

## Epidemiologic Study of Kawasaki Disease in Korea, 1997-1999: Comparison with Previous Studies During 1991-1996

We performed a retrospective epidemiologic survey on Kawasaki disease (KD) from 1997 to 1999 in Korea. We sent a questionnaire to 111 training hospitals, and summarized the data from 50 hospitals that responded. Data from a total of 3,862 cases were collected, which showed no difference in annual incidence and a seasonal predilection for summer. The male-to-female ratio was 1.51:1, and the mean age was 29.7 months. The prevalence of sibling cases was 0.26%, and the rate of recurrent cases was 2.3%. The proportion of patients with KD among total hospitalized pediatric patients was 1.19% in average, showing a significant difference according to the regions. Coronary arterial (CA) abnormalities were detected by echocardiography in 19.8% of cases (737/3,723) including dilatations in 601 cases (16.1%) and aneurysms in 191 cases (5.1%). Data from total 8,251 cases in the 1990s including the cases in the present study, in Korea showed a mean age of patients 28.9 months, male-to-female ratio 1.6:1, seasonal predilection for summer, prevalence of sibling cases 0.24%, rate of recurrent cases 2.3%, incidence of CA abnormalities 21.0%, and incidence of CA aneurysms 5.2%, with statistically significant decreasing trends in the male-to-female ratio and the rate of CA abnormalities.

**Key Words :** Coronary Aneurysm; Epidemiology; Mucocutaneous Lymph Node Syndrome; Prevalence

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## INTRODUCTION

Kawasaki disease (KD) is a systemic vasculitis which predominantly affects children under the age of 4 yr. It was first described by Kawasaki in 1967 (1). Afterward the disease has been reported worldwide, especially with a high prevalence in Asian countries including Japan and Korea.

It has been difficult to obtain reliable data on the nationwide incidence of KD in Korea. The first series of epidemiologic surveys were performed by Lee in the 1980s (2, 3). The nationwide multicenter study during 1991-1993 was started by Yun and his colleagues of Korean Pediatric Cardiology Society (4). After that, similar studies (5), including this one, have been continued on a 3-yr basis to determine the epidemiology and rate of cardiac sequelae of KD in Korea.

## MATERIALS AND METHODS

### Study design

For the epidemiologic study of KD in Korea as a task of

Korean Pediatric Cardiology, data were collected for KD patients diagnosed from January 1997 to December 1999 by a questionnaire. A questionnaire was sent to 111 training hospitals and the data from 50 hospitals were analyzed.

The items in the questionnaire included age, sex, age at onset, sibling case, recurrent case, geographical incidence and number of KD patients among total hospitalized pediatric patients, findings of echocardiography, findings of coronary angiography, myocardial infarction case, and death case.

### Diagnosis of Kawasaki disease

Diagnosis of KD was based on clinical features, which included fever for at least 5 days and four of the following five signs: bilateral conjunctival injections; oral mucosal changes, such as injected pharynx, dry cracked lips, or strawberry tongue; changes of hands and feet, such as redness and swelling in the acute phase, and periungual desquamation in the sub-acute phase; rash, primarily on the trunk, that may be maculopapular, erythema multiforme, or scarlatiniform; cervical lymph node greater than 1.5 cm in diameter (6).

Also included were the patients with dilatation or aneurysm

of the coronary artery (CA) on echocardiography, even if the aforementioned clinical criteria were not satisfied.

**Diagnostic criteria of Coronary Artery abnormalities**

Normal ranges for CA size defined according to the body weight or age were used. In 3 groups of children, that is, those weighing less than 12.5 kg, 12.5-27.5 kg, and more than 27.5 kg, normal ranges of internal lumen diameter (ILD) were 2.5 mm or less, 2.5-3.0 mm, and 3.0-5.0 mm, respectively (7). In children younger than 5 yr, ILD of 3.0 mm or less is considered normal, and in children aged 5 yr or older, ILD of 4.0 mm or less is considered normal (8). If the ILD of CA segment is enlarged less than 1.5 times of the upper normal limit, it is defined as dilatation, and if the ILD is enlarged 1.5 times or more, it is defined as aneurysm.

**Statistical analysis**

To evaluate the trends of data in the 1990s, we analyzed data of three studies by using chi-square for trend (Mantel-Haenszel chi-square) in the SAS System for Windows, Release 6.12. A *p*-value of <0.05 was considered to indicate a significant trend for decrease or increase.

**RESULTS**

**Yearly and monthly distribution**

The total number of patients with KD during the study period was 3,862. The subtotals of patients in 1997, 1998, and 1999 were 1,143, 1,419, and 1,300, respectively, which showed no difference in annual incidence. Monthly distribution of cases showed a high incidence from May to August (Fig. 1).

