Clinical Ophthalmology

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ORIGINAL RESEARCH

Sociodemographic and Visual Outcomes of Juvenile Idiopathic Arthritis Uveitis: IRIS® Registry Study

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Purpose: Understanding sociodemographic factors associated with poor visual outcomes in children with juvenile idiopathic arthritis-associated uveitis may help inform practice patterns.

Patients and Methods: Retrospective cohort study on patients <18 years old who were diagnosed with both juvenile idiopathic arthritis and uveitis based on International Classification of Diseases tenth edition codes in the Intelligent Research in Sight Registry through December 2020. Surgical history was extracted using current procedural terminology codes. The primary outcome was incidence of blindness (20/200 or worse) in at least one eye in association with sociodemographic factors. Secondary outcomes included cataract and glaucoma surgery following uveitis diagnosis. Hazard ratios were calculated using multivariable-adjusted Cox proportional hazards models.

Results: Median age of juvenile idiopathic arthritis-associated uveitis diagnosis was 11 (Interquartile Range: 8 to 15). In the Cox models adjusting for sociodemographic and insurance factors, the hazard ratios of best corrected visual acuity 20/200 or worse were higher in males compared to females (HR 2.15; 95% CI: 1.45–3.18), in Black or African American patients compared to White patients (2.54; 1.44–4.48), and in Medicaid-insured patients compared to commercially-insured patients (2.23; 1.48–3.37).

Conclusion: Sociodemographic factors and insurance coverage were associated with varying levels of risk for poor visual outcomes in children with juvenile idiopathic arthritis-associated uveitis.

Keywords: rheumatology, ophthalmology, uveitis, health inequity, social determinants of health

Introduction

Juvenile idiopathic arthritis (JIA), formerly referred to as juvenile rheumatoid arthritis, is the most common rheumatic disease in childhood and the most common systemic disease associated with pediatric uveitis.[1–3] JIA-associated uveitis is minimally symptomatic but associated with a high rate of sight-threatening complications.[4] Vision loss related to uveitis and its complications can result in lifelong visual impairment for a child, but may be prevented or reduced with early diagnosis and proper treatment.[3]

Barriers to care for JIA-associated uveitis may exist for numerous reasons and are associated with decreased remission rates in pediatric non-infectious uveitis.[5–9] These obstacles to care may be part of an individual's overall social determinants of health (SDOH), which are generally defined as

> the conditions in the environments where people are born, live, work, play, worship, and age which affect a wide range of health, function, and quality-of-life outcomes and risks.

Received: 22 December 2023
Accepted: 21 April 2024
Published: 8 May 2024

SDOH have been shown to impact access to healthcare and disease outcomes.[10,11] Because managing JIA-associated uveitis is complex and long term, SDOH likely impact treatment success and vision outcomes.[12–14]

The American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) provides nationwide data in the United States (US) that can be used to evaluate the relationship between sociodemographic factors and insurance coverage information with health and visual outcomes in patients with JIA-associated uveitis. As of July 1, 2022, there were 454 million patient visits from 75.4 million unique patients and 15,799 individual eye care clinicians in the database.[15] The IRIS Registry captures disease diagnoses, patient demographic information, and metrics of ocular health, including best-corrected visual acuity (BCVA) from participating practices' electronic health record (EHR) data. With access to this large and diverse database, we tested the hypothesis that sociodemographic factors and insurance coverage, as possible proxies for SDOH, are associated with different visual outcomes and complication rates for patients with JIA-associated uveitis.

Materials and Methods

This study was exempted from the University of Washington Institutional Review Board due to the use of de-identified data from the IRIS Registry. This study was performed in accordance with the Declaration of Helsinki.[16] Methods for collecting data from the IRIS Registry have been previously described.[17,18] Data was analyzed using IRIS Registry version: Chicago AMC_2021_12_24.

