



Original Article

Epidemiological features of Kawasaki disease in Korea, 2006–2008

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Abstract ***Background:** The aim of this study was to estimate the incidence and describe the epidemiological characteristics of Kawasaki disease among children in Korea.*

***Methods:** Questionnaires for surveying the epidemiology of Kawasaki disease were distributed to a total of 101 hospitals that conduct pediatric residency programs. Then, we retrospectively obtained the data, which covered a three-year period (2006–2008) and analyzed them.*

***Results:** During the three-year study period, a total of 9039 cases of Kawasaki disease were reported from 84 hospitals (response rate, 83.2%), comprising 5375 boys and 3664 girls (male : female ratio, 1.47:1). The outbreak rate per 100 000 children <5 years old was 108.7 in 2006, 118.3 in 2007 and 112.5 in 2008 (average rate, 113.1). The seasonal distribution showed a slightly higher incidence rate in winter and summer. The patients' mean age of onset was 32.6 months, while the proportions of sibling cases and recurrent cases were 0.17% and 2.2%, respectively. Coronary arterial abnormalities were detected during follow up by echocardiogram in 17.5% of all cases including dilatations (16.4%) and aneurysms (2.1%).*

***Conclusions:** The average annual incidence rate of Kawasaki disease in Korea has been continuously increasing, and reached 113.1/100 000 children <5 years old, which is the second highest rate in the world.*

Key words coronary aneurysm, epidemiology, Kawasaki disease, incidence.

Kawasaki disease (KD) is an acute febrile illness that predominantly affects children younger than 5 years of age. After its first description in 1967 by Dr Tomisaku Kawasaki,¹ KD has become the leading cause of acquired heart disease among children in developed nations. Although the incidence rates of KD vary among countries, it is much higher in children in Asian countries.^{2,3} Since the 1990s, a nationwide epidemiological survey has been conducted every 3 years in Korea. The epidemiological characteristics and changes in KD's incidence rate have been revealed through these surveys.^{4–6} This particular survey, which was conducted in 2009 and targeted KD patients who were admitted between 2006 and 2008, will display the recent epidemiological features of KD in Korea.

Methods

This epidemiological study of KD in Korea was carried out under the purview of the Korean Pediatric Heart Association. The data

were collected retrospectively using a questionnaire for KD patients newly diagnosed within a period of 3 years from January 2006 to December 2008 in all hospitals that have a pediatric residency program. A total of 101 general hospitals in Korea were approved by the Korean Hospital Association as pediatric resident training hospitals, where most of the KD patients were admitted. Hence, both mail- and internet-based questionnaires were sent in January 2009 to these hospitals. The survey format included a diagnostic criteria of KD itself and coronary artery (CA) abnormalities. Other items in the questionnaire were identical to those reported previously.^{4–6} Normal ranges for CA size were defined according to age or bodyweight. In children younger than 5 years old, an internal lumen diameter (ILD) of 3.0 mm or less is considered normal and in children aged 5 years or older, an ILD of 4.0 mm or less is considered normal. In three groups of children, that is, those weighing less than 12.5 kg, 12.5 kg–27.5 kg and more than 27.5 kg, the normal ranges of their ILD were 2.5 mm or less, 2.5–3.0 mm and 3.0–5.0 mm, respectively. If an ILD of a CA segment is enlarged to less than 1.5 times the normal upper limit, it is defined as a dilatation and if the ILD is enlarged to 1.5 times the normal upper limit or greater, it is defined as an aneurysm. Echocardiograms were usually repeated 2–4 weeks and 2 months after the first echocardiogram at admission, and thereafter as needed.

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Based on the Korean population data, the annual incidence of KD was calculated by dividing the number of newly diagnosed KD patients who were younger than 5 years old by the total number of children the same age, as reported for each year, between 2006 and 2008. This value was expressed as the number of patients per 100 000 children.

In order to evaluate the data trends during 2006–2008, we analyzed the data of each year using the χ^2 -test for trends (Mantel–Haenszel χ^2). Geographic differences in the incidence rate were compared using χ^2 -tests. Statistical analyses were carried out by using the SAS System for Windows (release 6.12) and a P -value <0.05 was considered statistically significant.

