ASO F. SALIH, MBCHB, DCH, FIBMS, MSC (*ped.* Cardiology) * ADNAN M HASAN, MBCHB, CAB ** JAMAL A. RASHID, MBCHB, DCH ***

Submitted 11/3/2017; accepted 31/12/2017

ABSTRACT

Background: Kawasaki disease is the most common cause of acquired heart disease in developed countries. Kawasaki disease it has been increasingly reported from developing countries. The aim of this study was to assess the clinical and epidemiological characteristics of Kawasaki disease in children of Sulaimaniyah city.

Subject and Methods: In this study all children diagnosed as Kawasaki disease included during the period between January 2010 and December 2014. The hospital records / pediatric cardiology clinic data were reviewed, and data were abstracted onto standardized forms.

Results: During the study period from January 2010 to December 2014, 36 patients were diagnosed as Kawasaki disease. Their mean age at diagnosis was 2.8 ± 2 years (range 6 months -9years). Most of the patients (30 patients 83.3%) were under age of 5 years, and the median age was 2.1 year. Male to female ratio was 1.76. Most of cases occurred during winter and spring season. Out of 36 patients, 16 (44.4%) patients had coronary disease, and 4 cases of coronary cases were classified as A4 and A5 class according to Japanese Classification of Severity of Coronary Artery Lesions. There was non-significant difference between coronary and non-coronary group regarding hemoglobin level, platelet count, ESR and WBC count.

Conclusions: Kawasaki disease is not uncommon in Sulaymaniyah, the clinical and epidemiological pattern is not different from other parts of the world. We need to increase the index of suspicion in order not to miss Kawasaki disease cases and avoid its serious cardiac complications.

			Duhok Med J	2017; 11 (2): 3	7-45.
Keywords:	Kawasaki disease,	Echocardiography,	Coronary disease		

A Kawasaki disease (KD) is a multisystem, generalized medium and small vessel vasculitis of unknown etiology, which is the most common cause of acquired heart disease among children living in developed countries ^{1, 2}. It is more common in males than in females, with a male-to-female ratio of $1.5:1^3$. The distribution of KD by age in childhood is characteristic; the disease occurs most frequently in young children, 50 percent are younger than 2 years of age, 80 percent are younger than 5 years of age, and cases seldom occur in those older than 12 years of age⁴⁻⁶.

*Assistant Professor, Department of Pediatrics, School of Medicine, Faculty of Medical Sciences, University of Sulaimani, Kurdistan Region, Iraq.

^{**}Professor, Department of Pediatrics, School of Medicine, Faculty of Medical ***Sciences, University of Sulaimani, Kurdistan Region, Iraq.

 ^{***}Assist Professor, Department of Pediatrics, School of Medicine, Faculty of Medical Sciences, University of Sulaimani, Kurdistan Region, Iraq.

Correspondence author to: Aso Faeq Salih, <u>asofaek@hotmail.com</u>, Mobil +9647701474701

The principal symptoms and signs include: 1. Fever persisting 5 days or more (inclusive of those cases in whom the fever has subsided before the 5th day in response to therapy).

2. Bilateral conjunctival congestion without exudates.

3. Changes of lips and oral cavity: Redding of lips, strawberry tongue, and diffuse injection of oral and pharyngeal mucosa.

- 4. Polymorphous exanthema.
- 5. Changes of peripheral extremities:
 - a. (Acute phase): Redding of palms and soles, indurative edema
 - b. (Convalescent phase): Membranous desquamation from fingertips.
 - c. Acute non-purulent cervical lymphadenopathy.

At least five items of 1 to 6 should be satisfied for diagnosis of KD. However, patients with four items of the principal symptoms can be diagnosed as KD when coronary aneurysm or dilatation is recognized by two-dimensional (2D) echocardiography or coronary angiography⁷.

with Treatment intravenous immunoglobulin and aspirin reduces the risk of coronary artery abnormalities when administered within 10 days of fever onset. Coronary artery aneurysms, the most serious consequence of KD, seen in 20% to 25% of untreated patients, and longconsequences include coronary term stenosis. early atherosclerosis. and myocardial infarction^{8, 9}.

