemoglobin level was lower in children in Group II as compared to Group I ($p = 0.001$), while there was no difference in parameters of inflammation. Cardiac abnormalities were noted in about 12% children but there was no statistically significant difference between the two groups.*

Conclusion. *In Chandigarh, KD occurs more frequently in children above 5 years of age as compared to the West. Older children with KD have a different clinical profile. However, cardiac complications do not differ between the 2 groups.*

Introduction

Kawasaki disease (KD) was first described in Japan in 1967 (1). This entity has now been reported worldwide, but reports from developing countries are still scarce (2). Although KD is seen in all age groups, the majority of patients are below 5 years of age (2-5). Patients older than 8 years are encountered only infrequently (6-9). Such patients are reported to have a different clinical presentation and may also have an increased risk of cardiac complications (8-11). However, there are no data on this aspect of KD from the developing world (12-16).

We have previously reported that approximately one-third of our patients with KD were above 5 years of age as compared to a figure of only 20% reported from the West (2). In this study, we have compared the clinical features of children with KD above and below 5 years of age. Ours would be the first study from the developing world, which has focused on age stratification of clinical features of the disease.

Patients and methods

Ninety-seven children with KD were identified during the period January 1994 to April 2006 from the Pediatric Allergy and Immunology Unit, Advanced Pediatric Center, Post Graduate Institute of Medical Education and Research, Chandigarh. Our institute serves as a tertiary care referral hospital for North India. Data were collected by review of the inpatient files and outpatient follow-up clinic records. KD was diagnosed according to standard criteria (detailed in one of our recent publications) (2). Patients were then divided into 2 groups – Group I: age > 5 years; Group II: age < 5 years. The usual laboratory investigations included complete blood count, platelet count, erythrocyte sedimentation rate, blood culture, liver and renal function tests, chest x-ray and an electrocardiogram. 2-D echocardiography was carried out by a cardiologist to look for coronary artery dilatation/aneurysms. Thallium scintigraphy of the heart was also carried out on follow-up in some of the cases.

Statistics

Statistical analysis was performed with SPSS for Windows, version 10.0. The descriptions of basic data, such as age and gender, are expressed as the mean ± standard deviation and percentage. The Student's t-test was used for comparison of continuous variable data. Pro-

Table I. Demography and clinical profile of children with KD.

	Group I (n = 38)	Group II (n = 59)
Age in years	8.12 ± 2.0 (Range 5.5-14.0)	2.83 ± 1.50 (Range 0.3-5.0)
Sex		
Male	27	39
Female	11	20
Duration of fever in days	11.2 ± 6.4	10.8 ± 6.0
Non-purulent conjunctivitis	25 (65.8	39 (66.1%)
Oral erythema	14 (36.8%)	25 (42.4%)
Strawberry tongue	20 (52.6%)	36 (61.0%)
Fissured lips	21 (55.3)	41 (69.5%)
Polymorphous rash	25 (65.8)	37 (62.7%)
Edema over dorsum of hands/feet*	10 (26.3%)	30 (50.8%)
Desquamation*		
At presentation	32 (84.2)	30 (50.8%)
At follow-up	5 (13.2%)	27 (45.8%)
Cervical lymphadenopathy	20 (52.6%)	33 (55.9%)
Arthralgia / arthritis*	8 (21.1%)	2 (3.4%)
Hepatomegaly	4 (10.5%)	10 (16.9%)

*p-value < 0.05.

portions were compared by chi-square test and Fisher's exact test wherever applicable.

Results

Of the 97 patients enrolled, Group I (>5 years) had 38 (39.2%) children while Group II (< 5 years) had 59 (60.8%). Twenty-five (25.8%) patients in Group I were between 5-8 years of age, while 13 (13.4%) were above 8. Table I shows the demographic and clinical features of children in the 2 groups. Mean age at presentation in Group I was 8.12 + 2.0 years while that in Group II was 2.83 ± 1.50 years.

Fever or history of fever was present in all cases, but 7 patients had presented to us in convalescent phase and had already become afebrile when they reached our institute. Forty-nine of the 97 children (50.5%) had fever of 10 or more days' duration (Table I). The time interval to make the diagnosis of KD was 11.2 ± 6.4 days in Group I, and 10.8 ± 6.0 days in Group II. Thus, children in Group II seemed to have presented slightly earlier than in Group I. This difference was even more prominent when children in Group II were compared with those in Group I aged 8 years and above, in whom the time interval was 13.9 ± 9.5 days. However, none of these differences were statistically significant.

Edema over hands and feet was seen in only 26.3% in Group I as compared to 50.8% of cases in Group II ($p < 0.05$). Desquamation at presentation was seen in majority of cases in Group I (84.3%) as compared to 50.8% in Group II. This difference was also statistically significant ($p = 0.001$). Arthralgia/arthritis was noticed more frequently in Group I as compared to Group II (21% *vs*. 3.4%; $p = 0.006$). Although oral erythema, strawberry tongue, fissured lips, cervical lymphadenopathy and hepatomegaly were seen with higher frequency in Group II, the differences were not statistically significant.

Among the laboratory investigations, hemoglobin level was lower in patients of Group II as compared to Group I (9.7 ± 1.7 *vs*. 11.7 ± 1.6 gm/dl; $p = 0.001$), but there seemed to be no difference in other parameters like total and differential white cell counts, platelet counts, erythrocyte sedimentation rates and serum albumin levels.

