

Kawasaki Syndrome Hospitalizations and Associated Costs in the United States

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SYNOPSIS

Objectives. To describe the epidemiologic characteristics of patients hospitalized with Kawasaki syndrome (KS) and estimate associated costs in the United States, using a large national hospital discharge dataset.

Methods. Hospitalization discharge records with KS for 1997 through 1999 for U.S. residents <18 years of age were selected from Solucient's hospital discharge records. These records are collected from most of the self-governing children's hospitals and approximately one-third of short-term, non-federal general hospitals in the United States.

Results. A total of 7,431 hospital discharges with a KS diagnosis were identified; 2,270 of the discharges were in 1997, 2,700 in 1998, and 2,461 in 1999. Boys comprised 60.0% of the discharges, and 76.4% of discharges were among children ages <5 years. For the 44 states and the District of Columbia with at least one hospital reporting KS, the average annual KS hospitalization rate was 10.2 per 100,000 children ages <5 years. The KS hospitalization rate for boys (12.0 per 100,000) was higher than that for girls (8.3 per 100,000) (risk ratio 1.45; 95% confidence interval 1.37, 1.52). Extrapolation to the U.S. population showed an estimated average annual KS hospitalization rate of 21.6. The median KS hospitalization cost for children <5 years of age during the study period was \$6,169.

Conclusions. The KS hospitalization rate was consistent with that of previous U.S. studies, although the extrapolated rate may be an overestimation. The median hospitalization cost for KS was higher than that for respiratory syncytial virus-associated bronchiolitis and diarrheal diseases. Large hospitalization datasets can be used to monitor the occurrence of KS in the United States.

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Kawasaki syndrome (KS) is characterized by an acute febrile vasculitis of unknown etiology. The vasculitis is most severe in medium-sized arteries and can result in a range of cardiovascular complications including coronary artery aneurysm, which can occur in about 20% of untreated KS patients.¹ In most cases, the coronary artery aneurysm will resolve completely or regress in size, but in some patients it may lead to long-term sequelae such as coronary artery stenosis or obstruction, and myocardial ischemia. Early treatment with intravenous immunoglobulin has been shown to markedly reduce the rate of occurrence of cardiac complications.²

About 80% of patients with KS are younger than 5 years of age and more than half of the patients are boys. In the United States, the incidence of KS among children <5 years of age is highest among Asians and Pacific Islanders, followed sequentially by blacks and whites.^{3,4} The incidence of KS in Japan is about five times the incidence in the continental United States and about two times the incidence in Hawaii.⁵ Studies have reported that a vast majority of KS patients are hospitalized in the United States, indicating that hospitalization data can be used to monitor the occurrence of KS.^{6,7} To describe the epidemiologic characteristics of patients hospitalized with KS and estimate the cost associated with these hospitalizations, we analyzed a large hospital discharge dataset with information collected from many hospitals within the United States.

METHODS

KS hospital discharge data were obtained from Solucient LLC for the period 1997–1999. Solucient is a private company that maintains the nation's largest health care database and provides information resources to many hospitals and large pharmaceutical manufacturers in the United States. Hospitalizations associated with KS were identified by using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code for KS (446.1).⁸ Hospitalizations with KS as a primary diagnosis or listed anywhere on the discharge record were included in the analysis. Non-U.S. resident and duplicate records were excluded, and our analysis was limited to hospitalizations among patients <18 years of age. Hospitalizations with a coronary artery aneurysm listed with KS were identified, using ICD-9-CM code 414.11.⁸

Solucient collects hospital discharge records from over 90% of self-governing children's hospitals that are members of the National Association of Children's Hospitals and Related Institutions (NACHRI) and care

for patients with conditions normally requiring a stay of less than 30 days. In addition, Solucient collects discharge records from approximately one-third of short-term, non-federal general hospitals in the United States. Information collected in the hospital discharge records included patients' demographic characteristics, residence ZIP Code, dates of hospital admission and discharge, length of hospital stay, and hospital charges. The hospital discharge database contains information on more than 17 million discharges occurring in the United States each year, including about 3.5 million discharges of pediatric-age patients. The database has been described in previous reports.^{9–11}

We examined KS-associated hospitalizations and rates by age, sex, and geographic regions. The geographic regions were defined on the basis of census region descriptions of the U.S. Bureau of the Census. The KS hospitalization rates were calculated for the states with at least one hospital reporting a KS hospitalization by using the 1997–1999 U.S. population estimates for the corresponding group as the denominator.¹² Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using Poisson regression analysis.¹³ The number of KS hospitalizations over time by month and year of admission was examined for a possible seasonal occurrence of KS. A possible seasonal variation in KS hospitalizations was further assessed by comparing the cumulative number of KS hospitalizations reported from December through May with that reported from June through November. The age and sex of patients with coronary artery aneurysm listed in the KS hospitalization records were compared with those without coronary artery aneurysm.

