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The Association of Race with Childhood Uveitis

Sheila T Angeles-Han[1,3], **Courtney McCracken**[1], **Steven Yeh**[1,3], **Kirsten Jenkins**[2], **Daneka Stryker**[1], **Curtis Travers**[1], **Kelly Rouster-Stevens**[1,2], **Larry B. Vogler**[1,2], **Scott R. Lambert**[1,3], **Carolyn Drews-Botsch**[4], and **Sampath Prahalad**[1,2]

[1]Department of Pediatrics, Emory University School of Medicine, Atlanta, GA

[2]Children's Healthcare of Atlanta, Atlanta, GA

[3]Department of Ophthalmology, Emory University School of Medicine, Atlanta, GA

[4]Rollins School of Public Health, Emory University, Atlanta, GA

Abstract

Purpose—To identify risk factors for a severe uveitis course among children with non-infectious uveitis.

Design—Retrospective cohort study

Method—This was a retrospective analysis of a prospectively collected database. Records of 94 children with uveitis were reviewed at enrollment and every 3-6 months (2011-2015). Severe uveitis was defined as a history of ocular complications or a visual acuity (VA) of ≤20/200. Children were compared by disease, VA, complications and race. Regression models were used to model risk factors for severe disease. When examining race, we focused on non-Hispanic African American and non-Hispanic White children only.

Results—Of 85 children with uveitis and complete ocular examinations, 27 (32%) had a history of a VA of ≤20/200. A subanalysis of non-Hispanic African American and White children showed an increased prevalence of VA ≤20/200 in non-Hispanic African Americans (18/25 (72%) vs. 4/43 (9%)). Non-Hispanic African Americans were more likely to be diagnosed at an older age (p=0.030), have intermediate uveitis (p=0.026), bilateral disease (p=0.032), a history of VA ≤20/50 (p=0.002), VA ≤20/200 (p<0.001), and a higher rate of complications (p<0.001). On multivariable analysis, non-Hispanic African American race was a significant predictor of blindness (OR=31.6, 95% CI (5.9– 168.5), p<0.001), after controlling for uveitis duration. Non-Hispanic African Americans also developed 2.2 times more unique complications per year of disease than non-Hispanic Whites when controlling for uveitis type and duration.

Corresponding author: Sheila T. Angeles-Han, MD, MSc, Division of Pediatric Rheumatology, Emory University, 2015 Uppergate Drive, Atlanta, GA 30307; Phone: 404-785-2000, Fax: 404-785-9096, sangele@emory.edu.

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Conclusions—There appear to be racial differences in the outcomes of children with uveitis. Non-Hispanic African American children with non-juvenile idiopathic arthritis associated uveitis may have worse visual outcomes with increased vision loss and ocular complications. These findings highlight the need for future studies in minority populations.

Pediatric non-infectious uveitis can lead to severe ocular complications and permanent vision loss[1]. Uveitis can occur as a primary disease without systemic associations (idiopathic uveitis) but can also be related to other diseases such as juvenile idiopathic arthritis (JIA), sarcoidosis, and Behcet's disease.

In North America, pediatric uveitis is most commonly associated with JIA, affecting 10-20% of children with inflammatory arthritis[2]. Three to 66% develop vision loss and ocular complications related to risk factors such as male gender, short duration between arthritis and uveitis diagnoses, a uveitis diagnosis prior to arthritis diagnosis, young age at uveitis onset, and a poor initial ocular examination (i.e. anterior chamber cell score ≥1+, initial visual acuity (VA) of 20/200 or worse, or presence of complications)[3-14]. However, few studies have examined risk factors in a prospective cohort of children. Early identification and treatment of those at greatest risk for severe disease may prevent devastating ocular sequelae.

Race plays a significant role in various autoimmune conditions such as JIA, systemic lupus erythematosus and sarcoidosis. In JIA, children of European descent predominantly develop oligoarticular disease, whereas non-European children develop polyarticular rheumatoid factor (RF) positive JIA with worse arthritis outcomes[15-17]. Since JIA subtypes differ in their association with uveitis, and race predisposes one to different JIA categories, race may influence uveitis risk. Less extensive investigation has been conducted in racial association with pediatric uveitis.

The primary objective of this study is to identify risk factors for a severe disease course among children with non-infectious uveitis, defined as a history of ocular complications or a VA of 20/200 or worse.

Patients and Methods

Data were collected retrospectively and prospectively. Some children in our cohort were enrolled after their initial uveitis diagnosis, requiring retrospective data collection. However, after enrollment, all data were collected prospectively, including that of children who were enrolled close to their time of uveitis diagnosis. Patients were managed in the Division of Pediatric Rheumatology of the Emory Children's Center. This study, including medical chart data collection from pediatric rheumatologists and ophthalmologists, was approved by the Institutional Review Board of Emory University and conformed to the requirements of the US Health Insurance Portability and Accountability Act. Informed consent was obtained from the parent/legal guardian, and assent was obtained from the children if applicable. Research adhered to the tenets of the Declaration of Helsinki.