Treatment included use of intravenous immunoglobulin (2 gm/kg single dose or 0.4 gm/kg x 4 days) and aspirin (75-80 mg/kg/day during the acute phase and 3-5 mg/kg/day thereafter). Intravenous immunoglobulin was administered to 89 out of 97 children with KD in our cohort. Corticosteroids were not used in any of our patients. More details about treatment are given in one of our recent publications on the subject (2).

Table II.

	Group I	Group II
Abnormal electrocardiogram	2	1
Abnormal chest x-ray	2	3
Abnormal echocardiography at diagnosis	5	7
Thallium scintigraphy scan		
Normal	9	18
Abnormal	3	2
Coronary angiography		
Normal	4	2
Abnormal	0	0

Electrocardiogram was performed in all cases but was abnormal in 3 of them: 2 in Group I and 1 in Group II (Table II). One child in Group I had persistent extrasystoles, ectopics, and premature ventricular contractions (2).

Our unit policy is to perform the first echocardiography examination during the acute phase and repeat it subsequently on follow-up approximately 6 -12 weeks later. Thallium scintigraphy scans are done approximately 6-12 months after diagnosis. All children with KD at our centre are advised long-term follow-up (2-17).

Twelve (12.4%) cases were found to have cardiac involvement based on echocardiography or thallium scintigraphy scans of the heart. Of these, 7 were from Group II and 5 from Group I. Echocardiography at diagnosis was done in 94 cases and was abnormal in 12 (12.8%). Left coronary artery dilatation (CAD) was seen in 4 cases, proximal left anterior descending CAD in 3, right CAD in 4, aneurysm of left anterior descending artery in 1, mild mitral regurgitation in 2 and mitral valve prolapse with tricuspid regurgitation in 1 case. These abnormalities regressed in 6 cases on follow-up.

Thallium scintigraphy scan of the heart was done in 27 cases on follow-up. Of these, 5 cases showed myocardial perfusion defects. Coronary artery angio-

graphy done in 3 of these 5 cases was, however, normal. There were no differences in the occurrence of cardiac complications between Groups I and II.

Discussion

KD is reported to be a disease of young children with 75-80% of cases being below 5 years (1, 18, 19). A survey from Japan found that less than 1% of cases occurred in children aged 9 years or older (20). There are similar reports from the United States and United Kingdom (21, 22). We have, however, previously reported that a significantly larger number of children with KD at our center were above 5 years (2). In the present study mean age of children with KD was 4.83 ± 3.2 years. As many as 39.2% of our patients were aged above 5 years, with 13.4% of these being above 8 years. Both these figures are much higher than what has previously been reported from the West (21, 23). We do not have an objective explanation for this finding. It could represent skewed data because of possible underdiagnosis of KD in infants and young children in our country (12, 16, 23). There is a distinct impression amongst many clinicians that younger children with KD in India (as also in other developing countries) are probably being misdiagnosed as having viral exanthemata (especially measles) and other febrile illnesses (2, 12, 16, 23). Moreover, our data are hospital based and it would be imprudent to extrapolate these figures to an epidemiological frame.

Published literature suggests that the clinical and risk profile of KD in older children may be different from that seen in younger children (7-10). However, a systematic age stratified study has never been carried out. In this analysis, we have compared the clinical features of children with KD above and below 5 years. As KD is usually considered to be a condition seen in only infants and young children, some delays in establishing the diagnosis in the older child may be understandable. For instance, Momenah *et al*. had reported that the time interval to make a diagnosis of KD for children aged 9 years and older, was twice that for patients aged 1-8 years (9). In our study, however, these differences were not apparent.

Non-purulent conjunctivitis, mucosal changes in oropharynx, cervical lymphadenopathy and hepatomegaly were seen more frequently in Group II as compared to Group I but the differences were not statistically significant. Edema over hands and feet was significantly more frequent in children in Group II, while desquamation at presentation was significantly more common in children in. Group I. One explanation for the latter clinical finding could be the fact that desquamation can often be very subtle and may be entirely missed in the very young, if not carefully looked for. It has already been reported that peeling of extremities appears to occur earlier in India as compared to reports from the United States and Japan (23). Joint symptoms were also significantly more frequent in children above 5 years as compared to younger children. Sittiwangkul *et al*. (24) from Thailand have reported that diarrhea was more common in infants as compared to older children with KD. Diarrhea, however, was a singularly infrequent symptom in our cohort.

It has been reported that cardiac complications are seen more frequently in extremes of pediatric age groups (6-10, 25). One explanation for this could be the delay, which often occurs in arriving at a diagnosis at these ages. It is also believed that the disease itself may be atypical at these ages. We, however, did not find a statistically significant difference in the occurrence of cardiac complications amongst children in the two age groups. Having said this, it must be kept in mind that there were only a few cases with cardiac complications in our cohort and extrapolating the data further may not be statistically valid.

Conclusion

In Chandigarh, we found the occurrence of KD to be significantly higher in children above 5 years of age as compared to the Western literature. The clinical profile of older children with KD is somewhat different from that seen in infants and young children. However, there seemed to be no difference in the occurrence of cardiac complications amongst children in the 2 age groups (*i.e*., above and below 5 years of age).

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