Patient Selection

The study population included children <18 years old with diagnoses of both JIA and uveitis who were actively followed in the IRIS Registry through December 2020 (Supplemental Figure 1). Participants were included regardless of whether they received a diagnosis of uveitis before or after a diagnosis of JIA. Diagnoses of JIA and uveitis were identified using International Classification of Disease 10th edition (ICD-10) codes (Supplemental Table 1), which included all subtypes of JIA with the exception of psoriatic arthritis which is listed as a separate ICD-10 code. This effectively created a start date for data collection in 2016.

Variables of Interest

We extracted the following variables of interest relevant to JIA-associated uveitis: age at uveitis diagnosis, duration of follow-up recorded in the IRIS Registry, BCVA and intraocular pressure at the initial uveitis diagnosis, the incidence of blindness defined as Snellen BCVA 20/200 or worse in at least one eye during the follow-up period, and rates of glaucoma or cataract surgery after JIA-associated uveitis diagnosis based on Current Procedural Terminology (CPT) codes (Supplemental Table 1). The need for cataract and glaucoma surgery was chosen as an indicator of complications related to JIA-associated uveitis as other commonly utilized clinical exam findings to assess visual outcomes and ocular complications are not available within the IRIS database (eg, posterior synechiae, cataract, band keratopathy, cystoid macular edema, and degree of inflammation).

Demographic and socioeconomic factors, including sex, race, and insurance status recorded in EHRs were utilized as proxies for SDOH.[19,20] We did not have methods to determine whether race was self-reported and/or staff-recorded from each contributing site. The IRIS Registry version used for the analysis has patient race categories of Asian, Black or African American, Native American and Alaskan Native, Native Hawaiian and Pacific Islander, Other, and White and allows one selection per patient. We combined the Asian, Native American and Alaskan Native, Native Hawaiian and Pacific Islander, and Other groups into a single analysis group due to low sample sizes ("Other"). Insurance coverage was organized into three categories: commercial, Medicaid, and other. The other insurance types in the IRIS Registry included government, military, miscellaneous, Medicare, Medicare Advantage, and no insurance.

Due to the structure of de-identified data in the IRIS Registry, each patient's age at diagnosis was inferred by subtracting the year of the date of diagnosis from their birth year. A given age at diagnosis in years calculated with this method corresponds to a range of possible true ages in months, resulting in an imprecise classification by years of age with overlap between successive age categories.

Statistical Analyses

Descriptive Visualizations

We generated locally estimated scatterplot smoothing (LOESS) curves for the average VA of patients' worst eyes over time as a function of sex, race, and insurance coverage. We also created Kaplan–Meier survival curves for the same predictors to model the proportion of patients developing the primary outcome, incidence of blindness defined as BCVA 20/200 or worse in at least one eye. For both visualizations, patients had to have a VA at baseline and the respective predictor to be included.

Survival Analyses

Patients with missing race, insurance data, or baseline VA measurement (at uveitis diagnosis) were excluded from the analytic dataset. Our primary outcome, 20/200 or worse in at least one eye, was analyzed using Cox proportional hazard models. Sex, race, and insurance type were our predictors of interest. Secondary analyses were performed to evaluate risk of sustained blindness which was defined as continued decreased visual acuity measures in at least one eye for at least 365 days.

We also developed Cox proportional hazards models for the risk of undergoing cataract or glaucoma surgery following uveitis diagnosis, with the same predictors as the Cox model for risk of blindness. All patients with uveitis and JIA diagnoses were included in this analysis. All analyses were performed with R statistical software version 3.6.1 and Python version 3.8.1.

Results

A total of 65,348,409 million unique patient records were evaluated for inclusion criteria in the IRIS Registry database (Supplemental Figure 1). We identified 1346 patients with both a JIA and uveitis diagnosis. A total of 979 (72.7%) were female, 364 (27.04%) were male, and 3 (0.22%) patients had unknown sex. There were 968 (71.92%) White patients, 74 (5.5%) Black or African American patients, 65 (4.83%) Other patients, and 239 patients of unknown race (17.76%). A total of 719 (53.42%) had commercial insurance, 339 (25.19%) had Medicaid, 72 (5.35%) had other insurance, and there were 216 (16.05%) patients with missing insurance information (Table 1).

