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Kawasaki Disease and Clinical Outcome Disparities Among Black Children

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Objective To determine whether Black children with Kawasaki disease exhibit disparities in prevalence, sequelae, and response to intravenous gamma globulin (IVIG) treatment.

Study design International Classification of Diseases codes were used to identify children with Kawasaki disease admitted to a tertiary center in the southeastern US. Subjects diagnosed and treated according to American Heart Association criteria were included. Demographic, laboratory, clinical, and echocardiographic data from the electronic medical record (2000-2015) were compared between Blacks and Whites.

Results Data from 369 subjects (52% Whites and 48% Blacks) were included in our analysis. No significant differences related to timely admission, IVIG treatment, or coronary artery (CA) abnormalities during hospitalization were observed. Blacks showed lower IVIG response rates than Whites for patients administered IVIG within 10 days of fever onset (86.6% vs 95.6%; $P = .007$). Blacks received more ancillary drugs (9.6% vs 2.6%; $P = .003$), and endured longer hospitalizations (mean, 5 ± 3.9 days vs 3.4 ± 2.2 days; $P = .001$). Blacks presented with higher C-reactive protein level and erythrocyte sedimentation rate and lower hemoglobin, albumin, and sodium levels. Blacks had a higher proportion of persistent CA abnormalities than Whites at second follow-up echocardiogram (14.5% vs 6.3%; $P = .03$), and at third follow-up echocardiogram (21.2% vs 6.9%; $P = .01$).

Conclusions Compared with White children, Black children with Kawasaki disease had higher IVIG refractory prevalence, more severe inflammation, more ancillary treatments, and longer hospitalizations. Despite no racial differences in time to diagnosis or initial treatment, there was greater CA abnormality persistence among Black children at follow-up. (*J Pediatr* 2021;229:54-60).

Substantial racial and ethnic variation in Kawasaki disease incidence occurs in the US and worldwide. Incidence among those of Japanese ethnicity exceeds that of Caucasians in the US by up to 20-fold.¹ The incidence of Kawasaki disease in the Black population exceeds that in Non-Hispanic Whites but is lower than in children of Asian descent.² Furthermore, studies have suggested that racial and ethnic discrepancies also exist for Kawasaki disease treatment response.³⁻⁵ Dionne et al reported that lower socioeconomic status is associated with delayed treatment, prolonged length of stay, and increased risk of large/giant coronary artery (CA) aneurysms; however, the lowest socioeconomic status quartile of the study cohort had a much greater proportion of Black children than the 3 higher quartiles combined, and thus the potential influence of race as a factor influencing these outcome measures could not be eliminated.⁶ A small retrospective study reported a lower risk of CA aneurysm in Black children.⁷ In contrast, 2 studies of Black children indicated that they were at greater risk of nonresponse to intravenous gamma globulin (IVIG) or had poorer CA outcomes.^{5,8} The hypothesis that Black race poses a risk factor for poorer Kawasaki disease outcomes requires further exploration. The Children's of Alabama hospital, is the only tertiary pediatric center in the state, serving a community in the deep South US with nearly proportionate White and Black populations. We performed a retrospective analysis to determine whether there were any differences in Kawasaki disease characteristics and clinical outcomes among Black children compared with White children, and if any identified disparities were due to differences in healthcare delivery or biological factors.

Methods

Once ethical approval was obtained, we identified patients with Kawasaki disease admitted to the Children's of Alabama hospital between January 2000 and May 2015. A hospital administrative database (PedCards) was queried using ICD-9

AHA	American Heart Association
CA	Coronary artery
CRP	C-reactive protein
IVIG	Intravenous gamma globulin
MIS-C	Multisystem inflammatory syndrome in children

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Supported by the National Institutes of Health, National Heart, Lung, and Blood Institute (R01 HL146130 [to S.S. and M.P.]) and the Quetelet Endowed Professorship Research Fund (to S.S.). The authors declare no conflicts of interest.

Portions of this study were presented at the American Heart Association Scientific Sessions 2019, Philadelphia, Pennsylvania, November 16-18, 2019.

0022-3476/\$ - see front matter. Published by Elsevier Inc.
<https://doi.org/10.1016/j.jpeds.2020.09.052>

(446.1) and ICD-10 (M30.3) codes for mucocutaneous lymph node syndrome (Kawasaki disease). The initial query yielded 587 records. We screened these records to remove duplicates and then excluded patients who did not meet our inclusion and exclusion criteria. Only those children with assigned race by parent report in their record as White or Black were included. Subjects were specifically excluded if they did not meet the American Heart Association (AHA) diagnostic criteria for Kawasaki disease,^{9,10} if they were transferred from an outside institution more than 36 hours after completing IVIG infusion, or if documentation received at patient transfer was inadequate. Non-IVIG response or IVIG refractoriness was defined as persistent or recurrent fever extending for 36 hours after completion of IVIG treatment.¹¹ Baseline demographics, hospital and laboratory clinical data, 2D echocardiography during hospitalization, and outpatient follow-up data were extracted from their electronic medical records manually and entered into REDCap.¹²

