

# Idiopathic uveitis presents different characteristics and outcome from juvenile idiopathic arthritis- related uveitis

Uveíte idiopática apresenta características e desfecho diferentes da uveíte associada à Artrite Idiopática Juvenil

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## How to cite:

Andrade RL, Zamora YF, Barbosa CM, Fraga MM, Nicacio AA, Muccioli C, et al. Idiopathic uveitis presents different characteristics and outcomes from juvenile idiopathic arthritis-related uveitis. Rev Bras Oftalmol. 2024;83:e0019.

## doi:

<https://doi.org/10.37039/1982.8551.20240019>

## Keywords:

Uveitis; Arthritis, juvenile; Eye diseases; Blindness

## Descritores:

Uveíte; Artrite juvenil; Oftalmopatias; Cegueira

## Received on:

Jul 25, 2023

## Accepted on:

Jan 20, 2024

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## Conflict of interest:

no conflict of interest.

## Financial support:

no financial support for this work.



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## ABSTRACT

**Objective:** To describe the clinical features and outcomes of patients with uveitis associated with juvenile idiopathic arthritis (JIA) and idiopathic uveitis.

**Methods:** This was an observational, retrospective study, conducted in a tertiary center. Patients under 18 years old who experienced at least one episode of uveitis and followed between 2000 and 2019 were included.

**Results:** A total of 82 patients were included, of whom 43 had idiopathic uveitis and 39 had uveitis associated with JIA. Anterior uveitis was the primary site of ocular inflammation (76.8%) and occurred in 24 and 39 patients with idiopathic uveitis and uveitis associated with JIA arthritis, respectively ( $p=0.02$ ). The complete response to corticotherapy was more frequent in uveitis associated with JIA ( $p=0.001$ ). Total and partial responses to biological disease modifying antirheumatic drugs were more frequent in uveitis associated with JIA ( $p=0.025$ ) and idiopathic uveitis ( $p=0.045$ ), respectively. There were 203 complications: cataracts were more frequently present in idiopathic uveitis ( $p=0.05$ ), while synechiae was more frequent in uveitis associated with JIA ( $p=0.02$ ).

**Conclusion:** Idiopathic uveitis and uveitis associated JIA frequently follow a chronic course and an increased risk of visual loss in childhood. The uveitis associated with JIA showed better response to systemic corticotherapy and total response to biologic disease modifying antirheumatic drugs more frequently.

## RESUMO

**Objetivos:** Descrever as características clínicas e desfechos dos pacientes com uveíte associada à Artrite Idiopática Juvenil (AIJ) e da Uveíte Idiopática.

**Métodos:** Este foi um estudo retrospectivo observacional conduzido em um centro terciário. Foram incluídos pacientes abaixo dos 18 anos de idade que apresentaram pelo menos um episódio de uveíte e que estiveram em acompanhamento médico entre os anos de 2000 e 2019.

**Resultados:** Foram incluídos 82 pacientes, sendo 43 com uveíte idiopática e 39 com uveíte associada à AIJ. A uveíte anterior foi o sítio primário de acometimento (76,8%) em 24 e 39 pacientes com uveíte idiopática e uveíte associada à AIJ, respectivamente ( $p=0.02$ ). Resposta total à corticoterapia foi mais frequente na uveíte associada à AIJ ( $p=0.001$ ). Respostas total e parcial às drogas antirreumáticas modificadoras de doença biológicas foram mais frequentes na uveíte associada à AIJ ( $p=0.025$ ) e na uveíte idiopática ( $p=0.045$ ), respectivamente. Foram encontradas 203 complicações: a catarata foi mais frequente na uveíte idiopática ( $p=0.05$ ), enquanto a sinéquia foi mais frequente na uveíte associada à AIJ ( $p=0.02$ ).

**Conclusão:** A uveíte idiopática e a uveíte associada à AIJ frequentemente apresentam um curso crônico e um risco elevado de perda visual na infância. A uveíte associada à AIJ apresentou melhor resposta à corticoterapia sistêmica e resposta total às drogas modificadoras de doença reumática biológicas mais frequentemente.

