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# An Evaluation of Hospitalizations for Kawasaki Syndrome in Georgia

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**Objective:** To evaluate and describe the epidemiologic characteristics of Kawasaki syndrome (KS) hospitalizations in Georgia.

**Design:** We reviewed hospital discharge data and corresponding medical records for Georgian patients discharged with a KS diagnosis during 1997 and 1998.

**Results:** During the study period, 233 KS hospital discharges were recorded in Georgia; 177 (76%) were for children younger than 5 years. Twenty-one (9%) of 233 of the hospital discharges represented multiple hospitalizations. Medical records for 211 KS discharges (91%), representing 197 patients (93%), were reviewed. For those 189 patients whose medical records were reviewed and had sufficient information, 139 (74%) either had a documented illness that met the Centers for Disease Control and Prevention (CDC) definition for KS (n=135) or had coronary artery abnormalities without meeting the CDC definition for KS (atypical KS; n=4). Eight patients had only a history of KS. Excluding multiple hospitalizations and patients with only a history of KS, 158 hospitalizations were for patients younger than 5 years (14.0 per 100 000 children); 110 of these patients met the KS or atypical KS definition (9.8 per 100 000 children).

**Conclusions:** Hospital discharge data are useful for KS surveillance. However, analysis of hospital discharge data may slightly overestimate the KS hospitalization rates because some discharges may represent multiple hospitalizations or hospitalizations of patients with only a history of KS. The incidence and epidemiology of KS in Georgia are consistent with findings from other continental US studies. Physicians should exercise their best clinical judgment in identifying and treating patients with KS who may not meet standard case definitions.

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KAWASAKI SYNDROME (KS), an illness of unknown origin, occurs worldwide, with the highest incidence in Japan.[1] In the United States and Japan, KS is the leading cause of acquired heart disease among children.[2] The most serious cardiac complications of KS are coronary artery abnormalities (CAA).[3] Timely treatment of patients with KS with intravenous immunoglobulin (IVIG) and aspirin has been reported to reduce the rate of occurrence of CAA.[1-3]

The epidemiologic characteristics of KS in the United States have been described in previous studies.[4-11] Some studies have analyzed hospital discharge data, and several of these studies have compared physician diagnosis of KS with a specific KS case definition.[5,7,11] A recent report[11] from a large, pediatric hospital in Utah showed that the proportion of patients diagnosed as having KS that did not meet a specific case definition increased from 27% during 1991 to 1994 to 45% during 1995 to 1997, indicating a need for a timely reevaluation of this issue among patients from a variety of hospitals in different settings.

In this study, we examined patients discharged with a diagnosis of KS using the Georgia hospital discharge data for 1997 and 1998. We reviewed the patients' medical records to compare their clinical signs and symptoms with the Centers for Disease Control and Prevention (CDC) case definition for KS[12] and to evaluate the usefulness of hospital discharge records for KS surveillance.

## RESULTS

During 1997 and 1998, 233 hospital discharges for KS in Georgia were identified; in 214 (92%) of these discharges, KS was listed as the primary diagnosis. The KS hospitalization rate for children younger than 5 years (n=177 hospitalizations) was 15.7 per 100 000 children. These 233 discharges represented 212 patients and were

## METHODS

Hospital discharge data for KS hospitalizations in Georgia during 1997 and 1998 were obtained from the Division of Public Health, Georgia Department of Human Resources, Atlanta. A KS hospitalization was defined as one with the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) discharge code 446.1 listed as one of the diagnoses on the discharge record.[13] The county of residence was used to examine the geographic distribution and define residence as urban (metropolitan statistical areas) or nonurban.[14]

Hospital discharge records for KS were examined, and patients as the unit of observation were identified for further study. Patients with multiple hospitalizations were identified by the medical record number and by using an algorithm based on the date of birth, sex, and county of residence and further assessed during the medical record review. For patients with multiple KS hospitalizations within 1 year, their hospitalizations were considered as part of the same episode of KS; the length of stay and the signs and symptoms were combined for analysis.

The hospitals that reported having discharged patients with a diagnosis of KS during the study period were contacted by letter and telephone to arrange for review of medical records. These medical records were then reviewed, and information was obtained on demographics, illness characteristics, treatment with IVIG, and the presence of CAA. The Institutional Review Board of the Georgia Department of Human Resources approved this study.

