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Uveitis Patterns and Severity: An Epidemiologic Study from a Tertiary Care Private Referral Center in Buenos Aires, Argentina

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ABSTRACT

Purpose: To report uveitis' spectrum in a private practice cohort in the city of Buenos Aires, Argentina. **Methods:** Retrospective review at Instituto de la Visión (November 2011-October 2015). Standard demographics, ethnicity and Native American aboriginal ancestry were recorded.

Results: Among 212 patients, median age 45 (6-97), 10% pediatric, 35% bilateral, 72% non-idiopathic, 36% infectious. Anterior uveitis presented in 50%, followed by posterior (32%), intermediate (9%) and panuveitis (8%). Frequent visits (\geq 6 per year) needed by 29%: posterior, non-idiopathic disease with 79% systemic immunosuppression requirement was their main presentation. Native American aboriginal ancestry was reported by 22.64% of the whole cohort and 37% of frequent visits' subgroup.

Conclusions: Unilateral, non-idiopathic, non-infectious anterior uveitis was the most frequent presentation, in agreement with reports coming from western developed cities. The multi-racial Argentinian population with specific Native American aboriginal ancestry might contribute to certain forms of posterior uveitis and their response to treatment. **ARTICLE HISTORY**

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KEYWORDS Ancestry; Argentina; epidemiology; severity; urban; uveitis

Under the designation of uveitis are regrouped a variety of inflammatory (infectious or autoimmune) ocular diseases, which when poorly treated, can potentially lead to blindness (uveitis is responsible for 5–10% of visual impairment worldwide).¹ The prevalence and phenotypic expression of uveitis vary with age, sex, diet and social habits but is also influenced by geographic location and ethnicity.² Important differences arise as well between rural and urban settings.³

Some uveitic entities by nature have a guarded prognosis. In most cases however, response to therapy can be anticipated, though the nature of this response will vary from case to case and from individual to individual. Therefore, it is difficult to establish universal criteria for severity and treatment response, though such criteria would be useful to judge response in different settings.^{4–6}

The present study is aimed at describing the epidemiological and clinical features of patients referred and managed in a private uveitis practice in the city of Buenos Aires, Argentina. The city of Buenos Aires is an autonomous district and the largest urban conglomerate in Argentina, with a permanent population of about 3 million people and a local catchment area of 13.5 million.⁷ The Instituto de la Visión is a private specialized ophthalmology clinic in which a uveitis department was created as a separate division in 2011. The clinic is considered a referral center for patients with complex eye diseases, but it is not part of the Argentinean Public Health System. Hence, patients treated there have health insurance or can pay for care out of pocket. The study reports on the incidence of both non-infectious and infectious uveitis over a period of 4 years (2011–2015) and describes the clinical features of this particular patient's population.

Materials and methods

This is a retrospective review study of all clinical files of patients referred to the Uveitis Clinic at the Instituto de la Visión in Buenos Aires, Argentina, from November 2011 to October 2015. The study followed the tenets of the Declaration of Helsinski for epidemiological studies and was approved and monitored by the Instituto de la Visión Ethics Committee for human trials. Charts of individual patients were reviewed only after obtaining informed consent.

Patients with infectious and non-infectious uveitis were retained in this analysis. Excluded were patients with a masquerade syndrome (either benign or malignant) and those with the eye involved in a surgical or traumatic injury without contralateral inflammatory eye disease. Patients with scleritis and episcleritis were also excluded.

At the initial visit, demographic data, age of onset, disease anatomic location, clinical course and systemic medical history were collected. Each patient was asked about their ancestry, with specific questioning regarding Native American ethnicity. Patients were classified as suffering from adult-onset disease if uveitis was first observed after 16 years of age and of pediatric origin if it had started prior to that age. At each visit, a complete ophthalmic evaluation was systematically performed (Snellen best corrected visual acuity, slit lamp biomicroscopy, applanation tonometry and dilated fundus examination). Ancillary ophthalmic tests (visual field, fundus autofluorescence, fluorescein angiography, indocyanine green angiography, optical coherence tomography, ultrasound biomicroscopy) were obtained as required on a case-by-case basis. Similarly, systemic investigations (blood tests, tomographic scans, magnetic resonance images, pet scans and biopsies) were ordered after analyzing preliminary clinical and ocular findings in a specific tailored approach. Ocular fluid samples were obtained when required during the patient's initial visit or follow-up, based on clinical picture and diagnosis' suspicion. Once obtained, the sample (aqueous humor and/or vitreous) was processed as per etiological hypothesis in a particular case (polymerase chain reaction when infectious etiology was suspected; cytokine analyses, flow cytometry and cytology whenever masquerade syndrome was considered).