## INTRODUCTION

Uveitis is a rare inflammatory eye disease in the pediatric population, accounting for 5 to 10% of all uveitis cases.<sup>(1-4)</sup> Although rare, it can be associated with a high risk for eye complications and severe visual loss.<sup>(1-4)</sup>

Uveitis can be either infectious or immune mediated. Non-infectious causes of uveitis in the pediatric population correspond to 69 to 95% of all uveitis, and juvenile idiopathic arthritis (JIA) is the most common systemic cause of uveitis in children, corresponding to 41 to 47% of cases.<sup>(5)</sup> However, the etiology of uveitis is not always possible to determine, being characterized as idiopathic uveitis (IU) that corresponds to 28 to 51% of cases.<sup>(2)</sup>

The most common clinical presentation of uveitis in children is anterior, bilateral, chronic, recurrent, asymptomatic, and is related to oligoarticular JIA.<sup>(4)</sup> The acute uveitis, when presenting with ocular hyperemia, pain, and photophobia, is frequently associated with the enthesitis-related arthritis (ERA) subtype.<sup>(3,6)</sup>

The complications secondary to uveitis are reported in 35.5 to 76% of pediatric uveitis patients.<sup>(3,6)</sup> Uveitis patients may develop secondary glaucoma, cataract, band keratopathy, and cystoid macular edema, which can result in visual loss and blindness,<sup>(3,6,7)</sup> despite treatment. Complications can also result from treatment with topical and systemic corticosteroids.<sup>(2,5,7,8)</sup> The initial treatment of anterior uveitis indicates the use of topical corticosteroids as the first-line agent.<sup>(3,8,9)</sup> In refractory cases, systemic immunosuppression should be initiated, with methotrexate being the first line agent.<sup>(3,8,9)</sup> In the absence of response to methotrexate, biological drugs, especially anti-tumor necrosis factor (TNF) agents, are indicated.<sup>(3,6,9)</sup> We decided to carry out this study because of the relevance of this important ocular manifestation and the scarcity of Brazilian publications.

We assessed the clinical characteristics and treatment outcomes in uveitis associated to juvenile idiopathic arthritis (JIA-U) and IU in a pediatric population from a tertiary center. Our objective was to assess demographic data, clinical findings (systemic and ocular), and treatment outcome in this population.

## METHODS

This observational, retrospective cohort study was carried out in a tertiary Pediatric Rheumatology care center in collaboration with the Department of Ophthalmology and included patients that were followed from January 2000 to January 2019. The clinical files of 463 patients were reviewed. Eighty-two patients with diagnosis of uveitis (of

whom 43 presented IU and 39 JIA-U) were included in this study. Other causes for uveitis such as infectious diseases, tubulointerstitial nephritis, and uveitis syndrome, masquerade syndromes, sarcoidosis, and other causes of autoimmune or autoinflammatory diseases, were ruled out. This study was approved by the Ethics Committee of the Federal University of São Paulo (Unifesp), under number 3.771.584.

The inclusion criteria were patients under 18 years old, of both sexes, and all ethnicities, who had experienced at least one episode of uveitis and classified as IU (defined as intraocular inflammation not attributed to any specific ocular or systemic cause) or JIA-U, according to the International League Against Rheumatism (ILAR)<sup>(5)</sup> and International Uveitis Study Group (IUSG).<sup>(10)</sup> The diagnosis of uveitis was performed by uveitis experts from the Ophthalmology Department. Patients with other causes of uveitis and incomplete patient records were excluded from the study. Patients with acute anterior uveitis associated with ERA were also excluded. Exams to rule out other causes of uveitis included: Mantoux test, bacterial and viral serologies, determination of angiotensin converting enzyme, calciuria, urine analysis, and chest X ray. Data about demographics (age and sex), clinical features (uveitis classification and course, and presence of antinuclear antibodies – ANA), complications, and clinical and surgical treatment were collected.