Table 1 Demographic and Baseline Characteristics

Characteristic	Overall n (%)	Median Age at Uveitis Diagnosis (IQR)	Median Duration in Years of IRIS Follow-up (IQR)
All Participants	**1346**	**11 (8–15)**	**4.6 (1.9–7.0)**
Sex			
Female (reference)	979 (72.2)	11 (7.5–14)	4.8 (2.1–7.2)
Male	364 (27.0)	12 (8–15)	4.2 (1.5–6.8)
Not Reported	3 (0.2)	13 (10.5–15)	5.3 (2.7–6.2)
Race			
Asian and Other[a]	65 (4.8)	12 (8–15)	4.1 (1.7–6.4)
Black or African American	74 (5.5)	12 (9–15)	5.2 (1.6–7.2)
Unknown	239 (17.8)	12 (8–15)	2.5 (0.6–5.3)
White (reference)	968 (71.9)	11 (8–14)	5.1 (2.5–7.3)
Insurance Coverage Type			
Commercial (reference)	719 (53.4)	11 (8–14)	4.8 (2.1–7.0)
Medicaid	339 (25.2)	11 (8–14)	5.2 (2.8–7.4)
Other	72 (5.4)	11 (8–15)	3.0 (1.4–4.9)
Missing	216 (16.1)	12 (8–15)	3.6 (0.9–6.8)

Notes: [a]Asian and Other category includes races defined in IRIS Registry as Native American and Alaskan Native, Native Hawaiian and Other Pacific Islander, and Other race.
Abbreviations: IQR, interquartile range; IRIS, Intelligent Research in Sight Registry.

The median age of diagnosis of JIA-associated uveitis was 11 years old (Interquartile Range [IQR]: 8.0 to 15.0). The median follow-up for patients was 4.6 years (IQR: 1.9–7.0). Further statistics by demographic and insurance group can be found in Table 1.

Out of the 1346 patients with JIA-associated uveitis, 1001 (74.4%) had available baseline VA data, 588 (43.7%) had VA data at one year after uveitis diagnosis, 424 (31.5%) at year 2, and 320 (23.8%) at year 3. The average baseline VA was 0.22 logMAR (Snellen VA 20/33, 95% CI: 0.19–0.25) in patients' worst eye and 0.07 logMAR (Snellen VA 20/23, 95% CI: 0.06–0.08) in their best eye (Table 2). A total of 46 (3.4%) patients were recorded as having any cataract surgery and 28 (2.1%) as having any glaucoma surgery following JIA-associated uveitis diagnosis (Supplemental Table 2).

In the LOESS curves generated for VA following uveitis diagnosis, the temporal trends in visual outcomes across the predictors of interest can be observed over a three year period (Figure 1). Males demonstrated worse visual acuity than females at uveitis diagnosis, with differences persisting until after three years following diagnosis. Black or African American patients demonstrated worse visual outcomes when compared to White and Other patients, while Medicaid-insurance patients had worse outcomes compared to commercial-insured and other insurance patients. Similarly, Kaplan–Meier curves showed a faster time to blindness and a larger proportion reaching blindness in males, Black or African American patients, and Medicaid-insurance patients compared to females, White patients, and commercially insured or other insurance patients, respectively (Figure 2).

Using the Cox proportional hazards model (n = 687), 103 of the 687 patients eligible for analysis developed the outcome BCVA ≤ 20/200. The risk of blindness was higher in males compared to females (Hazard Ratio [HR]: 2.15, [95% CI: 1.45–3.18]) when accounting for race and insurance status. The risk of BCVA ≤ 20/200 was 2.5 fold higher in Black or African American patients than in White patients (HR: 2.54, 95% CI: 1.44–4.48) when accounting for sex and insurance. Additionally, the risk of blindness was more than double in Medicaid than in commercially-insured patients (HR: 2.23, 95% CI: 1.48–3.37) when accounting for sex and race. The results of the Cox proportional hazards models are summarized in Table 3. The secondary analyses performed for risk of sustained blindness demonstrated similar results (Supplemental Table 3). There were no statistically significant hazard ratios for cataract or glaucoma surgery with the same predictors with a significant threshold of $p < 0.01$ (Supplemental Table 2).

