Profile of Kawasaki Disease in Adolescents: Is It Different?

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ABSTRAK

Latar belakang: *terdapat peningkatan populasi dewasa muda dengan penyakit arteri koroner yang memiliki penyakit Kawasaki saat usia anak, dan dokter spesialis jantung/penyakit dalam harus siap untuk merawat mereka. Penyakit Kawasaki (PK) pada remaja dan dewasa masih jarang dan belum banyak dikenal, karena itu penting untuk mempelajari data pasien dengan mengetahui kriteria diagnostik dan pedoman pengobatan untuk kelompok usia ini. Penelitian ini bertujuan membandingkan profil klinis penyakit Kawasaki (PK) antara kelompok pasien berusia lebih dari 10 tahun (remaja) dan kurang dari 10 tahun (anak).* ***Metode:*** *analisis dilakukan pada 1150 kasus PK selama periode Januari 2003-Desember 2016. Profil klinis saat fase akut dibandingkan antara kelompok pasien berusia lebih dari 10 tahun dengan kurang dari 10 tahun.* ***Hasil:*** *dari 1150 kasus PK ditemukan 17 kasus PK remaja (1,5%), dengan presentasi klinis yang lebih sering dijumpai adalah PK inkomplit (59%), lebih tinggi dibandingkan pada kelompok kurang dari 10 tahun (29%). Beberapa tanda klinis lebih sering dijumpai pada anak dibandingkan remaja, seperti konjungtivitis (85% pada <10 tahun; 65% pada >10 tahun), perubahan mukosa (94% vs. 77%), ruam (86% vs. 59%), dan perubahan tangan dan kaki (68% vs 41%). Sedangkan tanda klinis lain lebih sering dijumpai pada remaja seperti limfadenopati servikal (82% vs 39%) maupun dilatasi koroner (47% vs 29%). Pada pemeriksaan laboratorium (hemoglobin, leukosit, laju endap darah, dan C reactive protein) tidak didapatkan perbedaan bermakna antara 2 kelompok.* ***Kesimpulan:*** *penyakit Kawasaki pada remaja memiliki profil klinis yang berbeda dengan anak-anak. Mayoritas pasien remaja menunjukkan PK inkomplit. Beberapa gejala klinis seperti konjungtivitis, kelainan mukosa, ruam, dan perubahan tangan/kaki lebih sering dijumpai pada PK kurang dari 10 tahun, sedangkan limfadenopati servikal dan dilatasi koroner lebih sering ditemukan pada PK remaja. Rasio lelaki : perempuan jauh lebih tinggi pada PK remaja.*

Kata kunci: *penyakit Kawasaki, remaja.*

ABSTRACT

Background: *there is clearly growing population of young adults with potentially important coronary artery disease after Kawasaki disease (KD) during childhood, and cardiologist must be prepared to take care for them. As Kawasaki disease in adolescent and adult is rare and under-recognized, it is important to study data on patient presentations which may permit development of diagnostic criteria and treatment guidelines for this age group.This study aimed to compare the clinical profile of KD between adolescents (>10 years of age) and children ≤10 years.* ***Methods:*** *This is a cross sectional study. A total of 1150 KD cases (age 1-192 months) during the period of January 2003-December 2016 were analyzed. The clinical profile of subjects aged >10 years (adolescents) and ≤10 years (children) at acute phase of KD were compared.* ***Results:*** *we found 17 cases of KD in adolescents among 1150 total cases (1.5%). Incomplete KD was more often seen in adolescents compared to children ≤ 10 years of age (59% vs. 29%). Some clinical features were more frequently seen in children than in adolescents, e.g. conjunctivitis (85% in ≤ 10 years of age vs. 65% in > 10 years), mucosal changes*

(94% vs. 77%), rash (86% vs. 59%), and hand/foot changes (68% vs. 41%). While other clinical features were more often seen in adolescents, e.g., cervical lymphadenopathy (82% vs. 39%) and coronary dilatation (47% vs. 29%). Laboratory results (hemoglobin, leukocytes, erythrocyte sedimentation rate and C-reactive protein) did not differ much between the two groups. ***Conclusion:*** *Kawasaki disease in adolescents has some different clinical profile from that of younger age. Majority of adolescent patients have incomplete presentation. Some clinical features such as conjunctivitis, mucosal changes, rash, and hand/foot changes are more often seen in children ≤ 10 years compared to in adolescents, while cervical lymphadenopathy and coronary dilatation are more frequently seen in adolescents. The ratio of male to female is much higher in adolescents.*

Keywords: *Kawasaki disease, adolescents.*

INTRODUCTION

Kawasaki disease (KD) is an acute systemic vasculitis syndrome of unknown etiology that mainly affects infants and young children. KD was first reported by Tomisaku Kawasaki in 1967 in Japan.[1] KD typically affects young children, mostly below 5 years of age with the highest incidence between 1-2 years of age.[2] In Indonesia, it is estimated that over 2000 KD cases had been treated and presumably the majority of cases are still undiagnosed as the estimate incidence is approximately 5000 new cases per year.[2] Coronary artery aneurysm develops in 15 - 25% of untreated KD cases and may lead to myocardial infarction, sudden death, or ischemic heart disease.[3]