In the current report, the epidemiology and clinical features of 36 patients with KD, seen over a 5-year period at Sulaymaniyah Pediatric Teaching Hospital, Kurdistan Region/Iraq is presented.

PATIENTS AND METHODS

A retrospective descriptive study was done Sulaymaniyah Pediatric Teaching at Hospital that serve more than 1.5 million population in the Sulaymaniyah Governorate; Kurdistan Region/ Iraq. The study included all children diagnosed as KD in the period between January 2010 and December 2014. The hospital records and/or pediatric cardiology clinic charts were reviewed, and data were abstracted onto standardized forms. The data included age at onset, sex, the presence and duration of fever, skin and oral manifestations, LN enlargement, laboratory test (lowest hemoglobin, highest platelet count, highest pretreatment ESR. positive CRP). echocardiography features, treatment, outcomes, and follow-up. All cases were diagnosed according to the study group's diagnostic guidelines for Kawasaki disease base on the criteria of the Japan Kawasaki Disease Research Committee⁷. Patients were included in the study if they had at least five of the following¹⁰:

- 1. Fever persisting more than 5 days
- 2. Changes of extremities
- 3. Polymorphous exanthema
- 4. Bilateral conjunctival congestion
- 5. Changes of lips and oral cavity
- 6. Acute non purulent cervical lymphadenopathy

Echocardiography done with Accuson Cypress Siemens 3MH and 7 MH probes,through subcostal,apical, and parasternal views. Size of coronary arteries plotted on normal value chart against body surface area for each patient accordingly (coronary charts and percentiles)¹⁰. The coronary lesions were classified according to the Japan Kawasaki Disease Research Committee⁷:

A-1 Patients with no dilatation of coronary arteries, A-2 Patients with slight and transient dilatation of coronary arteries, which subsides within30 days after the onset of KD, A-3 Patients who have small coronary aneurysms at 30 days after the onset of KD, A-4 Patients who have medium coronary aneurysms at 30 days after the onset of KD, and A-5 Patients who have giant coronary aneurysms at 30 days after the onset of KD.

Echocardiographically all were evaluate every 2 weeks apart for the first 8 weeks of the illness. Patients with no evidence of coronary involvement were evaluated again after 6 months while patients with coronary involvement were evaluated 2-4 weeks every until the echocardiography finding become normal. Diagnostic coronary angio planned to perform in 6-12 months later in giant coronary disease cases.

Statistical analysis done using SPSS software program version 19, applying *t*-test to compare means and p-value < 0.05 was considered statistically significant.

RESULTS

A total of 36 patients with Kawasaki disease were evaluated. The mean age at diagnosis was 2.8 ± 2 years, ranging from 6 months to 9 years. Most of the patients were under age of 5 years (30 patients 83.3%), the median age was 2.1 years. Male to female ratio was 1.76, and most of cases occurred during winter and spring seasons, (Table 1).

Gender	No (%)
Male	23(64
Female	13(36)
Seasonal distribution	
Winter	11 (31)
Spring	15 (42)
Summer	8 (22)
Autumn	2 (5)
Age distribution	
< 1yr	5 (14)
1-2yr	7 (19)
2-3yr	10 (28)
3-4yr	5 (14)
4-5yr	3 (8)
>5 yr	6 (17)

Table 1: Demographic and epidemiologic

characteristics of the patients

Presenting signs and symptoms are shown in **Table 2.** Among the 36 patients; 16(44.4%) had coronary affection, 10 were males, (Figure 1).

