

# Racial/Ethnic Differences in the Incidence of Kawasaki Syndrome among Children in Hawai'i

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## Abstract

**Objective:** To describe the occurrence of Kawasaki syndrome (KS) among different racial/ethnic groups in Hawai'i.

**Methods:** Retrospective analysis of children <18 years of age, with a focus on children <5 years of age, living in Hawai'i who were hospitalized with KS using the 1996-2006 Hawai'i State Inpatient Data.

**Results:** Children <5 years of age accounted for 84% of the 528 patients <18 years of age with KS. The average annual incidence among this age group was 50.4 per 100,000 children <5 years of age, ranging from 45.5 to 56.5. Asian and Pacific Islander children accounted for 92% of the children <5 years of age with KS during the study period; the average annual incidence was 62.9 per 100,000. Within this group, Japanese children had the highest incidence (210.5), followed by Native Hawaiian children (86.9), other Asian children (84.9), and Chinese children (83.2). The incidence for white children (13.7) was lower than for these racial/ethnic groups. The median age of KS admission for children <5 years of age was 21 months overall, 24 months for Japanese children, 14.5 months for Native Hawaiian children and 26.5 months for white children.

**Conclusions:** The high average annual KS incidence for children <5 years of age in Hawai'i compared to the rest of the United States population reflects an increased KS incidence among Asian and Pacific Islander children, especially Japanese children. The incidence for white children was slightly higher than or similar to that generally reported nationwide.

## Introduction

Kawasaki syndrome (KS) cases were first reported in the United States in Hawai'i in 1976.<sup>1</sup> The KS incidence among children <5 years of age in Hawai'i has been much higher than that for children in the continental United States (9 to 19 cases per 100,000 children <5 years of age).<sup>2-8</sup> The incidence of KS in Hawai'i was 47.7 and 45.2 per 100,000 children <5 years of age during the mid-1990s and 1996-2001, respectively.<sup>4,5</sup> Furthermore, the occurrence of KS has been reported in community-wide outbreaks within Hawai'i and the continental United States.<sup>9,11,12</sup> In both Hawai'i and the continental United States, the incidence of KS has been reported to be high among children with Japanese and other Asian ancestry.<sup>4,5,7,9</sup> A large proportion of children living in Hawai'i have ancestral origins in Asia, which contributed to the overall high rate of KS among children in Hawai'i compared to rate estimates for the continental United States.<sup>2-6,9</sup>

In the present study, we analyzed records for patients <18 years of age hospitalized with KS during 1996 through 2006 using Hawai'i hospital discharge data to describe recent trends of KS and better understand the racial/ethnic-specific incidence of KS among children living in Hawai'i.

## Methods

Hospital discharge records with KS listed as a diagnosis from 1996 through 2006 for patients <18 years of age living in Hawai'i were obtained from the Hawai'i State Inpatient Database (SID).<sup>13</sup> The

Hawai'i Health Information Corporation (HHIC) partners with the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality (AHRQ) to produce the Hawai'i SID.<sup>13,14</sup> The HHIC is a non-profit corporation that was established in 1994 to collect all inpatient data submitted from Hawai'i's 25 acute-care hospitals, representing 100% of the hospitalizations in Hawai'i.<sup>13,14</sup> The KS hospital discharge data obtained on October 2008 included hospitalizations with KS reported by both community hospitals and military/Department of Defense hospitals for the study period.