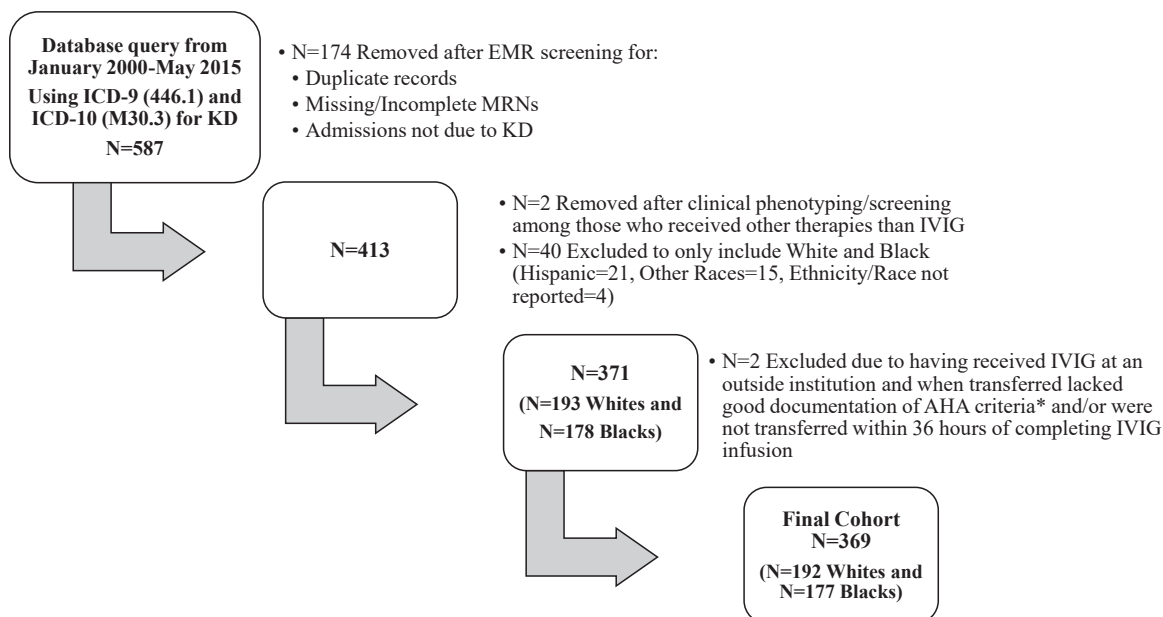
The z-scores for the left anterior descending, right CA, and left main CA were calculated using regression models as described by McCrindle et al¹³ (<http://www.parameterz.com/sites/coronary-arteries>). An abnormal echocardiogram was defined as having a z-score ≥ 2.5 or reported aneurysm in any of the 3 CAs.^{9,14} Hospital echocardiogram readings were classified as “yes” for changes if any increase in diameter ($>20\%$) occurred for any of the CAs.³ When available, data on the subsequent 3 follow-up outpatient echocardiogram examinations after discharge were extracted.

Descriptive statistics (frequency and percentage, median and IQR, mean \pm SD) of demographics, clinical, and laboratory variables were used to summarize the data in the 2 racial groups. Differences between the 2 groups were compared using the χ^2 and Fisher exact test for categorical variables and the Student *t* test and Wilcoxon rank-sum test for continuous variables where appropriate. If a patient had missing data for a particular variable, that patient was excluded from the analysis for that variable. SAS version 9.4 (SAS institute, Cary, NC) was used for the analyses, and all statistical tests of a 2-sided *P* value of $<.05$ were considered significant. Comparisons of racial clinical and laboratory characteristics were further stratified by IVIG responders and nonresponders using similar descriptive statistical methods.

Results

After applying the inclusion and exclusion criteria, we analyzed a final cohort of 369 patients, comprising 192 Whites and 177 Blacks (Figure 1). There were no significant differences in age at admission or sex between the 2 racial groups (Table I). White children presented more frequently with conjunctivitis (66.7% vs 55.4%; *P* = .03) and rash (72.4% vs 58.2%; *P* = .004) than Black children. There were no other significant differences in clinical presentation between the 2 groups.

Table II presents the clinical laboratory data by race and eventual response to IVIG. Hematologic variables at



*American Heart Association (AHA) Guidelines for KD diagnosis include: ≥ 5 days of fever and the presence of ≥ 4 of the 5 principal clinical features: bilateral non-purulent conjunctivitis, oral mucosal changes such as strawberry tongue and cracked lips, peripheral extremity changes, rash, and cervical lymphadenopathy of >1.5 cm.