The need and use of systemic, periocular and intraocular immunosuppressive drugs were recorded and correlated with the underlying etiology. Complications of particular interest in uveitis were also recorded as separate entities including retinal vasculitis in at least one complete retinal quadrant, retinitis, uveitis related macular edema requiring specific treatment (besides the treatment of uveitis itself), visual field damage in at least one eye, with a residual visual field of 20 degrees or less, retinal or choroidal neovascularization and phthisis bulbi related to uveitis.

For patients with more than 6 visits per year, a sub-analysis was carried out to determine the clinical characteristics leading them to require frequent visits.

Uveitis was classified anatomically according to the criteria of the Standardization of Uveitis Nomenclature Working Group (SUN)⁸ and the International Uveitis Study Group (IUSG).⁹

Granulomatous uveitis was defined by the presence of medium to large size keratic precipitates, iris nodules (either Köeppe or Busacca type) and/or optic disc or choroidal granulomas; the absence of these findings defined the nongranulomatous nature of the disease. Specific clinical entities were defined upon established clinical criteria and supporting laboratory evidence as needed.

A diagnosis of herpetic anterior uveitis was based on the presence of unilateral granulomatous inflammation, elevated intraocular pressure, granulomatous keratic precipitates and sectoral iris atrophy. Posterior segment herpetic disease was classified as Acute Retinal Necrosis (ARN),¹⁰ Progressive Outer Retinal Necrosis (PORN)¹¹ and cytomegalovirus (CMV) retinitis¹² according to established criteria.

Acute Anterior Uveitis (AAU), associated or not with HLA B27 haplotype, was characterized by recurrent, unilateral, sudden onset and alternating nature, non-granulomatous inflammation, with significant cellular and fibrinous anterior chamber reaction.¹³ HLA B27 – associated uveitis' clinical picture could also be represented by panuveitis and/or retinal vasculitis, following exclusion of other possible diagnosis.^{14,15}

Juvenile idiopathic arthritis (JIA) associated uveitis was defined as a chronic, anterior non-granulomatous uveitis (even granulomatous inflammation was also a rare but possible presentation), frequently associated with elevated flare and posterior synechiae and starting no later than 16 years old. Antinuclear antibodies (ANA) positivity was considered a risk factor for the development of complications but not required for the diagnosis.^{16–18}

Fuchs' uveitis was defined as a chronic, low grade anterior uveitis with or without anterior vitreous cells, characteristic fine, stellate granulomatous keratic precipitates, stromal iris atrophy, with or without heterochromia and absence of posterior synechiae and macular edema. While most cases were unilateral, if the above criteria were met and other etiologies have been properly ruled out, bilaterally was allowed.^{19–21}

Posner-Schlossman syndrome was characterized by recurrent attacks of acute, unilateral, mild anterior granulomatous uveitis with elevated intraocular pressure, in the presence of an open angle.^{22–24}

Behçet's disease (BD) was diagnosed according to the criteria of the International Study Group for BD²⁵; for Vogt-Koyanagi-Harada (VKH) disease, the 2001 revised diagnostic criteria were used.²⁶

Ocular sarcoidosis was classified as definite, presumed, probable and possible according to the criteria proposed by the International Workshop on Ocular Sarcoidosis.²⁷

White dot syndromes were defined based on the clinical criteria for each entity already described in literature.^{28,29} Multimodal images were applied to each case within this group of retino-choroidal diseases.^{30,31}

The diagnosis of tuberculous uveitis was based on the exclusion of other etiologies, the presence of an evocative clinical picture, a positive Mantoux test and a positive response to tuberculostatic treatment.³²

Toxoplasmic retinochoroiditis in the immunocompetent host was diagnosed on the basis of a focus of retinitis in the setting of mild granulomatous anterior segment inflammation, presence of retino-choroidal pigmented scar and positive IgG serology. In cases of primo infection, a scar was not present and both IgM and IgG had to test positive.³³

Any focus of retinitis affecting the immunosuppressed host and/or elderly patient was diagnosed clinically and confirmed by aqueous humor analysis.^{34–36} Any case of retinitis judged as unusual to be clinically diagnosed was treated upon the result of ocular fluid analysis.

Given the nature of this study, only descriptive statistics were used (mean, median and range) and were computed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

Results

During the study period, 238 patients were referred to the Uveitis Clinic for evaluation and management; among them, 26 did not have uveitis and were excluded from this analysis. The mean age of the remaining 212 patients was 45 years old (range 6–97), including 21 pediatric cases (10%). Male to female ratio was almost equal (107 to 105). Median follow up was 22,82 months.

Anterior uveitis was the most frequent anatomic presentation (107 cases, 50%), followed by posterior uveitis (68 cases, 32%), intermediate uveitis (20 cases, 9%) and panuveitis (17 cases, 8%). Disease was bilateral in 76 cases, being bilateral involvement most commonly present in posterior uveitis (28 patients). An etiology could be identified in 72% of cases, while an infectious etiology was present in 36% of individuals. Table 1 summarizes the main demographic features.

