Cardiology in the Young

cambridge.org/cty

An update on the epidemiology, length of stay, and cost of Kawasaki disease hospitalisation in the United States

Laxmi V. Ghimire[1,2], Fu-Sheng Chou[3,4,5], Narayan B. Mahotra[6] and Sharan P. Sharma[7]

[1]Section of Pediatrics and Section of Cardiology, Department of Medicine, Lakes Region General Hospital, Laconia, NH, USA; [2]Department of Pediatrics, University of New England Biddeford, ME, USA; [3]Division of Neonatology, Children's Mercy Hospital, Kansas City, MO, USA; [4]Department of Pediatrics, University of Missouri-Kansas City, Kansas City, MO, USA; [5]Department of Pediatrics, University of Kansas Medical Center, Kansas City, KS, USA; [6]Department of Clinical Physiology, Tribhuvan University, Institute of Medicine, Kathmandu, Nepal and [7]Department of Medicine, Lakes Region General Hospital, Laconia, NH, USA

Original Article

Cite this article: Ghimire LV, Chou F-S, Mahotra NB, and Sharma SP (2019) An update on the epidemiology, length of stay, and cost of Kawasaki disease hospitalisation in the United States. *Cardiology in the Young* **29**: 828–832. doi: 10.1017/S1047951119000982

Received: 24 December 2018
Revised: 31 March 2019
Accepted: 8 April 2019
First published online: 6 June 2019

Key words:
Kawasaki disease; coronary aneurysm; United States

Author for correspondence:
Laxmi V. Ghimire, MD, Section of Pediatrics and Section of Cardiology, Lakes Region General Hospital, Laconia, NH 03246, USA. Tel: +603 528-0995; Email: laxmivilasg@gmail.com

Abstract

Background: Kawasaki disease is an acute vasculitis of childhood and is the leading cause of acquired heart disease in the developed countries. *Methods:* Data from hospital discharge records were obtained from the National Kids Inpatient Database for years 2009 and 2012. Hospitalisations by months, hospital regions, timing of admission, insurance types, and ethnicity were analysed. Length of stay and total charges were also analysed. *Results:* There were 10,486 cases of Kawasaki disease from 12,678,005 children hospitalisation. Kawasaki disease was more common between 0 and 5 years old, in male, and in Asian. The January–March quarter had the highest rate compared to the lowest in the July–September quarter (OR=1.62, $p < 0.001$). Admissions on the weekend had longer length of stay [4.1 days (95 % CI: 3.97–4.31)] as compared to admissions on a weekday [3.72 days (95 % CI: 3.64–3.80), $p < 0.001$]. Blacks had the longest length of stay and whites had the shortest [4.33 days (95 % CI: 4.12–4.54 days) versus 3.60 days (95 % CI: 3.48–3.72 days), $p < 0.001$]. Coronary artery aneurysm was identified in 2.7 % of all patients with Kawasaki disease. Children with coronary artery aneurysm were hospitalised longer and had higher hospital charge. Age, admission during weekend, and the presence of coronary artery aneurysm had significant effect on the length of stay. *Conclusions:* This report provides the most updated epidemiological information on Kawasaki disease hospitalisation. Age, admissions during weekend, and the presence of coronary artery aneurysm are significant contributors to the length of stay.

Kawasaki disease is an acute febrile illness associated with self-limited vasculitis of unknown aetiology. It is characterised by fever lasting for more than 5 days, bilateral non-exudative conjunctivitis, erythema of the lips and oral mucosa, changes in the extremities, rash, and cervical lymphadenopathy. Coronary artery aneurysm or ectasia develops in approximately 15–25 % of untreated children. Other cardiac manifestations of Kawasaki disease include myocarditis, valvular insufficiency, ischemic heart disease, or sudden death.[1,2] Kawasaki disease is now the most common cause of acquired heart disease in children in the developed countries.[3] The goals of therapy include reduction of inflammation in the coronary arteries and the myocardium by intravenous immunoglobulin (IVIG) administration, and prevention of thrombosis through inhibition of platelet aggregation by aspirin administration. IVIG has reduced the incidence of coronary artery aneurysm, defined by absolute luminal dimension, from 25 % to 4 % in a recent report.[3] The epidemiology of Kawasaki disease in the United States has not been updated since previous small- and medium-sized studies.[4,5] In this report, we provide updated information on Kawasaki disease epidemiology. Additionally, by using a database consisting of more than 12 million children discharges from US hospitals, this report also provides information on variables contributing to Kawasaki disease hospitalisation including season and region, as well as variables contributing to length of stay (LOS) and hospital charge, which have not been reported previously.