Key: Electronic Medical Record (EMR); Medical Record Number (MRN); Intravenous Immune globulin (IVIG)

Figure 1. Flowchart for selecting the clinical cohort of patients with Kawasaki disease analyzed in this study.

Table I. Baseline, hospital presentation, treatment, and echocardiography findings during Kawasaki disease hospitalization by race

Variables	White (N = 192; 52%)	Black (N = 177; 48%)	P value
Age at admission, mo, mean ± SD	45.3 ± 32.5	40 ± 30.4	.11
Age at admission, mo, median (IRQ)	40 (20-68)	33 (15-56)	.26
Male sex, n (%)	114 (59.7)	108 (61.4)	.74
Time from fever to admission, d, mean ± SD	5.7 ± 3.6	5.2 ± 2.8	.05
Time from admission to IVIG, d, mean ± SD	0.8 ± 1.2	1 ± 1.4	.12
Time from IVIG to discharge, d, mean ± SD	2.5 ± 1.8	3.6 ± 3.4	.0005
Symptoms, n (%) [*]			
Conjunctivitis	128 (66.7)	98 (55.4)	.02
Rash	139 (72.4)	103 (58.2)	.004
Lymphadenopathy	56 (29.2)	45 (25.4)	.42
Oral symptoms	112 (58.3)	98 (55.4)	.56
Hand/foot	101 (52.6)	84 (47.5)	.32
Nonmucocutaneous [†]	19 (9.9)	18 (10.2)	.93
Hospital therapy, n (%)			
IVIG	175 (91.2)	164 (92.7)	.59
Aspirin	175 (91.2)	156 (88.1)	.34
Other therapy [‡]	5 (2.6)	17 (9.6)	.003
None	14 (7.3)	5 (2.8)	.04
IVIG response, n/N (%)	133/165 (80.6)	124/160 (77.5)	.54
Multiple IVIGs given, n/N (%)	31/165 (18.4)	33/154 (21.4)	.55
Time between IVIGs, d, mean ± SD	2.4 ± 2	3.8 ± 5.5	.65
Treated with IVIG within 10 d, n/N (%)	139/155 (89.7)	142/150 (94.7)	.10
IVIG response among those treated within 10 d, n/N (%)	133/139 (95.6)	123/142 (86.6)	.007
First echocardiogram as inpatient, n (%)	173 (90.1)	163 (92.6)	.39
Abnormal first inpatient echocardiogram, n (%)	23 (13.3)	26 (15.9)	.49
Had repeat echocardiogram, n/N (%)	14/172 (8.1)	23/163 (14.1)	.08
Changes from first to repeat echocardiogram, n/N (%)	2/14 (14.3)	10/23 (43.5)	.08
Repeat echocardiogram among those with abnormal echocardiography findings, n/N (%)	4/23 (17.4)	9/26 (34.6)	.16

Significant P values (<.05) are in bold type.

*More than 1 option may apply.

†Most common were gastrointestinal symptoms, such as diarrhea, emesis, and abdominal pain.

‡Other therapies: heparin, plavix, steroids, infliximab, and remicade.

admission were significantly different between Black and White children. Mean hemoglobin (10.6 ± 1.2 vs 11.2 ± 1.2 g/dL; $P < .0001$) and hematocrit ($31.2\% \pm 3.3$ vs $32.5\% \pm 3.1$; $P = .0002$) levels were lower in Black children, whereas potassium ($P = .04$) and creatinine ($P = .01$) levels were higher than Whites. Inflammatory measures at admission were higher in Black children, particularly C-reactive protein (CRP) (14.4 ± 10.2 vs 8.6 ± 7.7 mg/L; $P < .0001$) and erythrocyte sedimentation rate (70 ± 33.5 vs 58.5 ± 29.1 mm/hr; $P = .0007$). Admission albumin (3.4 ± 0.5 vs 3.6 ± 0.5 g/dL) and sodium (136.5 ± 3.4 vs 138.4 ± 3.1 meq/L) were also lower in Blacks ($P < .001$ for all). Few significant laboratory differences occurred between either Black or White children when comparing IVIG response. Discharge laboratory data were lacking for the majority of patients and is shown in **Table III** (available at www.jpeds.com). In general, laboratory variables for both groups trended toward normality at discharge. For this select patient group with data, we noted that discharge CRP levels, although lower than admission levels for both races, remained higher for Black children, and Black children had lower alanine aminotransferase levels than White children ($P = .04$).