As a routine in the Pediatric Rheumatology Unit, all patients underwent a regular ocular screening every 3 months. At each visit, complete ocular examination was performed and included best corrected visual acuity (BCVA) measure, slit lamp evaluation, intraocular pressure, and fundus examination. The uveitis was classified according to the primary site of inflammation in anterior, intermediate, posterior, or panuveitis.<sup>(11)</sup> The ocular disease was considered active when the ophthalmologic examination showed any of the following: cells and flare in the anterior chamber, keratic precipitates (PK's), hypopyon, iris nodules, vitreous cells, snowballs, snowbanks, and inflammatory active lesions in the retina or choroid, or vasculitis, whether associated with the symptoms or not. Recurrence was defined as when uveitis reactivation occurred after 3 months of inactivity without treatment. Chronic uveitis was defined as a persistent uveitis with relapse in less than 3 months after treatment suspension.<sup>(12)</sup>

The Sun Working Group Activity Criteria was used to define inactivity, worsening, improvement and also remission. Visual acuity measurement was converted from the Snellen fraction to LogMAR units.<sup>(12)</sup> Demographic and clinical data, laboratory exams, treatment outcomes,

and follow up, were collected from the patients' files. ANA detection was performed by immunofluorescence.<sup>(13)</sup> Rheumatoid factor (RF) was detected by latex agglutination technique.<sup>(14)</sup> Response to each treatment was defined by the authors as: total (when inactive ocular inflammation was achieved), partial (improvement in ocular inflammation without achieving inactive disease) and no response (worsening or no improvement of ocular inflammation). Indication for disease modifying anti-rheumatic drug (DMARD) use was the need for more than one ocular drop for over a month.

The statistical analyses for the categorical variables were presented as the absolute and relative frequencies, and for the numerical variables, the mean and standard deviation were considered. Chi-squared or Fisher's exact test was used for categorical variables and Mann-Whitney test for continuous variables. P values  $\leq 0.05$  were considered statistically significant.

## RESULTS

From the total of 82 patients included, 43 (52.4%) had a diagnosis of IU and 39 (47.6%) of JIA-U. The JIA subtypes according to the ILAR classification criteria<sup>(5)</sup> were oligoarticular in 27 (69.2%) patients and polyarticular in 12 (30.8%). Arthritis was the first manifestation of 76.9% of JIA-U. Antinuclear antibodies were positive in 28 (71.8%) patients with JIA-U and in 20 (46.5%) patients with IU. No patient with JIA-U or IU had positive RF. Only one out of 15 patients with JIA-U and two out of 25 with IU presented positive

**Table 1.** Demographic and clinical data of patients with idiopathic uveitis and uveitis associated to juvenile idiopathic arthritis

	IU (n=43)	JIA-U (n=39)	Total (n=82)	p-value
Demographic data				
Female	29 (67.4)	33 (84.6)	62 (75)	0
Current age, Years	16 $\pm$ 4.9	17 $\pm$ 8	16 $\pm$ 6.5	0.640
Age at uveitis diagnosis, years	7.3 $\pm$ 2.7	6.5 $\pm$ 4.9	6.9 $\pm$ 3.2	0.290
Age at JIA diagnosis, years	NA	5.7 $\pm$ 3.5	NA	NA
Clinical data				
Arthritis as first manifestation	NA	30 (76.9)	NA	NA
Clinical course of uveitis*				
Acute	2 (4.7)	5 (12.8)	7 (8.5)	0.190
Chronic	28 (65.1)	22 (56.4)	50 (61.0)	0.670
Recurrent	13 (30.2)	11 (28.2)	24 (29.3)	0.910
Primary site of uveitis				
Anterior	24 (55.8)	39 (100)	63 (76.8)	0.020
Intermediate	16 (37.2)	0	16 (19.5)	0.0001
Posterior	0	0	0	NA
Panuveitis	3 (7.0)	0	3 (3.7)	0.090
Positive ANA	20 (46.5)	28 (71.8)	48 (58.3)	0.130
Female	14 (32.6)	25 (64.6)	39 (47.6)	<0.001

Results expressed as n (%) or mean  $\pm$  standard deviation.