Materials and methods

Study population and variables

We analysed data from hospital discharge records on patients under 18 years of age using the national representative Kids Inpatient Database (KID) for years 2009 and 2012. The data were compiled by the Agency for Healthcare Research and Quality (AHRQ) and generated by the

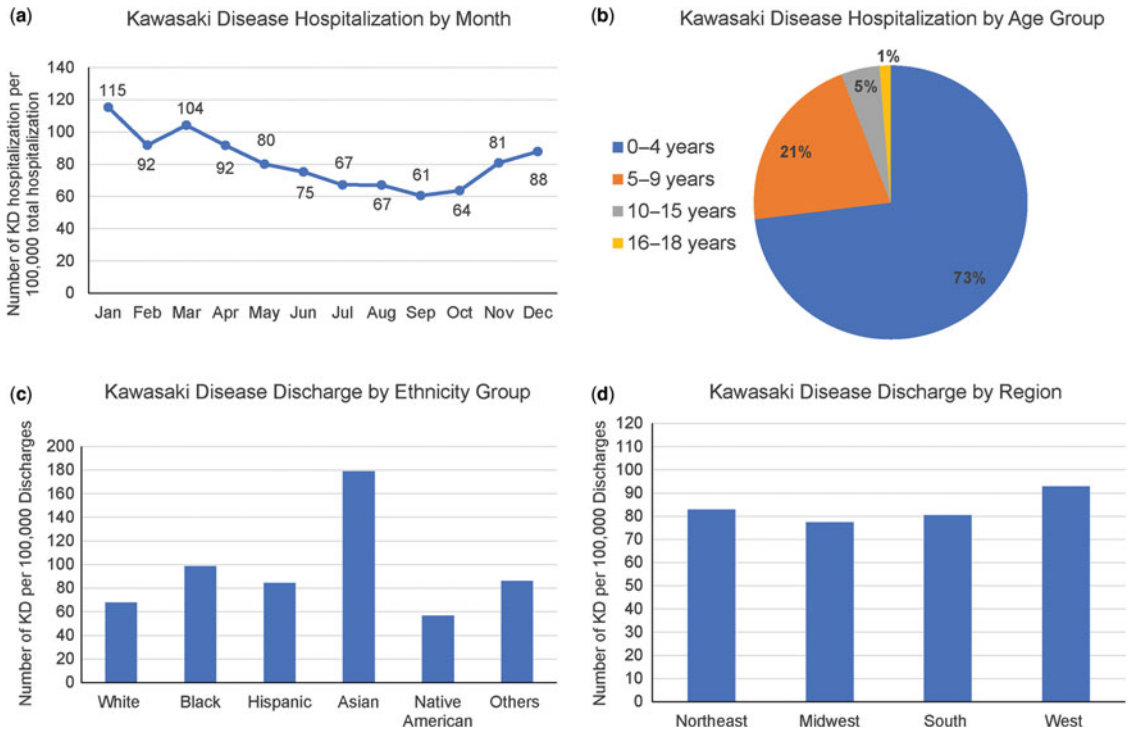

Figure 1. Kawasaki disease hospitalisation by month (***a***), age group (***b***), ethnicity group per 100,000 discharges (***c***), and region per 100,000 discharges (***d***). Data obtained from the national Kids Inpatient Database (KID) for years 2009 and 2012.