Subjects

Eligible children presenting with a diagnosis of non-infectious uveitis at less than 18 years of age were enrolled from the pediatric rheumatology outpatient clinics at Emory Children's Center from November 2011 to January 2015. They were followed prospectively from time of enrollment and returned for their usual follow up appointments every 3-6 months. Inclusion criteria included: 1) a diagnosis of non-infectious uveitis and 2) English speaking. Exclusion criteria included: 1) refusal to participate.

Data Collection

We reviewed rheumatology and ophthalmology medical records from time of diagnosis to time of presentation to our clinics and then every 3-6 months during the usual pediatric rheumatology follow up visit until March 1, 2015. Data collected at the baseline visit included date of birth, gender, self-described race and ethnicity, JIA category established by the International League of Associations for Rheumatology (ILAR) classification in children with arthritis [18], uveitis characteristics (onset date, diagnosis date, laterality, location, ocular complications such as cataracts, glaucoma, synechiae, band keratopathy, ocular hypertension, cystoid macular edema, amblyopia and other complications, and ophthalmic surgeries), ocular exams (best corrected visual acuity (VA), intraocular pressure, and anterior chamber cell score), labs (antinuclear antibody (ANA), rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), HLA-B27, and angiotensin converting enzyme (ACE)), and both past and current medications. Race was designated as American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White by self-report. Ethnicity was also self-reported as Hispanic or non-Hispanic. Since children without a diagnosis of JIA do not commonly undergo regular screening examinations, an accurate determination of disease duration is challenging. In this study, disease duration refers to time from uveitis diagnosis to analysis. Follow up data on arthritis, uveitis, labs and medications were collected at 3-6 month intervals (time of last study visit to current study visit) and during uveitis flares. Data from the ocular exam were recorded from every ophthalmology visit with varied intervals depending on disease activity. Not all patients had complete data from their initial ocular exam or subsequent visits as some patients had chronic uveitis prior to enrollment and records were unavailable.

Statistical Analysis

Statistical analyses were conducted using SAS 9.3 for Windows (Cary, NC). Statistical significance was assessed at the 0.05 level unless otherwise noted. Data are summarized using means and standard deviations, medians and interquartile ranges (25^{th} – 75^{th} percentile) or counts and percentages, when appropriate. Duration of uveitis was calculated as time between dates uveitis of diagnosis to last study visit. For statistical purposes, we converted Snellen VA to logMAR VA. We compared children 1) with JIA-associated uveitis to those with other forms of uveitis, 2) with a history of a VA of 20/200 or worse to those with a VA better than of 20/200, 3) with and without a history of ocular complications, and 4) of non-Hispanic African American and non-Hispanic White race, using Chi-square tests and two sample t-tests. In instances of small expected cell counts (<5), exact Chi-square

tests were used. When continuous data were skewed or non-normal, a nonparametric test (Mann Whitney-U or Kolmogorov-Smirnov test) was used in place of the two sample t-test.

Multivariable logistic regression was used to simultaneously model multiple risk factors for development of complicated disease (i.e., blindness or complications). Candidate predictors identified in the univariate analyses ($p < 0.1$) were entered into the model using backwards elimination. Variables were systematically removed until all variables in the model were significant at the 0.05 level or until a significant reduction in model fit was observed. In addition, other variables that were demonstrated to be associated with the risk of poor outcome and race (e.g., duration of disease defined as time from disease diagnosis to analysis) were included in the models. In addition, to compare the number of ocular complications among non-Hispanic African American and non-Hispanic White children, multivariable negative binomial models were used to model the number of unique complications developed while adjusting for disease duration. To further examine the role of non-Hispanic African American race with poor visual outcomes in a more homogenous cohort of children with uveitis, a subanalysis was performed in non-Hispanic White and non-Hispanic African American children with only JIA-associated uveitis or chronic anterior uveitis.

Results

Demographics and clinical characteristics of cohort

Demographic and clinical characteristics of 94 children with uveitis are presented in Table 1. Of these, 52 (55%) also had JIA, 30 (32%) had idiopathic uveitis, 6 (6%) were HLA-B27 positive, 2 (2%) had sarcoidosis, and 4 (4%) had other types of uveitis associated with vitritis, nodular scleritis, pars planitis, and sympathethic ophthalmia. There were 57 (61%) White and 28 (30%) African American children. Eleven (12%) of the children were Hispanic. The median (25^{th} - 75^{th}) age at uveitis diagnosis was 6.3 years (4.0 – 10.6). Many had anterior uveitis (N = 65 (74%)) with bilateral involvement (62 (70%)). Most common ocular complications included synechiae (41 (44%)) and cataracts (38 (40%)).

A majority of children (77 (83%)) were treated with subcutaneous and/or oral methotrexate during the course of their disease. Sixteen children did not require or refused immunosuppressive therapy and among those, 6 (37%) used steroid ocular drops alone, 1 (6%) NSAIDs alone, 1(6%) oral prednisone alone, and 8 (50%) a combination of NSAIDS and ocular drops. Approximately 36 (38%) required biologic therapy, but not beyond anti-tumor necrosis factor agents for treatment of uveitis.