The differences in presentation were not due to disparity in time to treatment (initiation of IVIG infusion) or healthcare delivery. Of near significance, the interval in days from fever

onset to admission was shorter for Blacks ($P = .05$), and there was no difference in time from admission to IVIG treatment ($P = .12$). For all patients receiving IVIG, regardless of the number of days from onset of fever to infusion, there were differences in response between the racial groups. Ninety-four percent of the Black children and 89.7% of the White children received IVIG within 10 days of fever onset, in accordance with the AHA guidelines (**Table I**). Among those treated with IVIG within the first 10 days after fever onset, Black children had a lower IVIG response rate compared with Whites (86.6% vs 95.6%; $P = .007$). More Black children than White children received alternative therapies (9.6% vs 2.6%; $P = .003$), and a smaller proportion of them were left untreated (2.8% vs 7.3%; $P = .04$). Black children also had a longer average length of hospital stay (4.5 ± 3.9 days vs 3.4 ± 2.2 days; $P = .002$) (**Figure 2**; available at www.jpeds.com).

Table I provides echocardiographic data for the patients during their Kawasaki disease hospitalization. The first echocardiogram was performed at an equivalent time in the 2 groups. The low proportion of patients without an initial inpatient echocardiogram underwent echocardiography as an outpatient before their admission. The percentage of abnormal echocardiograms was similar in the 2 groups, although there was a trend toward performing more subsequent echocardiograms during hospitalization in the

Table II. Laboratory results at admission for patients with Kawasaki disease by race and IVIG response

Parameter	White (N = 192; 52%)				Black (N = 177; 48%)				
	Overall	IVIG responders (N = 133; 80.6%)	Non-IVIG responders (N = 32; 19.4%)	P value*	Overall	IVIG responders (N = 124; 77.5%)	Non-IVIG responders (N = 36; 22.5%)	P value†	P value‡
Hospital admission									
WBC count, $\times 10^3/\mu\text{L}$	12.9 \pm 4.7	13.1 \pm 4.4 120	12.1 \pm 5.3 27	.30	13.9 \pm 6.1	14 \pm 6 110	14.3 \pm 5.8 35	.71	.10
Hemoglobin, g/dL [§]	11.2 \pm 1.2	11.2 \pm 1.2	11.3 \pm 1.1	.69	10.6 \pm 1.2	10.5 \pm 1.2	10.5 \pm 0.8	.68	<.0001
Hematocrit, % [§]	32.5 \pm 3.1	32.6 \pm 3	32.6 \pm 3	.96	31.2 \pm 3.3	31.2 \pm 3.4	30.6 \pm 2.7	.38	.0002
Platelets, $\times 10^3/\mu\text{L}$ [§]	439.6 \pm 177	438.2 \pm 174.8	419.2 \pm 162.3	.60	414 \pm 179.6	422.9 \pm 173	389.3 \pm 182	.32	.19
ESR, mm/h	58.5 \pm 29.1	56.3 \pm 28.2 110	63.7 \pm 31.9 28	.22	70 \pm 33.5	71.3 \pm 33.8 99	76.6 \pm 31.1 30	.45	.0007
Na, mEq/L	138.4 \pm 3.1	138.4 \pm 2.9 86	138 \pm 3.7 21	.66	136.5 \pm 3.4	136.9 \pm 3.4 75	135.5 \pm 3.1 24	.06	<.0001
K, mEq/L	4 \pm 0.5	4.03 \pm 0.5 90	3.9 \pm 0.4 21	.53	4.2 \pm 0.6	4.1 \pm 0.5 76	4 \pm 0.5 25	.42	.04
Chloride, mEq/L	101.7 \pm 3.3	101.4 \pm 3.4 89	101.6 \pm 2.8 20	.85	101.1 \pm 4.3	101.5 \pm 4.3 75	99.5 \pm 3.6 24	.05	.31
Bicarbonate, mEq/L	24.3 \pm 3	24.1 \pm 3.4 26	24.6 \pm 1.5 9	.67	23.4 \pm 3.5	23.5 \pm 3.7 23	23.6 \pm 2.5 5	.96	.26
BUN, mg/dL	8.3 \pm 3.5	8.2 \pm 3.5 87	9.6 \pm 4.1 20	.12	10.2 \pm 10.7	8.6 \pm 5.4 76	15.7 \pm 19.5 24	.08	.08
Creatinine, mg/dL	0.37 \pm 0.13	0.35 \pm 0.12 84	0.4 \pm 0.16 20	.15	0.42 \pm 0.17	0.41 \pm 0.1 70	0.46 \pm 0.2 23	.25	.01
Glucose, mg/dL	100.4 \pm 18	100.1 \pm 19.7 86	100.5 \pm 13 20	.94	100.9 \pm 17.5	100.3 \pm 18 75	106.8 \pm 24 24	.11	.81
Albumin, g/dL	3.6 \pm 0.5	3.6 \pm 0.4 90	3.7 \pm 0.4 22	.51	3.4 \pm 0.5	3.4 \pm 0.5 77	3.4 \pm 0.4 27	.93	.001
AST, U/L	64.7 \pm 74.8	66.2 \pm 84.6 87	64.8 \pm 31.7 23	.89	60.1 \pm 63.1	53.5 \pm 40 74	80.8 \pm 104 27	.19	.61
ALT, U/L	75.5 \pm 111.6	76.5 \pm 123.1 88	77.4 \pm 66.8 23	.96	58.3 \pm 54.4	47.4 \pm 42 74	91.8 \pm 71 27	.004	.13
Alkaline phosphatase, IU/L	246.9 \pm 139.3	245.4 \pm 130.7 87	251.5 \pm 124.2 23	.84	262.5 \pm 221.8	219.4 \pm 106 73	391.3 \pm 377 27	.02	.53
Total bilirubin, $\mu\text{mol/L}$	0.72 \pm 1.1	0.72 \pm 1.1 87	0.90 \pm 1.3 23	.51	0.79 \pm 1.3	0.51 \pm 0.53 72	1.3 \pm 2 27	.03	.68
CRP, mg/L	8.6 \pm 7.7	8.5 \pm 7.6 101	9.8 \pm 8.6 25	.45	14.4 \pm 10.2	14 \pm 10 98	16.5 \pm 9.6 28	.24	<.0001