Table 2: Signs and symptoms frequencies inKawasaki disease cases				
Clinical feature	Number of cases (%)			
Fever	36 (21)			
Conjunctival changes	32 (19)			
Oral cavity and lip	28 (17)			
changes				
Changes in extremities	30 (18)			
Exanthema	24 (14)			
Cervical	18 (11)			
lymphadenopathy				



Figure 1: Sex distribution among coronary affected Kawasaki disease cases.

The investigations done are shown in **Table3**. Among the coronary disease,

cases only one patient present with right coronary aneurysm, the rest were left coronary artery affection cases.

Table 3: Duration of Fever and Investigations in coronary and non-coronary Kawasaki disease					
Variable	Non coronary Group	Coronary Group	P value		
Number of cases	20	16			
Duration of fever before starting treatment	8.4+/-2.6	6.6+/-2.35	0.004		
Hemoglobin	10.5+/-1.36	11.1+/-1.3	0.325		
Platelet	487+/- 193	524+/- 96	0.527		
ESR	75+/- 21	81+/-29	0.497		
WBC count	14457+/-6127	17225+/-7566	0.240		

The severity of coronary artery affection shown in **table 4**

Table 4: Classification of Severity of Cor. ArteryLesions Based on Echocardiographic Findings				
Coronary disease class	No. of patients (%)			
A 1	2 (13)			
A 2	6 (36)			
A 3	4 (25)			
A 4	2 (13)			
A 5	2 (13)			

All patients received IVIG single dose 2gm/kg and Acetylsalicylic acid antiinflammatory dose. No recurrence noted in our cases but in one case the fever did not subside after the recommended IVIG dose in which case the coronary artery disease 2^{nd} diagnosed on the was echocardiographic examination on 18th day of illness although 1st echo was normal on 8th day of illness. Another patient presented with giant aneurysm (8mm) after 14 days of fever in which the intravenous immunoglobulin treatment was not received within the 10 days of illness, on subsequent echo. the measurement increased to 11mm at left main stem. The third patient developed giant aneurysm from the 2nd weeks and persisted as the same measure till 1 year follow up and

then regressed to 7mm on the end of the 2nd year. Subsequently we did coronary catheterization which supported the same diagnosis without other aneurysmal or stenotic lesions.

DISCUSSION

Most of KD cases (30, 83.4%) were below 5 years of age, this finding was similar to studies done in western Saudi Arabia (83.3%), ¹¹ in Korea $(71\%)^{12}$, in Iran $(77\%)^{13}$, and in Taiwan $(80\%)^{14}$. In addition the average age at diagnosis in our study (2.9 years) was nearly similar to other studies in Korea and Iran (2.8 years in both)^{12,13}.

Male to female ratio was (1.76:1), which is similar to Saudi Arabia study (1.7:1), ¹¹ and Iranian study $(1.5:1)^{15}$.

In the current study there was seasonal variation, in which we have two cases recorded during autumn and the peak of our cases was reported in winter, spring and early summer, similar to other studies done in Saudi Arabia¹⁶, Iran¹⁷ and United States of America¹⁸. However, in other studies KD had a peak incidence during other seasons¹⁹.

Duhok Medical Journal

The high rate of white blood cells, platelet count, ESR and positive C reactive protein was similar to other reports^{17, 19-22}.

There was no significant difference between the presentations of patients with coronary involvement and patients with no coronary involvement except for the duration of fever before commencing treatment. Similar results were found in studies in Iran¹⁷, and China²³.

In one of our patients, the fever continue in spite of using aspirin and IVIG without explanation, and later she was diagnosed as rheumatoid arthritis.

Delay in diagnosis and treatment, which occur more frequently in older children, are associated with an increased risk of coronary artery aneurysms as we have one case with giant aneurysm diagnosed after 14th day of illness²⁴.

If a child clearly meets criteria for Kawasaki disease, the decision to treat with intravenous immunoglobulin is not difficult, especially if surrogate markers support the diagnosis, if the coronary artery abnormalities were detected by echocardiogeraphy, continue the aspirin with a dose of 3-5 mg/kg PO qd long term²⁸.