KD is extremely uncommon in patients 9 years of age and older.[4,5] The recent epidemiologic survey in Japan found that only 0.95% cases occurred in children 10 years of age and older.[6] The clinical criteria that establish the diagnosis of KD are the same in all age groups.[7] Clinical findings at acute stage include fever persisting at least for 5 days, changes in the extremities (erythema of palms, soles, edema of hands, feet), polymorphous exanthema, bilateral conjunctival injection without exudate, changes in lips and oral cavity (erythema, strawberry tongue), unilateral cervical lymphadenopathy measuring >1.5 cm. Diagnosis of KD relies on the clinical presentation; laboratory tests are not specific, although anemia, leukocytosis, increased erythrocyte sedimentation rate, and increased C-reactive protein are frequently found on laboratory examination at acute stage. The diagnosis of KD may be missed in older children with fever of unknown origin.[8]

There is clearly a growing population of young adults with potentially important coronary artery disease after KD during childhood, and cardiologist must be prepared to take care for them.[9] Antecedent KD should be considered in the evaluation of all cases of sudden, unexpected death in young adults.[10] A history of Kawasaki-like illness in childhood should be sought for adult patients presenting with coronary artery aneurysms in the absence of generalized atherosclerosis disease.[11]

As Kawasaki disease in adolescent and adult is rare and under-recognized, it is important to study data on patient presentations which may permit development of diagnostic criteria and treatment guidelines for this age group. We conducted this study to compare the clinical profile of KD between adolescents (≥10 years) and children (<10 years).

METHODS

This is a cross-sectional study using a database of subjects with Kawasaki disease between January 2003 and December 2016 obtained from five hospitals in Jakarta and its surroundings (Cipto Mangunkusumo Hospital, Jakarta; Omni Hospital Alam Sutera, Tangsel; Harapan Kita Hospital, Jakarta; Siloam Hospital, Tangerang; Premier Bintaro Hospital, Tangsel). The choice of these hospitals was simply based on the author's (NA) access. Variables studied were age, gender, clinical presentations (fever, conjunctivitis, mucosal changes, cervical lymphadenopathy, rash, hand/foot changes), laboratory (hemoglobin, leukocyte, ESR, CRP) and echocardiogram (coronary artery dilatation). Diagnosis of KD was based on AHA (American Heart Association) consensus

criteria either for complete or incomplete cases.[7] The classic diagnosis of acute KD was based on fever persisting at least for 5 days, changes in the extremities (erythema of palms, soles, edema of hands, feet or peeling of fingers and toes at subacute stage), polymorphous exanthema, bilateral conjunctival injection without exudates, changes in lips and oral cavity (erythema, strawberry tongue), unilateral cervical lymphadenopathy measuring 1.5 cm or more. The presence of fever and ≥4 principal features allowed for the diagnosis of KD (complete KD). Patient with fever ≥5 days and <4 principal features was diagnosed as incomplete KD when coronary artery abnormality was detected by echocardiogram. For assessment of coronary artery dilatation, we used a Z score based on body surface area for right coronary artery (RCA), left main coronary artery (LMCA), and left anterior descending LAD.[7] All echocardiographic examinations were done by the author (NA) at the time of diagnosis, at 2 weeks and then 6-8 weeks. Initial coronary dilatations are usually transient ones, but could be regarded as sequelae of KD if they persist beyond 30 days.[12] Therefore, we determined the presence of coronary dilatation sequelae using the echocardiogram at >30 days.

Nearly all (98%) patients received intravenous immunoglobulin (2g/kg BW) with high-dose (80-100 mg/kg BW) aspirin on admission according to the AHA consensus. Eligibility criteria were all patients regardless of age who met the AHA criteria for complete or incomplete Kawasaki disease with complete data of laboratory tests (hemoglobin, leukocytes, ESR and CRP) and echocardiogram.

Laboratory tests were done on admission. Anemia was considered as hemoglobin level below 10 g/dL. Leukocytosis was considered leukocyte count of over 15.000/μL, ESR increase as ≥40 mm /hour and increase of CRP as ≥30 mg/L.[7] This study has been approved by the Ethics Committee Faculty of Medicine Universitas Indonesia with a reference number 420A/PT02. FK/ETIK/2012.

RESULTS

We found 1150 subjects with KD (age 1-192 months) during the period of January 2003 to December 2016. Among them there were 17 patients with age > 10 years (1.5%). While complete eligible data were obtained from 559 subjects, 542 from ≤ 10 years and 17 from > 10 years (adolescents).

In the adolescent group there were only 3 females out of 17 subjects, with male to female ratio of nearly 4:1 while the ratio in the ≤ 10 years group was around 1.5:1.

There was a difference between the two age groups in terms of the presence of mucosal changes (red lips and/or strawberry tongue) and rash which were less common in the adolescent group. On the other hand, cervical lymphadenopathy, incomplete KD and coronary artery dilatation were more commonly seen in the adolescent group.