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; WBC, white blood cell.

Data are mean \pm SD. An N value in the column indicates the number of patients for whom the data were available for the calculation. Significant P values (<.05) are in bold type. A comparison of White IVIG responders vs Black IVIG responders was performed. The P values from this comparison are similar to the comparison of Black and White overall P values.

*Comparison of White responders vs White nonresponders.

†Comparison of Black responders vs Black nonresponders.

‡Comparison of Black vs White overall values.

§No data were missing.

Black children. **Table IV** presents outpatient echocardiography data. Overall, the 2 groups had similar numbers of repeat echocardiograms and similar follow-up time frames; however, a significantly greater proportion of persistent CA dilation or aneurysm ($z > 2.5$) was observed in Black children compared with White children at follow-up (second follow-up echocardiogram abnormality, 14.5% vs 6.3%, $P = .03$; third follow-up echocardiogram abnormality, 21.2% vs 6.9%, $P = .01$) (**Table IV**). For those who had abnormal follow-up echocardiograms, there were no differences between the 2 racial groups' median z-scores for any of the 3 CAs.

Discussion

The subjects in this study were drawn from areas throughout Alabama, a state considered representative of populations in the deep southern US, where 65.3% of the population is White (not Hispanic or Latino) and 26.8% is Black.¹⁵ We

found that Black children with Kawasaki disease have a greater prevalence of IVIG refractoriness and greater persistence of CA abnormalities at follow-up. Two studies with much smaller populations paralleled our present findings.^{4,5} In those studies, Black children also exhibited a higher prevalence of IVIG resistance and greater persistence of CA abnormalities. Contradicting these findings, a single study of an urban center with a predominantly Black population suggested that African American descent was protective against developing CA aneurysms⁷; however, that study did not provide clearly defined criteria for CA and lacked a comparable size White population. Furthermore, time to treatment specifically by race has not been examined in previous studies. Thus, questions remained as to whether disease outcome disparities are related to disparities in socioeconomic status, timely access, or healthcare delivery or is linked to a true biological/genetic variation. In this study, from a region traditionally known for racial disparities including in access,¹⁶

Table IV. Follow-up echocardiography data during outpatient clinic visits

Parameter	White (N = 192; 52%)	Black (N = 177; 48%)	P value
Cardiology visit after discharge, n (%)	128 (66.7)	124 (70.5)	.43
Time from discharge to first echocardiogram, d, median (IQR)	28 (16-39)	25 (15-40)	.15
First follow-up echocardiogram			
Abnormality, n/N (%)	14/192 (7.3)	22/177 (12.4)	.09
LMCA-Z, median (IQR)	4.2 (3.6-7.5)	4.7 (3.3-6.6)	.39
LAD-Z, median (IQR)	8.5 (5.6-13.6)	6.1 (4-10.4)	.47
RCA-Z, median (IQR)	5 (3.4-7.2)	3.1 (2.5-5.2)	.20
Time from discharge to second echocardiogram, d, median (IQR)	159 (61-373)	100 (60-308)	.24
Second follow-up echocardiogram			
Abnormality, n/N (%)	8/127 (6.3)	18/124 (14.5)	.03
LMCA-Z, median (IQR)	3.3 (2.7-4.5)	3.8 (2.5-5.2)	.94
LAD-Z, median (IQR)	6.6 (4.1-9.6)	6 (3.8-8.6)	.88
RCA-Z, median (IQR)	5.4 (3.4-6.8)	4.2 (2.1-8.9)	.53
Time from discharge to third echocardiogram, d, median (IQR)	739 (297-1581)	636 (263-1622)	.41
Third follow-up echocardiogram			
Abnormality, n/N (%)	5/73 (6.9)	14/66 (21.2)	.01
LMCA-Z, median (IQR)	2.5 (2.4-3.9)	6.8 (3.8-8)	.17
LAD-Z, median (IQR)	12.1 (10-14.3)	4 (3-8.2)	.31
RCA-Z, median (IQR)	10.8 (2.1-19.5)	4.8 (4-6.3)	.50
Follow-up from discharge to third echocardiogram, y, mean \pm SD*	2.8 \pm 2.7	2.7 \pm 2.8	.77

LAD-Z, left anterior descending artery z-score; LMCA-Z, left main coronary artery z-score; RCA-Z, right coronary artery z-score.