Patients with severe coronary affectioncategories (A4 and A5), like the four patients we have, are at high risk for coronary sequels in the future and if coronary artery abnormalities fail to long-term regress bv time. pharmacological therapy and diagnostic follow-up are implicated²⁹.

In conclusion, KD is not uncommon in Sulaymaniyah, it seems that the clinical feature is not different everywhere in the world. We need from our pediatrician to be aware of it and not to miss Kawasaki disease cases to avoid its serious cardiac complication.

REFERENCES

- Barron KS .Kawasaki disease in children.Curr Opin Rheum. 1998, 10(1):29-37.
- 2- Kawasaki T. Acute febrile mucocutaneous lymph node syndrome with accompanying specific peeling of the fingers and the toes. Allergy 1967:178-222.
- 3- Burns JC, Glode MP. Kawasaki syndrome. Lancet. 2004: 533-544.
- 4- Holman R.C., Curns A.T., Belay E.D., Steiner CA, and Schonberger LB. Kawasaki syndrome:Hospitalizations in the United States,1997 and 2000. Pediatrics. 2003; 112:495-501.
- 5- Stockheim J. A., Innocentini N., and Shulman S. T. Kawasaki disease inolder children and adolescents. J. Pediatr. 2000; 137:250-252.
- 6- Yanagawa H., Nakamura Y., Yashiro M., Uehara R, Oki I, Kayaba K. Incidence of Kawasaki disease in Japan: The nationwide surveys of 1999-2002. Pediatr. Int. 2006; 48:356-361.
- 7- Japanese Circulation Society Joint Working for Group. Guideline diagnosis and management of cardiovascular sequelae in Kawasaki disease (JCS 2013)-digest version. Circ J. 2014: 7 8:2521 2562 www.jcirc.or.jp/guideline/pdf/JCS2013 _ogawas_d.pdf.
- 8- Melish ME, Marchette MJ, Kaplan JC, Kihara S, Ching D, Ho DD. Absence of significant RNA-dependent DNA polymerase activity in lymphocytes

from patients with Kawasaki syndrome. Nature. 1989; 337:288-290.

- 9- Hirata S, Nakamura Y, Matusmoto K, Yanagawa H. Long-term consequences of Kawasaki disease among first-year junior high school students. Arch Pediatr Adolesc Med. 2002; 156 (1):77-80.
- 10- Lai W, Mertens LL, Cohen MS, GevaT. Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult. eds 2009 Wiley-Blackwell Appendix 1: Normal Values for Cardiovascular Structures. http://onlinelibrary.wiley.com/doi/10.1 002/9781444306309.app1/pdfaccessed on August 18th 2011.
- Al-Harbi K. M.Kawasaki disease in western Saudi Arabia. Saudi Med J. 2010; 31(11):1217-1220.
- 12- Kim SH, Kim KH, Kim DS. Clinical Characteristics of Kawasaki Disease According toAge at Diagnosis. Indian Pediatrics. 2009; 46(17):585-590.
- 13- Ahmad S., Farah S. Kawasaki disease in Iran A report of 85 cases Iranianjournal ofpediatric society. 2007; 1(2):9-12.
- Mei-Chen T., Li-Chieh W., Hsin-Hui Y., Jyh-Hong L., Yao-Hsu Y., Bor-Luen C. Kawasaki disease and Henoch Schonlein purpura - 10 years' experience of childhood vasculitis at a university hospital in Taiwan. Journal of Microbiology, Immunology and Infection. 2012; 45:22-30.
- 15- Mohammad M., Abdolrazagh K. Kawasaki disease in Iranian children. Iran J Pediatr. 2007; 17 (3):241-246.

