Journal of Clinical and Basic Research (JCBR): 2018: Vol. 2: N.4.P: 54-5 Original Article

Prevalence of Kawasaki Disease in Children Admitted to Taleghani Medical Center in Gorgan, Iran

Fatemeh Cheraghali[1], Naghimeh Hajimoradloo[1], Gholamreza Roshandel[2], Mehrnaz Meftah[1], Somayeh Azadfar*[1]

1. Infectious Diseases Research Centre, Golestan University of Medical Sciences, Gorgan, Iran
2. Golestan Research Center of Gastroenterology and Hepatology (GRCGH), Golestan University of Medical Sciences, Gorgan, Iran

ABSTRACT

Background and objectives: Kawasaki disease is an acute systemic vasculitis of unknown etiology that affects infants and children under 5 years of age. The aim of this study was to investigate the epidemiology of this disease in the Golestan Province, Iran.

Methods: This cross-sectional study was performed on all patients (51 individuals) who had been admitted to the Taleghani Hospital in Gorgan (Iran) from September 2005 to October 2012. Characteristics of the patients were extracted from patients' records. Data were analyzed in SPSS (version 16.0) using chi-square test and independent t-test.

Results: Of 51 patients, 30 (58.8%) were male and 39 were under 2 years of age (76.47%). The annual incidence rate of Kawasaki disease in the Golestan Province was 37.39 per 100,000 persons. The most common clinical manifestations were skin rash (68.6%), conjunctivitis (51%) and changes of lip and oropharyngeal mucosa (60.8%). In terms of laboratory findings, erythrocyte sedimentation rate of greater than 35, positive C-reactive protein and anemia were found in 74.5%, 88.2% and 68.6% of the patients, respectively. In terms of cardiac involvement, echocardiography had been performed for 42 cases, of which 38 were normal and 5 were abnormal. Moreover, abdominal sonography had been performed on 37 cases, and one case had splenomegaly.

Conclusion: In the Golestan Province, Kawasaki disease is more prevalent among children under the age of 2 years. The most common clinical symptoms of this disease are skin rashes and changes in lip and oropharyngeal mucosa. Furthermore, the rate of cardiac complications is significantly low at this center.

KEYWORDS: Kawasaki, Gorgan, Epidemiology

Received: 2018/11/14 **Revised:2018/12/01** **Published:2019/01/11**

***Correspondence:** Somayeh Azadfar

Address: Infectious Diseases Research Centre, Golestan University of Medical Sciences, Gorgan, Iran

Telephone: +98-9113758412, +98-1732341280 **Email:** a.atrin@yahoo.com

[DOI: 10.29252/jcbr.2.4.54]

INTRODUCTION

Kawasaki disease (KD) is an important and dangerous disease with serious but preventable complications (1,2). In fact, this disease is an acute systemic vasculitis of unknown etiology that affects infants and children under 5 years of age, in a way that about 50% of affected children are less than 2 years old and 80% are less than 5 years old (3, 4). The disease has a winter/spring seasonal predominance in most countries but may also occur in other seasons (5). The incidence of KD is higher among Asians compared to other racial groups. KD is currently the most common cause of acquired heart disease in children in many countries (6, 7). Infectious and noninfectious factors, such as superantigens are debated as probable causes of the disease (8). Diagnosis is based on clinical findings and ruling out other diseases with similar manifestations (1). Diagnostic criteria for the disease include fever for at least 5 days, polymorphic exanthem, mucosal erythema, desquamation of the skin of fingers and toes, bilateral conjunctivitis and non-suppurative cervical lymphadenopathy (9). According to the American Heart Association, patients with fever for more than 5 days and an abnormal echocardiogram, even with less than four clinical symptoms, are considered classical cases of KD (10). Laboratory findings include leukocytosis, normocytic anemia, thrombocytosis (sometimes up to 1 million platelets) and high C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Pyuria and elevated liver enzymes may also be present in some cases (11). Seizure is a rarely seen in the patients and indicates cerebrovascular involvement (12). The most dangerous complication of the disease is coronary artery disease, which occurs in 20-25% of patients in the absence of proper treatment, and may lead to sudden death (13). Patients with acute KD should be treated with intravenous immunoglobulin (IVIG) and aspirin. If performed within the first 10 days, this treatment can reduce the risk of developing coronary artery disease to 2-4% (14). Given the importance of KD in children, its unknown etiology and serious complications, this study was conducted to investigate epidemiology of KD in the Golestan Province (Iran) between 2005 and 2012.

