

Kawasaki Syndrome in Hawaii

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Objective: To describe the incidence and epidemiology of Kawasaki syndrome (KS) in Hawaii.

Methods: Retrospective analysis of the State Inpatient Database for Hawaii residents hospitalized with KS during 1996 through 2001.

Results: During 1996 through 2001, 267 persons younger than 18 years of age living in Hawaii were hospitalized with KS; 226 (84.6%) were younger than 5 years of age. The average annual incidence for KS was 45.2 per 100,000 children younger than 5 years of age. The incidence was higher for children younger than 1 year of age than for those 1–4 years of age (74.3 and 37.5 per 100,000). The KS incidence for Asian and Pacific Islander children and for White children was 70.9 and 35.3 per 100,000, respectively. Incidence was highest among Japanese American children living in Hawaii (197.7 per 100,000). Honolulu County had the most KS patients (85.0%) and the highest incidence (53.1 per 100,000) among Hawaii counties. For children younger than 5 years of age hospitalized with KS, the median length of stay was 2 days, and the median hospital charge was \$9379.

Conclusion: During 1996 through 2001, the annual incidence rate for KS among children younger than 5 years of age in Hawaii was the highest in the United States. The incidence among Japanese American children in Hawaii was higher than that among other racial groups in the state and when compared with children living in Japan.

Key Words: Kawasaki syndrome, hospitalizations, epidemiology, children, infants, Hawaii

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Kawasaki syndrome (KS) was first described among Japanese children in 1967.¹ In Japan, the annual incidence of KS among children younger than 5 years of age increased from 73.8 per 100,000 in 1987 to 134.2 per 100,000 in 2000.^{2,3} The first cases of KS outside Japan were reported in Hawaii in 1976,⁴ and during the mid-1990s, the rate of hospitalizations with KS among children younger than 5 years of age living in Hawaii was 47.7 per 100,000 children.⁵ This rate was much higher than rates reported for children in the continental United States.^{5–12} Community-wide outbreaks of KS have been reported in Hawaii and elsewhere in the United States.^{13–18}

Previous studies indicate that the risk of developing KS is higher for children of young age, boys and children of Asian descent.^{5,7,9,10,12–14,16,17,19–24} A high proportion of children with ancestral origin from the various Asian countries (eg, Japan, China and the Philippines) live in Hawaii, where a higher incidence of KS has been reported.^{5,14} In our study, we examined hospital discharge data for KS patients to describe the incidence and epidemiology of KS in Hawaii, including the incidence of KS among the various racial groups.

METHODS

Hospital discharge records with KS listed as a diagnosis during 1996 through 2001 for Hawaii residents were obtained from the Hawaii State Inpatient Database.²⁵ The Hawaii Health Information Corporation (HHIC) partners with the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (AHRQ), to produce the Hawaii State Inpatient Database for Hawaii.^{26,27} The HHIC is a nonprofit corporation that was established in 1994 to collect all inpatient data submitted from Hawaii's 22 acute care hospitals.²⁶ The collected data report on >98% of the hospitalizations in Hawaii.

Hospitalizations for children younger than 18 years of age with an International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM)²⁸ code for KS (446.1) listed as one of the diagnoses on the discharge record were selected for our analysis. AHRQ and HHIC internally identified multiple KS hospitalizations for patients with KS

during the study period by matching admissions by date of birth, sex and residential zipcode (no unique identifiers were available), and questionable records were verified by the hospitals. For patients with multiple KS-associated hospitalizations, the first KS-associated hospitalization during the study period was selected for analysis, and the hospital length of stay and charges from subsequent hospitalizations were added to those for the first hospitalization.

We examined data by patients' age, sex, race, county of residence and admission month. To protect patient privacy, results for these characteristics were reported only if the data were for at least 5 patients. Race was examined as reported on the hospital discharge record. We also describe the expected primary payer, hospital length of stay and charges and accompanying diagnoses listed with KS-associated hospitalizations.

KS incidence (per 100,000 children) was calculated by using the number of patients hospitalized with KS and the population and live birth estimates from the U.S. census and natality data for Hawaii for 1996 through 2001; natality data were used for the infant (younger than 1 year of age) population.^{29,30} To examine the incidence of KS by race, the average annual incidence for the 6-year study period was estimated by using the number of patients and data from Census 2000 to represent the population for the study years.^{31,32} Persons indicated as part Native Hawaiian were considered Native Hawaiian, as reported by the census. Census 2000 provided the population classified by race listed alone or in combination with other races, which was different from previous census race classifications.^{31,32} We used the listed alone race categories for race-specific denominators. Incidence rates were compared by Poisson regression analysis.³³ The overall KS-associated hospitalization rate per 100,000 children was calculated by using the number of hospitalizations as the numerator. Wilcoxon rank sum tests were used to test for group differences for age and hospital length of stay.³⁴