Abnormality defined as echocardiogram measures resulting in a z-score <2.5 of any CA. The N for the median z-scores reported are only for those with an abnormal echocardiogram. Significant P values (<.05) are in bold type.

*10%-20% data missing.

we found no difference in time to admission after fever, follow-up, or healthcare delivery. In addition, racial differences in clinical presentation did not appear to impact the time to diagnosis or treatment. Because the diagnosis of Kawasaki disease depends on patients meeting published clinical and laboratory criteria, treatment with IVIG is not initiated until after 4 or 5 days of persistent fever. Overall, our data show no deviation from this practice in either race.

In contrast, although demographic characteristics and timing of admission and treatment were nearly equivalent in the 2 racial groups, we observed differences in laboratory values at admission. Compared with White children, in Black children the CRP level was nearly double, and erythrocyte sedimentation rate was also higher. Similar racial differences in inflammatory variables have been reported for children with Kawasaki disease in Tennessee.⁴ Our data suggest that the innate or inflammatory response to an unknown environmental trigger may be more extreme in Black children with Kawasaki disease. Previous studies have compared innate response in general European (Dutch) and African (Gabonese) children, but the differences in inflammatory responses were observed in relation to different pathogenic stimuli in 2 geographical regions and not in relation to race.¹⁷ In this study, we examined children living in the same state, suggesting that differences in immune response could potentially be due to genetics, although cultural or environmental exposure discrepancies cannot be ruled out. Studies in adults have shown that African ancestry specifically predicts a stronger inflammatory response to pathogens, and this response may have an evolutionary and genetic basis that could have broad implication for health disparities.^{18,19} Multiple studies have identified various genetic polymorphisms and copy number variations that influence Kawasaki disease

susceptibility and treatment response²⁰⁻²³; however, most of these studies included only Asian or White cohorts.²⁴ The only published genetic investigation to include a reasonable number of Black children with Kawasaki disease was too underpowered to allow a selective family-based genetic analysis for this race, although those subjects were included in the overall population analyses.²⁵

The finding of a greater inflammatory response to an unknown environmental trigger in Black children is interesting, considering the racial disparity in outcomes observed during the current COVID-19 pandemic.²⁶⁻²⁸ Kawasaki disease produces inflammatory and cytokine responses, which resemble those noted after infection with severe acute respiratory syndrome coronavirus 2.²⁹ Accordingly, multiple reports are emerging throughout the world that children are exhibiting symptoms from multisystem inflammatory syndrome in children (MIS-C), which resemble those of Kawasaki disease during the pandemic.³⁰⁻³³

The Black population exhibits poorer IVIG treatment response using both acute and chronic clinical outcome variables. Recommendations that patients with acute Kawasaki disease receive IVIG within 10 days of fever onset stem from randomized clinical trials.^{9,10} Although not significant, a higher percentage of Black children than White children received IVIG within this recommended window; however, the Black children's response to IVIG was poorer with greater refractoriness when treated within this window.

In general, delayed treatment is considered less likely to prevent CA dilation or CA aneurysm formation. Accordingly, the most recent clinical trials performed in North America, examining adjunct therapies for acute Kawasaki disease enrolled patients receiving IVIG within 10 days.³⁴⁻³⁶ The Etanercept as Adjunctive Treatment for Acute Kawasaki

Disease (EATAK) clinical trial prespecified racial subgroup analysis for treatment response. The study included a relatively small cohort of Black patients. Nevertheless, the prospective study found that Black patients showed greater refractoriness to IVIG, with some improvement seen when adding etanercept.³ The significant IVIG refractory rates among Blacks in our study possibly contributed to the disparity in receipt of more alternative treatments and longer hospital stays.

Our study found a greater persistence of CA abnormalities in Black children compared with White children, with no differences in follow-up times or rates. Nevertheless, following the most recent AHA definition of CA abnormality, >20% of Blacks who were still followed after their Kawasaki disease event (~2 years later) continued to show echocardiogram abnormalities, compared with 6% of Whites.^{9,14} The index z-score >2.5 also has been used as an outcome variable in recent clinical trials of patients with Kawasaki disease.⁹ In contrast, a previous study examining a Black cohort evaluated only the incidence of giant CA aneurysm and estimated it as 2%-7%, depending on the series.¹⁴ To date, the relationship between CA abnormality in children and the development of incident coronary atherosclerosis in adult life remains unclear. However, the persistence of CA abnormalities and lesions in children might be important for the Black population, who already exhibit higher rates of CA disease in adulthood. Future longitudinal studies that measure persistence of CA abnormalities and the future implications of this complication in adult cardiovascular health and other co-morbidities is warranted.