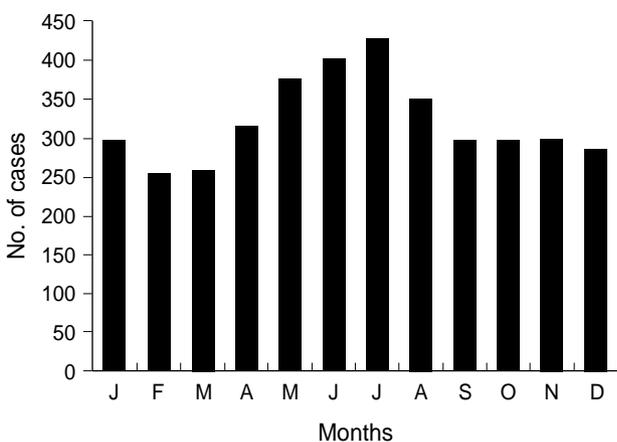


Fig. 1. Monthly distribution of cases with Kawasaki disease.

**Age and sex**

The mean age at diagnosis was  $29.7 \pm 16.2$  months, and the median age was 25 months with an age range from 1 month to 17.8 yr (Fig. 2). The disease occurred most commonly in children aged 4 yr or younger with an incidence of 83.4% (3,221/3,862). The male-to-female ratio was 1.51:1 showing a predilection for males (2,321/1,541).

**Sibling cases and recurrent cases**

The prevalence of sibling cases was 0.26% (10/3,862). The total number of recurrent cases was 90 (2.3%), including 85 cases with a single event recurrence, 4 cases with 2 events recurrence, and 1 case with 3 events recurrence.

**Geographical incidence and number of Kawasaki disease patients among total hospitalized pediatric patients**

The proportion of patients with KD among total hospitalized pediatric patients except patients in nursery was 1.19% in average (Table 1), and showed a significant difference according to regions with the highest incidence in Chungbuk area and the lowest incidence in Kwangju and Chonnam areas (Table 2).

Table 1. Yearly proportion of patients with Kawasaki disease among total hospitalized pediatric patients

Year	No. of patients		%
	KD	Total	
1997	1,143	116,639	0.98
1998	1,419	103,069	1.38
1999	1,300	104,359	1.25
Total	3,862	324,067	1.19

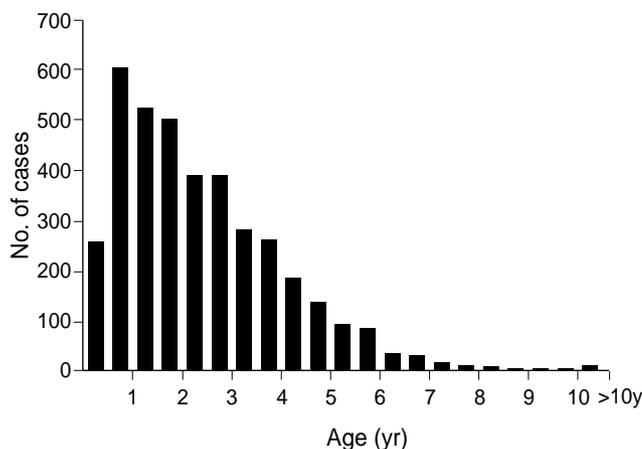


Fig. 2. Distribution of age at onset.

**Table 2.** Geographical incidence and number of patients with Kawasaki disease among total hospitalized pediatric patients

Region	No. of patients		%	Hospitals (No.)
	KD	Total		
Seoul	922	97,149	0.95	18
Incheon, Kyonggi	535	34,083	1.57	5
Taejon, Chungnam	104	7,736	1.34	1
Chungbuk	208	9,323	2.23	2
Chonbuk	120	9,842	1.22	1
Kwangju, Chonnam	319	34,155	0.93	5
Taegu, Kyongbuk	849	73,589	1.15	8
Busan, Kyongnam	627	46,599	1.35	8
Kangwon	178	11,593	1.54	2
Total	3,862	324,067	1.19	50

### Findings of echocardiography

Echocardiography was done in 97.4% of patients (3,723/3,862), and CA abnormalities were found in 19.8% of cases (737/3,723) including dilatations in 601 cases (16.1%) and aneurysms in 191 cases (5.1%). Categorization of these 737 cases in detail showed 546 cases (14.7%) with pure dilatation, 136 cases (3.6%) with aneurysm only, and 55 cases (1.5%) with dilatation and aneurysm. Morphologic classification of total aneurysms by echocardiography revealed 68 cases with saccular aneurysm, 61 cases with fusiform, and 62 cases without description.