RESULTS

Overall. During 1996 through 2001, a total of 287 hospitalizations with KS were reported in Hawaii for 267 persons younger than 18 years of age. Of these, 243 hospitalizations were for 226 children younger than 5 years of age (84.6%). Nineteen patients (16 children younger than 5 years of age) had more than 1 KS hospitalization, totaling 20 multiple hospitalizations (6.9 and 7.1% of all KS hospitalizations among children younger than 18 and younger than 5 years of age, respectively). Fewer than 5 KS patients younger than 5 years of age had a second hospitalization with KS as the primary diagnosis occurring ≥ 3 months after the first KS hospitalization.

The average annual incidence rate for KS among children younger than 5 years of age during 1996 through 2001 was 45.2 per 100,000 children (Table 1). The incidence rate by year during the study period was 38.7, 43.7, 48.0, 39.8, 46.1 and 56.0 per 100,000 children, respectively. The average annual KS-associated hospitalization rate (including multiple hospitalizations) was 48.6 per 100,000 children younger than 5 years of age.

Age, Sex and Race. The median age of children hospitalized with KS was 1 year (quartiles 0, 4; Fig. 1). Two-thirds (66.8%) of the KS cases were among children younger than 3 years of age. Age in months was reported for 61.2% of infants. Among infants, the median age at admission was 6 months (quartiles 5, 9). The incidence rate of KS among children younger than 5 years of age was nearly 6 times that of children 5–9 years of age ($P < 0.001$) and 15 times the incidence among children 10–17 years of age ($P < 0.001$). The incidence for infants was higher than that for 1- to 4-year-old children (74.3 and 37.5 per 100,000 children, respectively; $P < 0.001$; Table 1).

More KS hospitalizations for children younger than 5 years of age occurred among boys (57.1%), but the KS incidence did not significantly differ between boys and girls ($P = 0.08$; Table 1). However, a marked difference in incidence by sex was seen for infants, among whom the incidence for boys was twice that for girls ($P = 0.003$). The incidence for boys and girls 1–4 years of age did not differ. The median age for both boys and girls younger than 5 years of age was 1 year; the

TABLE 1. Characteristics of Children Hospitalized with KS and KS Incidence Rates by Age Group, Hawaii, 1996–2001

Characteristic	No. of Patients	Incidence*
Age group		
All ages	267	50.4
Younger than 1 yr	78	74.3
1–4 yr	148	37.5
5–17 yr	41	5.1
Children younger than 5 yr of age		
Total	226	45.2
Male		
Total	129	50.3
Younger than 1 yr of age	53	98.1
1–4 yr of age	76	37.5
Female		
Total	97	39.9
Younger than 1 yr of age	25	49.0
1–4 yr old	72	37.5
County of residence [†]		
Honolulu	192	53.1
Kauai	8	34.4
Maui	12	22.4
Hawaii	13	22.1

*Number of children hospitalized with KS per 100,000 children.

[†]County of residence was missing for 1 child. The county populations for children younger than 5 yr of age during 2000 were 361,717, 23,225, 53,457 and 58,779, respectively.³¹

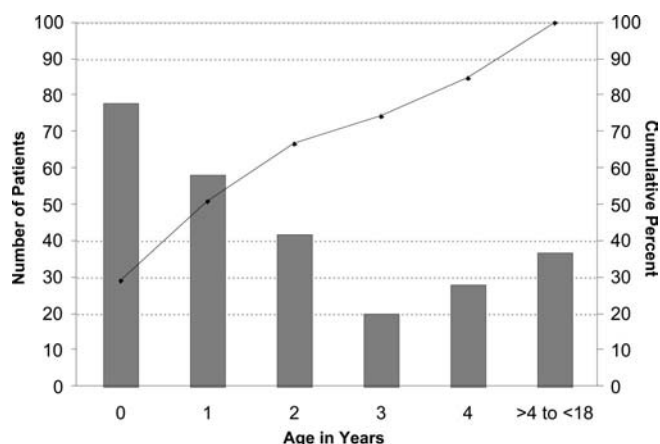


FIGURE 1. Number (■) and cumulative percent (—◆—) of children younger than 18 years of age hospitalized with Kawasaki syndrome by age, Hawaii, 1996–2001.

median age in months among infants was 6 months for both boys and girls.