Table 2 Visual Acuity at Baseline by Predictor

Characteristic	LogMAR VA at Uveitis Diagnosis – Worst[a] Eye Mean (95% CI)	LogMAR VA at Uveitis Diagnosis – Best[b] Eye Mean (95% CI)
Participants (n = 1001)	**0.22 (0.19–0.25)**	**0.07 (0.06–0.08)**
Sex		
Female (723)	0.18 (0.15–0.21)	0.06 (0.05–0.07)
Male (276)	0.32 (0.25–0.39)	0.08 (0.05–0.1)
Race		
Asian or Other[c] (51)	0.29 (0.17–0.41)	0.09 (0.03–0.15)
Black or African American (51)	0.4 (0.23–0.57)	0.11 (0.05–0.17)
Unknown (171)	0.33 (0.24–0.42)	0.11 (0.07–0.15)
White (728)	0.17 (0.15–0.2)	0.05 (0.04–0.06)
Insurance Coverage Type		
Commercial (548)	0.15 (0.12–0.18)	0.05 (0.04–0.06)
Medicaid (249)	0.39 (0.31–0.47)	0.12 (0.09–0.15)
Other (48)	0.3 (0.13–0.47)	0.08 (0.01–0.15)
Missing (156)	0.17 (0.11–0.23)	0.05 (0.03–0.08)

Notes: [a]Worst eye defined as eye with lower visual acuity at baseline or the only eye with data available. [b]Best eye defined as the eye with better visual acuity at baseline. [c]Asian and Other category includes races defined in IRIS Registry as Native American and Alaskan Native, Native Hawaiian and Other Pacific Islander, and Other race.
Abbreviations: LogMAR, Logarithm of the Minimum Angle of Resolution; VA, visual acuity; CI, confidence interval.