In patients with anterior uveitis, 30% were idiopathic cases (4 granulomatous uveitis, 29 non-granulomatous). Herpes uveitis was the most common infectious cause: anterior uveitis in 21 eyes and endotheliitis in 2. Among the remaining patients, HLA-B27 associated acute anterior uveitis (AAU HLAB27) was the most common diagnosis, followed by Fuchs' uveitis.

Among intermediate uveitis patients, 14 were idiopathic in nature (Table 2). Both eyes were involved in all idiopathic cases, as well as in sarcoidosis and multiple sclerosis but not in other etiologies.

Idiopathic cases were less frequent in posterior uveitis (9 patients, 13%) (Table 2). An infectious origin was present in 43% of cases, being toxoplasmosis the most frequent etiology. Behçet disease was the most frequent non-infectious cause.

Panuveitis was diagnosed in 17 patients (28 eyes). Infectious etiology was present in 5 (7 eyes), of which 5 eyes (3 patients) were tuberculosis related uveitis. Non-infectious etiologies were found in 12 patients (21 eyes), with VKH the most frequent diagnosis in this group (5 patients, 10 eyes), followed by sarcoidosis (2 patients, 4 eyes) and Behçet disease (2 patients, 3 eyes). Table 2 summarizes the distribution of different etiologies among different anatomic locations.

During the follow-up, visually significant cataract in the setting of uveitis developed in 16 patients (20 eyes); inflammatory glaucoma in 10 patients (11 eyes) and uveitis-related cystoid macular edema affected 20 patients (26 eyes).

Systemic immunosuppression was needed in 68 patients (32%); within this group, 8 received only oral prednisone; 31 received a combination of steroids and immunosuppressants and 29 received immunosuppressants without steroids (Table 3).

A slow-release steroid implant was injected in the vitreous cavity of 6 patients (11 eyes); in all cases the dexamethasone one was administered.

Sub-tenon triamcinolone acetonide (40 mg/ml) injections were administered to 4 patients (7 eyes).

Intravitreal methotrexate (400 microgrames/0.1 ml) was given to 4 eyes of 3 patients. One eye suffered from chronic cystoid macular edema secondary to unilateral idiopathic non-granulomatous anterior uveitis and responded very well to this approach. The other 3 eyes (2 patients) suffered from white dots syndrome (1 case of multifocal choroiditis and panuveitis, MCPU, and the other one of serpiginous choroiditis).

Table 1. Main demographic characteristics of the study population.

Age	45 years old (6–97)		
Pediatric cases	21 patients (10%)		
Gender	107 males – 105 females		
Duration	28.41 months (1–72)		
Laterality	65% unilateral – 35% bilateral		
Inflammation pattern	64% non-infectious – 36% infectious		
Etiology	72% non-idiopathic – 28% idiopathic		

Table 2. Anatomic involvement. Main number indicates cases while number in brackets refers to eyes. Idiopathic posterior uveitis includes idiopathic retinitis (1 patient, 1 eye) and idiopathic retinal vasculitis (8 patients, 8 eyes). HLA B27 related uveitis regroups acute anterior uveitis, intermediate, retinal vasculitis (posterior) and panuveitis cases.

Anterior	Intermediate	Posterior	Panuveitis
		1 (2)	
		2 (4)	
2 (4)		6 (11)	2 (3)
		3 (6)	
9 (9)	1 (1)		
20 (24)	1 (1)	2 (3)	2 (3)
33 (40)	14 (28)	9 (9)	1 (1)
		1 (2)	
		1 (1)	
5 (10)			
		4 (7)	
	• •		
1 (2)	2 (4)	. ,	2 (4)
		4 (8)	
1 (2)			
			5 (10)
Anterior	Intermediate	Posterior	Panuveitis
2 (2)	1 (1)		
23 (23)		4 (7)	
		1 (1)	
7 (7)			
. ,		3 (3)	
. (=)		. ,	1 (1)
		. ,	1 (1)
2 (3)	1 (1)	()	3 (5)
	2 (4) 9 (9) 20 (24) 33 (40) 5 (10) 1 (2) 1 (2) 1 (2) 23 (23) 7 (7) 1 (2)	2 (4) 9 (9) 1 (1) 20 (24) 1 (1) 33 (40) 14 (28) 5 (10) 1 (2) Anterior Intermediate 2 (2) 1 (1) 23 (23) 7 (7) 1 (2)	$\begin{array}{c} 1 & (2) \\ 2 & (4) \\ 2 & (4) \\ 6 & (11) \\ 3 & (6) \\ 9 & (9) \\ 1 & (1) \\ 20 & (24) \\ 11 & (1) \\ 20 & (24) \\ 11 & (2) \\ 133 & (40) \\ 14 & (28) \\ 9 & (9) \\ 1 & (2)$

JIA: Juvenile Idiopathic Arthritis. APMPPE: Acute Posterior Multifocal Placoid Pigment Epitheliopathy. MCPU: Multifocal Choroiditis and Panuveitis. VKH: Vogt Koyanagi Harada. IRVAN: Idiopathic Retinal Vasculitis, Aneurysms and Neurorretinitis. RRD: Rhegmatogenous Retinal Detachment. HIV: Human Immunodeficiency Virus.