Healthcare Cost and Utilization Project (HCUP) in collaboration with public and private state-wide data organisations.

Hospitalisations due to Kawasaki disease were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM) code (446.1: mucocutaneous lymph node disease) in the primary or secondary diagnosis field, and they were weighted with DISCWT to estimate the number of hospitalisations in the entire USA. ICD-9CM codes (414.11: aneurysm of coronary vessels) were used to identify patients who developed coronary artery aneurysm. Patient characteristics collected for this study included age, gender (male or female), and ethnicity (black, Hispanic, white, Asian or Pacific Islanders, native American). Hospital characteristics included hospital regions (Northeast, Midwest, South, or West).

Outcome variables

The outcomes of interest were trends in the annual hospitalisation rates of Kawasaki disease with respect to age, gender, and race. Annual Kawasaki disease-associated hospitalisation rates were calculated by using the number of hospitalisations as the numerator and the corresponding population derived from the US census for 2009 and 2012 as denominator. The number of hospitalisations by months, hospital regions, weekend, and ethnicity were also obtained. Additionally, we investigated LOS and total charges for hospitalisation for Kawasaki disease by ethnicity groups, weekday/weekend admissions, and insurance. In addition, we also identified patients who developed coronary artery aneurysms and categorised them according to age and ethnic groups. We also identified the contribution of several independent variables on LOS.

Statistical analysis

Descriptive statistics including mean, standard deviation, frequency, and percentage were computed. Chi-squared test and independent sample *t*-test were used for categorical and continuous variable comparisons, respectively. Linear regression analysis was used to calculate the effects of independent variables on outcome variables. The level of significance was chosen at 0.05, and all *p*-values were two-sided. Statistical analysis was performed using STATA software version 15.1 (StataCorp LP, TX, USA).

Results

Seasonal, regional, ethnicity group, and age variation

There were a total of 12,678,005 children hospitalisations during the study period, out of which 10,486 were from Kawasaki disease. Incidence of Kawasaki disease was calculated at 6.35 per 100,000 children. There were significant seasonal variations in Kawasaki disease hospitalisation, with highest during the month of January (115 cases per 100,000 discharges) compared to lowest during the month of September (61 cases per 100,000 discharges). The odds ratio (OR) was 1.9, with a $p < 0.001$ (Fig 1a). Similarly, the January–March quarter had the highest rate and the July–September quarter had the lowest (OR=1.62, $p < 0.001$).

Kawasaki disease was most common among children between 0 and 4 years old, comprising 73 % of total Kawasaki disease cases (Fig 1b). Hospitalisation was more common in male, with a male-to-female ratio of 1.4.

With regard to variations in Kawasaki disease hospitalisation according to ethnicity groups, Asian and pacific islanders were significantly higher as compared to whites (OR=2.64, $p < 0.001$) and other groups (Fig 1c). In terms of regional variation, West had the higher rate of hospitalisation compared to the rest of the country (Fig 1d). The regional variation may partly be explained by the highest density of the Asian population in the West.

https://doi.org/10.1017/S1047951119000982 Published online by Cambridge University Press

Table 1. Total Kawasaki disease cases and percentages of coronary artery aneurysm according to age category.

Age category (years)	Kawasaki disease cases	Coronary artery aneurysm cases	Rate of coronary artery aneurysm per 100 Kawasaki disease cases
<1	3426	130	3.81%
1–5	4233	73	1.72%
6–10	2215	47	2.13%
11–15	477	26	5.49%
16–18	134	11	8.59%

Coronary artery aneurysm

A total of 287 cases of coronary artery aneurysm were identified in children diagnosed with Kawasaki disease (2.7 %). On further analysis, we found variations in the incidence of coronary artery aneurysm according to the age groups. Children less than 1 year of age and more than 10 years of age were at increased risk of coronary artery aneurysm (Table 1). Among children younger than 1 year of age, the rate of coronary artery aneurysm was 3.81 % in comparison to 2.7 % in the entire paediatric population (OR=1.40, p = 0.001). We found that Hispanic children had higher coronary artery aneurysm followed by Asian population compared to white children (Table 2). In the subset of patients with coronary artery aneurysm, blacks had the longest stay compared with other ethnicity groups (Table 3).