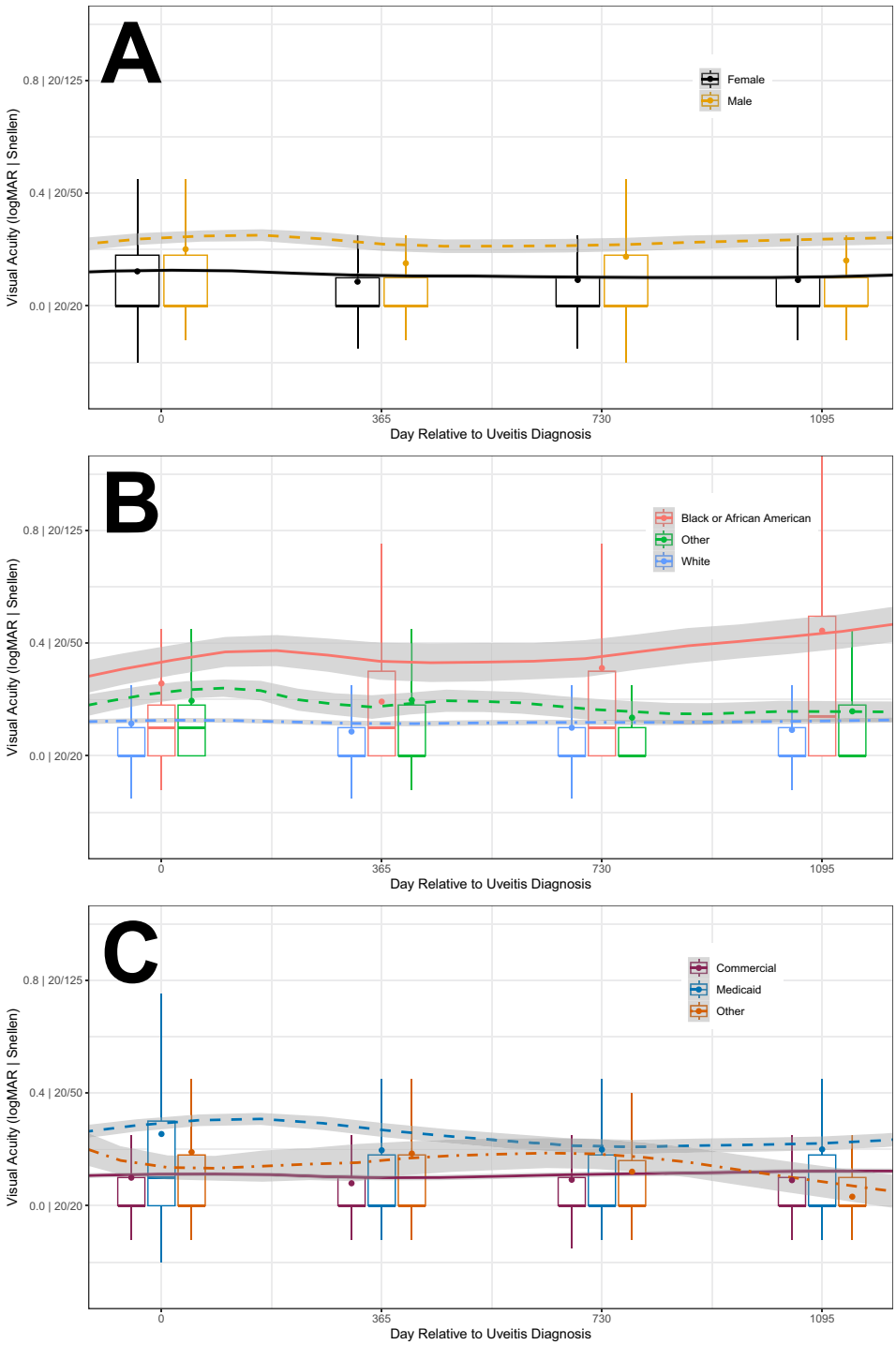

Figure 1 Visual Acuity Over Time After Uveitis Diagnosis. Boxplots displaying visual acuity for all patients at day 0, 365, 730, and 1095 from uveitis diagnosis. The minimum, 25th, 50th, 75th percentile and maximum visual acuity is represented in the box plot; the circle represents the mean. The LOESS curves are displayed continuously across the x-axis with the 95% confidence interval displayed in gray. The figure is shown for the respective subgroups: (**A**) Male and Female patients, (**B**) White, Black or African American, and Other participants, and (**C**) insurance type. Visual acuity data was tracked from all IRIS Registry visits available.

Discussion

Our review of 1346 children with JIA and uveitis in the IRIS Registry revealed that 15.0% of patients in our analytic set developed blindness in at least one eye after the initial uveitis diagnosis, with significant differences observed across sociodemographic and insurance groups that persisted over time. Patients who were male, Black or African American, or