The Ethical Board of Inje University Seoul Paik Hospital approved this survey.

Results

Response rate

To increase the response rate, the inquiries were sent twice to non-responding hospitals. We yielded a response rate of 83.2% (84/101), similar to that of the previous survey (83.3%).

Annual incidence rate and monthly distribution

A total of 9039 KD patients were reported: 2990 in 2006, 3127 in 2007 and 2922 in 2008. KD occurred predominantly among children <5 years of age (87.0%). The average annual incidences in children <5 years of age and those 5–9 years of age were 113.1 and 17.4 per 100 000, respectively. The yearly incidence rate per 100 000 children <5 years old was 108.7 in 2006, 118.3 in 2007, and 112.5 in 2008. The overall rate was 113.1. There was no statistically significant increasing trend according to the year of incidence ($P > 0.05$).

The average annual incidence per 100 000 children decreased as age increased: 167.2 in children aged 0–1 years, 143.6 in children aged 1–2 years, 114.7 for ages 2–3 years, 92.2 for ages 3–4 years, and 61.6 for ages 4–5 years. The average age- and gender-specific incidence for the study period was highest in the latter half of the first year of life for the boys and girls (boys, 254.8;

girls, 169.0, total, 213.4), and gradually decreased with age. They were also higher in boys than in girls, regardless of age (Fig. 1).

Monthly distribution of KD is shown in Figure 2. During the 3-year study period, although unusual outbreaks or prominent seasonal variation were not present, somewhat higher occurrences of KD were generally seen in the summer (June and July) and winter (December and January) months. The highest incidence of KD was observed in December with 877 children (9.7%), followed by June (9.6%), July (9.5%) and January (9.4%).

Age and gender

The mean age (\pm SD) at diagnosis was 32.6 ± 25.1 months with a range of 1 month to 18.9 years and the median age was 27 months. Almost 90% of the KD cases occurred in children who were <5 years old, and the peak age of onset was 7–12 months of age with a proportion of 15.7% (1419/9039).

The male : female ratio was 1.47:1, which shows a predilection for boys (5375/3664).

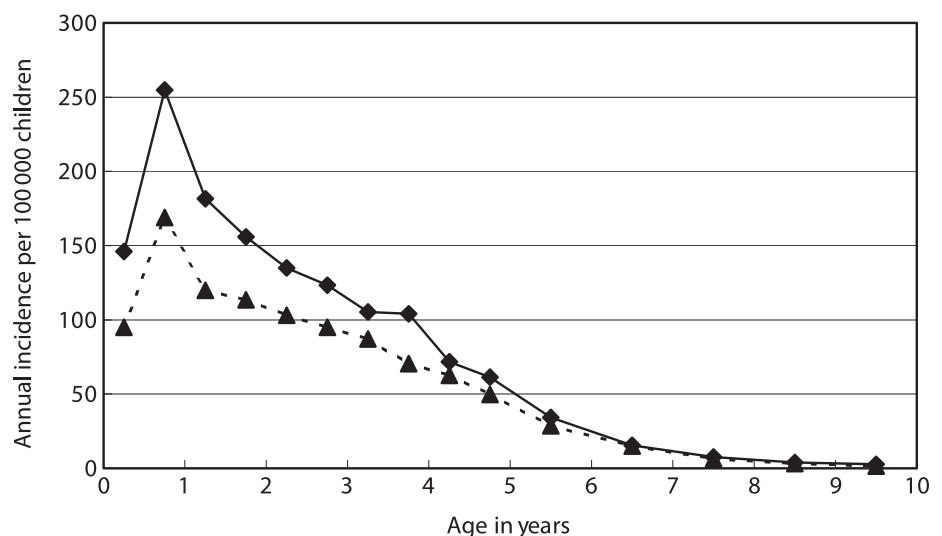
Sibling cases, recurrent cases and death

The prevalence of KD in siblings was 0.17% (15/9039). The total number of patients with recurrences was 202 (2.2%), including 188 patients with one recurrence, 13 patients with two recurrences and one patient with three recurrences. One death was reported in the acute stage of the disease.