Given the increased frequency of children with JIA-associated uveitis, we compared them to children with other uveitis types (Table 1). Children with JIA-associated uveitis were primarily White (38 (73%)), whereas almost half of those with other types of uveitis were African American (20 (48%)) ($p = 0.003$). Those with other types of uveitis were older at diagnosis ($p=0.006$), had intermediate ($p = 0.014$) and posterior location ($p = 0.029$), were more likely to have a history of a VA of 20/50 or worse ($p = 0.009$) or 20/200 or worse ($p = 0.009$), and several ocular complications.

Children with ocular complications and legal blindness

Overall, 49 children (58%) had a history of a VA of 20/50 or worse, and 27 (32%) had a history of a VA of 20/200 or worse. Among the 27 children with VA of 20/200 or worse, 9 (33.3%) had bilateral blindness. At last follow-up (median duration of follow-up: 4.3 years), 14 (52%) had improved visual acuity (VA better than 20/200), while 13 (48%) were still considered blind in one or both of their eyes. Of those with improved visual acuity (n = 14), 10 (71%) still have significant vision loss (VA of 20/50 or worse) while the remaining 4 (29%) have a VA of 20/40 or better. In addition, 62 (66%) of children had at least one ocular complication. These poor outcomes were significantly more common in children with non-JIA associated uveitis (Table 2). Those with a history of a VA of 20/200 or worse had worse logMAR VA on initial examination ($p < 0.001$), similar to children with ocular complications, but this did not reach significance (median logMAR VA 0.18 vs. 0.09, $p = 0.057$) (data not shown).

Children with uveitis compared by race

Since more African American children with uveitis appeared to experience poor visual outcomes, we explored uveitis characteristics by race and compared White and African American children and excluded those of Hispanic ethnicity (N = 76) (Table 3). Non-Hispanic African Americans were more likely older at uveitis diagnosis ($p = 0.030$), had intermediate uveitis ($p = 0.026$), bilateral involvement ($p = 0.032$), and ocular complications such as cystoid macular edema ($p = 0.004$). Although they were also more likely to have Medicaid insurance coverage ($p = 0.002$), there were no significant differences in treatment with methotrexate or biologics.

More non-Hispanic African Americans also had a history of VA of 20/50 or worse ($p = 0.002$) and 20/200 or worse ($p < 0.001$). However, non-JIA associated uveitis was more prevalent in non-Hispanic African American children relative to non-Hispanic White children ($p = 0.004$). When examining children with non-JIA associated uveitis only, the same trend was observed, as non-Hispanic African Americans still had an increased frequency of a VA of 20/200 or worse (13/18 (72.2%) vs. 1/14 (7.1%); $p < 0.001$) (data not shown). Among the 4 non-Hispanic White and 18 non-Hispanic African American children with VA of 20/200 or worse, 8 (36.4%) had bilateral blindness; all of whom were non-Hispanic African American. Eleven children (50%) have improved visual acuity (VA better than 20/200) but half remain blind as of last follow-up. Among the 4 non-Hispanic White children, 1 (25%) is currently blind, 2 (50%) have improved VA, but still have vision loss, and 1 has VA of 20/40 or better. In the 18 non-Hispanic African American children with blindness, 10 (55.6%) are still blind at last follow-up, 6 (33.3%) have improved VA with vision loss, and 2 (11.1%) have VA of 20/40 or better.

Predictors of severe uveitis

We examined the potential role of race on ocular complications and/or blindness while controlling for disease and uveitis duration (Table 4). We adjusted for disease duration since ocular complications and vision loss could develop over the course of disease. We again limited our analysis to non-Hispanic children. On univariate analysis, a diagnosis of other types of uveitis, as compared to JIA-associated uveitis, ($p < 0.001$), longer duration of

disease (p= 0.026), and non-Hispanic African American race (p = 0.012) were associated with ocular complications. On multivariable analysis, after adjustment for uveitis duration, uveitis not attributed to JIA (OR = 10.8; 95% CI [2.6 – 43.5]) was still a significant predictor of a history of complications; while the association with non-Hispanic African American race failed to reach significance (OR = 3.4; 95% CI [0.8 – 15.5]), but remained clinically significant. However, univariate analysis suggested that non-Hispanic African American children had, on average, more types of complications than non-Hispanic Whites (median number of complications: 3 vs 1, $p < 0.001$). To explore differences in the number of ocular complications of non-Hispanic African American and White children, we utilized a negative binomial model including race and uveitis disease type and included an offset parameter adjusting for varying durations of disease. We noted an increased rate in the development of unique complications in non-Hispanic African American children (rate ratio = 2.2; 95% CI [1.4-3.5]), and in children with a diagnosis of non-JIA associated uveitis (rate ratio = 1.9; [95% CI 1.2-3.1]). We noticed that non-Hispanic African American children who developed uveitis (rate ratio = 2.2; 95% CI [1.4-3.5]), and those whose uveitis was not attributable to JIA (rate ratio = 1.9; 95% CI [1.2-3.1]), developed complications at an accelerated rate relative to other children. After adjustment for duration of disease and disease type, non-Hispanic African Americans remained more likely to have cataracts (p = 0.009), band keratopathy($p < 0.001$), and cystoid macular edema (p = 0.015).