For selected variables, the weighted number of national KS hospitalizations was estimated by using Solucient's weighting methodology. To calculate the weights, the stratifying characteristics were based on age, sex, inpatient bed service, the U.S. census region, number of hospital beds, and teaching status of the hospital. The overall weighted rate was calculated using the 1997–1999 census data as the denominator.¹² We estimated the cost associated with KS hospitalizations on the basis of both the observed and the weighted numbers of hospitalizations, and compared the median cost of hospitalization for KS with that reported for several other common childhood diseases. The KS hospitalization costs in the database reflect the total hospital costs charged to the payer.

RESULTS

A total of 7,431 hospital discharges with a diagnosis of KS were identified in the Solucient hospital discharge

database for patients <18 years of age; 2,270 of the discharges were in 1997, 2,700 in 1998, and 2,461 in 1999. For 6,738 (90.7%) of the total discharges, KS was listed as a primary diagnosis in the hospital discharge record. Overall, 4,461 (60.0%) of the discharges were for boys and 5,674 (76.4%) of discharges were for children <5 years of age. The peak age of KS hospitalization was at 1 and 2 years of age (Figure 1). The median age of patients discharged with a KS diagnosis was 2 years. For the 44 states and the District of Columbia with at least one hospital reporting a KS discharge, the average annual KS hospitalization rate was 10.2 per 100,000 children <5 years of age. The KS hospitalization rate for boys (12.0) was significantly higher than that for girls (8.3) (RR 1.45; 95% CI 1.37, 1.52). The KS hospitalization rates for the Northeast and Midwest regions were significantly higher than that reported for the West region, probably due to a lower number of hospitals in the West region contributing to Solucient's database (Table 1).

Table 1. The age, sex, and geographic distribution of patients <18 years of age hospitalized with Kawasaki syndrome in hospitals contributing discharge data to Solucient, United States, 1997–1999

Characteristic	Number (percent)	Rate (RR; 95% CI) ^a
Age group (years)		
0–4	5674 (76.4)	10.2 (Reference)
5–9	1419 (19.1)	2.4 (0.24; 0.23, 0.25)
10–14	283 (3.8)	0.5 (0.05; 0.04, 0.06)
15–17	55 (0.8)	0.2 (0.02; 0.01, 0.02)
Sex		
Male	4461 (60.0)	12.0 (1.45; 1.37, 1.52) ^b
Female	2970 (40.0)	8.3 (Reference) ^b
Regions		
South	2558 (34.4)	9.6 (1.06; 0.99, 1.14) ^b
Midwest	1677 (22.6)	10.6 (1.17; 1.08, 1.26) ^b
Northeast	1638 (22.0)	12.6 (1.40; 1.29, 1.51) ^b
West	1558 (21.0)	9.0 (Reference) ^b
Year		
1997	2270 (30.6)	9.4 ^b
1998	2700 (36.3)	11.1 ^b
1999	2461 (33.1)	10.2 ^b
Total	7431 (100.0)	

^aRates were calculated after excluding six states that did not report a KS hospitalization and are expressed per 100,000 individuals for the corresponding groups.

^bThe hospitalization rates are for children <5 years of age.

Figure 1. Age distribution of patients <18 years of age hospitalized with a diagnosis of Kawasaki syndrome in hospitals contributing to Solucient data, United States, 1997–1999

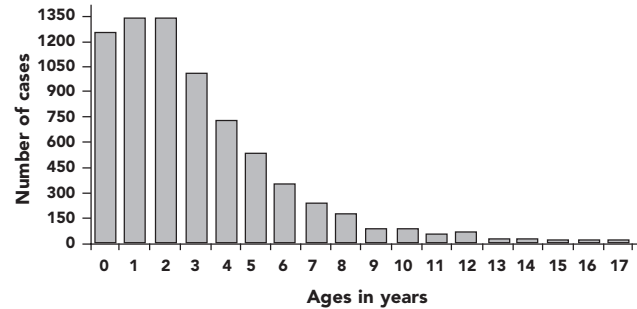
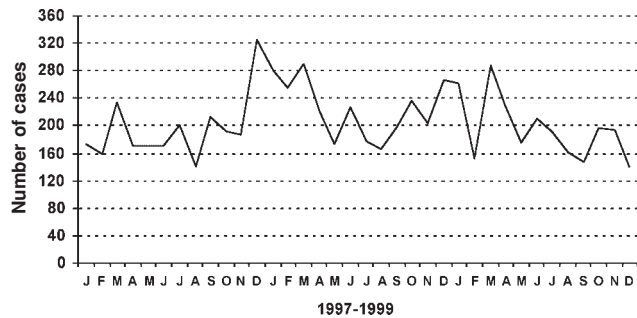