DISCUSSION

Kawasaki disease is the most common cause of acquired heart disease in children in the developed countries. The majority of KD patients are below 5 years of age;[2] there are few case reports of KD in adolescents and adults.

Table 1. Characteristics of Kawasaki disease subjects

Characteristics of subjects	Age	
	≤ 10 years (n=542)	> 10 years (n=17)
Age (mo), Mean (SD)	27 (16)	135 (14)
Median (min-max)	24 (1-120)	134 (121-192)
Gender, n (%)		
- Male	330 (61)	14 (82)
- Female	212 (39)	3 (18)
Clinical findings, n (%)		
- Fever	542 (100)	17 (100)
- Conjunctivitis	462 (85)	11 (65)
- Mucosal changes	509 (94)	13 (77)
- Cervical lymphadenopathy	214 (39)	14 (82)
- Rash	469 (86)	10 (59)
- Hand/foot changes	367 (68)	7 (41)
Complete (%)	386 (71)	7 (41)
Laboratory results, n (%)		
- Anemia	103 (19)	4 (24)
- Leukocytosis	299 (55)	7 (41)
- ESR increase	406 (75)	15 (88)
- CRP increase	412 (76)	14 (82)
Echocardiograpahy result, n (%)		
Coronary artery dilatation	159 (29)	8 (47)

The diagnostic criteria for KD were developed for children and have not been validated in adolescents or adults. Fortunately, KD is uncommon in patients over 9 years of age.[4,5]

We reported 17 cases in adolescents (10-16 years of age) out of 1150 total KD subjects (1.5%). This percentage is higher than that of survey in Japan which was 0.95% for subjects over 10 years of age, 6 but is likely lower than the findings of Momenah et al. which was 7.5% in children ≥9 years of age out of 133 total KD cases.[8] We do not know the reason for the differences.

In the adolescents, there were just 3 females out of 17 subjects with the ratio of male to female was nearly 4:1. While in the ≤ 10 years subjects the ratio was 1.5:1. It seems that the male to female ratio is higher in adolescents compared to the younger ones. This result is in accordance with the study of Stockheim et al. which reported the ratio of male vs female KD ≥8 years was 2.5:1.[13] Momenah et al. reported the ratio of male vs female in ≥ 9 years of age 1:1.8 We could not explain the reason for this, whether it is by chance or any other reason.

Incomplete cases were more frequently seen in adolescents (59% vs. 29%). The presence of coronary artery defects on echocardiogram can aid the diagnosis in those lacking the typical clinical features. As many cases of KD in adolescents have incomplete presentation, they might not be diagnosed until relatively late in their illness. This may lead to development of coronary aneurysms and cause long-term morbidity that may impair the quality of life, and although rare, mortality. It would be beneficial if there are specific diagnostic criteria in adolescents to avoid under-diagnosis. However, as the number of KD in adolescent is quite small, making specific diagnostic criteria for this age group would not be easy. In this study 5 out of 17 adolescent cases (30%) were diagnosed after day 10 of illness (delayed diagnosis). While in the ≤ 10 years group 103 out of 542 subjects (19%) were diagnosed after day 10. It seems more difficult to diagnose KD in the adolescents as the majority of cases (60%) were incomplete type. So far there was no mortality until convalescence period in both groups.

Our study showed that there were some differences in the clinical profile between the adolescents and the younger group. Some clinical features were more frequently seen in children ≤ 10 years than in adolescents such as conjunctivitis (85% in ≤ 10 years of age vs. 65% in > 10 years), mucosal changes (94% vs. 77%), rash (86% vs. 59%), and hand/foot changes (68% vs. 41%). Stockheim et al.[13] reported that fever, conjunctivitis and exanthem were observed with an equal rate in adults and children. Cervical lymphadenopathy was significantly more often seen in adolescent group (82% vs. 39%) as also reported by Seve et al. in adults.[14] Likewise, coronary dilatation was more often seen in adolescents than in younger group. This is in line with the study of Momenah et al.[8] but different from other studies which found that coronary aneurysms were seen more frequently in children.[13,14] Laboratory results (hemoglobin, leukocytes, ESR and CRP level) did not differ much between the two groups. It is rather hard to compare our results of the adolescent KD with other studies as there are very few studies and with very limited subjects.

The diagnosis of KD should be considered more often in adolescents and adults when patients present with fever, skin rash, and lymphadenopathy. As the main complication associated with KD is the development of coronary aneurysms which may cause long-term morbidity, awareness of the disease is essential to any physician either handling pediatric or adolescent patients. Once KD is diagnosed, immunoglobulin should be administered immediately to prevent the risk of coronary artery aneurysms.

CONCLUSION

Kawasaki disease can occur in adolescents with some different clinical profile than that of the classical findings of the disease in younger children. The ratio of male to female is much higher in adolescents and nearly 60% of them have incomplete presentations. Some clinical features are more often seen in children ≤10 years compared to adolescents such as conjunctivitis, mucosal changes, rash, and hand / foot changes. While cervical lymphadenopathy and coronary

artery dilatation were more frequently seen in adolescents. Physicians must be alert of the occurrence of KD in older children and adolescents or even adults to prevent coronary complications.

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