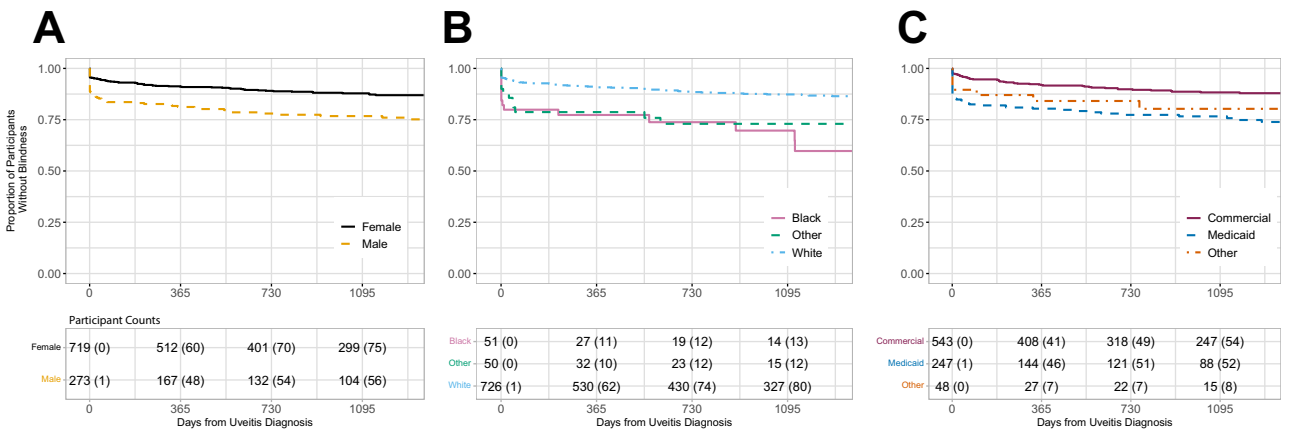

Figure 2 Proportion of Patients Without Visual Acuity ≤ 20/200 Relative to Uveitis Diagnosis (Kaplan–Meier Curves). Results are shown by (**A**) sex, (**B**) race, and (**C**) insurance status. Participant counts are given at yearly intervals in the tables below. The numbers in parentheses refer to the participants with the outcome at that time point. Later counts will not sum to their original values due to participant attrition.

were ever covered by Medicaid insurance had an increased risk of developing 20/200 or worse vision, compared to female, White, and commercially insured patients, respectively, when accounting for confounding variables.

Rates of severe vision loss 20/200 or worse at initial presentation have been reported in up to 24% of children with JIA-associated uveitis.[4,21,22] Treatment with long-term immunosuppressive medications has improved visual outcomes over time.[5,23–25] More recent population-based cohort studies of JIA uveitis children from the Nordic region and the Netherlands demonstrate blindness rates as low as 2% to 3.8%, as measured by visual acuity at last follow-up.[5,25] The earlier introduction of systemic immunomodulatory treatment is theorized to be a key factor for improved visual prognoses.[4,5,25] Our cohort included a more diverse patient population as compared to recent studies[5,25] and our results suggest that despite overall improvements in JIA-associated uveitis visual outcomes over the past few decades, not all populations may be experiencing progress similarly.

While we know that the rates and prevalence of JIA vary by sex, race, and ethnicity, literature on the visual outcomes of non-White populations with JIA-associated uveitis is rather limited.[26] Non-White race has previously been shown to be a risk factor for poor BCVA, but the sample size and the follow-up periods have been limited.[4,27] One study of 327 patients with JIA-associated uveitis from five US tertiary care centers found that non-White race was associated with

Table 3 Risk of Best-Corrected Visual Acuity 20/200 or Worse

Characteristic	HR (95% CI)	P-value
Sex		
Female (reference)	reference	reference
Male	2.15 (1.45–3.18)	<0.001
Race		
Asian or Other[a]	2.23 (0.98–5.31)	0.05
Black or African American	2.54 (1.44–4.48)	0.001
White (reference)	reference	reference
Insurance Coverage Type		
Commercial (reference)	reference	reference
Medicaid	2.23 (1.48–3.37)	<0.001
Other	1.01 (0.38–2.67)	0.99

Notes: [a]Asian and Other category includes races defined in IRIS Registry as Native American and Alaskan Native, Native Hawaiian and Other Pacific Islander, and Other race.

Abbreviations: HR, hazard ratio; CI, confidence interval.

>2.6-fold higher risk (95% CI: 1.99, 3.46, p < 0.01) of developing 20/200 or worse BCVA after controlling for age, sex, bilateral disease and duration of uveitis, though they did not control for insurance status or other socioeconomic factors.[4] In another study of 287 children with JIA, Black or African American patients were older at the time of the uveitis diagnosis (11.3 years old) compared to non-Hispanic White children (4.6 years old).[7] Additionally, despite a similar prevalence of uveitis between groups, Black or African American patients had higher rates of legal blindness compared to non-Hispanic White children (5/7, 71% vs 2/29, 7%; p < 0.001). We had a substantially larger group of Black or African American patients included in our analyses and found a similar trend - a 2.5-fold increased risk of blindness in Black or African American patients compared to White patients after controlling for sex and insurance type.

