Patterns and complications of uveitis among patients with Juvenile Idiopathic Arthritis

Ali M. Alawneh, MD, Ahmed E. Khatatbeh,MD**, Shehab A. Alabed, MD** ,*
*Marwan M. Otoum, MD**, Mohammad Shdefat, MD**, Shrouq R. Albtoush, MD****

ABSTRACT

Aim: to explore the frequency and types of uveitis among Juvenile Idiopathic Arthritis (JIA) patients and to identify uveitis complications and there impacts on vision.

Method: a prospective study conducted at the ophthalmology clinic of Queen Rania Al Abdullah Children Hospital between 1st Jan. 2017 and 1st Jan. 2018. All patients who were diagnosed with (JIA) were included in the study. Data were obtained regarding age, gender, type and duration of JIA, type and duration of uveitis, Antinuclear Antibody ANA status and treatment used. Ocular examination was performed including best corrected visual acuity using Snellen chart, anterior segment exam using slit lamp, posterior segment exam using 90D and 78D Volk lens and intra ocular pressure measurement using Goldmann applanation tonometry. The data was analyzed and compared with other studies worldwide.

Results: 54 children with a mean age of 9.4±2.4 years were diagnosed to have JIA. 74% of them were female (male to female ratio 1:3). The mean duration of JIA was 5.1 years±1.9 years. The most common type of JIA was oligoarticular (four joints in the first six months of the symptoms) type (67%) followed by polyarticular (22%) and systemic onset types (11%). A high ANA titer was noted in 70% of patients and rheumatoid factor was detected in 7% of patients.

Uveitis was encountered in 13 patients (24%). The mean age of the patients was (9.9±2.9) years and the mean duration of uveitis was (3.7±1.6) years with male to female ratio of (1:4). Only one uveitis patient (8%) had systemic onset type of JIA and another patient had polyarticular type (8%), while the remaining patients (84%) had oligoarticular type. Rheumatoid factor was not detected in any of the JIA associated uveitis patients. Uveitis was bilateral in 12 patients (92%). ocular complications were detected in 64% of eyes and visual impairment were seen in only 32% of eyes. Ocular complications were seen in 64% of eyes with uveitis. Cataract, glaucoma and band keratopathy were the most frequent ones.

Conclusions: A higher frequency of uveitis with lower rates of moderate to severe visual impairments and ocular complications were seen in JIA patients. long duration of uveitis, late referral, , delay in starting systemic treatment including the biologics and glaucoma were associated with moderate to severe visual impairment. The most common complications seen in JIA uveitis patients were cataract, glaucoma and band keratopathy.

Key words: Juvenile idiopathic arthritis, uveitis, visual impairment.
RMS August 2023; 30 (2): 10.12816/0061610

Introduction

Juvenile idiopathic arthritis (JIA) refers to arthritis of known etiology, and it affects children younger than 16 years of age for at least 6 weeks' duration. (1)

From the Department of:
* surgical retina
** medical retina
*** ophthalmologist
Correspondence should be addressed to:
Submission date: , Acceptance date: , Publication date: August 2023

It is the most common rheumatic disease of childhood. (2) There is a wide geographical variation regarding its prevalence, which ranges 7-400/100,000. (3) The diagnosis of JIA is mainly clinical. However, raised erythrocyte sedimentation rate, elevated C-reactive protein, negative rheumatoid factor (RF) and high anti-nuclear antibody titer (ANA) are frequently observed among JIA patients. (4)

Pediatric uveitis accounts for about 10% of uveitis cases. (5) JIA-associated uveitis occurs in 4-38% of JIA patients and accounts for 15-67% of pediatric uveitis. (2,4) Studies have reported that female gender, early age of onset, positive ANA and oligoarticular category of JIA are risk factors for developing uveitis in JIA patients. (5,6)

JIA-associated uveitis is usually asymptomatic, and children are incapable of providing accurate description of uveitis symptoms unless they face severe complications. Therefore, late diagnosis of uveitis may contribute to a high rate of ocular complications, which may cause visual impairment and blindness. (7) Ocular complications that may adversely affect the vision include band keratopathy, posterior synechiae, cataract, glaucoma, hypotony, macular edema, epiretinal membrane, and optic disc edema. (8)

The aim of this study is to explore the frequency and types of uveitis among JIA patients and identify uveitis complications and its impacts on vision.