Most patients younger than 5 years of age were Asian or Pacific Islander (81.5% of children with known race). The Asian and Pacific Islander children had a KS incidence of 70.9 per 100,000 children. Examination by more specific racial groups among the children younger than 5 years of age showed that the highest proportion of children hospitalized with KS in Hawaii was for Japanese American children (25.0%; Table 2). Japanese American children also experienced the highest incidence among children younger than 5 years of age (197.7 per 100,000), followed by the incidence for Native Hawaiian, Chinese and Filipino children (99.1, 81.3 and 64.8 per 100,000 children, respectively). The KS incidence for Japanese American children was twice that for

TABLE 2. Race of Children Younger Than 5 years of Age Hospitalized With KS, Hawaii, 1996–2001

Race*	No.	Incidence [†]
Japanese	50 (25.0) [‡]	197.7
Hawaiian	35 (17.5)	99.1
Chinese	9 (4.5)	81.3
Filipino	36 (18.0)	64.8
Other Asian	26 (13.0)	83.0
Other Pacific Islander [§]	7 (3.5)	9.8
White	29 (14.5)	35.3
Mixed/other race	8 (4.0)	5.1

*Race was not reported for 26 patients. The percentages are based on the number of patients with reported race (N = 200).

[†]Number of children hospitalized with KS per 100,000 children estimated by using the total number of patients by reported race during the 6-year study period and the corresponding data from the Census 2000 to represent the population for each of the study years.

[‡]Numbers in parentheses, percent.

[§]Census for Other Pacific Islanders includes persons who provide a response of Pacific Islander groups, such as Samoan, Tongan, Guamanian or Chamorro, Fijian, Polynesian and others or Pacific Islander not specified.³²

Native Hawaiian children ($P = 0.002$) and >5.5 times higher than that for White children living in Hawaii ($P < 0.001$). **Location and Admission Month.** In Hawaii, most (85%) children hospitalized with KS resided in Honolulu County (Table 1). KS incidence for children younger than 5 years of age varied geographically within Hawaii. The incidence for children residing in Honolulu County was higher than that for children residing in the other 3 counties (Hawaii, Maui and Kauai). During the study period, there was not a clear seasonal pattern in KS hospital admissions. However, 33.6% of the patient admissions occurred in January through March, whereas fewer cases were seen during April through June (20.4%).

Expected Payer, Hospital Stay and Charges. During the study period, private insurance was the expected primary payer for 80.9% of the children younger than 5 years of age, whereas Medicaid was indicated for 17.3%. Private insurance was the expected primary payer for 78.1% and Medicaid for 14.6% of the 5- to 17-year-old children. The median length of hospital stay was 2 days (quartiles 2 and 3) for children younger than 5 years of age hospitalized with KS (Table 3). The median length of stay for children 5–17 years of age was 3 days (quartiles 2 and 4). No deaths were reported among children hospitalized with KS.

The median charge for a KS hospitalization for children younger than 5 years of age was \$9379 (mean, \$10,113; Table 3), and the median charge for 5- to 17-year-old patients was \$13,620 (mean, \$13,861). The total hospitalization charges associated with KS averaged \$380,921 per year for children younger than 5 years of age and \$475,639 per year for all children younger than 18 years of age.

Other Conditions Associated with KS. KS was the first listed hospital discharge diagnosis for 96.0% of the children younger than 5 years of age hospitalized with KS and was the first listed diagnosis for 87.8% of the children 5–17 years of age. Diagnoses listed most frequently with KS on the hospitalization records for children younger than 5 years of age included volume depletion (ICD-9-CM code 276.5; 9.3%) and unspecified otitis media (ICD-9-CM code 382.9; 7.1%). Among children 5–17 years of age, the most frequently listed diagnoses were volume depletion (ICD-9-CM code 276.5; 17.1%) and sodium deficiency (ICD-9-CM code 276.1; 12.2%).

DISCUSSION

We found that the average annual KS incidence rate among children younger than 5 years of age in Hawaii during 1996 through 2001 was 45.2 per 100,000 children, and this finding is consistent with previous reports that Hawaii has the highest incidence of KS.^{5,14} KS incidence for the continental United States has ranged from 9 to 19 cases per 100,000 children younger than 5 years of age.^{5–12} The high KS incidence in Hawaii is likely because approximately one-half

TABLE 3. Expected Primary Payer, Hospital Length of Stay and Hospital Charges for Children Younger Than 5 Years of Age Hospitalized With KS, Hawaii, 1996–2001

Variable	No. of Children*	% of Children Hospitalized*
Total	226	100
Primary payer		
Medicaid	39	17.3
Private insurance/HMO	182	80.5
Self-pay/unknown	5	2.2
	Mean (minimum, maximum)	Median (quartiles)
Length of stay (days)	3.0 (0, 17)	2 (2, 3)
Charges (\$)	\$10,112 (\$877, \$47,191)	\$9379 (\$5926, \$12,689)