Excluding cases of toxoplasmic retinochoroiditis, retinal vasculitis affecting at least one retinal quadrant was present in 20 patients (26 eyes) and retinitis in 6 (9 eyes) Tables 4 and 5.

Five eyes presented with unilateral phthisis bulbi secondary to active persistent intraocular inflammation despite treatment. Their diagnosis is summarized in Table 6.

Nine patients (14 eyes) developed permanent severe visual field loss (defined as 20 or less degrees of visual field in at least one eye). Only 3 patients within this group suffered from uveitis-related glaucoma. In the remaining 11 ones, visual field loss was related to uveitic optic nerve damage (optic neuropathy in the setting of syphilitic uveitis, Behçet disease or herpetic posterior uveitis) Table 7.

Choroidal neovascularization occurred in 4 patients (6 eyes) while 1 developed bilateral retinal neovascularization in the setting of IRVAN syndrome (Idiopathic Retinal Vasculitis, Aneurysms and Neuroretinitis) Table 8.

Sixty-two patients (106 eyes) had 6 or more visits in one year. Median age in this group was 37.54 years old, distributed equally between men and women. Posterior involvement was most frequently observed (29 patients, 49%). Disease was idiopathic in 14 cases (23%). Patients with the following diagnosis were more likely to require frequent follow ups: Behçet's disease (9 patients), VKH syndrome (5 patients), sarcoidosis (4 patients) and HLA B27 non-anterior uveitis (retinal vasculitis in 3 patients and panuveitis in 1).

 Table 3. Distribution of systemic immunosuppressive treatment modalities among different etiologic diagnosis. Main number indicates cases while number in brackets refers to eyes.

			Combined treatment (steroids and
Diagnosis	Steroids	Immunosuppressants	immunosuppresants
VKH	3 (6)		2 (4)
Sarcoidosis	3 (6)	3 (6)	
APMPPE	1 (2)		
Behçet's disease			10 (20)
Birdshot			3 (6)
Serpiginous Choroiditis		1 (1)	2 (4)
Ampiginous Choroiditis			2 (4)
MCPU		4 (6)	
HLA B27 panuveitis			2 (3)
HLA B27 posterior uveitis		2 (3)	
JIA associated uveitis		4 (8)	
Idiopathic intermediate uveitis	4 (8)	7 (14)	2 (2)
Lupus related intermediate uveitis			1 (1)
Childhood sarcoidosis		1 (2)	
Idiopathic Uveitis and RRD			1 (1)
Idiopathic retinitis		1 (1)	
ldiopathic retinal vasculitis		5 (6)	3 (4)
IRVAN		1 (2)	
Toxocariasis	1 (1)		1 (1)

VKH: Vogt Koyanagi Harada. APMPPE: Acute Posterior Multifocal Placoid Pigment Epitheliopathy. MCPU: Multifocal Choroiditis and PanUveitis. JIA: Juvenile Idiopathic Arthritis. RRD: Rhegmatogenous Retinal Detachment. IRVAN: Idiopathic Retinal Vasculitis, Aneurysms and Neurorretinitis.

 Table 4. Vasculitis affecting at least one complete retinal quadrant (excluding toxoplasmic retinochoroiditis).

Diagnosis	N* of Patients (N* of Eyes)
Behçet's disease	8 (16)
Idiopathic retinal vasculitis	8 (10)
HLA-B27 associated retinal vasculitis	2 (3)
HLA-B27 associated panuveitis	1 (2)
IRVAN	1 (2)

IRVAN: Idiopathic Retinal Vasculitis, Aneurysms and Neuroretinitis.

 Table 5. Retinitis affecting at least one complete retinal quadrant (excluding toxoplasmic retinochoroiditis).

Diagnosis N* of Patients (N* of Eyes)		Host immune status
ARN	1 (1)	Immunocompetent
ARN	1 (2)	Immunosuppressed
CMV retinitis	2 (4)	Immunosuppressed
Behcet's disease	1 (1)	Immunosuppressed
Idiopathic retinitis	1 (1)	Immunosuppressed

ARN: Acute Retinal Necrosis. CMV: Cytomegalovirus.