We also found that Medicaid patients in the IRIS Registry had a 2.2-fold higher risk of developing BCVA 20/200 or worse compared to their commercially insured peers while accounting for sex and race. Insurance carrier type has been shown to affect clinical outcomes in other pediatric ophthalmic diseases.[28] JIA-associated uveitis outcomes are likely impacted by access to overall systemic treatment for JIA. One study showed differences in public and private insurance delays in approval for biologic disease-modifying antirheumatic drugs.[29] Furthermore, low household income and reliance on public insurance have been associated with persistent disability and higher JIA disease activity.[14] Similarly, patients on Medicaid coverage have been shown to score worse on pediatric disability scales in a tertiary rheumatology clinic after controlling for race, JIA onset, and duration.[30] Delayed access to treatment due to costs and varying reimbursement rates per insurance or delayed diagnosis and/or referral to an ophthalmologist likely impact visual outcomes.[30]

In our large cohort, we found that males have a significantly higher risk of blindness than females when controlling for race and insurance status. This discrepancy in vision is notable at the baseline exam and continues throughout follow-up. This is consistent with other studies which note that males are more likely to have severe uveitis at presentation[31] as well as a higher risk of ocular complications and severe vision loss.[32–34] Specifically, males are at greater risk of vision-threatening ocular complications, including posterior synechiae, cystoid macular edema, papillitis, and cataracts.[32,33,35] Ayuso et al demonstrated that males more often present with an initial manifestation of uveitis rather than arthritis leading to a diagnosis of JIA, which could suggest increased ocular complications at presentation due to the insidious nature of JIA uveitis.[35] However, the initial presentation of uveitis was not shown to be associated with blindness in their study, although male gender was. The etiology of the differences in visual outcomes between males and females remain unclear.[31–33,35] Given a known higher prevalence of JIA-associated uveitis in females, both rheumatologists and ophthalmologists should be aware of the trend toward worse visual acuity outcomes in male patients to properly identify and refer patients who are at high risk of vision loss.

Several limitations exist with our study. The IRIS Registry data is primarily from community ophthalmology practices and includes few academic medical centers.[36] As opposed to other publications studying large cohorts of children with JIA-associated uveitis followed at tertiary care referral centers,[3,4] our population could reflect a different demographic. The median age of JIA uveitis diagnosis in our study was 11 years old, which is older than that cited in Smith et al, who studied 527 patients from 3 different academic institutions with a median age of 9.4 years. However, our age appears in line with that of Gregory et al, who evaluated 327 patients from 5 referral centers and found a median age of 15.6 years for the first ophthalmologic clinic visit with uveitis diagnosis in JIA patients. Regardless, due to the IRIS Registry data including mostly community ophthalmology practices, it is possible our study is not capturing patients referred directly (or for follow-up) to the tertiary care referral center. As academic eye centers often follow a significant portion of children with Medicaid insurance, this may have implications on our population's sociodemographic and insurance distribution.[37] Additionally, rates of cataract and glaucoma surgery in our study were lower than that found in Smith et al and Gregory et al, which may also reflect this difference if patients more likely to require surgery are subsequently referred to the academic institution for intervention, and there is a limited pediatric population within the IRIS Registry.

JIA uveitis diagnosis relies on ICD-10 diagnosis codes input by the physician, thus there is the possibility of coding errors. We cannot determine the method of refraction when obtaining BCVA measurements in the IRIS registry. Still, we would assume cycloplegic refraction is performed in the pediatric population given routine practice. Medication data was too limited to provide reliable statistics for our analytic cohort. Many clinical exam findings commonly used to assess

ocular complications and severity of uveitis are not available within the IRIS database (eg, posterior synechiae, cataract, band keratopathy, cystoid macular edema, and degree of inflammation), although we did assess for rates of cataract and glaucoma surgery in our study cohort. We did not include ICD codes for the psoriatic JIA subtype, and we did not use a lookback period with our analyses. Some patients may have had an existing uveitis diagnosis before seeing an IRIS Registry provider or before the implementation of ICD-10 coding, which could have led to an overestimation of the age at the uveitis onset. However, the discrepancy would have been randomly distributed among the subgroups, minimally impacting the overall conclusion.