\* In one patient with juvenile idiopathic arthritis it was not possible to determine the clinical course of uveitis. IU: idiopathic uveitis; JIA-U: uveitis associated to juvenile idiopathic arthritis; JIA - juvenile idiopathic arthritis; NA: not applicable; ANA: antinuclear antibody.

tuberculin skin test and were treated for latent tuberculosis once tuberculosis disease had been ruled out.

The demographic and clinical data of these patients were described in table 1. Anterior uveitis was present in 63 (76.8%) patients, having been diagnosed in all patients with JIA-U and in 24 patients with IU. For the IU group, 16 (37.2%) patients presented intermediate uveitis, and 3 (7.0%) presented panuveitis. No posterior uveitis was observed in either group.

Table 2 shows the uveitis treatment. The main systemic route of corticosteroids was oral and only two patients with JIA-U underwent intravenous pulse therapy with methylprednisolone due to severe and persistent ocular inflammation. The total response to systemic corticotherapy was more frequent in JIA-U (p=0.001).

**Table 2.** Treatment approach and response to medications of patients with idiopathic uveitis and uveitis associated to juvenile idiopathic arthritis

	IU (n=43)	JIA-U (n=39)	Total (n=82)	p-value
Corticotherapy				
Topical corticosteroids	38 (88.4)	32 (82.1)	70 (85.4)	0.620
Systemic corticosteroids	30 (69.8)	19 (48.7)*	49 (58.8)	0.560
Response to systemic corticosteroids				
Total	n=30	n=18†	n=48	
Partial	2 (6.7)	10 (55.6)	12 (25)	0.001
No response	28 (93.3)	6 (33.3)	34 (70.8)	0.010
Patients using synthetic DMARDs				
Methotrexate	n=38	n=38	n=76	
Cyclosporine	37 (97.4)	34 (89.5)	71 (93.4)	0.480
Leflunomide	9 (23.8)	8 (21.0)	17 (22.4)	0.680
Azathioprine	1 (2.6)	8 (21.0)	9 (11.8)	0.020
No response	0	1 (2.6)	1 (1.3)	0.330
Number of synthetic DMARDs/patients				
One	n=38	n=38	n=76	
Two	34 (89.5)	21 (55.3)	55 (72.4)	0.070
Three or more	4 (10.5)	13 (34.2)	17 (22.4)	0.020
Response to synthetic DMARDs/patients				
Total	n=38	n=38	n=76	
Partial	21 (55.3)	20 (52.6)	41 (53.9)	0.870
No response	15 (39.5)	13 (34.2)	28 (36.8)	0.700
No information	0	4 (10.5)	4 (5.3)	0.040
Patients using biological DMARDs				
Adalimumab	n=8	n=15	n=23	
Infliximab	8 (100)	13 (86.7)	21 (91.3)	0.640
Etanercept	3 (37.5)	4 (26.7)	7 (30.4)	0.120
Tocilizumab	1 (12.5)	4 (26.7)	5 (21.7)	0.520
Abatacept	1 (12.5)	3 (20.0)	4 (17.4)	0.720
No response	0	2 (13.0)	2 (8.7)	0.310
Number of biological DMARDs/patients				
One	n=8	n=15	n=23	
Two	4 (50.0)	9 (60.0)	13 (56.5)	0.760
Three or more	4 (50.0)	3 (20.0)	7 (30.4)	0.210
Response to biological DMARDs/patient				
Total	n=8	n=15	n=23	
Partial	0	3 (20.0)	3 (13.0)	0.200
No response	3 (37.5)	7 (46.7)	10 (43.5)	0.025
No information	4 (50.0)	4 (26.7)	8 (34.8)	0.045
No response	1 (12.5)	3 (20.0)	4 (17.4)	0.150
No information	0	1 (6.6)	1 (4.3)	NA

Results expressed as n (%).

\* Three patients with uveitis associated with juvenile idiopathic arthritis used corticosteroid therapy for arthritis and not for uveitis; † one patient did not have data on the response to corticotherapy. IU: idiopathic uveitis; JIA-U: uveitis associated with juvenile idiopathic arthritis; DMARDs: disease-modifying antirheumatic drugs.

