

Incidence Survey of Kawasaki Disease in 1997 and 1998 in Japan

Hiroshi Yanagawa, MD*; Yosikazu Nakamura, MD, MPH‡; Mayumi Yashiro‡; Izumi Oki, MD‡; Shizuhiro Hirata, MD‡; Tuohong Zhang, MD§; and Tomisaku Kawasaki, MD||

ABSTRACT. *Objective.* To describe the results of a nationwide epidemiologic survey of Kawasaki disease for the 2-year period 1997 and 1998.

Design. We sent a questionnaire to all hospitals with 100 beds or more throughout Japan (2663 hospitals) requesting data on patients with Kawasaki disease. Study items included name, sex, date of birth, date of initial hospital visit, diagnosis, address, recurrence, sibling cases, gammaglobulin treatment, and cardiac lesion in the acute stage or 1 month after onset.

Results. Of the 2663 hospitals, 68.5% responded, reporting 12 966 patients—7489 males and 5477 females. Of the total patients reported, 6373 (incidence rate of 108.0 per 100 000 children <5 years old) occurred in 1997, and 6593 (111.7) in 1998. More than one half of the patients (54.9%) were <2 years old and 81.6% were <4 years old. In males, the incidence rates of cardiac lesions were 27.2 in the acute stage and 10.1 a month after onset. In females, the rates were 16.7 and 5.2, respectively. The incidence rates of cardiac lesions were highest in the youngest age group (<6 months old) both in the acute stage and 1 month after onset. The rates decreased with increasing ages. Although frequency of giant aneurysms was not high at the acute stage, it did not decrease 1 month after onset.

Conclusion. The incidence rates have been steadily increasing for 11 years since 1987. The rate in 1998 was over 1.5 times higher than that in 1987. The age and sex distributions were identical in each survey. Although most of the cardiac lesions at the acute stage decreased to half or less 1 month after onset, giant aneurysms did not decrease and existed persistently after 1 month. *Pediatrics* 2001;107(3). URL: <http://www.pediatrics.org/cgi/content/full/107/3/e33>; *Kawasaki disease, epidemiology, incidence, nationwide survey.*

ABBREVIATIONS. KD, Kawasaki disease; GG, gammaglobulin.

The Japan Kawasaki Disease Research Committee has continuously conducted nationwide epidemiologic surveys since the committee was first established in 1970.¹⁻⁷ Recently, the results of the survey for the Kawasaki disease (KD) patients treated during the 2-year period of 1997 to 1998 have

been finalized. This article reports the basic analysis of the survey.

METHODS

The participants of this survey are KD patients who were diagnosed at hospitals with 100 beds or more during the 2-year study. A questionnaire form was sent to the hospitals with a pamphlet describing the diagnostic criteria of the disease including color pictures of typical lesions of the skin, eyes, hands, and feet. The mailing list of the hospitals for this survey was obtained from the 1998 hospital directory edited by the Ministry of Health and Welfare of the Japanese Government. The number of hospitals thus obtained was 2663.

Items included in the questionnaire were name, sex, date of birth, date of initial hospital visit, diagnosis, address, recurrence, sibling cases, gammaglobulin (GG) treatment, and cardiac lesion in acute stage or 1 month after onset. The cardiac disorders in this series were defined as 1 of the following findings: coronary aneurysms including dilatation, coronary stenosis including narrowing, myocardial infarction, and valvular lesions. We observed the cardiac disorders at both the acute stage and 1 month after onset.

RESULTS

Of the 2663 hospitals surveyed, 1825 (68.5%) responded. They reported 12 966 patients—7489 males and 5477 females. Of the total patients reported, 6373 (incidence rate of 108.0 per 100 000 children of age <5 years old) occurred in 1997, and 6593 (111.7) in 1998. Male/female ratios of the incidence rates were 1.31 in 1997 and 1.29 in 1998. More than half of the patients (54.9%) were <2 years old (57.1% in males, 51.9% in females; significantly higher in males; $P < .01$) and 81.6% (82.1% in males, 80.9% in females; not significant) were <4 years old. Seventy-six patients (.59%) were 10 years of age or older. The proportions were 0.77% in males and 0.33% in females (significantly higher in males; $P < .01$; Table 1).