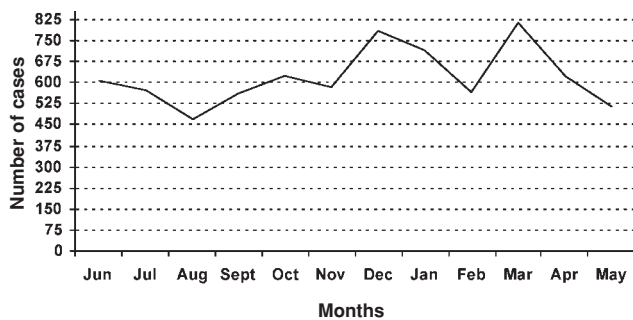
Figure 2. Kawasaki syndrome hospitalizations among patients <18 years of age by month and year of admission in hospitals contributing to Solucient data, United States, 1997–1999



KS hospitalizations by month of admission for each of the three years is shown in Figure 2, and reveals that the highest two monthly totals each year occurred in January, March, or December. Cumulatively, the increased number of cases in these three months is illustrated in Figure 3. For the six-month period from December through May, a total of 4,014 (54%) KS hospitalizations were reported compared with 3,417 (46%) hospitalizations reported for June through November.

Coronary artery aneurysm was reported on 197 (2.7%) of the 7,431 hospitalizations. Patients with coronary artery aneurysm were more likely to be boys (RR 1.76; 95% CI 1.29, 2.40), <1 year old (RR 2.61; 95% CI 1.96, 3.48), or >8 years of age (RR 1.80; 95% CI 1.15, 2.84). The rate of KS-associated coronary artery aneurysm based on Solucient's records was about 2.7 per million children <5 years of age. Six patients with KS died (hospital case-fatality rate 0.08%); their ages

Figure 3. Cumulative number of Kawasaki syndrome hospitalizations among patients <18 years of age by month of admission in hospitals contributing to Solucient data, United States, 1997–1999



ranged from 6 months to 17 years (median: 8.5 years), and five were boys.

The average annual estimated cost associated with KS hospitalizations among patients <18 years of age in the Solucient database was at least \$18.4 million, and the overall median length of hospital stay was three days (range: 1–55 days). The total hospitalization cost during 1997–1999 was in excess of \$55.1 million. The median cost of KS hospitalizations was \$6,447 for patients <18 years of age, and \$6,169 for patients <5 years of age. This latter median hospitalization cost for children <5 years of age was higher than that reported during a comparable period for hospitalizations due to respiratory syncytial virus (RSV)-associated bronchiolitis, diarrheal diseases, and rotavirus disease (Table 2). The median hospitalization cost for KS patients with coronary artery aneurysm was \$7,439 for all ages and \$7,025 for children <5 years of age.

Extrapolation of Solucient data to the total U.S. population showed that a total of 15,988 KS hospitalizations may have occurred during 1997–1999, for an estimated average annual hospitalization rate of 21.6 per 100,000 children <5 years of age. The average annual estimated cost associated with KS hospitalizations among patients <18 years of age after extrapolation of Solucient data to the U.S. population was \$38.6 million.

DISCUSSION

Our analysis of Solucient’s large hospital discharge database containing information from many hospitals across the United States indicated that the number of KS-associated hospitalizations during 1997–1999 was relatively stable. The age and sex distribution of KS

Table 2. Estimated median hospitalization cost associated with Kawasaki syndrome compared with that associated with other childhood diseases for children <5 years of age, United States

Disease	Median hospitalization cost ^a
Kawasaki syndrome	\$6169
RSV-associated bronchiolitis ¹⁸	\$4320
Diarrheal diseases ¹⁹	\$2307
Rotavirus disease ¹⁹	\$2303