In our cohort, the Black children also had significantly lower hemoglobin, sodium, and albumin values at presentation compared with the White children; however, the clinical importance of this disparity remains unclear. Previous studies in Asian populations have shown that derangements in these laboratory values are associated with no initial response to IVIG and a higher rate of CA aneurysm.³⁷ The Kobayashi and other risk scores developed in Japanese populations to predict IVIG response incorporate some of these variables.³⁸ Studies evaluating these risk scores in non-Japanese populations have found relatively poor predictability, specifically in North American populations.^{38,39} These studies evaluated predominantly White populations and did not specifically address risk score analyses in Blacks. The longer hospital length of stay among Blacks further supports the tenet that Black children are more severely affected. Future studies that provide insight on reasons for prolonged hospitalizations and the effects it may pose not only to the child and the hospital, but to the families of these children needs to be addressed.

Limitations of our study relate principally to its retrospective nature, which includes missing data or was limited by what was reported in notes from healthcare professionals in the electronic medical record. Laboratory data are not routinely collected for patients with Kawasaki disease in most centers following treatment except in special circumstances or for patients with poor clinical evolution. Therefore,

there is a paucity of second laboratory values for our cohort. Likewise, some longitudinal data were missing because patients were frequently not followed, specifically after normal CA results. We noted a trend toward obtaining more repeat inpatient echocardiograms in Black children, which may possibly be related to the longer hospital stays and the higher rate of nonresponders prompting requests for additional studies (Figure 2). The vast majority of patients were seen again after an abnormal echocardiogram, thereby minimizing important data loss and protecting the integrity of our CA persistence results. For this same reason, a decrease in the number of overall echocardiograms performed over time could affect the positivity rate. Furthermore, this drop in the denominator for echocardiography may be due to patients continuing their follow-up elsewhere. Categorical risk level of CAs was not feasible due to the small numbers of those with abnormal z-scores. Our results are from a single center and may lack generalizability to other populations. Finally, there also may be selection bias, because these were patients referred to or hospitalized at a tertiary care hospital.

For the most part, race has rarely been accounted for in predictive models or during statistical analyses for clinical trials. Therefore, evaluation of these risks scores by race, specifically in Blacks is warranted. ■

We thank the participating patients and their parents for providing their information, as well as the research staff who helped during the data extraction process at Children's of Alabama.

Submitted for publication Jun 23, 2020; last revision received Sep 16, 2020; accepted Sep 21, 2020.

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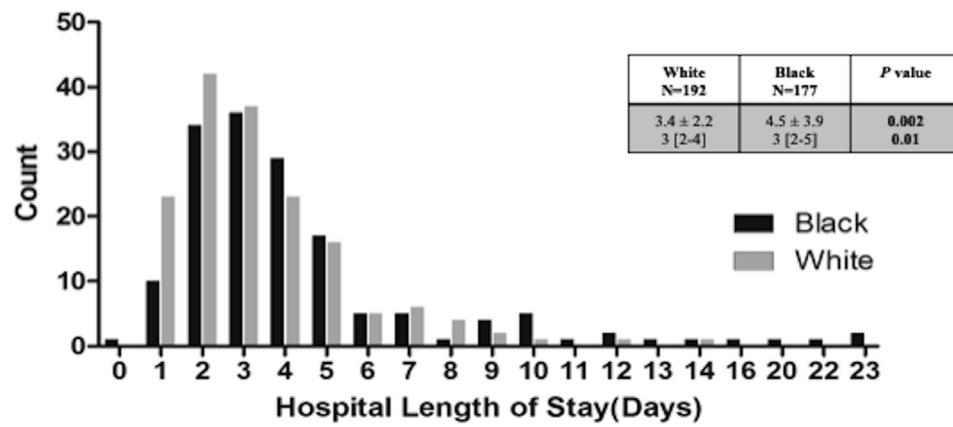
Data Statement

Data sharing statement available at www.jpeds.com.

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Note: Mean ± SD and Median [Q1-Q3] values are reported and significant *P* values at <0.05 are shown in bold font.

Figure 2. Hospital length of stay for patients with Kawasaki disease, by race.