All hospitalizations for children with an International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM)<sup>14</sup> code for KS (446.1) listed as any one of up to 20 diagnoses on the discharge record were selected for our analysis. Multiple hospitalizations for patients during the study period were identified internally by AHRQ and HHIC through matching admissions by date of birth, sex, and residential zip code (no unique identifiers were available). The records for patients with more than one KS hospitalization were further examined to estimate a rate of KS recurrence. To analyze records by patient, the first KS hospitalization during the study period was selected for analysis; therefore, the patient's age was derived from their first admission with KS and the number of hospitalization days for each patient was summed from all of their KS hospitalizations. Race/ethnicity was described by using the race/ethnicity classification of the children from the hospital discharge records; for those records with missing race/ethnicity, appropriate hospital staff were contacted to review the medical records. Race/ethnicity was not available for 118 (22.3%) children <18 years of age. Race/ethnicity for patients recorded as "mixed or other race" and patients with a missing race/ethnicity was recorded as "other/unknown" by some of the hospitals (54 children <5 years of age had a recorded race of "mixed or other", and 42 patients had a missing race/ethnicity), therefore "mixed or other race" and "other/unknown race" were both considered as unknown for this study. Due to the small number of patients with race/ethnicity coded as either Black or as Hispanic, analysis of these racial/ethnic groups is not provided separately in this study. Thus, for the present study, race/ethnicity was examined for Asian and Pacific Islander and white children; Asian and Pacific Islander children were further analyzed by specific racial/ethnic classifications.

The average annual KS-associated incidence rates were estimated by age group for children <18 years of age, and by sex and race/ethnicity for children <5 years of age. The incidence estimate was calculated as the number of children hospitalized with KS per 100,000 of the corresponding population. In addition, the average annual KS-associated hospitalization rate for children <5 years of age was calculated by using the total number of KS hospitalizations for children <5 years of age per 100,000 children <5 years of age. The KS-associated incidence is reported unless otherwise indicated. The National Center for Health Statistics Bridged Race Vintage

population estimates for the population of children <18 years of age in Hawai'i for 1996 through 2006 were used for the denominator for overall rates, rates by age group, general race group (white and Asian/Pacific Islander), and sex.<sup>16,17</sup> The average annual incidence rate for each detailed racial/ethnic group was estimated for the 11-year study period; the denominator for each of these groups was calculated by summing the 2000 Census with the corresponding census data for each of the other study years (the population for each detailed race group was based on the Census 2000 proportion of each detailed race group).<sup>18</sup> Census 2000 is the most recent census data that provides the population classified by race listed alone or in combination with other races, which was not available in earlier census race classifications.<sup>19</sup> The listed-alone race categories were used for race/ethnicity-specific denominators. Persons indicated as part-Native Hawaiian were considered Native Hawaiian, as reported by the census.<sup>19</sup> Incidence rates were compared using Poisson regression analysis, and age in months for groups was compared using the Wilcoxon rank-sum test.

## Results

During 1996 through 2006, 528 children < 18 years of age accounted for 582 hospitalizations with KS. The 1996-2006 average annual KS-associated incidence rate for children <18 years of age was 16.3 patients per 100,000 children (Table 1). The average annual incidence rate for children <5 years of age (50.4) was significantly higher than those for children 5-9 and 10-17 years of age (8.6 and 0.7, respectively;  $p<0.001$ ). The incidence for children <1 year of age was significantly higher than that for children 1-4 years of age (77.4 and 43.6, respectively;  $p<0.001$ ). The median age of admission for children <18 years of age hospitalized with KS was 2 years of age.

Of the 528 children < 18 years of age, 441 (83.5%) were <5 years of age and accounted for 487 hospitalizations. Forty-four patients <5 years of age (10%) had more than one KS hospital stay, accounting for 9.4% of the hospitalizations. Approximately 1.1% of all KS patients <5 years of age had a second hospitalization with KS as the primary diagnosis occurring  $\geq 3$  months after the first KS hospitalization during the study period.

The 1996-2006 average annual KS-associated incidence rate for children <5 years of age was 50.4 patients per 100,000 children (Table 1). The annual incidence was relatively stable during the study period and ranged from 45.5 to 56.5. The average annual KS-associated hospitalization rate was 55.7 hospitalizations per 100,000 children.

For children <5 years of age, the incidence for boys was higher than the incidence for girls (55.2 and 45.3, respectively;  $p=0.04$ ; Table 1). Among infants, the KS incidence rate was significantly higher for boys than that for girls ( $p=0.001$ ); there was no significant rate difference by sex among children in the 1-4 year old age group.

