ABSTRACT. Objective. To evaluate the epidemiologic pattern of Kawasaki disease (KD) in the United States over 10 years.

Methods. The National Inpatient Sample, a stratified national sample of >900 hospitals in 22 states of the United States, was used. Data on hospital discharges from 1988–1997 were analyzed. Patients <18 years of age with a discharge diagnosis of KD were identified.

Results. There were 6442 patients with KD admitted to 651 hospitals. Median age at hospital admission was 2 years. Peak incidence by year of age was 1 year old. Children <2 years old accounted for 36.6% of all cases; <5 years old, 75.6%; and <10 years old, 95.6%. The age distribution seems to be wider than reported from Japan. The incidence for children <5 years old was 8.1 per 100,000 people in 1988, and increased to 18.5 in 1997. There were 3905 males (60.6%) and 2537 females (39.4%), for a male-to-female ratio of 1.54. The incidences were higher in winter and spring (December to May) and dropped to a nadir between July and September. No apparent change in seasonal pattern was noted over 10 years. The South census region showed a seasonal change 2 to 3 months ahead of other regions. The overall in-hospital mortality rate was 0.17%. The mortality rate in children ≥10 years (1.4%) was significantly higher in than children <10 years (0.11%).

Conclusions. KD affects mainly children under 5 years of age, with a peak incidence in children 1 to 2 years of age. The incidence of KD was rising over the study period. There is a male predominance. Although KD occurs year-round, the lowest incidence is seen from July through September. Such seasonal variation did not change over the 10 years. Seasonal pattern may vary in different geographic regions. Mortality from KD is rare, although children ≥10 years are at higher risk. Pediatrics 2002;109(6). URL: http://www.pediatrics.org/cgi/content/full/109/6/e87; Kawasaki disease, epidemiology, United States.

Abbreviations. KD, Kawasaki disease; NIS, Nationwide Inpatient Sample; IVIG, intravenous immunoglobulin; AHA, American Heart Association.
for each year of the study period was calculated by interpolating the census data.

**Case Selection**

For this study, pediatric patients (0 through 17 years of age) with a diagnosis code in the database indicating KD (International Classification of Diseases, Ninth Revision, Clinical Modification code 446.1) were selected as the study population. Each patient in the database is assigned a unique sequence number, which allows identification of patients with multiple hospitalizations. For patients with multiple hospitalizations for KD, only the first hospitalization (determined by the month and year of hospitalization) was entered into the analysis.

To evaluate the geographic variation of KD epidemiology, the 22 states were grouped into 4 regions according to each state’s census region designation. States in the West census region are Arizona, California, Colorado, Hawaii, Oregon, Utah, and Washington. States in the Midwest census region are Iowa, Illinois, Kansas, Missouri, and Wisconsin. States in the Northeast census region are Connecticut, Massachusetts, New Jersey, New York, and Pennsylvania. States in the South census region are Florida, Georgia, Maryland, South Carolina, and Tennessee.

### Statistical Analysis

Descriptive continuous data, such as hospital charges and length of stay, are presented as mean ± standard deviation and median when appropriate. Continuous variables were compared using the Student t test. Categorical variables and proportions were compared using χ² test or Fisher exact test. A P value <.05 was considered statistically significant. Statistical analyses were performed using SPSS 8.0 for Windows (SPSS Inc, Chicago, IL).

### RESULTS

A total of 6442 patients <18 years of age were admitted to 651 hospitals in 22 states over the 10-year study period. Table 1 lists the number of cases and hospitals from each year of the study period. The total number of cases in each hospital ranged from 1 to 297 cases. The highest number of average annual cases for a hospital was 50 cases per year. There were 890 cases of KD among children 0 to 17 years of age from the 1997 NIS data. Considering that NIS data represents 20% all hospital discharges in the United States, an estimated 4500 cases of KD occurred in the United States in 1997.