Method

This was a prospective study conducted at the ophthalmology clinic of Queen Rania Al Abdullah Children Hospital between January 2017 and January 2018. All patients diagnosed with JIA were included in the study. The patients were screened for uveitis at the ophthalmology clinic. Patients with ocular diseases and complications not related to uveitis like congenital or steroid induced cataract and glaucoma were excluded from the study. Initially, data were obtained regarding age, gender, type and duration of JIA, type and duration of uveitis, ANA status, and treatment used. Detailed ocular examination including best corrected visual acuity using Snellen chart, anterior segment examination using slit lamp, posterior segment examination using 90D and 78D Volk lens and intra ocular pressure measurement using Goldmann applanation tonometry. The obtained data were analyzed and compared with the findings of other studies conducted in regional countries and worldwide.

Results

A total of 54 children aged between 3 and 15 years (mean 9.4±2.4 years) were diagnosed with JIA at Queen Rania Al Abdullah Children Hospital. Of them, 74% were female (male to female ratio 1:3). The duration of JIA ranged from 6 months to 12 years (mean 5.1 years±1.9 years). The most common type of JIA was oligoarticular type (67%), followed by polyarticular (22%) and systemic onset types (11%). High ANA titer was noted in 70% of patients, and RF was detected in 7% of patients.

Uveitis was encountered in 13 patients (24%). The mean age of the patients was 9.9±2.9 years, and the mean duration of uveitis was 3.7±1.6 years with male to female ratio of 1:4. Only one uveitis patient (8%) had systemic onset type of JIA, one patient had polyarticular type (8%), and the remaining patients (84%) had oligoarticular type. RF was not detected in any patient with JIA-associated uveitis. Uveitis was bilateral in 12 patients (92%).

Table I : represents a comparison between JIA patients who developed uveitis and those who did not.

	JIA without uveitis (41 patients)	**JIA with uveitis (13 patients)**
Mean age (years)	9.2	9.9
Age of onset of JIA	4.6	3.3
Male to female ratio	1:2.4	1:5
Oligoarticular type	25 patients (61%)	11 patients (84%)
Systemic onset type	11 patients (27%)	1 patient (8%)
Polyarticular type	5 patients (12%)	1 patient (8%)
Positive ANA	28 patients (68%)	10 patients (77%)
Positive rheumatoid factor	4 patients (10%)	0%

Table II: represents the best corrected visual acuity among eyes with JIA associated uveitis.

BCVA	**Number of eyes**	**Percentage**
>0.5 to 1.0	17	68%
>0.3 to 0.5	4	16%
0.1 to 0.3	2	8%
<0.1	2	8%

The risk factors for moderate to severe visual impairment were long duration of uveitis, late referral, delay in starting systemic treatment including the biologics, and glaucoma. Age and gender did not show any significant association with deterioration of vision.

Uveitis complications were reported in 16 eyes (64%), and **Table III** represents the types of complications encountered in those patients.

Complication	Number of eyes	percentage
Band keratopathy	7	28%
Posterior synechiae	6	24%
Cataract	7	28%
Pseudophakia	4	16%
Aphakia	2	8%
glaucoma	7	28%
Vitreous haze	2	8%
vasculitis	2	8%
Macular edema	1	4%

The most common complication responsible for visual impairment in JIA patients was cataract, followed by band keratopathy. However, glaucoma was most commonly associated with severe visual impairment. The most common form of uveitis was chronic anterior uveitis (68%), followed by recurrent anterior uveitis (24%) and pan uveitis (8%).

Discussion

Uveitis is the most common extra articular manifestation of JIA. It can result in serious ocular morbidities due to the high rate of associated complications (9). Although the prevalence of JIA is not yet studied in Jordan, JIA is commonly seen in pediatric medical practice. In our study, the mean age of the patients was 9.4 years and the mean duration of JIA was 4.9 years. In addition, the mean age of JIA onset worldwide has a wide range of variability; it can be as low as 2.8 years in the USA to as high as 7.3 years in Switzerland (10,11). This variability could be implicated by genetic factors. In the present study, the mean age of JIA onset was 4.3 years.

As reported in many global studies, oligoarticular JIA is the most common form at a rate of 64% in our study. However, it was higher than that found in Germany (41%) and lower than that found in Japan (81%). (12,13) In the present study, the rate of uveitis was much higher than that found in other parts of the world like Japan (6.1%), Germany (12%) and the USA (18%)(10,12,13). However, a few studies have reported a high rate of uveitis of up to 30% of JIA patients (14). In addition, the rate of uveitis was reported to be 31%, 17%, and 8% in oligoarticular, poly articular and systemic onset types of JIA, respectively. The high rate of uveitis among JIA patients, particularly in oligoarticular subtype, necessitates frequent and routine ocular screening of JIA patients to detect uveitis and prevent ocular morbidity and blindness. JIA patients with uveitis were associated with significant (P value <0.05) lower age of JIA onset, higher female to male ratio, higher rate of ANA titer, and lower rate of RF titer. These results are in line with the findings of other studies but with variable percentage. Although positive rheumatoid factor was associated with lower rates of uveitis and seems to be a protective factor we think that this might be a distinct form of arthritis which is not associated with uveitis rather than JIA. These factors were considered as risk factors for the development of uveitis in JIA patients (5). Uveitis may precede the onset of arthritis in 3-7% of cases (2) while in our study, all patients were previously diagnosed with JIA before the onset of uveitis. This may be because uveitis is a