MATERIAL AND METHODS

In this cross-sectional study, we investigated all patients diagnosed with KD who had been referred to the Taleghani Medical Center in Gorgan (Iran) from September 2005 to October 2012. Demographic characteristics, clinical features, laboratory findings and cardiac complications were retrieved from the patients' records. Inclusion criteria consisted fever for more than five days along with four of the following clinical manifestations: bilateral conjunctivitis, polymorphous red rashes over extremities, especially on the trunk, changes of the oral cavity and lips (redness and dryness of the lips, strawberry tongue and pharyngeal erythema), changes in the extremities (erythema of the hands and feet and desquamation of the skin of the fingers and toes in later stages of the disease), cervical lymphadenopathy (with diameter of ≥ 1.5 cm), ESR value of ≥35, leukocytosis (white blood cell count >15,000/mm^3) and anemia (hemoglobin <10.5 g/dl).

Statistical analysis was carried out in SPSS 16.0 using the chi-square test and independent t-test. P-values less than 0.05 were considered statistically significant.

RESULTS

Overall, we found 51 children with KD. Of these patients, 37 (72.5%) were living in urban areas and 39 (76.47%) were under 2 years of age. The annual incidence rate of KD in the Golestan Province was 37.39 per 100,000 persons. The incidence of KD in children younger than 2 years (55.52 per 100,000 persons) was significantly higher than in children older than 2 years (24.77 per 100,000 persons) (P=0.002). The incidence of KD in children who were living in urban areas (58.74 per 100,000 persons) was significantly higher than in those who were

[DOI: 10.29252/jcbr.2.4.54]

living in rural areas (20.69 per 100,000 persons) (P=0.0001).

Frequency distribution of patients based on seasons was as follows: 16 cases (31.4%) in spring, 13 cases (25.4%) in summer, 11 cases (21.6%) in autumn and 11 cases (21.6%) in winter. All patients had received IVIG. The mean (SE) duration from the onset of symptoms until admission and from hospitalization until IVIG administration was 8.6 (0.7) days and 46.5 (9.96) hours, respectively. The mean (SE) duration of fever in the patients was 7.2 (0.75) days. The mean (SE) duration from IVIG administration until cessation of fever was 2.1 (0.38) days. The most frequent clinical manifestations in patients with KD were skin rash (68.6%), bilateral conjunctivitis (51%) and changes in the lips and oropharyngeal mucosa (60.8%) (Table 1).