### Age and Incidence

Median age at hospital admission was 2 years. Peak incidence by year of age was 1 year old (20.7% of all cases). Children <2 years old accounted for 36.6% of all cases, <5 years old accounted for 75.6%, and children <10 years old accounted for 95.6% cases (Fig 1). The incidence of KD was calculated based on the 1990 US census data and the assumption that the NIS data represent 20% of all hospital discharges in the United States. For children <5 years of age, the incidence increased from 8.1 per 100 000 children <5 years old in 1988 to 18.5 in 1997. Figure 2 shows the incidence of KD over the 10-year study period. The incidence increased from 1988 to 1991, remained relatively unchanged till 1996, and rose again in 1997. The incidence for children <10 years old increased from 5.0 per 100 000 children <10 years old in 1988 to 11.7 in 1997. The pattern of incidence changes over time in children <10 years old, which was similar to that of children <5 years old as shown in Fig 2.

### Gender

There were 3905 males (60.6%) and 2537 females (39.4%), for a male-to-female ratio of 1.54. As shown in Fig 3, the number of males exceeds the number of females in all ages. The male-to-female ratio for infants (<1 year) was 1.52, and the ratios for children <5 years and <10 years were the same at 1.50. The male-to-female ratio for children ≥10 years old was 3.0, which is significantly different from children <10 years old (P < .01). There was no significant geographic variation in the male-to-female ratio. The male-to-female ratio was 1.58 for West, 1.52 for Midwest, 1.55 for Northeast, and 1.53 for South. However, variation in male-to-female ratio was noted in different months of the year. The male-to-female ratio varied from 1.29 in January to 1.90 in November (P < .01).

### Seasonal Variation

The 10-year study period was divided into two 5-year periods (1988–1992 and 1993–1997) to determine whether the seasonal pattern had changed over time. The 2 periods show similar seasonal pattern with lowest incidence in July through September (Fig 4). The incidences were higher in winter and spring (December to May). No apparent change in seasonal pattern of KD was noted over 10 years.

All 4 regions showed seasonal variation in the number of cases by month (Fig 5). In the South, the number of cases decreased in March and stayed low until October. In contrast, the number of cases in the West started to decrease in June, decreased further in July, and stayed low until December when it started to rise again. Northeast and Midwest showed seasonal patterns similar to that of the West. Therefore,
the South census region showed a seasonal change 2 to 3 months ahead of other regions.

Hospitalization and Outcomes

Of the days of the week when patients were admitted to the hospitals, the number of admissions was high on Monday (16.4% of all admissions), decreased on Tuesday (15.8%) and Wednesday (15.8%), decreased further on Thursday (15.0%), and rose again on Friday (16.9%). The number of admissions was lowest on weekends (Saturday 10.6% and Sunday 9.6%).

The overall median hospital length of stay was 3 days (mean 4.3 ± 4.8 days), ranging from 0 to 146 days. The median length of hospital stay decreased from 5 days in 1988 to 4 days in 1989 and to 3 days...
from 1990 to 1997. The median hospital charge was $5652 (mean $8025 ± 12 016), ranging from $198 to $426 060 (without adjustment for inflation rate over time).

There were 11 in-hospital deaths, yielding an overall mortality rate 0.17%. The deaths occurred from day 1 to day 24 of hospitalization. The majority of deaths (7) occurred in the first week of hospitalization. There were 2 deaths in infants (<1 year of age).

The mortality rate of infants (0.20%) was not different from children >1 year of age (0.17%). Four deaths occurred in children ≥10 years old (all males), yielding a mortality rate of 1.40% in children 10 to 17 years old, which was significantly higher than mortality rate of 0.11% in children <10 years old (P < .01). The relative risk for mortality comparing children ≥10 years old with children <10 years old is 12.3. The causes of death in these cases could not be deter-
mined because of insufficient clinical information provided in the database.

**DISCUSSION**

This study provides epidemiologic information on KD in the United States over 10 years, during which the incidence of KD increased. Seasonal variation in the number of KD cases was noted, and the seasonal pattern seems different in the South. Length of hospitalization for KD shortened between 1988 and 1990. This possibly was attributable to the increasing adoption of the combined single intravenous immunoglobulin (IVIG) infusion treatment strategy, which was published in 1991.16