- 16- A.Lardhi . A Kawasaki disease: A university hospital experience. Saudi journal of medicine and medical science. 2013; 1(1): 35-39.
- 17- Shamsizadeh A, Kajbaf T, Razavi M, and Chreaghian B. Clinical and epidemiological characteristics. jundishapur J Microbiol. 2014; 7(8): e11014.
- 18- Chang RK. Hospitalizations for Kawasaki disease among children in the United States, 1988-1997. Pediatrics. 2002; 109(6):e87.
- 19- Huang WC, Huang LM, Chang IS, Chang LY, Chiang BL, Chen PJ, Wu MH, Lue HC, Lee CY. Epidemiologic features of Kawasaki disease in Taiwan, 2003- 2006. Pediatrics. 2009; 123(3):e401–5.
- 20- Park YW, Han JW Park IS, Kim CH, Cha SH, Ma JS Lee JS, Kwon TC Lee SB et al . Kawasaki disease in Korea, 2003-2005. Pediatr Infect Dis J. 2007; 26 (9):821–3.
- 21- Özdemir H, Çiftçi
 E, Tapısız A, İnce E, Tutar E, Atalay S
 et al. Clinical and epidemiological
 characteristics of children with Kawasaki disease in Turkey. J Trop Pediatr.
 2010; 56(4):260–2.
- 22- Singh S, Bansal A, Gupta A, Kumar RM, Mittal BR. Kawasaki disease: a decade of experience from North India. Int Heart J. 2008; 46(4):679–689.
- 23- Du ZD, Zhang T, Liang L, Meng X, Li T, Kawasaki T, et al. Epidemiologic picture of Kawasaki disease in Beijing from 1995 through 1999. Pediatr Infect Dis J. 2002; 21(2):103-7.

Duhok Medical Journal

- 24- Hiromi M, Masahiro I, Mayumi Y, Ritei U, and Yosikazu N. Late intravenous immunoglobulintreatment in patients with Kawasaki disease. Pediatrics. 2012; 129(2); e291– e297.
- 25- Kushner HI, Bastian JF, Turner CH, Burns JC. Rethinking the boundaries of Kawasaki disease: toward a revised case definition. Perspect. Biology Med. 2003; 46(2):216-33.
- 26- Sundel RP, Burns JC, Baker A, Beiser AS, Newburger JW. Gamma globulin re-treatment inKawasaki disease. J Pediatr.1993; 123(4):657-9.
- 27- Brogan PA, Bose A, Burgner D, Shingadia D, Tulloh R, Michie C, Klein N, Booy R, Levin M, Dillon MJ.

Kawasaki disease: an evidence based approach to diagnosis, treatment, and proposals for future research. Arch Dis Child. 2002; 86(4):286-90.

- 28- Wright DA, Newburger JW, Baker A, Sundel RP. Treatment of immune globulin resistant Kawasaki disease with pulsed doses of corticoid steroids. J Pediatr. 1996; 128(1):146-9.
- 29- Nathan J. and Davinder S.G. Kawasaki Disease: A Clinician's Update. International journal of pediatrics. 2013; article ID645391, 7 pages,<u>http://dx.doi.org/10.1155/2013/6</u>45391

ثوختة

نەخۆشى كاواساكى لە سلى مانىدا / كوردستانى عىراق

ثیشة کی: نه خوشی کاواساکی باوتریین نه خوشی وه رگیراوی دله له ولاته پی شکهوتو و مکاندا . همرو ها نه خوشی کاواساکی له ولاته گهشهکردو و مکاندا پارهی سهندو وه. ئامانج لهم تویزین هوه ی هو هیه که ناسه ره و مکان و نی شانهکانی ی هم ناخوشی یه دی اری بکریت له مندالدا له شاری سلی مانی به متای به ی ی ی هو ان هی کی شهی دلی ان همیه.