Table 6. Phthisis bulbi related to active persistent inflammation despite treatment.

Diagnosis	N* of Patients (N* of Eyes)
Behcet's disease	2 (2)
Idiopathic intermediate uveitis	1 (1)
HLA B27 associated panuveitis	1 (1)
Congenital toxoplasmosis	1 (1)

Systemic immunosuppression was used in 49 cases. The remainder received one or more intravitreal dexamethasone implants, sub-tenon triamcinolone or intraocular immunosuppressants (13 patients, 20.96%).

Sixteen patients (25.80%) within this group of frequent visits presented retinal vasculitis not related to toxoplasmosis in at least 1 retinal quadrant and 3 (4.83%) presented retinitis.

Table 7. Permanent visual field damage related to uveitis (remnant visual field	
less than 20 degrees).	

Diagnosis	N* of Patients (N* of Eyes)	Uveitic glaucoma
CMV retinitis	2 (4)	No
Acute Retinal Necrosis	2 (3)	No
Fuchs' uveitis	2 (2)	Yes
Behçet's disease	1 (2)	No
Tuberculosis related uveitis	1 (1)	Yes
Syphillis	1 (1)	No

CMV: cytomegalovirus

Diagnosis	N* of patients (N* of eyes)	Choroidal neovascularization	Retinal neovascularization
Serpiginous choroiditis	2 (3)	Yes	No
MCPU	1 (2)	Yes	No
Sarcoidosis probable	1 (1)	Yes	No
IRVAN	1 (2)	No	Yes

MCPU: Multifocal Choroiditis and PanUveitis. IRVAN: Idiopathic Retinal Vasculitis, Aneurysms and Neuroretinitis.

Permanent visual field damage in at least one eye affected 7 patients (11.29%) while neovascularization (either choroidal or retinal) developed in 5 (8.06%).

Native American aboriginal ancestry was reported by 48 patients within the whole cohort (22.64%) and 23 out of 62 patients (37%) within the group of 6 or more visits.

During the median 23 months of follow-up,¹⁻⁴⁸ visual acuity improved in 99 patients (46.69%), remained stable in 91 (42,92%) and worsened in 22 (10.37%).

Discussion

Here, we report the clinical characteristics of a cohort of uveitis patients from a single private practice in the city of Buenos Aires, Argentina. The anatomic and etiologic distribution resembles that of any other community-based urban center from a developed country. Anterior, non-infectious, non-idiopathic uveitis make up the majority of cases, with HLA-B27 associated AAU the most frequent etiology. Similar findings were reported from tertiary referral centers in New Zealand and Australia (both countries located at a similar latitude but with different ethnicity and economic development).^{37,38}

The ethnography of Argentina is highly diverse due to the massive immigration during the mid-19th and 20th centuries.³⁹ Waves of migrants arrived mostly from Europe but also from Syria and Lebanon as well as a significant influx of Jewish origin. Most Argentinians are the offspring of these immigrants with almost 97% of the urban population from European or partial European descent. This particular ethnic composition should suggest a uveitis' spectrum very similar to those published in European series on uveitis. Indeed, in this urban cohort of patients, anterior, non-idiopathic, non-infectious uveitis was the most common presentation. A series from Barcelona, Spain, found a similar anatomic distribution, although panuveitis was more prevalent than

Table 9. Comparison of our results with the ones reported in similar studies performed in other countries.

	Present Study	Wong et al. ³⁷	Hart et al. ³⁸	Llorenc et al. ⁴⁰	Liberman et al. ⁴¹	Gonzalez Fernandez et al. ⁴²
	Buenos Aires, Argentine	Auckland, New Zealand	Melbourne, Australia	Barcelona, Spain	Santiago, Chile	Sao Paulo, Brazil
Number of patients	212	1148	1236	1022	611	1053
Timeframe analysis	2011-2015	2008-2014	2014-2015	2009-2012	2002-2012	2012-2013
Nost frequent anatomic subtype	Anterior	Anterior	Anterior	Anterior	Anterior	Posterior
Most frequent etiology	Idiopathic anterior uveitis	HLA-B27 associated anterior uveitis	HLA-B27 associated anterior uveitis	Herpetic	Vogt-Koyanagi-Harada syndrome	Toxoplasmosis
Infectious etiologies (%)	36%	19.6%	13.4%	29%	28.7%	46.34%
Ethnic variations	Yes	Yes	Not reported	Yes	Not reported	Not reported

intermediate uveitis in their cohort.⁴⁰ Interestingly, they report 22% of patients being non-Spanish in origin; among this subgroup, 47% of VKH and 36% of toxoplasmosis occurred in those from South America. In South America, a series from Santiago de Chile⁴¹ also found anterior uveitis as the most common anatomic presentation while another one from Sao Paulo, Brazil, reported posterior uveitis related to toxoplasmosis as the most frequent diagnosis.⁴² Table 9 summarizes our own results and those from these epidemiologic studies conducted elsewhere.