Length of stay

There was a weekend effect for the total length of Kawasaki disease hospitalisation, with children admitted during weekend staying longer than when the admissions were during a weekday [4.1 days (95 % CI: 3.97–4.31) versus 3.72 days (95 % CI: 3.64–3.80), p < 0.001].

When comparing LOS among different ethnicity groups, blacks had the longest LOS and whites had the shortest [4.33 days (95 % CI: 4.12–4.54 days) versus 3.60 days (95 % CI: 3.48–3.72 days), p < 0.001].

We further subcategorised LOS according to insurance types, and found that patients without insurance (self-pay) had the longest stay. In addition, we found that patients with government insurance stayed longer than those who had private insurance [4.0 days (95 % CI: 3.9–4.1) versus 3.6 days (95 % CI: 3.5–3.7), $p < 0.001$] (Table 4).

We performed linear regression analysis to assess the effect of co-variates on LOS. Co-variates in the model included age, admission during weekend, hospital region, ethnicity group, insurance type, coronary artery aneurysm, and gender. We found that age, admissions during weekend, and the presence of coronary artery aneurysm each significantly affected LOS after adjusting for other co-variates (Table 5). On the other hand, ethnicity group, gender, and insurance types did not have significant association with LOS (Table 5).

We applied the same model to a subset of Kawasaki disease patients who developed coronary artery aneurysm, and found that only the insurance type was significantly associated with LOS (p = 0.045) (Table 5).

Table 2. Coronary artery aneurysm according to ethnicity.*

Race	Aneurysm +/total patients	% of patients with aneurysm
White	100/3866	2.58%
Black	33/1712	1.92%
Hispanic	72/2058	3.50%
Asian	22/820	2.68%
Native Americans/Indians	**<11/61	4.91%
Others	21/571	3.67%

*Because of some patients not reporting races, the total number in races does not equal to the total sample size.
** The number of Native Americans/Indians who developed coronary aneurysms were <11, the value not reported due to HCUP guidelines for the KID.

Table 3. Length of stay according to ethnicity in coronary artery aneurysm subpopulation.

Ethnicity	Number of patients	Mean length of stay with 95%CI
White	100	4.8(4.00–5.64)
Blacks	33	10.2(6.45–14.0)
Hispanics	72	5.8(4.54–7.1)
Asians	22	5.3(3.43–6.83)
Native Americans	***<11	1.5(1.4–4.4)
Others	21	7.3(4.1–10.4)

*** The number of Native Americans/Indians who developed coronary aneurysms were <11, the value not reported due to HCUP guidelines for the KID.

Table 4. Comparison of total length of stay and charge between timing of admission, presence of coronary artery aneurysm, ethnicity groups and insurance types.

Groups	Length of stay in days	Charges in US dollars
Admissions		
Weekday	3.72 (3.64–3.80)	31294 (30367–32221)
Weekend	4.1 (3.97–4.31)	34303 (32356–36251)
Presence of coronary artery aneurysm		
No	3.76 (3.68–3.83)	31178(30420–31994)
Yes	5.95 (5.21–6.67)	56089(44512–68381)
Race		
White	3.60 (3.48 to 3.72)	29899 (28605–31193)
Black	4.33 (4.12 to 4.54)	34861(32203–37518)
Hispanic	4.01 (3.85 to 4.19)	37347(35234–39459)
Asian	3.64 (3.26 to 3.67)	32951(30381–35521)
Native American	3.56 (2.76 to 4.35)	27493(19204–35782)
Others	3.92 (3.61 to 4.23)	32647(29207–36086)
Insurance types		
Medicaid	4.0(3.9–4.1)	31132(29838–32427)
Private including HMO	3.6(3.5–3.7)	31968(30813–33123)
Self-pay	4.2(3.6–4.9)	39962(32211–47714)
Others	3.6(3.3–3.9)	34187(30436–37937)

Data presented as mean (95% CI).

https://doi.org/10.1017/S1047951119000982 Published online by Cambridge University Press

Table 5. Relationship between co-variates on the length of stay of children with Kawasaki disease and the subpopulation with coronary artery aneurysm.