Proportions of KD patients among total pediatric hospitalizations and their geographic pattern

The proportion of patients with KD among the total pediatric hospitalizations in the general ward, except the nursery, was 1.20% (9039/751 949) on average. The yearly proportion was 1.22% (2990/244 459) in 2006, 1.26% (3127/248 142) in 2007, and 1.13% (2922/259 348) in 2008. The proportions of different geographic regions in descending order were Kangwon (2.08%), Chungbuk (1.63%), Incheon and Kyonggi (1.44%), Daejeon and Chungnam (1.39%), Kwangju and Chonnam (1.34%), Daegu and Kyongbuk (1.26%), Seoul (1.08%), Chunbuk (1.03%), Busan

Fig. 1 Annual incidence of Kawasaki disease by age and gender. (—◆—) Boys (—▲—) Girls.



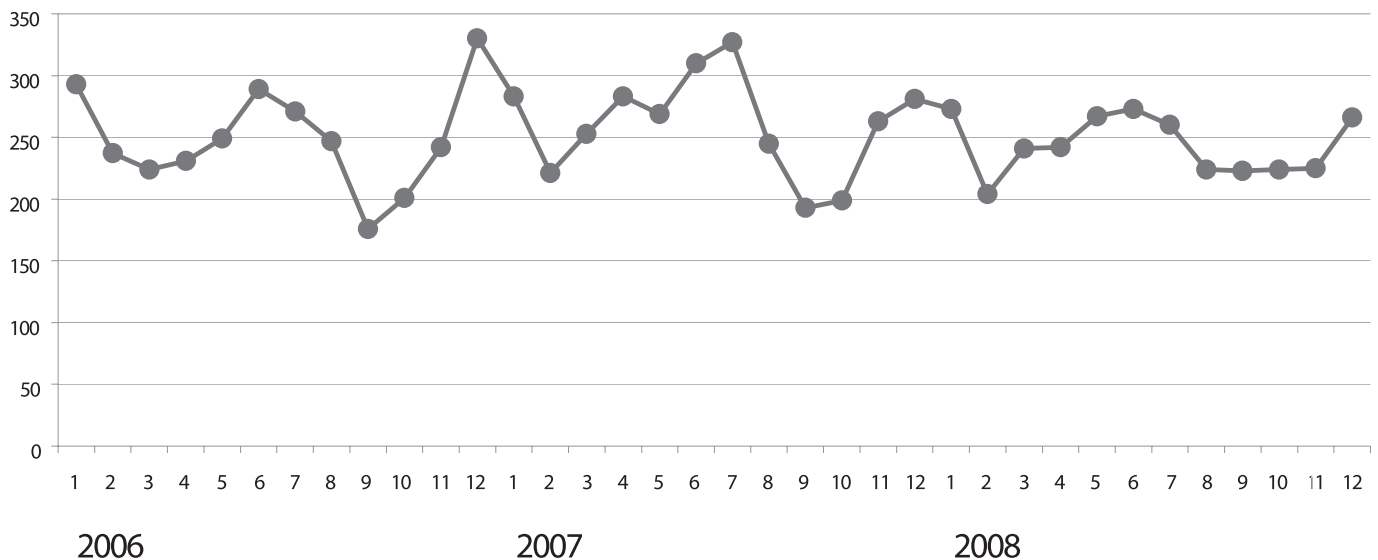


Fig. 2 Monthly distribution of Kawasaki disease cases.

and Kyongnam (0.88%) and Jeju (0.52%). Even though comparisons of differences in the proportion of KD patients among total pediatric hospitalizations for different periods or regions constitute an indirect method of comparison, these data showed a significant difference according to region ($P < 0.0001$) with the highest proportion of 2.08% in Kangwon province, located in the north-east part of the country, and the lowest proportion of 0.52% on Jeju island, located in the south of the peninsula.