Asian and Pacific Islander children <5 years of age accounted for 91.6% of the children <5 years of age for whom race information was available; the KS incidence was 62.9 per 100,000. Among Asian and Pacific Islander children, the incidence was higher for infants than that for children 1-4 years of age. The Asian and Pacific Islander infant incidence was higher than that for white infants (104.6 and 4.8 per 100,000 children, respectively,  $p<0.0001$ ). Among all racial/ethnic groups <5 years of age in Hawai'i, Japanese children

Table 1.— Characteristics of Children Hospitalized with Kawasaki Syndrome (KS) and KS Incidence Rates Among Children <18 and <5 Years of Age, Hawai'i, 1996–2006.

Characteristic	Number of Patients (%) <sup>a</sup>	Incidence (per 100,000) <sup>b</sup>
<b>Total (&lt;18 years of age)</b>	528 (100)	16.3
Age group (years) <1	136 (25.8)	77.4
Age group (years) 1–4	305 (57.8)	43.6
Age group (years) 5-9	77 (14.6)	8.6
Age group (years) 10-17	10 (1.9)	0.7
<b>Gender</b>		
Boys	306 (58.0)	18.3
Girls	222 (42.0)	14.2
<b>Children &lt;5 years of age</b>		
<b>Gender</b>		
Boys	249 (56.5)	55.2
<1 year	89 (35.7)	98.2
1–4 years	160 (64.3)	44.4
Girls	192 (43.5)	45.3
<1 year	47 (24.5)	55.3
1–4 years	145 (75.5)	42.8

<sup>a</sup> Proportion of patients is based on the primary group of patients with known data. Percentages may not add to 100% due to rounding.

<sup>b</sup> Average annual incidence rate is the number of children hospitalized with KS per 100,000 children from the corresponding group in the census data during the study period.<sup>16</sup>

had the highest incidence (210.5), followed by Native Hawaiian children (86.9), other Asian children (84.9), and Chinese children (83.2; Table 2). The KS incidence for Japanese children was more than twice that for Native Hawaiian children ( $p=0.01$ ) and much greater than that for white children (13.7;  $p<0.0001$ ).

The median age for children <5 years of age was 21 months (25th and 75th percent quartiles of 10 and 36 months, respectively; Figure 1). The median age of admission for Japanese children <5 years of age was 24 months, and was significantly higher than the median age of Native Hawaiian children (14.5 months;  $p=0.03$ ) and not statistically different from that for white children (26.5 months).

No clear seasonal pattern in KS hospital admissions for children <5 years of age was observed; admissions occurred throughout the study period with a small peak seen in December/January. The median length of hospital stay was 2 days (quartiles = 2 and 3.5 days). No in-hospital deaths were reported among children hospitalized with KS.

## Discussion

The average annual KS-associated incidence among children <5 years of age in Hawai'i for 1996-2006 was 50.4 per 100,000 children. This relatively high KS incidence reflects the high incidence among Asian and Pacific Islander children, especially Japanese children. This incidence was approximately 2.5 times higher than the upper range of the reported incidence for the continental United States (9 to 19 cases per 100,000 children <5 years of age).<sup>2-8</sup> As reported

Table 2.— Race/ethnicity of children hospitalized with Kawasaki syndrome (KS) and KS incidence rate estimates among children <18 and <5 years of age, Hawai'i, 1996–2006.