Similarly, in univariate analysis, non-Hispanic African American race ($p<0.001$), other types of uveitis (p = 0.009), earliest ESR (p =0.002, and VA on initial ocular exam ($p < 0.001$) were significant predictors of blindness. Due to the small number of patients with data from their initial ocular exam, logMAR VA was not included in multivariable models. In addition, because ESR was highly associated with type of uveitis ($r_s = 0.40$; $p < 0.001$), it was also excluded. In multivariable analysis, after controlling for duration of disease, only non-Hispanic African American race remained a significant predictor of blindness (OR = 31.6; 95% CI [5.9 – 150.0]).

Sub-analysis of children with JIA-associated uveitis and chronic anterior uveitis

We recognize that the categories and patterns of uveitis can differ based on their association with different types of systemic inflammatory diseases. Hence, we conducted a sub-analysis of children with JIA-associated uveitis and chronic anterior uveitis alone, and we them compared by non-Hispanic African American and White race. Non-Hispanic African American children were still older at diagnosis (p = 0.012), their uveitis was less likely to be secondary to JIA (p = 0.019), had an increased history of a visual acuity of 20/200 or worse (p = 0.003), and more cataracts (p = 0.018), synechiae (p = 0.030), and band keratopathy (p = 0.005). They had a similar initial ocular exam and treatment with DMARDs and biologics. Although the odds decreased, non-Hispanic African American children still had an increased odds of a history of blindness (OR = 10.58; 95% CI [1.76 – 63.75]) with an increased rate of complications compared to non-Hispanic White children (rate ratio = 2.39; 95% CI [1.13 – 5.07]).

Discussion

We report that non-Hispanic African American race and uveitis that is not associated with JIA are potential predictors of a severe disease course in pediatric non-infectious uveitis. Non-Hispanic African American children had worse visual outcomes with an accelerated rate of ocular complications, and an increased likelihood of vision loss. Race may have an effect on a child's uveitis course, even accounting for the fact that non-Hispanic African-American children with uveitis are more likely to have ocular disease that is not attributable to JIA. This difference in outcome was also evident when considering a homogenous group of patients with JIA-associated uveitis and anterior chronic uveitis only.

Risk factors for the development of uveitis in children with JIA are well established and incorporated in the American Academy of Pediatrics screening schedule [19]. However, there are few reports on markers of severe pediatric uveitis. In general, predictors of vision loss include male gender, intermediate uveitis, severe disease at baseline examination, and history of prior surgery before presentation[3,11,20-23]. Similarly, predictors for ocular complications include young age at diagnosis, increased cells and flare, increased disease duration before treatment, presence of keratic precipitates, and intermediate uveitis [11,23]. For JIA-associated uveitis specifically, additional risk factors for complications include short duration between diagnosis of arthritis and uveitis and a positive ANA[23,24]. We did not find a difference in visual outcomes based on gender and ANA status, but our other findings remain consistent with these studies.

Approximately 1/3 of our uveitis cohort had a history of a VA of 20/200 or worse (legal blindness). This was more common in children with other types of uveitis (8/38 (47%)), compared to JIA-associated uveitis (9/47 (19%)). This finding is similar to another cohort wherein 24% of 75 JIA-associated uveitis children presented with blindness[24]. Importantly, we found that non-Hispanic African American children with uveitis were much more likely to experience legal blindness- 70% were non-Hispanic African American despite only 30% of the entire cohort being non-Hispanic African American. Likewise, all children with a history of bilateral blindness were non-Hispanic African American, and approximately half had one blind eye at last follow up. Even after including only children with JIA-associated uveitis and chronic anterior uveitis, non-Hispanic African American children still had more reports of legal blindness (62% vs. 13%).

Children with non-JIA-associated uveitis had a higher rate of complications after adjusting for duration of disease, similar to another report of children with idiopathic uveitis who experienced more severe inflammation[11]. Even after focusing on children with JIA-associated uveitis and chronic anterior uveitis only, they still developed more types of complications per year of duration of disease. After adjusting for disease duration and disease type, non-Hispanic African American race was no longer a statistically significant predictor of history of complications although a clinically significant increased risk of complications was present. Despite our larger cohort of African American children compared to other studies, we are not adequately powered to detect this association.