As shown in Fig 1, incidence rate of KD has increased since 1987. The regression analysis (dependent variable: incidence rate; independent variable: calendar year) provides the regression coefficient for calendar year in males of 3.8 (95% confidence interval: 3.2–4.4) and that in females of 3.1 (2.5–3.6). The results mean that the incidence rate significantly increased.

Figure 2 shows age-specific incidence rates by sex and year. The rates for males 3 to 5 months old (240.8 per 100 000 children) in 1997 and 9 to 11 months old (240.1) in 1998 were the highest. The rates for females were the highest in those 3 to 5 months old in both years (162.8 in 1997 and 173.8 in 1998). There was a small trough between 3 and 5 months and 9 and 11 months in both years in males and in 1998 in females.

We observed the monthly distribution of the incidence rates in 1997 and 1998. The variation of the

From the *Saitama Prefectural University; ‡Department of Public Health, Jichi Medical School; §Department of Health Policy and Management, School of Public Health, Peking University; and ||Japan Kawasaki Disease Research Center, Tokyo, Japan.

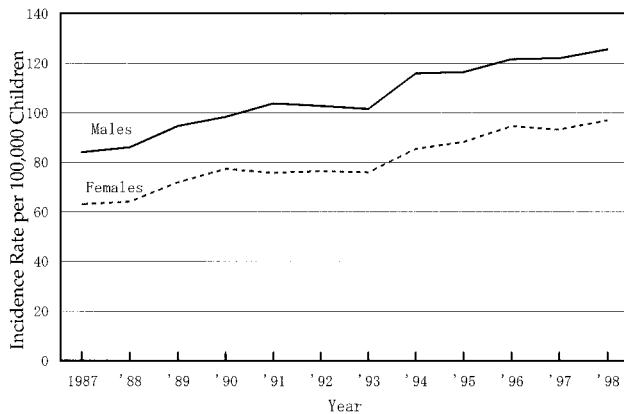
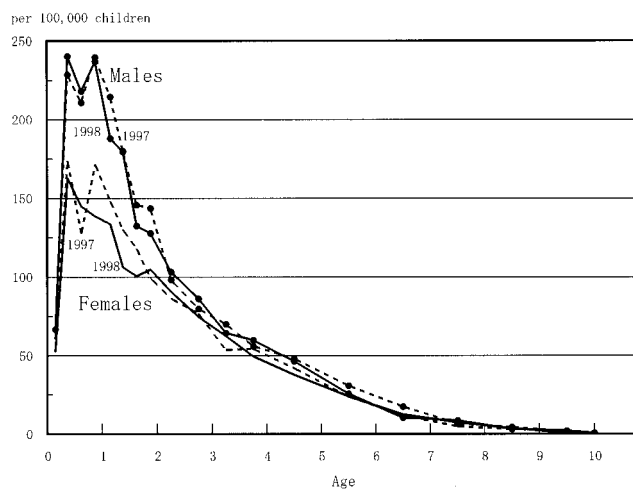
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Reprint requests to (H.Y.) Saitama Prefectural University, 820 Sannomiya, Koshigaya-shi, Saitama-ken, 343-8540, Japan. E-mail: yanagawa-hiroshi@spu.ac.jp

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TABLE 1. Number of Patients by Sex, Year, and Age

	Total	<1 Year	1 Year	2 Years	3 Years	4 Years	5-9 Years	10 Years+	Unknown
Total	12 966	3795	3327	2049	1405	1030	1276	76	8
Gender									
Males	7489	2297	1981	1104	765	571	705	58	8
Females	5477	1498	1346	945	640	459	571	18	0
Year of onset									
1997	6373	1885	1585	1045	706	497	612	37	6
1998	6593	1910	1742	1004	699	533	664	39	2

**Fig 1.** Annual incidence rates by sex, 1987-1998.**Fig 2.** Age-specific incidence rates by sex.

incidence rates transformed to annual rates between months was 82.5 per 100 000 children (October) to 123.4 (June and December) in 1997 and 98.2 (November) to 143.9 (January) in 1998. Although the seasonal distribution was not clear, the incidence rates were lower in the fall (September, October, and November) in both 1997 and 1998.