silent and asymptomatic disease in most of the JIA patients. Moreover, patients will not attend the ophthalmology clinic unless there is significant decline in vision (15). In Jordan, there is no routine or programmed ocular examination for preschool and school children. This may hinder the detection of uveitis in cases that may precede the onset of arthritis.

Visual impairments are commonly seen in JIA-associated uveitis due to the high rate of ocular complications resulting from uveitis, which may approach 73% (18). In the present study, ocular complications were detected in 64% of eyes, and visual impairment were seen in only 32% of eyes. These rates were lower than the global values. Only 16% of eyes showed moderate to severe visual impairment (≤0.3) and 8% eyes showed visual acuity of less than 0.1. In comparison, Gregory et al reported that 40% of eyes had visual acuity of 20/50 or less and 24% of eyes were found to have visual acuity of 20/200 or less (19). The policy at Queen Rania Al Abdullah Children Hospital is to immediately start systemic immune modulating therapy, including biologics for JIA patients with chronic uveitis, which might be the main reason for those lower rates. Risk factors for moderate to severe visual impairments were long duration of uveitis, late referral, delay in starting systemic treatment including the biologics, and glaucoma. So, 3 out of 4 of the risk factors are modifiable and adjustable. Therefore, a new policy should be adopted, particularly in peripheral hospitals, to control those risk factors before significant visual impairment takes place. These results are in line with other studies, except for gender, as age and gender did not show any significant association with deterioration of vision. Meanwhile, Edelsten et al. reported a higher rate of complications and visual impairment among males compared to females (19,20).

Uveitis complications were seen in 64% of eyes. This rate is higher than the rates in adults (21). This is attributed to the nature of uveitis, i.e., chronic and asymptomatic, among JIA patients (white eye). In addition, children are not aware and are unable to express their complaints related to uveitis.

The most common complications seen in JIA uveitis patients were cataract, glaucoma, and band keratopathy. However, glaucoma was associated with a higher risk for severe visual impairment. Glaucoma may develop in those patients as a result of damage to the trabecular meshwork drainage system or because of the steroids used to treat uveitis. In addition, angle closure resulting from anterior or posterior synechiae may also lead to glaucoma.

Finally, the present study is the first in Jordan to describe the frequency of uveitis among JIA patients and the rates of ocular complications and visual impairments seen in those patients. The sample size was relatively small, but higher frequency of uveitis with lower rates of moderate to severe visual impairments and ocular complications were seen in JIA patients at Queen Rania Al Abdullah children hospital compared to studies conducted in the USA and Europe. Genetic and geographical factors might be implicated in this issue. More comprehensive data should be obtained from other medical sectors to calculate more accurate rates and prevalence. In addition, this study showed that most of the risk factors for moderate to severe visual impairments are controllable, so effective measures should be activated to reduce visual morbidities.

Conclusions

Higher frequency of uveitis with lower rates of moderate to severe visual impairments and ocular complications were seen in JIA patients. Long duration of uveitis, late referral, delay in starting systemic treatment including the biologics, and glaucoma were associated with moderate to severe visual impairment. The most common complications seen in JIA uveitis patients were cataract, glaucoma and band keratopathy.