While a European ancestry is frequent, a unique and important ethnic segment of the Argentinian population has Indigenous American Indian ancestry. At a maternal chromosomic level, 56% of Argentinians have some Native American ethnicity, particularly in non-urban settings.⁴³ The occurrence of VKH disease in the Argentinian population, the most frequent etiology of panuveitis in our series, is probably related to this particular ethnic background, as it was also reported in other parts of the Americas, including Mexico, Canada and Alaska.^{44–46}

In our cohort, Behçet's disease represented 15% and 16% of all non-infectious posterior uveitis and panuveitis respectively. These figures are relatively high considering the geographical location of Argentina, far away from the Silk Road.⁴⁷ HLA-B51 is highly prevalent in certain Indigenous Amerindians populations and may explain this high prevalence.⁴⁷ The disease was traditionally considered almost non-existent in the Americas⁴⁸ but could have easily been overlooked if not properly assessed.

As we analyzed our data, we noticed the presence of a particular subgroup of individuals characterized by frequent visits (defined for the purpose of this study as 6 or more in a year). Patients falling into this category suffered from noninfectious, non-idiopathic posterior uveitis, and required systemic immunosuppression and/or frequently intraocular treatment. Retinal vasculitis, retinitis and retinal or choroidal neovascularization were more often observed, and they were more prone to severe visual field loss, glaucoma or hypotony and phthisis bulbi development. The prevalence of patients reporting Native American aboriginal ancestry among them was 37%. There did not appear to be a bias based on access to care. The observed severity in this group might be related to their genetic background, a subject that will require further study.

Our study does have biases: it is limited to one private practice setting, in one urban center in Argentina. Social inequality is a well-known phenomenon in South America and Argentina is no stranger to this situation. Our study was performed in a private tertiary referral center located in the city of Buenos Aires, the richest one in the country. Even though our population is highly representative of the urban Argentinian middle class, given a possible difference in access to care, we are not able to assimilate our results to the whole Argentinian population. A study involving patients from private and public hospitals and multiple urban and rural settings would be needed to provide a more comprehensive view of uveitis in Argentina. These could be linked to populations studies looking at the genetic makeup of patients which could help to further elucidate links between genetics and uveitis.

In summary, we report on the spectrum of uveitis in an urban cohort of Argentinian patients. While our results are comparable to published series from the western world, there is a particular tendency for certain form of uveitis to be present more frequently in the Argentinian population. There manifestations may also depend on the genetic make-up of the patients.

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References

- de Smet MD, Taylor SR, Bodaghi B, et al. Understanding uveitis: the impact of research on visual outcomes. *Prog Retin Eye Res.* 2011;30(6):452–470. doi:10.1016/j.preteyeres.2011.06.005.
- Tsirouki T, Dastiridou A, Symeonidis C, et al. A focus on the epidemiology of uveitis. *Ocul Immunol Inflamm*. 2018;26(1):2–16. doi:10.1080/09273948.2016.1196713.