Regarding synthetic DMARDs (sDMARDs), a total of 38 (97.4%; n=39) patients with JIA-U and 38 (88.4%; n=43) patients with IU used them to control ocular inflammation in case they needed more than one drop/eye for longer than one month. Methotrexate was the first choice of sDMARDs in both groups of patients, with a total of 71 (93.4%; n=76) prescriptions. Forty-one (53.9%; n=76) patients showed a total response to sDMARDs (methotrexate, cyclosporine, leflunomide and azathioprine). Twenty-eight (36.8%; n=76) patients had partial response to a sDMARD, requiring the addition of biological DMARDs (bDMARDs), such as anti-TNF agents or anti-interleukin 6, or local treatment for disease activity control. Prescription of more than one sDMARDs for uveitis control was greater in the group of JIA-U (two sDMARDs,  $p=0.02$ ; three sDMARDs,  $p=0.04$ ). A total of 23 (28.0%; n=82) patients used bDMARDs, of which 15 (38.5%; n=39) patients were due to JIA-U and 8 (18.6%; n=43) due to IU. Adalimumab was the first choice of bDMARDs in both groups and it was prescribed in 21 (91.3%; n=23) patients. Regarding bDMARDs response, a total response was significantly more common in JIA-U patients ( $p=0.025$ ), while partial response was significantly more frequent in IU group ( $p=0.045$ ) (Table 2).

Concerning ocular complications, 53 (64.6%) patients presented some kind of sequelae lesion, of whom 34 (64.2 %; n=53) belonged to the IU group and 19 (35.8%; n=53) to the JIA-U. The main ocular complications in the IU group were band keratopathy (36 eyes), cataract (34 eyes), and anterior/posterior synechiae (23 eyes). Secondary glaucoma/ocular hypertension was observed in 15 eyes of 12 patients; of whom two eyes received intravitreal triamcinolone and 1 eye was injected with subtenon triamcinolone. Nine of these glaucomatous patients used oral corticosteroids. In the JIA-U group, the main ocular complications were: anterior/posterior synechiae (19 eyes), band keratopathy (15 eyes) and secondary cataract (13 eyes). The presence of cataracts was more frequently found in the IU group ( $p=0.05$ ) and anterior/posterior synechiae in JIA-U ( $p=0.02$ ). Eleven (12.8%; n=86) eyes of 11 patients with IU, and 8 eyes (10.3%; n=78) of 6 patients with JIA-U had visual acuity of less than 20/400. A total of seven eyes from six patients had total blindness, due to phthisis bulbi (four eyes), band keratopathy (two eyes), and optic atrophy (one eye) (Table 3). There was no difference between the two groups regarding the frequency of loss of visual acuity ( $p=0.43$ ).

**Table 3.** Ocular complications in patients with idiopathic uveitis and uveitis associated with juvenile idiopathic arthritis

Complications	IU (n=144 complications)	JIA-U (n=59 complications)	Total (n=203 complications)	p-value
Band keratopathy	36 (25.0)	15 (25.4)	51 (25.1)	0.950
Cataract	34 (23.6)	13 (22.0)	47 (23.2)	0.050
Anterior/ posterior synechiae	23 (16.0)	19 (32.2)	42 (20.7)	0.020
Glaucoma/ eye hypertension	15 (10.4)	3 (5.0)	18 (8.9)	0.240
Macular edema	11 (7.6)	1 (1.7)	12 (6.0)	0.110
Retinal detachment	7 (4.9)	5 (8.6)	12 (6.0)	0.330
Epiretinal membrane	4 (2.8)	0	4 (2.0)	0.200
Choroidal neovascular membrane	3 (2.1)	0	3 (2.0)	0.200
Posterior capsule opacity	3 (2.1)	2 (3.4)	5 (2.5)	0.590
Vitreous hemorrhage	3 (2.1)	0	3 (1.5)	0.260
Phthisis bulbi	3 (2.1)	1 (1.7)	4 (2.0)	0.850
Optic atrophy	1 (0.7)	0	1 (0.5)	0.520
Visual loss				
VA less than 20/400	13/86 (15.1)	8/78 (10.3)	21/164 (12.8)	0.670
Total blindness	4 (2.8)	3 (5.1)	7 (3.4)	0.430

Results expressed as n (%).