Co-variates	p-Value on total Kawasaki disease patients	p-Value on patients with coronary artery aneurysm only
Age	<0.001	0.09
Gender	0.65	0.77
Race	0.37	0.61
Insurance types	0.10	0.045
Hospital region	0.45	0.56
Admission during weekend	<0.001	0.52
Presence of coronary artery aneurysm	<0.001	Not applicable

Hospitalisation charge

Total hospitalisation charge was also significantly higher in patients who were admitted on the weekend as compared to those admitted during weekdays (Table 4). The total charge was highest among Hispanic children, reaching statistical significance as compared to charges for white and Asian children (Table 4). Children with coronary artery aneurysm were hospitalised longer with higher hospital charge as compared to those without coronary aneurysm (Table 4). As expected, hospital charges were highest among self-pay patients compared to either government or private insurance.

Discussion

This report provides the most updated Kawasaki disease hospitalisation rate by using the HCUP hospitalisation data derived from the Kids Inpatient Database national database. The rate of Kawasaki disease hospitalisation in children <5 years old is 18.5 per 100,000 which is higher than the reported rate of 17.6 per 100,000 in 2000.[6] However, the hospitalisation rate due to Kawasaki disease has been continuing to decline since 2003.[7] Other epidemiological parameters such as variation in race, sex and age were very similar.[6,7]

Previous studies reported increased incidence of Kawasaki disease during the winter and spring seasons, which our findings confirmed.[6] Furthermore, our study again showed that the Asian population is at the highest risk for hospitalisation due to Kawasaki disease, similar to findings from a prior report.[8] Recently, a genome-wide association study found that human leukocyte antigen determinant was associated with increased susceptibility to Kawasaki disease in Asian children but not in Europeans, which may explain our findings.[9]

Coronary artery aneurysm

The coronary artery aneurysm rate in our analysis was 2.7 %, similar to but lower than a recent study reporting a rate of 4 % following treatment with IVIG, further emphasising the benefit of IVIG and the time-sensitive nature of this treatment.[3] We further found that the risk of coronary artery aneurysm formed an U-shape distribution, with higher rates observed among children who were less than 1 year and older than 10 years of age similar to the findings from previous studies.[10,11]

Compared to children without coronary artery aneurysm, those with coronary artery aneurysm had longer hospital stay, implying a sicker subpopulation requiring longer monitoring and management in the hospital setting.

It is possible that the rate of coronary artery aneurysm is underestimated due to miscoding or misclassification. Another possible cause of underestimation would be delayed appearance and diagnosis after the patient has already been discharged from the hospital. In this case, the diagnosis would have been made outpatient, and would therefore have not been included in this dataset.

Ethnicity, insurance type, and length of stay

In our study population, we found that LOS varied significantly among ethnicity groups, with Hispanics and black children staying significantly longer than white children. This finding applied to the total population as well as the subpopulation with coronary artery aneurysm. However, in a linear regression model, we did not find significant contribution of ethnicity to LOS. Similarly, ethnicity also did not significantly contribute to LOS in children with coronary artery aneurysm.

Insurance type also affected LOS. Generally speaking, the United States has a multi-payer system, which can be broadly divided into three groups: the first group consists of those who rely on government insurance and the second group are those who purchase private insurance either through their employer at work or directly from the insurance companies. The third group consists of those patients who do not have any type of health insurance, either voluntarily or unwillingly. Patients in the third group are required to pay out of pocket. We found that self-pay and Medicaid patients stayed longer than those patients who have private insurance. It is possible that healthcare providers are more conscious about LOS when their patients have private insurance to avoid refusal of reimbursement by their insurance companies. Nonetheless, in our regression model, the contribution of insurance type to overall LOS was not significant in the study population.