Table 1. Frequency of clinical manifestations of KD in patients

	Gender		Place of residence		Age	
	Female	Male	Urban	Rural	> 2 years	< 2 years
Erythema and desquamation of the perineal region	7 (33.3 %)	6 (20 %)	10(27 %)	3(21.4 %)	9(28.1 %)	4 (21.1 %)
Conjunctivitis	10 (47.6 %)	16 (53.3 %)	18(48.6 %)	8(57.1 %)	15(49.9 %)	11(56.9 %)
Loss of consciousness	2 (9.5 %)	1 (3.3 %)	3(8.1 %)	0	2(6.3 %)	1(5.3 %)
Skin rash	12 (57.1%)	23 (76.7 %)	27(73 %)	8(57.1 %)	22(8/68 %)	13(68.4 %)
Cough	3 (13.3 %)	9(30 %)	8(21.6 %)	4(28.6 %)	10(31.3)	2(10.5 %)
Desquamation and edema of extremities	6(28.6 %)	14(46.7 %)	14(37.8 %)	6(42.9 %)	11(34.4 %)	9(47.4 %)
Pharyngitis	16(76.2 %)	15(50 %)	22(59.5 %)	9(64.3 %)	17(53.1 %)	14(73.3 %)
Restlessness	4(19 %)	7(23.3 %)	9(24.3 %)	2(14.3 %)	8(25 %)	3(15.8 %)
Seizure	3(14.3 %)	1(3.3 %)	4(10.8 %)	0	3(9.4 %)	1(5.3 %)
Hepatosplenomegaly	0	1(3.3 %)	1(2.7 %)	0	0	1(5.3 %)
Unilateral lymphadenopathy	7(33.3 %)	10(33.3 %)	16(43.2 %)	1(7.1 %)	6(18.8 %)	11(57.9 %)
Lips and oral mucosal changes	16(76.2 %)	15(50 %)	22(59.5 %)	9(64.3 %)	17(53.1 %)	14(73.3 %)
Rhinorrhea	6(28.6 %)	7(23.3 %)	8(21.6 %)	5(35.7 %)	8(25 %)	5(26.3 %)
Otitis	0	2(6.7 %)	2(5.4 %)	0	1(3.1 %)	1(15.3 %)
Diarrhea	2(9.5 %)	5(16.7 %)	7 (18.9 %)	0	6(18.8 %)	1(5.3 %)
Gallbladder hydrops	0	2(6.3 %)	2(5.4 %)	0	2(6.3 %)	0
Fever for more than 4 days	16(76.2 %)	20(66.7 %)	24(64.9 %)	12(85.7 %)	25(78.1 %)	11(75.9 %)
Fever for less than 4 days	5(23.8 %)	10(33.3 %)	13(35.1 %)	2(14.3 %)	7(21.9 %)	8(42.1 %)

Laboratory findings of the patients with KD are presented in Table 2.

Table 2. Laboratory findings of patients with KD

Finding	Number of positives / number of tested patients (%)
leukocytosis (white blood cell count >15,000/mm3)	19/51 (37.3 %)
CRP (+)	45/48 (88.2 %)
ESR ≥35	38/51 (74.5 %)
Anemia (hemoglobin <10.5 g/dl)	35/50 (68.6 %)
AST elevation	23/40 (45.1 %)
ALT elevation	11/41 (11.6 %)

[DOI: 10.29252/jcbr.2.4.54]

Pyuria	11/51 (21.6 %)
Platelets > 450,000 per μL	17/51 (33.8 %)

In terms of cardiac involvement, echocardiogram had been performed for 42 cases, of which 38 were normal and 5 were abnormal. Electrocardiogram had been performed for 30 cases and reports were normal. Abdominal sonography was performed on 37 cases, and one case had splenomegaly.

DISCUSSION

Similar to previous studies, KD was more common in males. Three patients were younger than 6 months of age. The incidence of KD was significantly higher in children younger than 2 years. Given the fact that the clinical diagnosis should be made by ruling out other disease, particularly infectious diseases and vasculitis, suspicion, early diagnosis and timely treatment can prevent the development of complications (15). The annual incidence of KD in the Golestan Province was 37.31 per 100,000 persons. Although the prevalence of this disease is higher in Asian countries, but the annual incidence rates vary widely between these countries. For example, in Taiwan, the annual incidence rate of KD was 69 per 100,000 children under 5 years of age between 2003 and 2006 (16). The highest annual incidence rate has been reported from Japan (218 per 100,000 children under 5 years of age) and Korea (113 per 100,000 children under 5 years of age) (17). In a study by Zhang et al., the rate of KD was 1.39 to 11.07 (5.26 ± 3.97) per 100,000 children under 5 years of age (18). In this study, the disease was more prevalent in spring and summer, which is similar to the results of studies in China and Hong Kong (18). The prevalence of KD in Taiwan, Japan and Korea was also highest in summer. The peak incidence rate for KD occurs in spring and winter in Australia, the United States and Europe and in spring and summer in Korea and China (3, 19).