IU: idiopathic uveitis; JIA-U: uveitis associated with juvenile idiopathic arthritis; VA: visual acuity.

A total of 70 surgical procedures due to ocular complications were performed, of which 54 procedures (in 30 eyes) belonged to the IU group ( $p=0.01$ ). The procedures included in the IU group were: cataract surgery in 20 eyes (66.7%; n=30 eyes), treatment with intravitreal triamcinolone in 7 eyes (23.3%; n=30), phototherapeutic keratectomy in 7 eyes (23.3%; n=30), trabeculectomy surgery due to uncontrolled intraocular pressure in 6 eyes (20%; n=30), subtenon corticosteroids injection in 3 eyes (10%; n=30), treatment with anti-vascular endothelial growth factor (anti-VEGF) due to choroidal neovascular membrane in 3 eyes (10%; n=30), laser posterior capsulotomy in 3 eyes (10%; n=30), laser photocoagulation in 2 eyes (6.7%; n=30), vitrectomy via pars plana (VVPP) in 2 eyes (6.7%; n=30) and cyclophotocoagulation due to uncontrolled glaucoma in 1 eye (3.3%; n=30). In patients with JIA-U, among 16 procedures (in 16 eyes), cataract surgery was performed on 11 eyes (68.8%; n=16 eyes), VVPP in 4 eyes (25%; n=16) and glaucoma surgery in 1 eye (6.2%; n=16).

Recurrences were observed in 52 (63.4%) patients: 37 (86%) patients from the IU group and 15 (38.5%) patients from the JIA-U group, without statistically significant difference among them. Patients with JIA-U that experienced recurrences had more ocular complications ( $p=0.017$ ) and surgical treatment ( $p=0.05$ ) than patients from the same group without recurrences. Similar results were found in the IU group where the patients with recurrences were more frequently submitted to surgical treatment ( $p=0.013$ ); however, they did not present more ocular complications.

## DISCUSSION

Non-infectious uveitis in childhood represents a real challenge due to the chronic nature of the disease, the high number of ocular complications secondary to inflammation, and also due to the frequent systemic and ocular complications associated with treatment. Several studies agree that IU is the most common diagnosis across tertiary centers.<sup>(15-18)</sup> The mean age of uveitis diagnosis (6.9 years) of our patients was consistent with the literature.<sup>(17)</sup> Similarly to previous studies, females were more representative in all included patients (about 55%).<sup>(4)</sup> Anterior uveitis was the most common site of ocular inflammation in both groups, representing all cases of JIA-U patients. In general, anterior uveitis is considered the most frequent ocular type of uveitis in children.<sup>(4)</sup> Also, a chronic course of uveitis was present in the majority of the studied patients, followed by recurrent, and lastly, acute uveitis.<sup>(15,19)</sup> Positive ANA was observed more frequently in JIA-U patients than in IU patients in our study. Our results corroborated the fact that the risk of chronic anterior uveitis in JIA patients is higher in those with positive ANA.<sup>(20,21)</sup> On the other hand, no case of JIA-U with positive RF, which is described as a protective factor for uveal involvement, was found.<sup>(22)</sup> Almost half of IU patients had positive ANA. We must be cautious when interpreting this result because 12.6% of healthy Brazilian children have this antibody.<sup>(23)</sup>

Regarding treatment approach, it was observed that more than half of the patients included required systemic corticosteroids to control uveitis. A significant difference between topical (prednisolone acetate) and systemic corticosteroids use in both groups was not observed. In this sense, patients with JIA-U presented better responses to systemic corticosteroids than patients with IU.