Patients were classified on the basis of the CDC KS case definition.[12] This case definition includes the presence of fever for 5 or more days, or fever until the date of IVIG administration if it is given before the fifth day of fever, and any 4 of the following 5 criteria: (1) bilateral conjunctival injection, (2) oral changes (erythema of the lips or oropharynx, strawberry tongue, or drying or fissuring of the lips), (3) peripheral extremity changes (edema, erythema, or desquamation), (4) rash, and (5) cervical lymphadenopathy (at least one node ≥1.5 cm in diameter). Patients whose illness did not meet these criteria, but who had fever and CAA, were classified as having atypical KS.[12]

The epidemiologic and clinical characteristics of patients whose illness met the CDC criteria for KS or atypical KS were compared with those whose illness did not. Categorical variables were compared using the $\chi^2$ or Fisher exact test (2-tailed), as appropriate, and continuous variables were compared by using the Wilcoxon rank sum test.[15] Average annual KS hospitalization and incidence rates (per 100 000 children) for children younger than 5 years in Georgia were calculated by using the Georgia state census population.[16,17] Risk ratios with 95% confidence intervals were calculated using Poisson regression analysis.[18]

from 40 different hospitals in Georgia (**Figure 1**A); 21 (9%) of the 233 discharges were for multiple hospitalizations of 18 patients (8%). Of these 18 patients, 15 (83%) were readmitted or transferred within 1 month of the previous discharge; records of 2 of the remaining 3 patients were reviewed, and only 1 met the KS case definition. Medical records for 211 KS discharges (91%), representing 197 patients (93%), were reviewed. Most patients with KS (75%) were hospitalized in urban hospitals. Eight hospitals that reported discharging 9 patients with KS did not participate in the study.

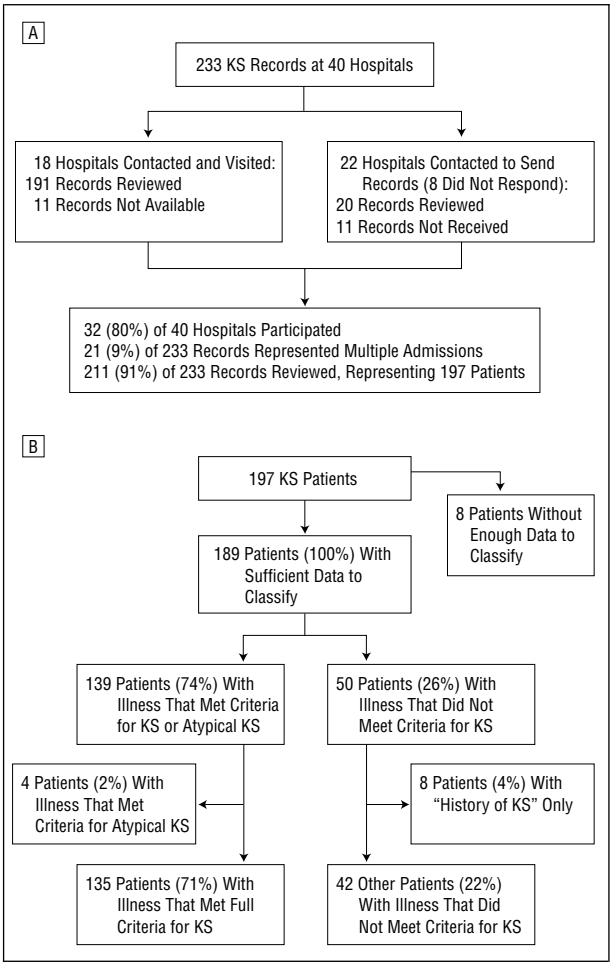


**Figure 1.** A, Flowchart of study of Kawasaki syndrome (KS) hospitalizations, Georgia, 1997-1998. B, Flowchart of study of the medical records of patients with physician-diagnosed KS, Georgia, 1997-1998.

Sufficient data to assess the KS case status were available for 189 of the 197 patients whose medical records were reviewed (**Table 1**). The case definition for KS (n=135) or atypical KS (n=4) was fulfilled by 139 (74%) of the 189 patients (Figure 1B). Of the 135 patients whose illness met the KS case definition, 53 met all the criteria, 19 met at least 4 criteria with the status of 1 criterion unknown, and 63 met 4 of 5 criteria. Eight (4% of the total patients) of the 50 patients who did not meet the case definition for KS or atypical KS had only a history of KS reported at the time of hospitalization; 5 of these 8 patients were the only patients 18 years or older, and 2 patients were younger than 5 years. Therefore, 139 (76%) of 184 patients met the KS case definition when restricting to patients younger than 18 years and 139 (77%) of 181 when excluding patients with only a history of KS. Excluding multiple hospitalizations (n=17) and those with only a history of

KS (n=2) for children younger than 5 years, there were 158 patients younger than 5 years.