*Some characteristics were not fully reported. Percentage is based on the number of patients with the reported information.

of the state population is Asian or Pacific Islander,³¹ racial groups in which high KS incidence has been documented.^{7,12–16} Active surveillance for KS in Hawaii during 1979 through 1983 showed that the annual incidence for Oahu ranged from 21 to 100 cases per 100,000 children younger than 5 years of age and that the rate for Japanese American children was higher than that for White children and for children living in Japan.^{15,16}

In our study, the incidence of KS was much higher for Asian and Pacific Islander children than for other children younger than 5 years of age living in Hawaii. Asian and Pacific Islander children accounted for ~80% of the hospitalized children younger than 5 years of age, yet they represented just under 50% of the population of children younger than 5 years of age in Hawaii.³¹ We also found that Japanese American children had the highest rate of KS among racial groups in Hawaii and that this rate was higher than the reported incidence for children in Japan.³ KS incidence varies among the different Asian countries,⁹ which may reflect actual differences in the KS incidence, differences in access to health care or physician awareness of KS and, possibly, differences in geographic location or culture among the Asian populations. In the current study, disparities in KS incidence among the various Asian racial groups living in Hawaii existed despite the expectation that these groups had similar access to health care and physician diagnostic practices.

Most (85%) of the KS patients hospitalized in Hawaii occurred among children younger than 5 years of age, with more than one-half of the cases being younger than 2 years of age, which was consistent with other KS studies.^{12,15,24} The highest KS incidence was among infants, which was also consistent with findings in earlier studies.^{6,12} Previous studies have also reported that more KS occurs among boys than among girls,^{4,6,7,12,16,21,35} and we found a marked difference in KS incidence between male and female infants.

KS incidence varied by county of residence in Hawaii. Most (85%) of the children hospitalized with KS resided in Honolulu County, where 72% of all children younger than 5 years of age resided.³¹ Also Honolulu County had the highest

incidence among the Hawaiian counties, which may partly be because this county has the highest population density in the Hawaiian Islands. Clustering of KS around areas of high population density has been reported in Japan as well.³⁶ In addition, there is a greater proportion of Japanese Americans living in Honolulu County (~18% of the population) than in the other 3 counties (11–14%).³¹ It is also possible that the difference in the incidence among counties may reflect a greater likelihood of physician diagnosis of KS in Honolulu County.

We estimated the incidence of KS for Hawaii residents by excluding nonresidents and multiple hospitalizations for patients. We found that 7.1% of KS hospitalizations for children younger than 5 years of age living in Hawaii represented multiple hospitalizations. Other studies have reported that ~10% of their KS hospitalization records were for multiple hospitalizations.^{10,35} Fewer than 5 of the KS patients were hospitalized again with a principal diagnosis of KS, possibly representing a KS recurrence. The recurrence rate previously was reported to be ~1% in North America and 3% in Japan.³⁷

Hospital discharge data are useful for studying the occurrence and epidemiology of KS because most children with KS are hospitalized;^{7,9,10} however, there are limitations to using such data. First, because physician diagnosis of KS was used to identify hospitalized KS cases, children who did not meet the Centers for Disease Control and Prevention (CDC) case definition for KS may have been included in our study.^{10,21} Some of these cases likely include patients with atypical KS. For epidemiologic studies, the CDC case definition is generally more specific, but it is less sensitive than a physician diagnosis. Medical chart reviews of KS cases identified through state hospital discharge data indicated that >70% met the CDC case definition for KS.^{10,35} Incompleteness of records or miscoding of KS as a different condition may have reduced the reported number of children hospitalized with KS. Furthermore patient's race was not reported for 26 of the KS patients younger than 5 years of age, resulting in an underestimate of the KS incidence among some race

groups. Finally the higher incidence for Japanese American children living in Hawaii than children living in Japan may also be affected by the methodology used in the present study as compared with the studies in Japan.^{2,3}

We found that the incidence of KS among children younger than 5 years of age living in Hawaii was higher than that reported for the continental United States. This difference may be attributable to the high proportion of children of Japanese ancestry residing in Hawaii and also, in part, to the higher rates among white children in Hawaii. We also found that the KS incidence for Japanese American children living in Hawaii was higher than that for children living in Japan, which may indicate the influence of environmental risk factors, as opposed to a purely genetic predisposition, in the etiology of the disease. Given the high KS incidence among children and infants in Hawaii, the monitoring of KS and its effect on children living in Hawaii continues to be important.

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