The incidence of KD was recently studied and reviewed by Belay et al.13 Using data collected from 4 West Coast health maintenance organizations, the authors found that the incidence for children <5 years old ranged from 9.0 to 19.1 per 100 000 persons per year. Other studies have reported similar incidences: Connecticut, 18.8, in 1993–1996; San Diego, 9.3 to 15.5, in 1994–1998; and Washington State, 6.5 to 15.2, in 1985–1989. In this study, the incidence per 100 000 children <5 years old was similar to previous studies: from 8.1 in 1988 to 18.5 in 1997 with a trend of increasing incidence over 10 years. The trend of increasing KD incidence has been reported by Taubert who used data from a survey of children’s hospitals.18 Increasing incidence of KD over time was also seen in Japan.4 The highest incidence of KD reported in the United States was from Hawaii with an incidence 47.7 per 100 000 children <5 years old.9 Studies from Japan reported a much higher incidence of 108.0.7

Increasing recognition of KD diagnosis and awareness of the need for hospitalization and treatment for KD by clinicians may have contributed to the increasing incidence of KD seen in this study. However, it is also possible that more children who do not meet the diagnostic criteria (recently revised by the American Heart Association [AHA]) are diagnosed with KD. In a study from a tertiary children’s hospital, Witt et al.20 reported that 36% of the children diagnosed with KD did not meet the AHA criteria. In addition, the proportion of children who did not meet the diagnostic criteria rose from 1991 to 1997. It may be difficult to extrapolate experience from a single institution to a nationwide trend of increasing diagnosis of patients who do not meet AHA criteria. However, if this trend existed in other hospitals or regions, the incidence of KD may continue to rise.

Another possible contributing factor to the increase of KD incidence is the fast growing Asian-American population in the United States. From 1990 to 2000, Asian-American population has increased by 52.4% in the United States.21 The proportion of US population who are Asian-American has increased from 2.78% in 1990 to 3.64% in 2000.21 How much of the increase in KD incidence is attributable to increasing Asian-American population and how the continuing increase in Asian-American population is going to affect the incidence of KD in the future requires additional investigation.

The peak age of KD has been reported at 1 to 2 years by previous studies. In Japan, patients <2 years old accounted for 54.1% of all KD cases in 1995–1996.22 In contrast, patients <2 years old only accounted for 36.6% of cases in this US sample. Patients ≥10 years old accounted for <1% of cases in Japan, but accounted for 4.4% in this study. Other studies from single institution experience in the United States have also reported a high proportion of

**Fig 5.** Seasonal variation in the number of KD cases in 4 census regions: West, Midwest, Northeast, and South.
children ≥10 years old (5.6%–7.5% of all cases).\textsuperscript{23,24} Therefore, the age distribution of cases in the United States seems to be wider compared with cases in Japan. This finding has important clinical implications, because older children with KD are more likely to be diagnosed late, have a higher rate of cardiovascular complications,\textsuperscript{23,24} and have a higher mortality rate as reported in the present study. Factors such as differences in demographic (eg, race and ethnic composition) and geographic characteristics (eg, climate, altitude) between the United States and Japan may contribute to such a difference. Future studies are needed to examine this speculation.

Although all studies on KD have shown a male predominance, the male-to-female ratio had ranged widely from 1.16 to 1.85 in different studies.\textsuperscript{7,13,14,17} It is likely that the variations in the male-to-female ratio reported by previous studies are attributable to small sample sizes and different geographic areas and time frames from which data were obtained. In the present study, the male-to-female ratio from this national sample was 1.54, which seems to be between the ratios previous reported. This ratio also seems to be slightly larger than the 1.36 reported by a recent survey in Japan.\textsuperscript{7}

The seasonal variation of KD has been reported previously. Bell et al\textsuperscript{8} reported the 1976–1980 data from Centers for Disease Control and Prevention surveillance and found seasonal variation of cases reported to the Centers for Disease Control and Prevention. This pattern was later reported from the 1991–1993 surveillance by Khan et al.\textsuperscript{14} A similar seasonal pattern was also noted from studies in Japan.\textsuperscript{22,25} In the present study, seasonal variation was also found, and this pattern remained similar over the 10 years of the study period. Cases from the South region showed a pattern different from other regions: peak incidence in December through February and remained lower from March to September. The decrease of incidence in the South began in March, which was 3 months earlier than other regions. It is speculated that such regional variation in the seasonal pattern may be attributable to differences in the climate of these regions. In support of this, Bronstein et al\textsuperscript{12} found the incidence of KD in San Diego correlates with temperature and rainfall. Future studies are needed to investigate the effect of climate on the epidemiology of KD.