Race plays a significant role in various autoimmune conditions, including JIA and systemic lupus erythematosus, but there have been few studies describing uveitis in African American children. An incidence and prevalence study from the Pacific Ocular Inflammation Study noted that of 224 adult uveitis cases, only 2% were Black[25]. However, Black patients with uveitis had the highest incidence at 39.6 cases per 100,000 patient years. Nguyen et al. reported an increased uveitis prevalence in African American adults with inflammatory bowel disease compared to Whites (8.1% vs. 1.6%, OR = 5.5, 95% CI: 2.3-13.0, $p < 0.001$)[26]. A 2 year prospective study of Bantu-speaking Black patients in South Africa noted that of 355 new uveitis cases, there were 40 children with anterior uveitis and one with posterior uveitis, with a rate of 11 per 100,000 population per year [27]. Uveitis has been described in 6-8% of African children with JIA with varied ANA positivity, although sample sizes ranged from 2-13[15,28-32]. The incidence of uveitis was similar in children of European and non-European ancestry (14.4% vs. 12.8%) in a Toronto JIA cohort. However, risk was increased in European children and decreased in non-European ancestries when compared to the general Toronto population[15]. We previously reported on data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry, a large multicenter registry of children and adolescents with pediatric rheumatic disease based in North America, and showed that in 3967 children with JIA, only 13 of 220 (5.6%) non-Hispanic African American children compared to 446 of 3747 (12%) non-Hispanic White (NHW) children developed uveitis[30]. Hence, reports of uveitis prevalence in African American children has varied.

There is less extensive data on racial differences in the course of pediatric uveitis. African American adults have been reported to have increased hypotony and a 2-fold increase of incident glaucoma in those randomized to implants or systemic therapy[33,34]. A severe course has been described in 22 African children with various types of uveitis (idiopathic, Still's disease, and sympathetic ophthalmia) [35]. However, Woreta et al. found no associations between race and ocular complications, a VA or 20/50 or worse, or a VA of 20/200 or worse in their JIA cohort, although there were only 5 blacks and 64 white patients[23]. We recently demonstrated increased blindness in a small cohort of non-Hispanic African American children with JIA-associated uveitis ((5/7) 71% vs. (2/29) 7%)[36]. Thus, reports vary on the course of disease in children of African descent.

The increased disease severity noted in our non-Hispanic African American children could be secondary to biologic differences or variance in health-care access. Although our non-Hispanic African American patients increasingly utilized Medicaid insurance health care, the duration of follow up and treatment were comparable. There are several potential reasons why non-Hispanic African American children were older at diagnosis, had a worse initial ocular examination and more complications. This could be secondary to a delay in referral and diagnosis or due to underlying genetic differences in relation to prevalence and outcome. Several studies have shown racial and ethnic disparities in healthcare access and outcomes in children[37,38]. Most studies in non-Hispanic White children with JIA-associated uveitis show associations with the HLA-DRB1 allele, and one study highlighted the association of HLA-DR8, but not HLA-DR5, with chronic non-granulomatous anterior uveitis in African Americans [39]. It is crucial to understand the reasons for the differences in outcomes in regards to race so we can better address deficiencies in treatment or access.

We report a higher proportion of non-Hispanic African American patients than previous studies, due to our location in the Southeastern United States. However, a 1997 report of uveitis prevalence in the Southeastern US was similar to our cohort and thus is representative of the region [40]. Of 385 patients, 31% were African American and 67% were White. Additionally, as in our sample, most of the African American patients had idiopathic uveitis. The larger proportion of non-Hispanic African American children in our population allows us to examine questions regarding differences in outcomes associated with race. We also focused on a non-Hispanic population since outcomes may vary based on ethnicity. We are exploring outcomes in this cohort.

There is a potential referral bias since patients with mild disease responsive to topical therapy may not be referred. Likewise, our institution is a tertiary care medical center which may bias towards referral of only severe cases needing immunosuppression. However, we are the largest pediatric rheumatology group in Georgia, and our group sees many children for their initial uveitis workup regardless of the need for immunosuppressive therapy.

Accurate determination of the duration of uveitis is difficult. Many children are asymptomatic at onset, and routine eye examinations may not be performed, even in children with JIA. Hence, we used the time of diagnosis of uveitis in our analysis but recognize that uveitis may have been active beforehand.

Since many patients are referred from various centers throughout Georgia and surrounding Southeastern states, we do not always have their complete ophthalmology records. Hence, we were unable to confirm the significance of the initial ocular examination in our cohort. There was not a protocol that stated specific complications to identify, hence some complications may have been missed. Timing of the onset of complications was not known in all children, and we were unable to perform survival analysis. However, we anticipate that this will be possible in the future as our cohort increases.

To address these issues, our group is designing future studies to examine racial differences in response to therapy, timing of referral or seeking care, and the genetics of uveitis. We also plan to have standardized protocols for identifying complications.

Given our limited sample size and single center experience, we were unable to adjust our significance level to control for testing of multiple hypotheses. A larger cohort of children or an external validation sample would be needed to confirm our findings.

In conclusion, we newly demonstrate that there are racial differences in the visual outcomes of children with uveitis. Our findings highlight the potential role of race and its implications on treatment of disease and complications. We may need to treat non-Hispanic African American children with uveitis earlier and more aggressively with systemic therapy. The impact of race should be further explored in a large, racially diverse cohort since identifying high risk children will enable early optimal treatment and potentially prevent vision threatening complications associated with severe disease. To our knowledge, this is the largest report on a childhood uveitis course in non-Hispanic African American children.