Table 2 compares the geographical differences in the incidence rates in 1997 and 1998. The country was divided into 8 regions from the north to the south. The average annual incidence rates were within the range of 118.7 and 83.2. The highest one was in Kinki (including Kyoto, Osaka, and Kobe) followed by Kanto-Koshinetsu (including the Tokyo metropolitan area) and Shikoku. In 5 regions, the rates were higher in 1998 (1998/1997 ratios were highest in Shikoku; 1.15 and lowest in Chugoku; 0.87).

TABLE 2. Differences in Incidence Rates per 100 000 Children by Area in 1997 and 1998

	Average of 1997 and 1998	1997	1998	1998/1997 Ratio
All Japan	109.9	108.0	111.7	1.03
Hokkaido	98.1	101.2	95.0	.94
Tohoku	83.2	78.0	88.3	1.13
Kanto-Koshinetsu	115.5	112.1	118.8	1.06
Tokai-Hokuriku	97.3	98.1	96.4	.98
Kinki	118.7	115.0	122.3	1.06
Chugoku	101.7	108.7	94.6	.87
Shikoku	114.4	106.3	122.5	1.15
Kyushu-Okinawa	98.2	97.7	98.7	1.02

Table 3 shows the proportion of patients with cardiac disorders by sex and age in the acute stage and 1 month after onset. The average proportion was 20.1% at the acute stage and 7.0% after 1 month. The proportion was higher in males at both the acute stage and 1 month after. It was highest at youngest age groups in males and females at both the acute stage and 1 month after.

The incidence rates (per 100 000 children <5 years of age) of the patients with cardiac disorders were also compared in Fig 3. In males, the average incidence rates were 27.2 in the acute stage and 10.1 per month after onset. In females, the rates were 16.7 and 5.2, respectively. The incidence rates were highest in the youngest age group (<6 months old) both at the acute stage and 1 month after onset. The rates decreased with increasing ages. In each age group, the rates of males were higher than those of females, without exception.

Figure 4 shows the proportion of each type of cardiac disorder both in the acute stage and after acute stage (1 month after onset). The most frequent lesions at the acute stage were dilatation (17.05% in males, 13.4% in females), which decreased to <30% after 1 month. Aneurysm decreased to ~60% of the acute stage. Notably, the frequencies of giant aneu-

TABLE 3. Proportion of Patients With Cardiac Lesions at the Acute Stage and One Month After Onset by Sex and Age (%)

	Total	Age				
		<6 Months	6-11 Months	1 Year	2 Years	5 Years
Acute stage						
Total	20.1	26.8	18.3	17.4	19.8	23.2
Males	22.0	30.1	18.3	19.0	22.1	26.3
Females	17.6	22.2	18.2	15.1	17.1	19.0
After 1 mo						
Total	7.0	11.8	6.2	5.7	6.5	7.9
Males	8.2	13.7	6.5	6.7	7.9	9.2
Females	5.5	9.2	5.7	4.2	4.8	6.3

Fig 3. Incidence rates of patients with cardiac lesions at the acute stage and 1 month after onset by age and sex.