The pattern for the day of hospital admission may reflect patients' care-seeking behavior. Parents may take their children to doctors before the weekend comes, which could explain the higher number of admissions on Fridays, and may wait until Monday to see a doctor if their children become ill over the weekend, which could explain the higher number of admissions on Mondays.

Outcomes of children affected by KD are generally good. Mortality attributable to KD is rare. Deaths are usually from cardiovascular complications. Checchia et al\textsuperscript{26} reported that 9 patients with KD from the United States who required cardiac transplantation because of coronary and myocardial involvement. The mortality rate in the present series was 0.17%. This rate seems to be slightly higher than 0.08% reported from the Japanese series.\textsuperscript{22} The higher mortality rate in the United States could be explained by the higher proportion of children ≥10 years old who had a higher in-hospital mortality rate than children <10 years old.

**Limitations**

There was a significant amount of missing data in the coding of race and ethnicity of the patients. Therefore, the incidence by race and ethnicity of the study population could not be analyzed. The incidence of coronary aneurysm, a major long-term sequela of KD, cannot be reliably calculated from the NIS database either. Because the NIS database is compiled from multiple states that do not necessarily follow a uniform reporting system, many may not have reported secondary diagnosis. In addition, treatment using IVIG, which has become a standard for preventing coronary aneurysm formation in patients with KD, could not be determined in the NIS data. IVIG treatment was listed as the Principal Procedure in many patients. However, many patients had KD and “diagnostic echocardiography” listed as the Principal Procedure but did not have IVIG listed.

There is also a potential for overestimating KD using an administrative database. Patients who do not meet the AHA criteria and are discharged with a diagnosis of “rule out Kawasaki disease” are likely to be coded as KD. In the NIS database, it is not possible to estimate how many patients who do not meet the AHA criteria are being diagnosed as KD because detailed clinical information is not listed in the database.

**CONCLUSION**

KD affects mainly children under 5 years of age, with a peak incidence in children 1 to 2 years of age. This study suggests that the incidence of KD is rising over time. An active surveillance system may be needed to determine the cause of increasing KD incidence. Compared with reports from Japan, the age distribution of patients in the United States seems wider. There is a male predominance with male-to-female ratio 1.54 to 1. Although KD occurs year-round, the lowest incidence is seen from July through September. Such seasonal variation did not change over the 10 years of study, although the seasonal pattern varied in different geographic areas. Mortality from KD is rare, although children ≥10 years old are at higher risk.

**ACKNOWLEDGMENTS**

Dr Chang was a postdoctoral fellow of the Agency for Healthcare Research and Quality and received an institutional research grant from the Harbor-UCLA Research and Education Institute. I thank Margaret Keller, MD, and James Joyce, MD, for reviewing this manuscript, and Silvia Rodriguez for proving secretarial assistance.

**REFERENCES**

3. Laupland KB, Dele Davies H. Epidemiology, etiology, and management


15. HCUP NIS data sources, hospitals and inpatient stay. Available at: http://www.ahrq.gov/data/hcup/nistab3.htm


20. Witt MT, Minich LL, Bohnsack JF, Young PC. Kawasaki disease: more patients are being diagnosed who do not meet American Heart Association criteria. Pediatrics. 1999;104(1). Available at: http://www.pediatrics.org/cgi/content/full/104/1/e10


Ruey-Kang R. Chang

Pediatrics 2002;109:e87
DOI: 10.1542/peds.109.6.e87

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/109/6/e87

References
This article cites 17 articles, 2 of which you can access for free at:
http://pediatrics.aappublications.org/content/109/6/e87.full#ref-list-1

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Hospital Medicine
http://classic.pediatrics.aappublications.org/cgi/collection/hospital_m edicine_sub
Infectious Disease
http://classic.pediatrics.aappublications.org/cgi/collection/infectious_ diseases_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints

Ruey-Kang R. Chang

*Pediatrics* 2002;109:e87

DOI: 10.1542/peds.109.6.e87

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://pediatrics.aappublications.org/content/109/6/e87