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Biography

Sheila T. Angeles-Han, MD, MSc is an Assistant Professor of Pediatrics and Ophthalmology at the Emory University School of Medicine in Atlanta, Georgia. She completed her pediatrics residency at the University of Illinois at Chicago, her pediatric rheumatology fellowship at the Hospital for Special Surgery in New York, and her Masters of Science in Clinical Investigation at Cornell University. Dr. Han's clinical and research career is dedicated to improving the outcomes of children with uveitis by identifying risk markers for disease development and severe course. She also developed the first measure of vision related function and quality of life in pediatric uveitis, "Effects of Youngsters' Eyesight on Quality of Life" (EYE-Q).

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Table 1

Comparison of Juvenile Idiopathic Arthritis-associated Uveitis (JIA-U) and Other Types of Childhood Uveitis

Characteristics N = 94 unless otherwise specified N (%) unless otherwise specified	Overall N=94	JIA-associated uveitis N=52 (55.3%)	Other types of uveitis N=42 (44.7%)	p-value
Demographics				
Age at most recent visit, *Median (25^{th} – 75^{th})*	11.8 (8.5 – 14.9)	13.3 (8.4 – 14.6)	13.3 (9.2 – 15.0)	0.225
Gender, female	66 (70.2%)	40 (76.9%)	26 (61.9%)	0.173
Race				
White	57 (60.6%)	38 (73.1%)	19 (45.2%)	0.003 [b]
African American	28 (29.8%)	8 (15.4%)	20 (47.6%)	
Other	9 (9.6%)	6 (11.5%)	3 (7.1%)	
Hispanic	13 (13.8%)	10 (19.2%)	3 (7.1%)	0.184
Insurance				
Private	54 (57.5%)	31 (59.6%)	23 (54.8%)	0.863
Medicaid	37 (39.4%)	19 (36.5%)	18 (42.9%)	
None	3 (3.2%)	2 (3.9%)	1 (2.4%)	
Disease Characteristics				
Age at uveitis diagnosis (years), *Median (25^{th} – 75^{th})*	6.3 (4.0 – 10.6)	4.8 (3.5 – 10.4)	8.7 (5.3 – 10.7)	0.006 [b]
Location of Disease [a] (N = 88)				
Anterior	65 (73.9%)	38 (80.9%)	27 (65.9%)	0.110
Intermediate	5 (5.7%)	0 (0.0%)	5 (12.2%)	0.014 [b]
Posterior/Panuveitis	4 (4.6%)	0 (0.0%)	4 (9.8%)	0.029 [b]
Unknown	14 (15.9%)	9 (18.0%)	5 (12.2%)	0.373
Bilateral Disease [a] (N = 89)	62 (69.7%)	34 (72.3%)	28 (66.7%)	0.562
Worst Ocular Exam [a] (N=85)				
Slit lamp exam (cells),				
0 & 0.5+	19 (22.4%)	11 (23.9%)	8 (20.5%)	0.797
1+ and worse	66 (77.6%)	35 (76.1%)	31 (79.5%)	
Intraocular Pressure *Median (25^{th} – 75^{th})*	20.0 (17.0 – 26.0)	19.0 (17.0 – 25.0)	21.0 (17.0 – 28.0)	0.282
Visual acuity 20/50 or worse	49 (57.7%)	21 (44.7%)	28 (73.7%)	0.009 [b]
Visual acuity 20/200 or worse	27 (31.8%)	9 (19.2%)	18 (47.4%)	0.009 [b]
Type of Complications				

Characteristics **N = 94 unless otherwise specified** **N (%) unless otherwise specified**	**Overall N=94**	**JIA-associated uveitis N=52 (55.3%)**	**Other types of uveitis N=42 (44.7%)**	**p-value**
Cataracts	38 (40.4%)	16 (30.8%)	22 (52.4%)	0.038 [b]
Glaucoma/ocular hypertension	16 (17.0%)	9 (17.3%)	7 (16.7%)	1.000
Synechiae	41 (43.6%)	16 (30.8%)	25 (59.5%)	0.007 [b]
Band Keratopathy	28 (29.8%)	13 (25.0%)	15 (35.7%)	0.364
Cystoid Macular Edema	22 (23.4%)	8 (15.4%)	14 (33.3%)	0.052
Initial Ocular Exam [a]				
≥1+ cells at first exam, (N=46)	29 (63.0%)	16 (61.5%)	13 (65.0%)	1.000
Intraocular pressure > 21, (N=25)	2 (8.0%)	1 (7.7%)	1 (8.3%)	1.000
LogMAR Visual acuity, (N=42) *Median (25^{th} – 75^{th})*	0.18 (0.00 – 0.40)	0.18 (0.00 – 0.30)	0.18 (0.10 – 0.48)	0.622
Labs [a]				
ANA[c] positive (N=92)	37 (40.2%)	28 (54.9%)	9 (22.0%)	0.003 [b]
Earliest ESR[d] (N=89) *Median (25^{th} – 75^{th})*	11.0 (6.0 – 29.0)	22.0 (8.0 – 38.0)	9.0 (3.0 – 14.0)	<0.001 [b]
HLA[e]-B27 positive (N=62)	16 (25.8%)	6 (18.8%)	10 (33.3%)	0.250
Medication Use [a] (N = 93)				
Methotrexate Oral	57 (61.3%)	36 (70.6%)	21 (50.0%)	0.055
Methotrexate Subcutaneous	65 (69.9%)	38 (74.5%)	27 (64.3%)	0.365
Infliximab	27 (29.0%)	17 (33.3%)	10 (23.8%)	0.364
Adalimumab	17 (18.3%)	12 (23.5%)	5 (11.9%)	0.184

[a] Indicates missing data;

[b] p = <0.05; Chi-square tests, two sample t-tests, non-parametric test (Mann Whitney-U or Kolmogorov-Smirnov test).