Age, sex, urban residence, and characteristics of treatment received did not differ significantly between those patients whose illnesses met and did not meet the KS definition (**Table 2**). Intravenous immunoglobulin was given to 97% of those whose illness met the KS case definition, 90% of those whose illness did not meet the definition, and 75% of those with insufficient data to classify. Among those patients whose illness met the KS case definition, the proportions for individual symptom criteria were as follows: oral mucosal changes, 98%; rash, 97%; conjunctival injection, 94%; extremity changes, 86%; and cervical adenopathy, 58%. For those patients whose illness did not meet the case definition, both extremity changes (29%) and cervical adenopathy (21%) were infrequently reported. Among patients younger than 18 years, the proportions of patients meeting the KS case definition did not differ between those with a primary diagnosis of KS and those with a secondary KS diagnosis (132 [76%] of 174 and 7 [70%] of 10, respectively).

At least one echocardiogram report was available for review for 122 (90%) of the 135 patients whose illness met the KS case definition, all 4 patients with atypical KS, and 30 (71%) of the 42 patients who did not meet the criteria. Fifteen (12%) of the 122 patients had evidence of CAA. Seven of these 15 patients had an echocardiogram positive for CAA within 10 days of KS onset; the remaining 8 patients did not have an echocardiogram within 10 days of onset. All of those 15 patients with CAA had dilations of the arteries, and 4 also had aneurysms. All patients with CAA received IVIG treatment; however, 8 (53%) of 15 of these patients received it within 10 days of illness onset compared with 97 (94%) of 103 patients without CAA who had a known date of IVIG treatment ($P<.001$). For the 7 patients with CAA and delayed IVIG treatment, the treatment was administered a median of 15 days after illness onset.

Most hospitalizations (79%) for patients whose illness met the KS or atypical KS case definition were for children younger than 5 years (Table 2, **Figure 2**). Hospitalizations occurred year-round, with a peak during May and June (26%). The geographic distribution of KS cases was consistent with the distribution of the population of children younger than 5 years in Georgia. No deaths were reported for patients with KS.

For children younger than 5 years, the average annual incidence for patients with physician-diagnosed KS was 14.0 per 100 000 children; for those children whose illness met the criteria for KS or atypical KS, the average annual incidence was 9.8 per 100 000 children (**Table 3**). Although a higher proportion of boys had KS than girls, the difference was not significant. The incidence between patients younger than 1 year and those 1 to 4 years old did not differ. The incidence for Asian children was highest and was at least 4 times greater than that for white children. The incidence for Asian children was almost twice that for black children, although it was not significantly higher.

**Table 1. Number of Patients Discharged With a Diagnosis of Kawasaki Syndrome (KS) by Criteria Status, Georgia, 1997 and 1998**

| Category of KS Criteria | No. (%) of Patients |
|---|---|
| KS case definition | 135 (68.5) |
| Atypical KS | 4 (2.0) |
| Fever criterion and 3 of 5 standard criteria* | 31 (15.7) |
| Fever criterion and 2 of 5 standard criteria* | 12 (6.1) |
| Fever criterion and 1 of 5 standard criteria* | 1 (0.5) |
| Fever criterion and 0 of 5 standard criteria* | 1 (0.5) |
| Not meeting fever criterion | 5 (2.5) |
| Remote history of KS only† | 8 (4.1) |
| **Total** | **197** (100) |

*If a criterion was unknown for a given patient, it was assumed to be absent. For 8 of these patients, insufficient data were available to determine if they met the KS definition.

†Patients hospitalized with only a history of KS, although KS was listed as a diagnosis.

## COMMENT

In this statewide review of medical records of Georgian children hospitalized with KS, 74% of patients with an *ICD-9-CM* code for KS listed on their discharge record met the CDC case definition for KS or atypical KS. This proportion is comparable to the 73% reported by Dykewicz et al,[7] whose study was based on hospital discharge data

**Table 2. Characteristics of Patients With a Diagnosis of Kawasaki Syndrome (KS) by Case Definition Status, Georgia, 1997 and 1998**

| Characteristic | Met KS Case Definition* (n = 139) | Did Not Meet KS Case Definition† (n = 42) | *P* Value |
|---|---|---|---|
| Median age, mo (range) | 31 (3-148) | 35 (4-173) | .5 |
| Male, No. (%) | 78 (56) | 27 (64) | .4 |
| Urban residence, No. (%) | 108 (78) | 29 (69) | .2 |
| Received IVIG, No. (%)‡ | 134 (97) | 38 (90) | .1 |
| Received >1 IVIG treatment, No. (%) | 18 (13) | 3 (7.1) | .4 |
| Median No. of days in hospital (range) | 3 (0-13) | 3 (1-13) | .6 |
| Median No. of days to IVIG treatment (range) | 6 (0-54) | 6 (1-24) | .3 |
| Median No. of days with fever (range) | 5 (1-51) | 6 (1-15) | .5 |

*Met Centers for Disease Control and Prevention case definition for KS or atypical KS.