- Acharya NR, Tham VM, Esterberg E, et al. Incidence and prevalence of uveitis: results from the Pacific Ocular Inflammation Study. *JAMA Ophthalmol.* 2013;131(11):1405–1412. doi:10.1001/ jamaophthalmol.2013.4237.
- Nelson WW, Rice JB, White AG, et al. Predictors of high-cost patients with noninfectious inflammatory eye diseases. *Clin Ther*. 2019;41(11):2331–2342. doi:10.1016/j.clinthera.2019.09.011.
- Cordero-Coma M, Salazar-Mendez R, Yilmaz T. Treatment of severe non-infectious uveitis in high-risk conditions (Part 2): systemic infections; management and safety issues. *Expert Opin Drug Saf.* 2015;14(9):1353–1371. doi:10.1517/14740338.2015.1061992.
- Cordero-Coma M, Salazar-Mendez R, Yilmaz T. Treatment of severe non-infectious uveitis in high-risk conditions (Part I): pregnancy and malignancies, management and safety issues. *Expert Opin Drug Saf.* 2015;14(7):1071–1086. doi:10.1517/14740338.2015.1044969.
- worldpopulationreview. https://worldpopulationreview.com/worldcities/buenos-aires-population. 2021 Accessed April 17th, 2021.
- Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature working G. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. *Am J Ophthalmol.* 2005;140:509–516.
- Deschenes J, Murray PI, Rao NA, Nussenblatt RB. International uveitis study G. International Uveitis Study Group (IUSG): clinical classification of uveitis. *Ocul Immunol Inflamm*. 2008;16(1):1–2. doi:10.1080/09273940801899822.
- Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for acute retinal necrosis syndrome. *Am J Ophthalmol.* 2021;228:237–244. doi:10.1016/j.ajo.2021.03.057.
- Holland GN. The progressive outer retinal necrosis syndrome. Int Ophthalmol. 1994;18(3):163–165. doi:10.1007/BF00915966.
- Jabs DA. Cytomegalovirus retinitis and the acquired immunodeficiency syndrome-bench to bedside: LXVII Edward Jackson Memorial Lecture. Am J Ophthalmol. 2011;151(2):198–216 e1. doi:10.1016/j.ajo.2010.10.018.
- Chang JH, McCluskey PJ, Wakefield D. Acute anterior uveitis and HLA-B27. Surv Ophthalmol. 2005;50(4):364–388. doi:10.1016/j. survophthal.2005.04.003.
- Wakefield D, Chang JH, Amjadi S, Maconochie Z, Abu El-Asrar A, McCluskey P. What is new HLA-B27 acute anterior uveitis? *Ocul Immunol Inflamm.* 2011;19(2):139–144. doi:10.3109/09273948. 2010.542269.
- Dodds EM, Lowder CY, Meisler DM. Posterior segment inflammation in HLA-B27+ acute anterior uveitis: clinical characteristics. *Ocul Immunol Inflamm*. 1999;7(2):85–92. doi:10.1076/ocii.7.2.85.4015.
- Qian Y, Acharya NR. Juvenile idiopathic arthritis-associated uveitis. *Curr Opin Ophthalmol.* 2010;21(6):468–472. doi:10.1097/ ICU.0b013e32833eab83.
- Keenan JD, Tessler HH, Goldstein DA. Granulomatous inflammation in juvenile idiopathic arthritis-associated uveitis. J AAPOS. 2008;12(6):546–550. doi:10.1016/j.jaapos.2008.05.012.
- Heiligenhaus A, Heinz C, Edelsten C, Kotaniemi K, Minden K. Review for disease of the year: epidemiology of juvenile idiopathic arthritis and its associated uveitis: the probable risk factors. *Ocul Immunol Inflamm*. 2013;21(3):180–191. doi:10.3109/09273948.2013.791701.
- Jones NP. Fuchs' heterochromic uveitis: a reappraisal of the clinical spectrum. *Eye (Lond)*. 1991;5(Pt 6):649–661. doi:10.1038/eye. 1991.121.
- Jones NP. Fuchs' heterochromic uveitis: an update. Surv Ophthalmol. 1993;37(4):253-272. doi:10.1016/0039-6257(93) 90009-V.
- 21. Beneyto P, Fernandez MJ, Garcia A, Ibanez M, Garcia-Aparicio A, Morente P. Fuchs' heterochromic cyclitis without heterochromia: a diagnostic approach. *Arch Soc Esp Oftalmol.* 2007;82(6):355–359. doi:10.4321/s0365-66912007000600007.
- Jap A, Sivakumar M, Chee SP. Is Posner Schlossman syndrome benign? *Ophthalmology*. 2001;108(5):913–918. doi:10.1016/S0161-6420(01)00551-6.