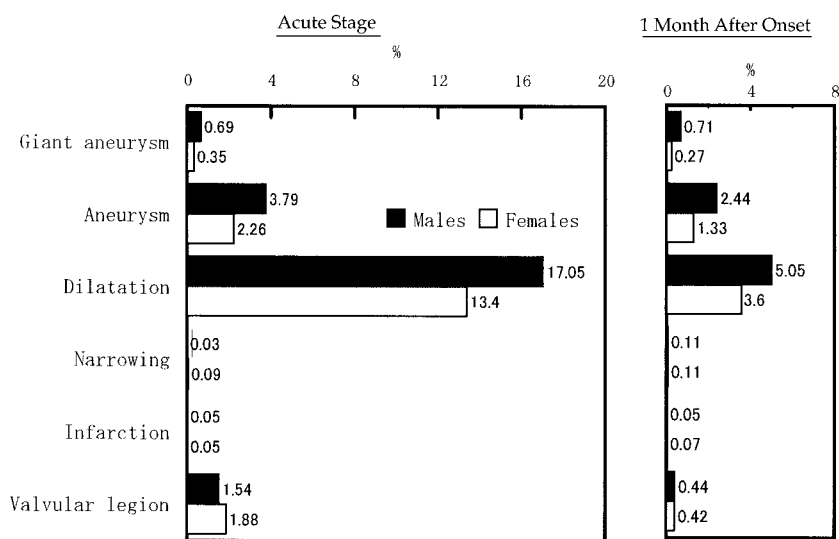
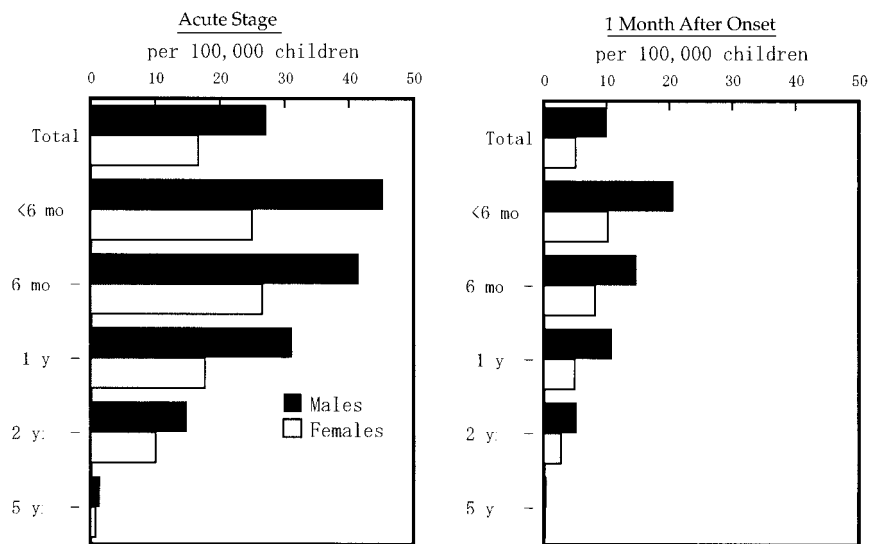


Fig 4. Proportion of patients with cardiac lesions at the acute stage and 1 month after onset by type and sex.

rysm were not high in males and females at the acute stage but did not decrease after 1 month.

DISCUSSION

Since 1970, 15 nationwide epidemiologic surveys have been conducted by the Japan Kawasaki Disease Research Committee and a total of 153 803 patients were reported by the end of 1998. It was estimated by the past study that >90% of total KD patients, including those referred from either small hospitals or clinics, were treated in hospitals with 100 beds or more.⁸ Although we cannot escape the bias attributable to the ruling out of patients who were treated at these facilities and the hospitals that failed to respond to our inquiry, we believe that the results of our study are the most reliable nationwide data in Japan. The response rates (68.5% in this survey) were stable in recent surveys (within the range of 65.5%–68.9% in the recent 5 surveys). Therefore, the comparability of the epidemiologic pictures with former surveys was maintained.

The incidence rates have been steadily increasing

for 11 years since 1987. The rate in 1998 (111.7 per 100 000 children) was over 1.5 times higher than that in 1987 (73.8). The current study shows the statistically significant increase both in males and females. There are 2 factors that increase the incidence rate: the increase of the number of patients and the decrease of the number of children. The annual number of KD patients increased year by year, and after 1993, the annual number was over 6000. Because recognition of the patients, diagnostic criteria, and survey method were not changed in the last 10 years, we are convinced that the recent trend is an actual increase in the occurrence in Japan, although we do not know the reason.

The age and sex distributions have been identical in each survey. It was not clear why there was a trough near the peak of the incidence curve in this survey. We will carefully follow this point in the next survey for 1999 and 2000. The seasonal distribution of incidence rates being lower in autumn was also the same as in former surveys.

For the first time in the history of the KD epi-

miologic surveys in Japan, the changes in the cardiac lesions at onset and 1 month after onset were compared in this survey. We found that most of the lesions decreased to one half or less after 1 month of onset. However, giant aneurysms existed persistently after 1 month. Detailed analysis on the factors influencing the fate of the cardiac lesions will be shown elsewhere.

The proportion of the patients with cardiac lesions 1 month after onset has decreased year by year. This reduction is possibly attributable to the increase in the proportion of patients treated with GG and an increase in the dosage. In the early 1980s, the GG treatment for KD started in Japan. In 1990, the Japanese Medical Insurance System authorized a regimen of 200 mg/kg for 5 days as a standard treatment for KD, and reimbursement of the expenses for the standard treatment were approved by the insurance system. In 1995, a new regimen of 400 mg/kg per day for 5 days was authorized.

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