ریکین ظةکولینیَ: ئەم تویزینەوە ئەنجام دراوە لەسەر نەخۆشى كاواساكى لە ماوەى ٢٠١٤ -٢٠١٤ لە بەشى دلّى مندالان لە نەخۆشخانەى مندالانى فیركارى شارى سلیمانى ھەموو حالمتەكان بەپى ى ناسەرمومكانى لیزنەى نەخوشى كاواساكى ژاپۆنى.

نَةَنجام: ژمارەى ٣٦ نەخۆش لەر مارەيەدا بە كاراساكى تەراو ديارى كرارە كەنارەندى تەمەنيان ٢+/_٨,٢سالە (٦ مانگ – ٩ ساڵ) ، وە زۆربەى نەخۆشەكان (٣٠ نەخۆش ٨٣,٣%) لە ژير تەمەنى ٥ سالەرەن، ريّژەى كور بۆ كچ ١,٧٦، وە زۆربەى حالەتەكان لە وەرزى زستان و بەھار رووى داوە. لە كۆى گشتى ١٦ نەخۆش (٤,٤ %)نەخۆشى بۆريەكانى ماسولكەى دليان گەررە بور بور، كە ٤ نەخۆش لەرانە لە جۆرى (A4,A5) يۆلينى نەخوشى كاراساكى دلى ژاپۆنى دانراون. ھەروەھا جيارازى نىيە لە ريّژەى خەستى خۆين و خرۆكە سېييەكان و خەپلەكانى خۆين لە ھەردور گروپەكە.

دةرىئةنجام: له دەرەنجامى ليكۆلينەوەكە ئەوە ساغ بووەوەكە نەخوشى كاواساكى ناسراوە لە سليمانيدا و جياوازى نى يە لە ولاتانى تر . ھەروەھا پيريستمان بەرچاوروونيەكردنى پزيشكانى خۆمان ھەيە لەكوردستان بۆ ناسينەوەو ديارى كردنى ئەم نەخوشى يە لە سەرەتاكانييدا .

الخلاصة

مرض الكواساكي في السليمانية / كردستان العراق

الخلفية والأهداف: مرض الكواساكي من الامراض الشائعة في الدول المتقدمة و في وقتنا الحاضر المرض اصبح شائعا في الدول النامية . الغرض من الدراسة متابعة مرضى الكاواساكي في السليمانية و متابعةالاعراض المتلازمة له.

طرق البحث: الدراسة اجريت على الاطفال اللذين يشكون من المرض الكاواساكى من فترة ٢٠١٠ الى ٢٠١٤ فى قسم قلب الاطفال / مستشفى الاطفال التعليمى فى السليمانية ، المشخصة حسب الاعراض المتبعة من مجلس الكاواساكى اليابانية .

النتائج: شخصت ٣٦ حالة خلال مدة الدراسة كحالة كاواساكى كاملة ، معدل العمر كان ٢+/- ٢,٦ سنة (٦ اشهر -٩ سنة) . اكثرية المرضى (٨٣,٣) كانوا دون عمر ٥ سنوات . نسبة الذكور الى الاناث ١,٧٦، و اكثرية الحالات شخصت فى الشتاء و الربيع . شخصت ١٦ حالة (٤٤,٤%) كتوسع شرايين التاجية للقلب و اربعة حالات صنفت بتصنيف (A4,A5) حسب الاعراض المتبعة من مجلس الكاواساكى اليابانية للقلب.واستنتجت ايضا انه ليس هناك اية فى نسبة الدم ، كريات البيضاءو صفائح الدم بين المجموعتين.

الإستنتاجات: استنتجت من الدراسة ان فى وقت الحاضر مرض الكاواساكى منتشر فى السليمانية و ليس هناك اختلاف فى انتشار و اعراض المرض مقارنة بمناطق العالم. و استنتجت ايضا اننا نحتاج الى توعية الاطباء الاطفال حول اعراض و مضاعفات مرض الكاواساكى لغرض تشخيصه فى المراحل الاولى.