### Findings of coronary angiography

Coronary angiography was performed in 0.7% (27/3,862) of patients, and abnormal findings of CA were found in 81.5% (22/27) of cases. Total abnormal lesions included 16 dilatations, 15 aneurysms, 3 stenoses, and 1 occlusion.

### Myocardial infarction and death

There was no case with myocardial infarction. Death was reported in one case, however, the cause of the death seemed to be unrelated to the KD.

### Comparison with previous studies during 1991-1996

These epidemiologic studies have been done every 3 yr from 1991. Adding 1,709 cases of the 1st study (4) during 1991-1993 and 2,680 cases of the 2nd study (5) during 1994-1996, to the 3,862 cases of the present study, the cumulative number of patients was 8,251.

Data of the total 8,251 cases in the 1990s in Korea showed a mean age of patients of 28.9 months, the male-to-female ratio of 1.6:1, a seasonal predilection for summer, the prevalence of sibling cases 0.24%, the rate of recurrence 2.3%, the incidence of CA abnormalities 21.0%, and the incidence of CA aneurysms 5.2% (Table 3). Among these data, the male-to-

**Table 3.** Comparison of three epidemiologic studies

Item	91-93	94-96	97-99	Mean	p-value
Response rate (%)	31/50 (62)	58/107 (54)	50/111 (45)	139/268 (52)	
No. of patients	1,709	2,680	3,862	2,750	
Mean age (mos)	27.0	28.9	29.7	28.9	
Sex ratio (M/F)	1.7	1.6	1.5	1.6	<0.05
SP <sup>1</sup> (mo)	5, 6, 7, 8	1, 5, 6, 7	5, 6, 7, 8		
Sibling cases (%)	0.18	0.26	0.26	0.24	ns*
Recurrent cases (%)	2.9	1.7	2.3	2.3	ns*
CA <sup>2</sup> abnormality (%)	25.2	20.1	19.8	21.0	<0.001
CA <sup>2</sup> aneurysm (%)	4.9	5.4	5.1	5.2	ns*

\*ns, not significant ( $p$ -value >0.05); <sup>1</sup>SP, seasonal predilection; <sup>2</sup>CA, coronary artery.

female ratio and the rate of CA abnormalities showed statistically significant decreasing trends. However, the rate of sibling cases, rate of recurrent cases, and incidence of CA aneurysms showed no significant increasing or decreasing trend.

## DISCUSSION

KD, also known as mucocutaneous lymph node syndrome, is an acute febrile, multisystemic vasculitis of unknown etiology, which almost exclusively affects young children. The peak incidence of KD usually falls between 1 and 2 yr of age, compared with the peak incidence between 6 months and 1 yr of age in the present study, and 80% of cases occur in children aged 4 yr or younger (9), in accordance with the incidence of 83.4% in the present study. Race-specific incidence rates demonstrate that the children of Japanese and Korean ancestry are of greatest risk. In Japan, the yearly incidence per 100,000 children under 5 yr of age was around 90 in both 1991 and 1992 (10), which were more than 10 times higher than the rates reported in Western countries. Boys are affected more often than girls with ratio of 1.3-1.5 to 1 (6, 9, 11), which is similar to the ratio of 1.51 in the present study. The rate in the present study showed a statistically significant decreasing trend, meaning of which is not yet clear. The recurrence rate of KD is 1-3%, and the prevalence of KD among siblings of patients was reported to be about 2% (6, 11).

KD is known to be a major cause of acquired heart disease in children nowadays, because of its prolonged and significant cardiac involvement, especially the development of coronary aneurysms that might lead to a myocardial infarction and sudden death. Thus all patients with KD should have an echocardiographic evaluation. Echocardiography exhibits mild diffuse dilation of CA during the acute phase in 30-50% of patients. If not treated, or treated by only aspirin, CA aneurysms develop in 20-25% of patients. However, the incidence of coronary aneurysms has been lowered to 3-5% with intravenous gamma-globulin treatment (6, 9, 11). The statistically significant decreasing trend of CA abnormalities in the present study is

thought to be related to the increasing usage of intravenous gamma-globulin in the 1990s.

A mortality rate of about 1-2% was reported in patients with KD in the mid-1970s. But the mortality rate in Japan has declined to approximately 0.04%, with improved recognition and appropriate treatment of the disease (6, 9, 11).

There are some limitations in this kind of survey, such as a retrospective nature of the investigation and low response rate to the questionnaire. However, we believe that the data from this study reflect the nationwide trend and change in the incidence of KD in Korea.

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