- Green RJ. Posner-Schlossman syndrome (glaucomatocyclitic crisis). *Clin Exp Optom*. 2007;90(1):53–56. doi:10.1111/j.1444-0938.2006.00088.x.
- Rodier-Bonifas C, Cornut PL, Billaud G, Lina B, Burillon C, Denis P. Cytomegalovirus research using polymerase chain reaction in Posner-Schlossman syndrome. J Fr Ophtalmol. 2011;34 (1):24–29. doi:10.1016/j.jfo.2010.10.008.
- 25. Criteria for diagnosis of Behçet's disease. International study group for Behçet's disease. *Lancet*. 1990;335(8697):1078–1080.
- Read RW, Holland GN, Rao NA, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an international committee on nomenclature. *Am J Ophthalmol.* 2001;131 (5):647–652.
- 27. Herbort CP, Rao NA, Mochizuki M, Members of Scientific Committee of First International Workshop on Ocular S. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop On Ocular Sarcoidosis (IWOS). Ocul Immunol Inflamm. 2009;17(3):160–169. doi:10.108 0/09273940902818861.
- Quillen DA, Davis JB, Gottlieb JL, et al. The white dot syndromes. *Am J Ophthalmol.* 2004;137(3):538–550. doi:10.1016/j.ajo.2004. 01.053.
- Crawford CM, Igboeli O. A review of the inflammatory chorioretinopathies: the white dot syndromes. *ISRN Inflamm*. 2013;2013:783190. doi:10.1155/2013/783190.
- Yeh S, Forooghian F, Wong WT, et al. Fundus autofluorescence imaging of the white dot syndromes. *Arch Ophthalmol.* 2010;128 (1):46–56. doi:10.1001/archophthalmol.2009.368.
- Knickelbein JE, Sen HN. Multimodal imaging of the white dot syndromes and related diseases. J Clin Exp Ophthalmol. 2016; 7 (3). doi: 10.4172/2155-9570.1000570.
- Gupta A, Bansal R, Gupta V, Sharma A, Bambery P. Ocular signs predictive of tubercular uveitis. *Am J Ophthalmol.* 2010;149 (4):562–570. doi:10.1016/j.ajo.2009.11.020.
- 33. Dutton GN. Toxoplasmic retinochoroiditis-a historical review and current concepts. *Ann Acad Med Singap*. 1989;18:214–221.
- Johnson MW, Greven GM, Jaffe GJ, Sudhalkar H, Vine AK. Atypical, severe toxoplasmic retinochoroiditis in elderly patients. *Ophthalmology*. 1997;104(1):48–57. doi:10.1016/S0161-6420(97) 30362-5.
- Fardeau C, Romand S, Rao NA, et al. Diagnosis of toxoplasmic retinochoroiditis with atypical clinical features. Am J Ophthalmol. 2002;134(2):196–203. doi:10.1016/S0002-9394(02)01500-3.
- Robert-Gangneux F, Binisti P, Antonetti D, Brezin A, Yera H, Dupouy-Camet J. Usefulness of immunoblotting and Goldmann-Witmer coefficient for biological diagnosis of toxoplasmic retinochoroiditis. *Eur J Clin Microbiol Infect Dis.* 2004;23 (1):34–38. doi:10.1007/s10096-003-1048-6.
- Wong A, McKelvie J, Slight C, Sims J. Land of the long white cloud: the spectrum of uveitis at a tertiary referral center in New Zealand. *Ocul Immunol Inflamm.* 2017;25(sup1):S115–S21. doi:10.1080/ 09273948.2016.1203957.
- Hart CT, Zhu EY, Crock C, Rogers SL, Lim LL. Epidemiology of uveitis in urban Australia. *Clin Exp Ophthalmol.* 2019;47 (6):733–740. doi:10.1111/ceo.13517.
- Devoto FJ. Argentine migration policy and movements of the European population (1876-1925). *Estud Migr Latinoam*. 1989;4:135-158.
- Llorenc V, Mesquida M, Sainz de la Maza M, et al. Epidemiology of uveitis in a Western urban multiethnic population. The challenge of globalization. *Acta Ophthalmol.* 2015;93(6):561–567. doi:10.11 11/aos.12675.
- Liberman P, Gauro F, Berger O, Urzua CA. Causes of uveitis in a tertiary center in Chile: a cross-sectional retrospective review. *Ocul Immunol Inflamm.* 2015;23(4):339–345. doi:10.3109/ 09273948.2014.981548.

- Gonzalez Fernandez D, Nascimento H, Nascimento C, Muccioli C, Belfort R Jr. Uveitis in Sao Paulo, Brazil: 1053 new patients in 15 months. *Ocul Immunol Inflamm*. 2017;25(3):382–387. doi:10.3109/ 09273948.2015.1132741.
- Caputo M, Amador MA, Sala A, Riveiro Dos Santos A, Santos S, Corach D. Ancestral genetic legacy of the extant population of Argentina as predicted by autosomal and X-chromosomal DIPs. *Mol Genet Genomics*. 2021;296:581–590. doi:10.1007/s00438-020-01755-w.
- 44. Arellanes-Garcia L, Bautista N, Mora P, Ortega-Larrocea G, Burguet A, Gorodezky C. HLA-DR is strongly associated with Vogt-Koyanagi-Harada disease in Mexican Mestizo patients. *Ocul Immunol Inflamm*. 1998;6(2):93–100. doi:10.1076/ocii.6.2.93.4049.
- 45. Kryshtalskyj MT, Roy M. Vogt-Koyanagi-Harada Syndrome in a Canadian First Nations Population. *Ocul Immunol Inflamm*. 2021;1-7. doi:10.1080/09273948.2020.1849737.
- Roy M. Analysis of uveitis in a Canadian aboriginal population. Can J Ophthalmol. 2014;49(2):128–134. doi:10.1016/j.jcjo.2013. 09.020.
- Verity DH, Marr JE, Ohno S, Wallace GR, Stanford MR. Behcet's disease, the Silk Road and HLA-B51: historical and geographical perspectives. *Tissue Antigens*. 1999;54(3):213–220. doi:10.1034/ j.1399-0039.1999.540301.x.
- Arbesfeld SJ, Kurban AK. Behcet's disease. New perspectives on an enigmatic syndrome. J Am Acad Dermatol. 1988;19(5 Pt 1):767–779. doi:10.1016/S0190-9622(88)70233-9.