†Patients with illness that did not meet the KS case definition, excluding patients with a history of KS (n = 8) and patients with insufficient data to classify (n = 8).

‡Intravenous immunoglobulin (IVIG) treatment is unknown for 1 patient whose illness met the KS case definition.

and other sources of data. Exclusion of patients with a history of KS indicated that 77% of physician-diagnosed KS cases met the KS case definition. This percentage is greater than the 64% reported in a similar study recently published by Witt et al[11]; however, it may reflect the difference in the KS case definitions used. Witt and colleagues used a case definition requiring fever for 5 days or more regardless of the timing of IVIG treatment, and early treatment could reduce the duration of fever.

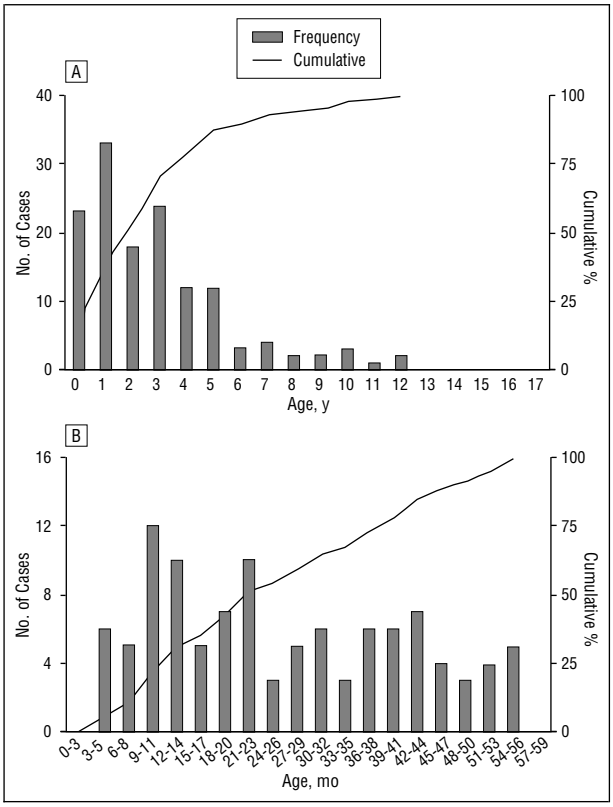


**Figure 2.** A, Age distribution by year of patients whose illness met the Kawasaki syndrome (KS) case definition, Georgia, 1997-1998 (n=139). B, Age distribution by month of patients younger than 5 years whose illness met the KS case definition, Georgia, 1997-1998 (n=107).

Our data should not be interpreted to imply that the patients not meeting the CDC case definition did not have KS, because several factors other than misdiagnosis of an illness similar to KS could account for this discrepancy. First, increased awareness of KS and its complications may lead to reluctance of clinicians to withhold effective IVIG therapy for patients whose illnesses do not meet the KS diagnostic criteria. The administration of IVIG early in the course of the disease may also prevent the appearance of the typical clinical signs of KS. Second, incomplete documentation of KS clinical signs may have affected our findings that relied exclusively on retrospective review of medical records. Notably, the 2 criteria reported least frequently in patients not meeting the case definition—cervical adenopathy and extremity changes—may have been less rigorously documented. Third, some patients with KS may have an atypical presentation without exhibiting the full range of signs and symptoms of the disease. Such patients may actually benefit from early diagnosis and treatment to reduce the likelihood of cardiac complications. Physicians should exercise their best clinical judgment in identifying and treating these patients.