According to the results, fever for at least 4 days was observed more frequently in females and those living in rural areas. Moreover, fever for more than 4 days was present in 78% of patients under the age of 2 years. The mean duration from IVIG administration until fever cessation was 1.2 days, which is longer than the duration reported by Zhang et al. (18).

The most common clinical manifestations among patients with KD were skin rash (68.6%), conjunctivitis (51%) and changes of lip and oropharyngeal mucosa (60.8%), all of which were less frequent compared to other studies (18, 20, 21). Lymphadenopathy is another diagnostic feature of KD, which was present in 33.3% of the cases. A study in Oman reported that the frequency of lymphadenopathy was 27% among patients with KD (24).

In terms of laboratory findings, ESR of greater than 35, positive CRP and anemia were found in 74.5%, 88.2% and 68.6% of the patients, respectively. These results are similar to the findings of a study by Sadeghi et al. (26). However, the frequency of anemia in our study was lower than that reported by other studies, which could be due to genetic factors and difference in stage of disease and study area (12).

Cardiac involvement was detected in 5 cases (11.9%), which is similar to results of Mahmoudzadeh et al. (12%) (23) but lower than the rates observed in some studies (9, 12, 26).

CONCLUSION

Our results indicate that KD is more prevalent in children under 2 years of age. The most common clinical symptoms of KD are skin rashes and changes in the lip and oral mucosa. The number of cardiac complications in this study is significantly less than other studies, which could indicate the early diagnosis of the disease at this center. Until development

[DOI: 10.29252/jcbr.2.4.54]

of a suitable diagnostic test for KD, IVIG administration within the 10 first days of fever is recommended for all children with KD in order to reduce the risk of developing complications.

ACKNOWLEDGMENTS

This article has been derived from results of a research project approved by the Department of Research and Technology of Golestan University of Medical Sciences (project number: 910830170). We would like to thank the personnel of Taleghani Medical Center in Gorgan for their kind cooperation.

DECLARATIONS

Funding

This study was financially supported by the Golestan University of Medical Sciences, Iran.

Ethics approvals and consent to participate

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Shulman ST. Unclassified infectious diseases. In: Feigin RD, Cherry JD. Text book of pediatric infectious disease. Philadelphia: W.B. Saunders Co 2004; 1.

2. Kordidarian R, Kazemi A, Nikyar A, et al. Assessing Kawasaki disease in children at Alzahra hospital (1995-1999). The Journal of Qazvin Univ. of Med. Sci. 2008; 11(4):42-47. [In Persian]

3. Burgner D, Harnden A. Kawasaki disease: What is the epidemiology telling us about the etiology?. Int J Infect Dis .2005; 9(4): 185-194. [DOI:10.1016/j.ijid.2005.03.002]

4. Rezai M, Siadati S, Khotaei G, et al . Isolation of Kawasaki disease-associated with bacterial sequence from peripheral blood leukocytes. J Mazandaran Univ Med Sci. 2008; 18 (64) :22-28. [In Persian]

5. Mosaiebi Z, Movahedian A, Heidarzadeh M, et al. Evaluation of clinical and paraclinical findings of Kawazaki patients among children admitted in Kashan Shahid Beheshti hospital during 1998-2008. Journal of Kashan University of Medical Sciences (FEYZ). 2010; 14 (3): 249-255. [In Persian]

6. Golestan M, Bahjati M, Akhavan- karbasi S, et al. Review of Kawasaki Patients in Yazd. JSSU. 2009; 16 (4) :21-25. [In Persian]

7. Burns JC, Glodé MP. Kawasaki syndrome. Lancet 2004;364(9433):533-44. [DOI:10.1016/S0140-6736(04)16814-1]

8. Rahbari-Manesh A, Salamati P, Ghaforian S, et al. Relationship between ESR, CRP, platelet count and coronary artery disease in Kawasaki disease. Iranian Journal of Pediatrics 2005; 15(2):139-144.[In Persian]

9. Ayazi P, Mohammadzadeh G, Arian far F. Clinical symptoms and laboratory findings of Kawasaki disease in children. The Journal of Qazvin University of Medical Sciences. 2007; 11 (1) :28-33. [In Persian]

10. Jeong EJ, Park HJ. Clinical Analysis of AtypicaKawasaki Disease: Comparison of Kawasaki Disease Between Typical and Atypical Types. J KoreanPediatr Soc. 2001; 44(12): 1448-53.