Racial information was obtained from the electronic health record. While this data is assumed to be mostly self-reported, it is likely subject to variability in institutional patient registration practices and is limited to only one choice in the IRIS Registry. While we saw a discrepancy in the age at diagnosis across racial groups, we were unable to test whether this was due to a delay in diagnosis or another factor. Though limitations may exist regarding whether our patient population sampled within the IRIS registry is representative of the JIA uveitis population, our racial distribution of patients is similar to that reported in other studies of children with JIA using large, multiethnic cohorts.[7,26] Additionally, studies focusing on visual outcomes of JIA uveitis in children from minority groups are rare, thus our results contribute further insight to the literature. Lastly, previous research has demonstrated that a small proportion of JIA patients may develop blindness many years after diagnosis.[5] Still, with a median follow-up time of 4.6 years, we should have captured the vast majority of cases of blindness. More importantly, we also found similar results with prolonged blindness as the outcome. We included patients with variable durations of follow-up due to a low number of cases. In doing so, some of our visualizations may be biased toward patients with longer durations of follow-up; however, we found similar results in the survival analyses, which account for differences in follow-up.

Conclusion

In conclusion, sociodemographic factors, including race and insurance coverage, are associated with the clinical outcomes of children with JIA-associated uveitis. Despite overall improvements in visual outcomes due to advances in available therapies for JIA-associated uveitis, clinicians should be aware of these disparities and potential barriers to care when evaluating patients with JIA and JIA-associated uveitis. Future efforts may serve to better understand the mechanisms behind the differences we observed by measuring the impact of other social determinants of health.

Acknowledgments

Cecilia S Lee and Laura C Huang are co-senior authors for this study.

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Flora Lum, MD; American Academy of Ophthalmology, San Francisco, CA, Emily Chew, MD; National Eye Institute, Bethesda, MD, Julia A. Haller, MD; Wills Eye Hospital, Philadelphia, PA, Leslie G. Hyman, PhD; Wills Eye Hospital, Philadelphia, PA, Alice C. Lorch, MD, MPH; Department of Ophthalmology, Mass Eye and Ear, Harvard Medical School, Boston MA, Joan W. Miller, MD; Department of Ophthalmology, Mass Eye and Ear, Harvard Medical School, Boston MA, Suzann Pershing, MD; Department of Ophthalmology, Stanford University School of Medicine, Palo Alto, California.

Funding

National Institutes of Health grants K23EY029246, R01AG060942, OT2OD032644, the Latham Vision Research Innovation Award (Seattle, WA), the Klorfine Family Endowed Chair, the C. Dan and Irene Hunter Endowed Professorship, the Karalis Johnson Retina Center, and by an unrestricted grant from Research to Prevent Blindness. The sponsors or funding organizations had no role in the design or conduct of this research.

Disclosure

Dr. A. Lee reports support from the US Food and Drug Administration, grants from Amazon, Carl Zeiss Meditec, iCareWorld, Meta, Microsoft, Novartis, NVIDIA, Regeneron, Santen Pharmaceutical, and Topcon, personal fees from Alcon, Boehringer Ingelheim, Genentech/Roche, Gyroscope, Janssen, Johnson & Johnson, and Verana Health outside of

the submitted work, and nonfinancial support from Microsoft, Optomed, and Heidelberg, outside of the submitted work. Dr. C. Lee reports personal fees from Boehringer Ingelheim. This article does not reflect the opinions of the Food and Drug Administration. The authors report no other conflicts of interest in this work.

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