RSV = Respiratory syncytial virus

^aMedian hospitalization cost for KS is for 1997–1999, whereas the costs for RSV-associated bronchiolitis, diarrheal diseases, and rotavirus disease are expressed in 1998 U.S. dollars.

patients identified in this large dataset were similar to those reported in other studies in the United States.^{3–5} Similarly, the KS hospitalization rate for children <5 years of age (10.2) was within the range reported in previous studies for the continental United States.^{5,14} The KS hospitalization rate from the observed number of hospitalizations may be underestimated because KS patients admitted to hospitals not contributing to Solucient’s hospital discharge database are not included in our analysis. On the other hand, the extrapolated rate (21.6) may have overestimated the KS hospitalization rate. Multiple hospitalizations for the same episode of KS, which have been consistently reported to account for as many as 10% of KS hospitalizations,^{3,15,16} may have led to an overestimation of the incidence of KS. We believe that the KS hospitalization rate is higher than 10.2 per 100,000 children <5 years of age, and perhaps lower than the weighted rate of 21.6. The higher rate of KS among boys than girls has been documented in previous studies.^{1,15} Although the West region appears to have a lower KS hospitalization rate than other regions, this difference is probably due to a lower number of hospitals in the West region contributing their hospital discharges to the database. In addition, our data did not include KS hospitalizations from Hawaii, a state with the highest reported incidence of KS in the United States.^{3,5}

In the past, a clear seasonal variation in the occurrence of KS was primarily reported during epidemic years. The seasonal variation was less clear during non-epidemic years.¹ In a Japanese nationwide epidemiologic survey of KS, a lower number of patients in the fall with absence of a clear seasonal variation was reported for the non-epidemic years of 1995 and 1996.¹⁷ The large number of KS hospitalizations in our study

enabled us to closely examine the possible seasonal occurrence of KS in the United States during what would be considered as non-epidemic years. Although a tendency for more KS hospitalizations during December, January, and March was observed, KS hospitalizations occurred consistently throughout the year.

Hospital discharge datasets such as Solucient's can be used to monitor the occurrence of KS in the United States. Hospital discharge data are readily available and should be exploited for surveillance of diseases that commonly lead to hospitalization of patients. Because a vast majority of KS patients are hospitalized in the United States, hospital discharge data can be a very good source of information for KS surveillance.^{5,7} A Georgia study evaluating the usefulness of hospital discharge data for KS surveillance indicated that the ICD-9-CM code for KS identified the physician diagnosis of KS in over 90% of the discharges. The study also indicated that the accuracy of such databases for KS surveillance can be increased, whenever possible, by excluding multiple hospitalizations for the same person and by limiting the analysis to patients <18 years of age.¹⁵ In our study, we excluded duplicate records and limited our analysis to patients <18 years of age. However, we were unable to control for possible multiple hospitalizations because critical variables such as date of birth were not available to create an appropriate algorithm. Several studies have consistently reported that about 10% of hospital discharge records may represent multiple hospitalizations for the same episode of KS.^{3,15,16}

In our study, we have estimated for the first time the cost associated with KS hospitalizations. The median hospitalization cost for KS was higher than that reported for RSV-associated bronchiolitis, diarrheal diseases, and rotavirus disease.^{18,19} This may be due to the expensive treatment of KS patients with high dose intravenous gamma globulin, which is recommended as the mainstay treatment for KS to reduce the occurrence of cardiac complications. However, the overall hospitalization costs associated with bronchiolitis, diarrheal diseases, and rotavirus disease were higher than for KS, owing to their relatively higher incidence in the United States. The annual KS-associated hospitalization cost based on Solucient data may have underestimated the hospitalization cost for KS because patients admitted to hospitals not contributing to Solucient were not included in our analysis. Moreover, the hospitalization cost underestimates the overall expenditure related to KS because costs associated with outpatient care of KS patients are not included in our study. Many KS patients would have had some of their clinical and laboratory investigations performed be-

fore hospital admission and also as a follow-up after discharge from the hospital to monitor the progression of their illness. The median cost of hospitalization was higher by about \$1,000 for KS patients with coronary artery aneurysm than for those without coronary artery aneurysm.

In summary, our analysis of Solucient's large hospital discharge database confirmed the epidemiologic characteristics of KS patients reported in previous studies, including a higher KS incidence among boys and the occurrence of KS throughout the year with a tendency for more cases during winter and spring. Patients who developed coronary artery aneurysm were more likely to be boys, infants <1 year of age, or older children >8 years of age. Hospital discharge data analysis can be a valuable tool for monitoring the occurrence of KS in the United States.

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