11. Singh GD, Wong M, Issacs D. Diagnosis,treatment and outcome of Kawasaki disease in an Australian tertiary setting: A review of three years experience. J Pediatr Child Health. Cardiol 1997;6: 181-5.

12. Nakamura Y, Yashiro M, Uehara R, et al. Use of laboratory data to identify risk factors of giant coronary aneurysms due to Kawasaki disease. Pediatr Int; 2004 ; 46(1): 33-8. [DOI:10.1111/j.1442-200X.2004.01840.x]

13. Yoshikawa H, Abe T. Febrile convulsion during the acute phase of Kawasaki disease. Pediatr Int; 2004. 46(1): 31-2. [DOI:10.1111/j.1442-200X.2004.01850.x]

[DOI: 10.29252/jcbr.2.4.54]

14. De Zorzi A, Colan SD, Gauvreau K et al. Coronary artery dimensions may be misclassified as normal in Kawaski disease. Journal of Pediatrics.1998; 133(2):254-58. [DOI:10.1016/S0022-3476(98)70229-X]

15. Kasiri K, Khoshdel A, Mokhtariyan K. A case report: An atypical Kawasaki syndrome following aseptic meningitis in a 9-month old infant . J Shahrekord Univ Med Sci. 2008; 10 (3) :90-94. [In Persian]

16. Park Y, Kim C, Han J, Lee J, et al. Epidemiological features of Kawasaki disease in Korea, 2006–2008. Pediatrics International. 2011; 53(1): 36–39. [DOI:10.1111/j.1442-200X.2010.03178.x]

17. Yim D, Burgner D, Cheung M. Echocardiography in Kawasaki Disease.(2012) Echocardiography - In Specific Diseases. 2012. In Tech. [DOI:10.5772/32175]

18. Zhang X, Sun J, Zhang Z, Liu Sh. Epidemiologic Survey of Kawasaki Disease in Jilin from 1999 Through 2008. Pediatr Cardiol. 2012; 33(2):272–279. [DOI:10.1007/s00246-011-0121-7]

19. Harnden A, Takahashi M, Burgner, D. Kawasaki disease. BMJ. 2009; 5(338): 1514. [DOI:10.1136/bmj.b1514]

20. Durongpisitkul K, Sangtawesin Ch, Khongphatthanayopthin A, et al. Epidemiologic Study of Kawasaki Disease and Cases Resistant to IVIG Therapy in Thailand. Asian pacific journal of allergy and immunology. 2006; 24(1): 27-32.

21. YM N, RYT S,LY S, NC F, et al. Kawasaki disease in Hong Kong,1994 to 2000. Hong Kong Med J. 2005; 11(5): 331-335.

22. Gheini S, Hemati M, Arghavanifard P. Characteristics of Kawasaki patients in Kermanshah Hospitals during 1997-2000 .Behbood. 2004; 8(3): 51-62.

23. Mahmoudzadeh H, Nikibakhsh AA, Gheibi SS, et al. A survey on kawasaki disease in imam khomeini hospital, Urmia. Urmia medical journal. 2008; 19 (3) :236-241. [In Persian]

24. Bahatnagar SK, Paul G, Subramanina R, et al. Kawazaki disease in Oman-a clinical study. J Trop Pediatr 2003; 49:361-6. [DOI:10.1093/tropej/49.6.361]

25. Mansouri M, Ghotbi N, Naderi B. Reports of children with kawasaki disease hospitalized in pediatric. Behbood 2009;13(1): 84-91. [In Persian]

26. Sadeghi E., Amin R., Ajamee GH. Kawasaki syndrome: the Iranian experience, Eastern Mediterranean Health J, 2001, 7(1-2): 16-25.

.

[DOI: 10.29252/jcbr.2.4.54]