[c] ANA = Antinuclear antibody.

[d] ESR = Erythrocyte Sedimentation Rate.

[e] HLA = Human Leukocyte Antigen.

Table 2
Comparison of a History of a Visual Acuity of 20/200 or Worse in Childhood Uveitis

Characteristics N = 85 unless otherwise specified N (%) unless otherwise specified	VA of 20/200 or worse		p-value
	Yes N=27 (31.8%)	No N=58 (68.2%)	
Demographics			
Age at most recent visit, *Median (25^{th} – 75^{th})*	11.9 (9.1 – 15.7)	11.4 (8.3 – 14.8)	0.329
Gender, female	18 (66.7%)	44 (75.9%)	0.435
Race			
Caucasian	5 (18.5%)	46 (79.3%)	<0.001[b]
African American	19 (70.4%)	7 (12.1%)	
Other	3 (11.1%)	5 (8.6%)	
Hispanic	2 (7.4%)	8 (13.8%)	0.074
Insurance			
Private	13 (48.2%)	36 (62.1%)	0.466
Medicaid	13 (48.2%)	21 (36.2%)	
None	1 (3.7%)	1 (1.7%)	
Disease Characteristics			
Type of uveitis			
JIA-associated uveitis	9 (33.3%)	38 (65.5%)	0.009
Age at uveitis diagnosis (years), *Median (25^{th} – 75^{th})*	6.6 (4.8 – 9.0)	6.0 (3.5 – 11.8)	0.728
Location of Disease [a] (N = 82)			
Anterior	17 (65.4%)	44 (78.6%)	0.204
Intermediate	2 (7.7%)	3 (5.4%)	0.682
Posterior/Panuveitis	3 (11.5%)	1 (1.8%)	0.056
Unknown	4 (15.4%)	8 (14.3%)	0.897
Bilateral Disease [a] (N = 80)	21 (77.8%)	37 (69.8%)	0.453
Type of Complications			
Cataracts	21 (77.8%)	15 (25.9%)	<0.001[b]
Glaucoma/ocular hypertension	10 (37.0%)	4 (6.9%)	0.001[b]
Synechiae	19 (70.4%)	19 (32.8%)	0.002[b]
Band keratopathy	17 (63.0%)	10 (17.2%)	<0.001[b]
Cystoid macular edema	14 (51.9%)	8 (13.8%)	<0.001[b]
Initial Ocular Exam [a]			
≥1+ cells at first exam (N=45)	6 (60.0%)	22 (62.9%)	1.000
LogMAR Visual acuity (N=42) *Median (25^{th} – 75^{th})*	0.40 (0.18 – 1.00)	0.18 (0.00 – 0.30)	<0.001[b]

Characteristics **N = 85 unless otherwise specified** **N (%) unless otherwise specified**	**VA of 20/200 or worse**		**p-value**
	Yes **N=27 (31.8%)**	**No** **N=58 (68.2%)**	
Labs [a]			
ANA[c] positive (N=84)	12 (46.2%)	22 (37.9%)	0.631
Earliest ESR[d] (N=80) *Median (25th – 75th)*	7.0 (2.0 – 16.0)	17.0 (7.0 – 36.0)	0.002[b]
HLA[f]-B27 positive (N=56)	4 (22.2%)	10 (26.3%)	1.000
Medication Use [a] (N = 84)			
Methotrexate Oral	14 (51.9%)	38 (66.7%)	0.232
Methotrexate Subcutaneous	21 (77.8%)	42 (73.7%)	0.791
Infliximab	13 (48.2%)	14 (24.6%)	0.045[b]
Adalimumab	4 (14.8%)	13 (22.8%)	0.563

[a] Indicates missing data;

[b] p = <0.05; Chi-square tests, two sample t-tests, non-parametric test (Mann Whitney-U or Kolmogorov-Smirnov test).

[c] ANA = Antinuclear antibody.

[d] ESR = Erythrocyte Sedimentation Rate.

[e] HLA = Human Leukocyte Antigen.