Finally, it has been suggested that an association between ethnicity groups and insurance type exists.[12] Therefore, we further analysed whether insurance type mediates LOS among different ethnicity groups. Interestingly, we found that LOS in whites remained significantly shorter as compared to that in blacks and Hispanics even after adjusting for insurance types.

Weekend effect

Weekend effect is an interesting finding in our report. The patients who were admitted over the weekend tend to stay longer. This is likely due to the lack of proper diagnostic resources such as echocardiography on the weekend. Correspondingly, hospitalisation charge was also higher on the weekend. Although LOS contributed to the total charge, with an adjusted R^2 of 0.46, additional hidden factors seemed to exist. Due to the limitations of the dataset, we were not able to further investigate.

Limitation

The main strength of our study is a large sample size available through a national database. However, like any administrative database, it is prone to coding errors. Coding practice also differs between different hospitals and regions. Other limitation may include variations in hospital charge across different states, which may have also contributed to differences in hospital charges among different ethnic groups. It merits further analysis with state-specific dataset which is not available in the dataset used for this study.

https://doi.org/10.1017/S1047951119000982 Published online by Cambridge University Press

Conclusion

In conclusion, our study provides an update on the epidemiology of Kawasaki disease hospitalisation by using a large national database. The rate of Kawasaki disease remains high among Asian children, as well as during winter and spring months, suggesting an interaction between environment and genetic pre-disposition in Kawasaki disease pathogenesis. Age, admission during weekend, and the presence of coronary artery aneurysm significantly affect LOS, while race, gender, insurance types did not meet statistical significance.

Author ORCIDs. Laxmi Ghimire 0000-0001-5880-3496

Acknowledgements. None.

Financial Support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of Interest. None.

References

1. Dajani AS, Taubert KA, Gerber MA, et al. Diagnosis and therapy of Kawasaki disease in children. Circulation 1993; 87: 1776–1780.
2. Kato H, Sugimura T, Akagi T, et al. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up study of 594 patients. Circulation 1996; 94: 1379–1385.
3. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation 2017; 135: e927–e999.
4. Uehara R, Belay ED. Epidemiology of Kawasaki disease in Asia, Europe, and the United States. J Epidemiol 2012; 22: 79–85.
5. Burns JC, Herzog L, Fabri O, et al. Seasonality of Kawasaki disease: a global perspective. PLoS One 2013; 8: e74529.
6. Holman RC, Curns AT, Belay ED, Steiner CA, Schonberger LB. Kawasaki syndrome hospitalizations in the United States, 1997 and 2000. Pediatrics 2003; 112: 495–501.
7. Okubo Y, Nochioka K, Sakakibara H, Testa M, Sundel RP. National survey of pediatric hospitalizations due to Kawasaki disease and coronary artery aneurysms in the USA. Clin Rheumatol 2017; 36: 413–419.
8. Kitano N, Suzuki H, Takeuchi T. Patient age and the seasonal pattern of onset of Kawasaki's disease. N Engl J Med 2018; 378: 2048–2049.
9. Onouchi Y. Genetics of Kawasaki disease. Circ J 2012; 76: 1581–1586.
10. Belay ED, Maddox RA, Holman RC, et al. Kawasaki syndrome and risk factors for coronary artery abnormalities: United States, 1994-2003. Pediatr Infect Dis J 2006; 25: 245–249.
11. Callinan LS, Tabnak F, Holman RC, et al. Kawasaki syndrome and factors associated with coronary artery abnormalities in California. Pediatr Infect Dis J 2012; 31: 894–898.
12. The Henry J. Kaiser Family Foundation. Key facts on health and health care by race and ethnicity – section 4: health coverage. 2016. Available at: https://www.kff.org/report-section/key-facts-on-health-and-health-care-by-race-and-ethnicity-section-4-health-coverage/. (Accessed: 23rd February 2019).

https://doi.org/10.1017/S1047951119000982 Published online by Cambridge University Press