Concerning DMARDs use, it is known that they are not only prescribed as corticosteroids but also control the long-term course of uveitis.<sup>(24)</sup> Our results showed that methotrexate was the first choice of treatment in both studied groups, consistent with the literature.<sup>(25,26)</sup> However, additional topical steroids or synthetic/biologic DMARDs drugs are often required, as observed in our results. Furthermore, the use of two or more DMARDs for uveitis control was found more frequently in the JIA-U group. More than half of the patients had a total response to DMARDs prescription.

In children with refractory uveitis or intolerance to sDMARDs (mainly methotrexate), bDMARDs are recommended.<sup>(26)</sup> In our study, biologic drugs were indicated in both groups, with no statistical difference regarding the number of medications used per patient or their response.

This data is similar to that reported by Heiligenhaus et al.<sup>(27)</sup> It is important to highlight that the data from our study was collected between 2000 and 2019, and the routine use of biologic drugs (especially monoclonal anti-TNF agents) as standard treatment for non-infectious uveitis non-responsive to methotrexate started in 2010. Consequently, from this date, the chronic use of systemic corticosteroids has been progressively reduced.<sup>(28)</sup>

Uveitis in childhood is frequently associated with a high level of ocular complication due to delayed diagnosis and is secondary to oligosymptomatic cases in most children, especially those at young age. Also, the chronic course of the disease and the corticosteroids used to control the ocular inflammation can favor the presence of these complications. Since most patients had been taking corticosteroids at the time of the onset of the complication, it is hard to confirm if this complication was related to refractory uveitis, or chronic use of corticosteroids. In our study, a higher frequency of ocular complications was observed, probably related to the fact that patients followed in a tertiary referral center tend to have more severe diseases, with poor outcome, in addition to the aforementioned factors. In this sense, anterior segment complications were the main ocular complications in both groups. Patients with JIA-U had a higher risk of developing anterior/posterior synechiae due to the anterior uveitis involvement present in all patients of this group. On the other hand, patients with IU had more frequently cataracts. A different result was found by Al-Haddad et al, in which vitreous haze was reported as the main ocular complication in IU.<sup>(4)</sup> Visual loss is strongly associated with the presence of ocular complication regardless of uveitis etiology.<sup>(29)</sup> Visual acuity in the logMAR unit was greater than 1.3 in one tenth of the analyzed eyes. Total blindness was observed in seven eyes from six patients. A delay in referral to a tertiary care center has been reported as a risk factor for poor visual outcome.<sup>(30)</sup> The ocular complications present at the time of uveitis diagnosis and treatment with biological drugs (because those drugs were introduced later) could also explain the dramatic course in these patients regarding visual acuity. The presence of recurrences in more than half of patients was associated with higher number of sequelae and higher frequency of surgeries, especially in JIA-U patients.

The authors are aware of the limitations of this study, including its retrospective nature and the ophthalmologic exam performed by different experts. However, all patients were assessed by uveitis specialists, with a standardized ocular evaluation and management. This makes

our study clinically relevant because it presents the clinical-demographic characteristics of the two main causes of uveitis in the pediatric population in tertiary centers. Additionally, this study warns ophthalmologists, pediatricians, and pediatric rheumatologists, of the importance of prompt diagnosis and treatment to avoid complications.

## CONCLUSION

We conclude that idiopathic uveitis and uveitis associated to juvenile idiopathic arthritis as the main causes of uveitis in children frequently present with a chronic course and a high risk of ocular complications, increasing the risk of loss of visual acuity in childhood. The uveitis associated to juvenile idiopathic arthritis showed greater response to systemic corticosteroid therapy. There was no significant difference between the groups in relation to uveitis response to synthetic disease modifying antirheumatic drugs. Total response to biological disease modifying antirheumatic drugs was more frequently observed in the uveitis associated to juvenile idiopathic arthritis group. The presence of cataracts and anterior/posterior synechiae were more frequent in idiopathic uveitis and uveitis associated to juvenile idiopathic arthritis groups respectively. Recurrences and surgical treatment were equally frequent in both groups, although procedures were more frequently performed in the idiopathic uveitis group.

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