Table 3
Comparison of Non-Hispanic African American and White Race in Childhood Uveitis

Characteristics N = 76 unless otherwise specified N (%) unless otherwise specified	Race		p-value
	African American N=27 (35.3%)	White N=49 (64.5%)	
Demographics			
Age at most recent visit, *Median (25^{th} – 75^{th})*	13.6 (9.9 – 16.5)	10.3 (8.9 – 14.8)	0.084
Gender, female	15 (55.6%)	36 (73.5%)	0.132
Insurance			
Private	8 (29.6%)	34 (69.4%)	0.002[b]
Medicaid	18 (66.7%)	13 (26.5%)	
None	1 (3.7%)	2 (4.1%)	
Uveitis Disease Characteristics			
Type of uveitis			
JIA-associated uveitis	8 (29.6%)	32 (65.3%)	0.003[b]
Age at uveitis diagnosis (years), *Median (25^{th} – 75^{th})*	9.2 (5.5 – 11.3)	5.3 (3.7 – 10.5)	0.030[b]
Uveitis duration at most recent visit (years), *Median (25^{th} – 75^{th})*	3.8 (2.8 – 4.6)	3.4 (1.3 – 6.1)	0.718
Location of Disease [a] (N = 70)			
Anterior	16 (66.7%)	35 (76.1%)	0.400
Intermediate	4 (16.7%)	1 (2.2%)	0.026[b]
Posterior/Panuveitis	2 (8.3%)	1 (2.2%)	0.226
Unknown	2 (8.3%)	9 (19.6%)	0.219
Bilateral Disease [a] (N = 71)	23 (85.2%)	27 (61.4%)	0.032[b]
Worst Ocular Exam [a], (N = 68)			
Slit lamp examination (cells),			
0 & 0.5+	5 (20.8%)	12 (27.3%)	0.770
1+ and worse	19 (79.2%)	32 (72.7%)	
Intraocular Pressure *Median (25^{th} – 75^{th})*	22.5 (17.5 – 34.5)	19.0 (18.0 – 24.0)	0.086
Visual Acuity 20/50 or worse	20 (80.0%)	22 (51.2%)	0.002[b]
Visual Acuity 20/200 or worse	18 (72.0%)	4 (9.3%)	<0.001[b]
Type of Complications			
Cataracts	18 (66.7%)	15 (30.6%)	0.004[b]
Glaucoma/ocular hypertension	8 (29.6%)	6 (12.2%)	0.073
Synechiae	16 (59.3%)	17 (34.7%)	0.054

Characteristics **N = 76 unless otherwise specified** **N (%) unless otherwise specified**	**Race**		**p-value**
	African American N=27 (35.3%)	**White N=49 (64.5%)**	
Band keratopathy	16 (59.3%)	9 (18.4%)	<0.001[b]
Cystoid macular edema	13 (48.2%)	8 (16.3%)	0.004[b]
Initial Ocular Exam [a], (N = 37)			
≥1+ cells at first exam	5 (50.0%)	17 (63.0%)	0.708
Intraocular pressure > 21	2 (28.6%)	0 (0.0%)	0.123
LogMAR Visual acuity *Median (25th – 75th)*	0.40 (0.18 – 0.70)	0.14 (0.00 – 0.18)	0.014[b]
Labs [a]			
ANA[c] positive *N=76*	11 (40.7%)	19 (38.8%)	1.000
Earliest ESR[d], *N=71* *Median (25th – 75th)*	9.0 (2.0 – 18.0)	14.0 (7.0 – 34.0)	0.076
HLA[e]-B27 positive, *N=51*	1 (5.3%)	12 (37.5%)	0.018[b]
Medication Use [a] (N = 75)			
Methotrexate Oral	13 (48.2%)	32 (66.7%)	0.144
Methotrexate Subcutaneous	21 (77.8%)	31 (64.6%)	0.301
Infliximab	10 (37.0%)	13 (22.8%)	0.258
Adalimumab	4 (15.4%)	12 (25.0%)	0.300

[a] Indicates missing data;

[b] p = <0.05; Chi-square tests, two sample t-tests, non-parametric test (Mann Whitney-U or Kolmogorov-Smirnov test)

[c] ANA = Antinuclear antibody.

[d] ESR = Erythrocyte Sedimentation Rate.

[e] HLA = Human Leukocyte Antigen.

Table 4

Risk factors for Ocular Complications or a Visual Acuity of 20/200 or Worse in Childhood Uveitis

Multivariable Models	Outcome	Risk Factors	Risk (95% CI)[1]	p-value
1 [a]	Visual acuity 20/200 or worse	Non-Hispanic African American	31.64 (5.94 – 168.49)	<0.001 [c]
		Non-JIA uveitis	1.32 (0.27 – 6.41)	0.731
		Uveitis duration	1.26 (1.00 – 1.59)	0.053
2 [a]	Any history of complication	Non-Hispanic African American	3.41 (0.75 – 15.49)	0.113
		Non-JIA uveitis	10.75 (2.62 – 43.48)	0.001 [c]
		Uveitis duration	1.44 (1.14 – 1.82)	0.003 [c]
3 [b]	Number of Complications	Non-Hispanic African American	2.21 (1.40, 3.49)	<0.001 [c]
		Non-JIA uveitis	1.94 (1.22, 3.11)	0.005 [c]

[a] For models 1 and 2, risk is presented as odds ratios with 95% confidence intervals.

[b] For model 3, risk is presented as a rate ratio, expressed as number of distinct complications / duration of disease in non-Hispanic African Americans compared to Caucasians or non-JIA uveitis compared to JIA-associated uveitis.

[c] p = <0.05.