Race/ethnicity <sup>a</sup>	<18 years of age		<5 years of age	
	Number of Patients (%) <sup>b</sup>	Incidence (per 100,000) <sup>c</sup>	Number of Patients (%) <sup>b</sup>	Incidence (per 100,000) <sup>c</sup>
Japanese	131 (32.4)	57.8	104 (30.8)	210.5
Native Hawaiian	75 (18.6)	27.7	60 (17.8)	86.9
Chinese	21 (5.2)	23.8	18 (5.3)	83.2
Filipino	81 (20.0)	19.0	70 (20.7)	64.5
Other Asian <sup>d</sup>	57 (14.1)	25.0	52 (15.4)	84.9
Other Pacific Islander <sup>e</sup>	12 (3.0)	8.5	12 (3.6)	8.6
White	27 (6.7)	5.0	22 (6.5)	13.7

<sup>a</sup> Race/ethnicity was not reported for 118 patients <18 years of age and 96 patients <5 years of age, therefore the rates and percentages are based on patients with reported race. Incidence rates are not presented for the Black and Hispanic race/ethnic groups, as there were few children reported in these categories. Percentages may not add to 100% due to rounding.

<sup>b</sup> Proportion of patients is based on the primary group of patients with known data.

<sup>c</sup> The average annual incidence rate is the number of children hospitalized with KS during the study period per 100,000 children from the corresponding group. This incidence was estimated by using the 2000 Census for detailed race data, and the census data for the other study years as the proportion of the detailed race groups for the Census 2000 data.<sup>17</sup>

<sup>d</sup> Census for other Asians includes persons who provide a response of Korean, Vietnamese, Cambodian, Hmong, Laotian, Asian Indian, and others, or other Asian not specified.<sup>18</sup>

<sup>e</sup> 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.<sup>18</sup>

in previous studies, the KS incidence approximates 90% of the KS hospitalization rate; this percentage takes into account multiple KS hospitalizations.<sup>3,20</sup> Although the KS incidence in Hawai'i was strikingly higher than in the continental United States, the median age of children <5 years of age with KS in Hawai'i (22 months) and in the overall US population (23–24 months) was similar.<sup>7,8</sup> The incidence of KS varies by race/ethnicity; studies have described a particularly high KS incidence among Asian children.<sup>4,7–9</sup> The high KS incidence among children <5 years of age in Hawai'i is likely due to the large population of Asian children in Hawai'i. The incidence for white children was lower than the incidence for the other reported racial/ethnic groups in Hawai'i and was slightly higher than or similar to those estimated for white children in the general US population.<sup>7,8</sup> The reported KS hospitalization rate for non-Hispanic white children in the general US population was 11.4 (95% CI=10.5–12.4) for 2000 and 12.0 (95% CI=10.2–13.8) for 2006.<sup>7,8</sup> The observed average annual KS incidence for Japanese-American children <5 years of age remains the highest among children of racial/ethnic groups living in Hawai'i, and appears to be slightly higher than or similar to that reported for children <5 years of age living in Japan where the KS incidence rate was 184.6 cases per 100,000 children <5 years of age for 2005–2006.<sup>21</sup>

The observed differences in KS incidence by race/ethnicity in Hawai'i likely reflect important racial/ethnic differences in genetic susceptibility to KS. Other factors such as environmental factors, access to health care, the index of suspicion and awareness of physicians for KS, and geographic location or culture among Asian populations may affect KS incidence.<sup>4</sup> At the Ninth International Kawasaki Disease Symposium, several investigators reported on progress in identifying genetic susceptibility factors for KS.<sup>22, 23</sup>

Approximately 10% of the hospitalizations represented multiple admissions for KS. A small number of patients were admitted for a hospitalization with KS as the primary diagnosis at least three months after an initial KS hospitalization, representing an estimated recurrence rate of 1.1%. This rate falls close to previously reported recurrence rates in North America (1%) and Japan (approximately 3%).<sup>24</sup>