References

1. **Saurenmann, R. K., Levin, A. V., Feldman, et al.** Prevalence, risk factors, and outcome of uveitis in juvenile idiopathic arthritis: A long- term followup study. Arthritis & Rheumatism 2007; 56: 647-657.
2. **Sarah L. NC, Ethan S, Athimalaipet VR.** Juvenile idiopathic arthritis-associated uveitis. Pediatric Rheumatology 2016;14:2.
3. **Barut K, Adrovic A, Şahin S, Kasapçopur Ö.** Juvenile Idiopathic Arthritis. Balkan Med J. 2017;34(2):90-101.
4. **Majumder PD, Biswas J.** Pediatric uveitis: An update. Oman J Ophthalmol. 2013;6(3):140–50.
5. **Moradi A., Amin RM, and Thorne JE,** "The Role of gender in juvenile idiopathic arthritis-associated uveitis, J Ophthalmology 2014; 461078, doi10.1155/2014/4610787.
6. **Christoph T., Jens K., Claudia S. et al.** Risk Factors and Biomarkers for the Occurrence of Uveitis in Juvenile Idiopathic Arthritis: Data From the Inception Cohort of Newly Diagnosed Patients With Juvenile Idiopathic Arthritis Study. Arthritis Rheumatol. 2018; 70(10): 1685–1694.
7. **de Boer J, Wulffraat N, Rothova A.** Visual loss in uveitis of childhood. Br J.Ophthalmol. 2003;87(7):879–84.
8. **Anthony CG, John HK, Ebenezer D, et al.** Risk Factors for Loss of Visual Acuity among Patients with Uveitis Associated With Juvenile Idiopathic Arthritis: The SITE Study. Ophthalmology. 2013 Jan; 120(1): 186–192.
9. **Qian Y, Acharya NR.** Juvenile idiopathic arthritis-associated uveitis. Curr Opin Ophthalmol. 2010;21(6):468–472.
10. **Angeles-Han ST, McCracken C, Yeh S, et al.** Characteristics of a cohort of children with Juvenile Idiopathic Arthritis and JIA-associated Uveitis. Pediatric Rheumatol. Online J. 2015;13:–19.
11. **Sabri K, Saurenmann RK, Silverman ED, et al.** Course, complications, and outcome of juvenile arthritis-related uveitis. J AAPOS. 2008;12(6):539–45
12. **Heiligenhaus A, Niewerth M, Ganser G, et al.** German uveitis in childhood study group. Prevalence and complications of uveitis in juvenile idiopathic arthritis in a population-based nation-wide study in Germany: suggested modification of the current screening guidelines. Rheumatology. 2007;46:1015–1019.
13. **Yasumura J, Yashiro M, Okamoto N, et al.** Clinical features and characteristics of uveitis associated with juvenile idiopathic arthritis in Japan: first report of the pediatric rheumatology association of Japan (PRAJ). Pediatr Rheumatol Online J. 2019;17(1):15. Published 2019 Apr 11.
14. **Moradi A, Amin RM, Thorne JE.** The role of gender in juvenile idiopathic arthritis-associated uveitis. *J Ophthalmol*. 2014;2014:461078. doi:10.1155/2014/461078.

15. **Cosickic A, Halilbasic M, Selimovic A, Avdagic H.** Uveitis Associated with Juvenile Idiopathic Arthritis, our Observations. Med Arch. 2017;71(1):52–55. doi:10.5455/medarh.2017.71.52-55.
16. **Lazarević D, Nikolić I, Ratković-Janković M, Vojinović J.** Outcome of Juvenile Idiopathic Arthritis Associated Uveitis in Two Disease Subtypes. Arch Rheumatol. 2017;32(1):26–31. Published 2017 Jan 6. doi:10.5606/ArchRheumatol.2017.6060
17. **Asproudis I, Felekis T, Tsanou E, et al.** Juvenile idiopathic arthritis-associated uveitis: Data from a region in Western Greece. Clin Ophthalmol. 2010;4(4):343–347. Published 2010 Apr 26.
18. **Kump LI.. Cervantes RA.,.Androudi SN, et al.** Visual Outcomes in Children with Juvenile Idiopathic Arthritis–Associated Uveitis. Ophthalmology 2006; 113(10): 1874-1877.
19. **Gregory AC 2nd, Kempen JH, Daniel E, et al.** Risk factors for loss of visual acuity among patients with uveitis associated with juvenile idiopathic arthritis: the Systemic Immunosuppressive Therapy for Eye Diseases Study. Ophthalmology. 2013;120(1):186–192.
20. **Edelsten C, Lee V, Bentley CR, et al.** An evaluation of baseline risk factors predicting severity in juvenile idiopathic arthritis associated uveitis and other chronic anterior uveitis in early childhood. Br J Ophthalmol. 2002;86(1):51–56.
21. **Cunningham ET, Smith JR, Tugal-Tutkun I, et. al.** Uveitis in Children and Adolescents. Ocular Immunology and Inflammation 2016; 24(4): 365-371.
22. **Heinz C., M. Koch JM, Zurek-Imhoff B, Heiligenhaus A.** (2009) Prevalence of Uveitic Secondary Glaucoma and Success of Nonsurgical Treatment in Adults and Children in a Tertiary Referral Center, Ocular Immunol Inflamm 2009; 17(4: 243-248.