Table III. Laboratory results at discharge in patients with Kawasaki disease by race and IVIG response

Variables	White (N = 192; 52%)				Black (N = 177; 48%)				
	Overall	IVIG responders (N = 133; 80.6%)	Non-IVIG responders (N = 32; 19.4%)	P value*	Overall	IVIG responders (N = 124; 77.5%)	Non-IVIG responders (N = 36; 22.5%)	P value†	P value‡
Hospital discharge									
WBC count, $\times 10^3/\mu\text{L}$	11 \pm 4.6	10.7 \pm 4.1 29	11.3 \pm 4.7 11	.67	13.8 \pm 9.2	12.2 \pm 5 23	18.1 \pm 15 10	.25	.11
Hemoglobin, g/dL	10.2 \pm 1	10.2 \pm 0.9 31	10 \pm 1.2 12	.46	9.7 \pm 1.7	9.8 \pm 1.7 26	9.3 \pm 1.6 10	.45	.09
Hematocrit, %	29.6 \pm 3.2	30 \pm 2.7 28	27.9 \pm 3.8 10	.06	29.2 \pm 4.6	29.7 \pm 4.7 25	27.7 \pm 3.8 10	.28	.68
Platelets, $\times 10^3/\mu\text{L}$	473.8 \pm 167.1	448.6 \pm 174 27	513.6 \pm 135 8	.33	523.8 \pm 269.5	511 \pm 218 24	611 \pm 364 10	.43	.34
ESR, mm/h	79.7 \pm 38.4	71.6 \pm 39.1 25	101.3 \pm 36.4 10	.04	91.7 \pm 43.8	96.2 \pm 42.3 22	83.4 \pm 50.4 7	.50	.22
Na, mEq/L	140.1 \pm 2	139.9 \pm 1.7 19	140.7 \pm 2.7 6	.45	139 \pm 2.4	139.2 \pm 2.4 21	138.2 \pm 2.4 6	.36	.06
K, mEq/L	4.3 \pm 0.6	4.2 \pm 0.5 16	4.3 \pm 0.6 6	.80	4.3 \pm 0.6	4.3 \pm 0.6 14	4.3 \pm 0.3 4	.89	.90
Chloride, mEq/L	104.5 \pm 3.1	104.5 \pm 2.8 19	104.8 \pm 4.4 6	.84	104.2 \pm 2.9	104 \pm 2.6 21	103 \pm 3.7 6	.26	.67
Bicarbonate, mEq/L	25.5 \pm 2.7	25.4 \pm 2.6 16	25.8 \pm 3.4 5	.80	24.3 \pm 3.1	24.1 \pm 3 14	25 \pm 3.7 4	.63	.19
BUN, mg/dL	9.5 \pm 4.7	8.4 \pm 3.3 16	12.8 \pm 7.2 5	.25	7.3 \pm 3.4	7.1 \pm 3.1 14	8 \pm 4.9 4	.67	.11
Creatinine, mg/dL	0.35 \pm 0.1	0.33 \pm 0.08 16	0.38 \pm 0.04 5	.32	0.35 \pm 0.1	0.3 \pm 0.1 14	0.3 \pm 0.2 4	.71	1.0
Glucose, mg/dL	93 \pm 8.1	92.8 \pm 8.8 16	92 \pm 5.9 5	.85	93.5 \pm 15	92 \pm 15.2 14	98.7 \pm 14 4	.44	.90
Albumin, g/dL	3.3 \pm 0.4	3.2 \pm 0.4 17	3.4 \pm 0.3 6	.31	3.1 \pm 0.5	3.0 \pm 0.5 14	3.2 \pm 0.5 4	.59	.16
AST, U/L	61.3 \pm 51	66.3 \pm 60 12	49.2 \pm 21 5	.55	69.8 \pm 72.8	70.8 \pm 80 10	65 \pm 4.2 2	.92	.71
ALT, U/L	81.8 \pm 82.4	97 \pm 93 12	45.4 \pm 28 5	.10	35.9 \pm 31.4	34.9 \pm 34 10	41 \pm 19.7 2	.81	.04
Alkaline phosphatase, IU/L	276.4 \pm 211	325.9 \pm 235 12	157.6 \pm 41.1 5	.03	175.2 \pm 37.4	178.8 \pm 40 10	157 \pm 2.8 2	.47	.07
Total bilirubin, $\mu\text{mol/L}$	0.5 \pm 0.3	0.5 \pm 0.3 12	0.4 \pm 0.2 5	.40	0.5 \pm 0.5	0.38 \pm 0.3 10	0.9 \pm 0.9 2	.59	.77
CRP, mg/L	4.7 \pm 5	5.6 \pm 5.3 22	4.2 \pm 4.5 9	.49	8.4 \pm 8.2	9.6 \pm 8.7 23	3.3 \pm 1.6 6	.003	.04

Data are mean \pm SD. An *N* value in the column indicates the number of patients for whom the data were available for the calculation. Significant *P* values (<.05) are in bold type. A comparison of White IVIG responders vs Black IVIG responders was performed. The *P* values from this comparison are similar to the comparison of Black and White overall *P* values.

*Comparison of White responders vs White nonresponders.

†Comparison of Black responders vs Black nonresponders.

‡Comparison of Black vs White overall values.