This study used statewide hospital discharge data with KS listed as a diagnosis and has some limitations. These data are physician diagnosis-based and likely include patients that may not meet the epidemiologic KS case definition.<sup>3,25</sup> In addition, incompleteness of records and diagnostic miscoding may have occurred. Patients' race/ethnicity was classified at the hospital into one racial/ethnic group, where a patient may be of more than one race/ethnicity. Incompleteness of patient's race/ethnicity on hospital records (21.8%), which includes the classification of other and unknown race together, may have led to underestimation of the KS incidence among some of the race/ethnic groups. The 2000 Census data for Hawai'i were used to estimate the incidence of KS for the racial/ethnic groups; population estimates for each racial/ethnic group alone were used, which does not account for persons of mixed race/ethnicity. Furthermore, the assignment of patients' race/ethnicity by the hospitals in Hawai'i might differ from the race/ethnicity of the census denominator and thereby alter the incidence in some racial/ethnic groups. Overall, differences between the incidence determined in the present study with incidences reported for Asian countries and the United States may be partially influenced by differences in reporting, diagnosis, and study design.<sup>4, 10</sup>

The incidence of KS in Hawai'i remains high, reflecting the high incidence among Asian and Pacific Islander children, especially Japanese children. White children, compared to Asian and Native Hawaiian children, had a lower incidence in Hawai'i, which was similar to or slightly higher than the rates reported for white children in the continental United States. Further efforts in the study of KS, and the monitoring of the occurrence of KS among children in Hawai'i, including racial/ethnic incidence differences, remain important.

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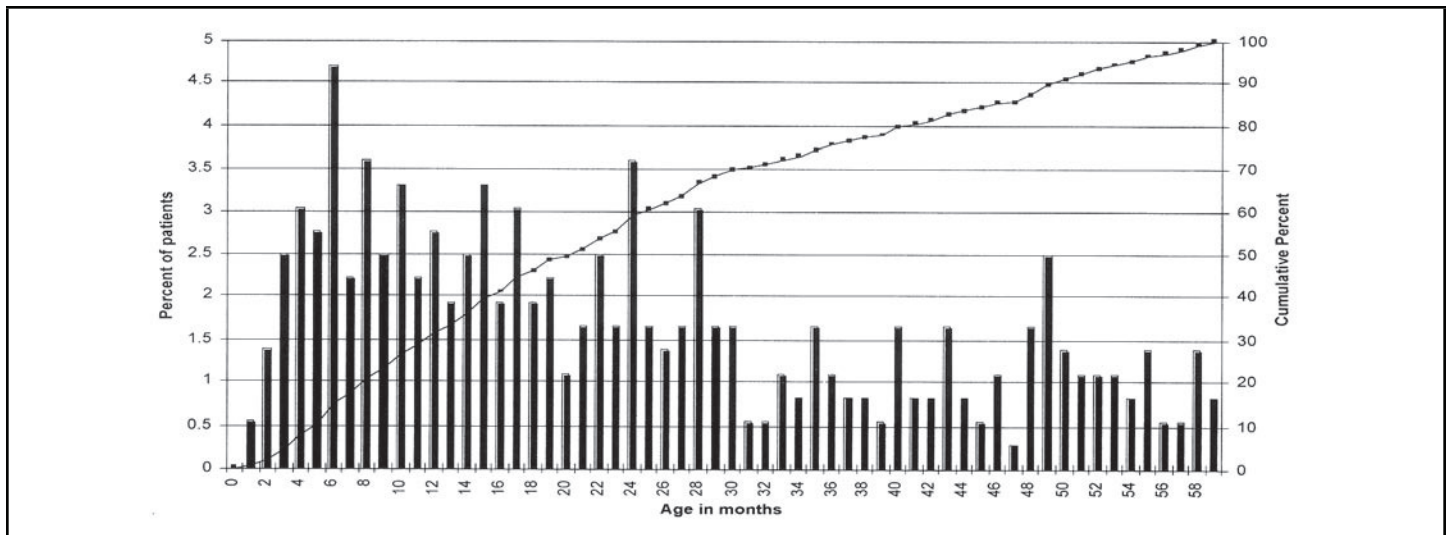


Figure 1.— Proportion of Children <5 Years of Age Hospitalized with KS by Month of Age, Hawai'i, 1996-2006.

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