Echocardiographic findings

Echocardiography was carried out during hospitalization and follow up in 95.9% of all patients (8671/9039), and CA abnormalities were observed in 17.5% of the cases (1518/8671), including dilatations in 1425 cases (16.4%) and aneurysms in 184 cases (2.1%). Categorization of these 1518 cases showed 1334 cases (15.4%) with pure dilatation, 93 cases (1.1%) with aneurysm only, and 91 cases (1.0%) with dilatation and aneurysm.

Findings of coronary angiography

Coronary angiography was performed in 46 patients (0.51%). Abnormalities, including 20 aneurysms, 20 dilatations, and three stenoses were described in 29 patients out of all the patients.

Discussion

KD is an acute, self-limited vasculitis that occurs in children of all ages, but the cause of KD remains unknown. KD has been reported among all racial and ethnic groups. Although the incidence of KD is more frequent among Asians, the incidence varies considerably among different Asian countries. In Japan, since 1970, nationwide epidemiological surveys have been conducted every 2 years, which showed increased occurrences of KD patients year by year.^{7,8} Based on the recent 19th survey, the number of patients with KD and its incidence rate are continuously increasing, and the average annual incidence rate in 2005 and 2006 was 184.6, which was the highest rate in the world.⁹

Additionally, due to a decreasing birth rate in Japan, the nominal incidence rate has increased more rapidly than an actual increase in the number of patients.

In Korea, with the support of the nationwide medical insurance system, most KD patients are diagnosed and treated in a general hospital setting, not a primary care setting. This is because KD patients are generally transferred to, and admitted to, hospitals with pediatric residency programs where the patients can undergo echocardiography by pediatric cardiologists and receive proper treatment with intravenous immunoglobulin. The response rate was 82.1% in the survey during 2000–2002, 83.3% in the survey during 2003–2005 and 83.2% for the survey in this report. These response rates were similar, so we do not think that changes in response rates influence the true incidence rate of KD. However, given that in an epidemiological study like this, underestimation is the rule, the actual incidence rate is probably higher than those seen in the surveys, especially when taking into consideration patients admitted to hospitals that failed to respond to our inquiry, or non-hospitalized KD patients, due to a late diagnosis. Considering a relatively high response rate and the aforementioned situation in our country, we believe that this study represents the epidemiological picture of KD in Korea.

The Korean Pediatric Heart Association has conducted a nationwide epidemiological study every 3 years since 1991. Reviewing the three surveys conducted in the 2000s, including this one, the average annual incidences in children <5 years of age were 86.4, 105.0 and 113.1 per 100 000 between 2000 and 2002, 2003–05 and 2006–08, respectively.^{5,6} The average annual incidence in this study is higher than the rates seen in our previous reports from 2000 through to 2005. Similarly to Japan, these differences might be mainly ascribed to the decrease in the population <5 years of age owing to the continuously decreasing birth rate rather than a change in the yearly occurrences of KD itself.

Taiwan reported an average annual incidence of 69 per 100 000 children <5 years from 2003 to 2006.³ According to

limited epidemiological data of KD from China, the reported annual incidence rates of KD per 100 000 children <5 years old were 16.79–36.76 in Shanghai from 1998–2002¹⁰ and 40.9–55.1 in Beijing from 2000–2004.¹¹ Hong Kong reported an annual incidence of 26 per 100 000 from 1994–1997 and 39 from 1997–2000.¹²

Summarizing the aforementioned data of recent epidemiological studies, Japan has the highest annual incidence in the world (184.6 per 100 000 children <5 years of age between 2005 and 2006),⁹ followed by Korea (113.1 per 100 000 children <5 years of age between 2006 and 2008) and Taiwan (69 per 100 000 children <5 years of age between 2003 and 2006).³ Compared to the higher incidence rates in Asian countries, the incidence of KD in Western countries, especially European countries, is significantly lower. The reported annual incidences per 100 000 children <5 years of age in the USA and Canada are 20.8 and 20.6, respectively.^{13,14} As the cause of this disease remains unknown, the reason for these differences in the incidence among various races and countries is also unknown.

In conclusion, a notable finding in our study is that the average annual incidence rate in Korea has been continuously increasing and reached 113.1/100 000 children <5 years old, which is the second highest rate in the world.

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