Two findings of our review are relevant for reducing the likelihood of overestimating KS incidence in future studies that use hospital discharge data. First, multiple hospitalizations, resulting from transfer to a different facility or rehospitalization for the same KS episode, may have occurred for 18 patients. The use of a unique patient identifier, if available, or an algorithm based on variables such as age, sex, and dates of hospitalization might allow detection of these multiple hospitalizations without review of the medical records. Second, 8 patients had only a history of KS and were hospitalized for an unrelated illness; 5 of these patients were 18 years or older. None of the cases that met the KS definition were 18 years or older. Therefore, the specificity of KS surveillance based on hospital discharge data could be improved by restricting the analysis to patients younger than 18 years. Other factors that may affect the incidence in a statewide hospitalization study, but may not be easily accounted for, include the possibility of diagnostic

**Table 3. Kawasaki Syndrome (KS) Incidence for Characteristics of Children Younger Than 5 Years, Georgia, 1997 and 1998***

| | All Patients With KS | | Met KS Case Definition | |
|---|---|---|---|---|
| **Characteristic** | **Rate† (No.)** | **RR (95% CI)** | **Rate† (No.)** | **RR (95% CI)** |
| Age, y | | | | |
| <1 | 12.3 (28) | 0.9 (0.6-1.3) | 10.1 (23) | 1.1 (0.7-1.7) |
| 1-4 | 14.5 (130) | Reference | 9.7 (87) | Reference |
| Sex | | | | |
| Male | 16.0 (92) | 1.3 (1.0-1.8)‡ | 10.4 (60) | 1.1 (0.8-1.7) |
| Female | 12.0 (66) | Reference | 9.1 (50) | Reference |
| Race§ | | | | |
| White | 8.0 (58) | Reference | 5.3 (38) | Reference |
| Black | 18.4 (69) | 2.3 (1.6-3.3) | 14.7 (55) | 2.8 (1.8-4.2) |
| Asian | 32.0 (8) | 4.0 (1.9-8.4) | 24.0 (6) | 4.6 (1.9-10.8) |
| **Total** | 14.0 (**158**) | | 9.8 (**110**) | |

*The 2 categories of patients are patients with physician-diagnosed KS, excluding multiple hospitalizations and patients with only a history of KS, and patients whose illness met the case definition for KS or atypical KS. RR indicates relative risk; CI, confidence interval.

†The KS incidence is expressed per 100 000 children of corresponding group.

‡Confidence limit equals 1.0 owing to rounding ($P>.05$).

§For all patients with KS, 5 were of another race and the race for 18 was unknown; for patients meeting the KS definition, 4 and 7 patients were of another race or unknown race, respectively.

**What This Study Adds**

Kawasaki syndrome, an illness of unknown origin, is the leading cause of acquired heart disease among children. The study compares the clinical signs and symptoms of patients with KS identified in hospital discharge data with the CDC case definition and describes the epidemiologic characteristics of these patients. The findings indicate that 77% of patients with physician-diagnosed KS met the case definition. Hospital discharge data are useful for surveillance of KS.

miscoding, nonhospitalization for KS, and patients seeking treatment in another state.

The estimated true annual incidence of hospitalized cases of KS in Georgia during 1997 to 1998 was probably between 11 and 14 cases per 100 000 children younger than 5 years. The minimum estimate is derived from the documented KS incidence of 9.8 per 100 000 children and adjusted for the proportion of KS hospital discharges of patients with the case status unknown. The maximum estimate assumes that each patient's diagnosis of KS is accurate regardless of some patients' illnesses not meeting the case definition. The estimate of the true annual KS incidence is within the range of those reported in other studies in the continental United States (4.0-19.1 per 100 000 children younger than 5 years).[4-7,9,10,19,20]

The epidemiologic characteristics of children hospitalized with KS in Georgia are similar to those reported in other US studies.[5-9,12,19-23] The highest incidence of KS in Georgia was among Asian children, followed by black and white children, as reported in previous studies. Seven of the 15 patients with KS with CAA received their IVIG treatment 10 days or more after illness onset, although they met the case definition for KS. The reasons for delayed IVIG administration in these patients are unclear. Nevertheless, every effort should continue to be made to identify and treat patients as early as possible to reduce the likelihood of cardiac complications.

In conclusion, the findings of this study indicate that hospital discharge data are useful for surveillance of KS. The accuracy of hospital discharge data can be increased by excluding multiple hospitalizations for the same person and by limiting the analysis to patients younger than 18 years. Because the KS clinical signs lack specificity, an accurate diagnosis of KS in some patients and determination of its true incidence may pose challenges to both clinicians and epidemiologists. Overcoming these challenges may largely depend on the identification of the etiologic agent and development of a specific diagnostic tool.[4] In the meantime, physicians should exercise their best clinical judgment in identifying and treating patients with KS who may not meet the standard case definition to reduce the likelihood of cardiac complications.

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