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RESEARCH ARTICLE

PREVALENCE AND PATTERN OF OCULAR INVOLVEMENT IN PATIENTS ATTENDING ALEXANDRIA UNIVERSITY RHEUMATOLOGY CLINIC: A Pilot study

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Abstract

Ocular involvement is well known in most rheumatic diseases including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, Behçet disease, anti-phospholipid syndrome and others. Their clinical expression and outcome vary between different populations. Although there are epidemiological studies on uveitis from different geographic areas, registry of pattern of eye affection among rheumatic patients in Egypt is highly deficient.

Objective:

To identify the prevalence and pattern of immune eye involvement in patients referred to Alexandria University outpatient rheumatology clinic during the period from January to December 2014.

Methods:

A cross sectional analysis of a cohort of 1500 patients with immune diseases attending the outpatient rheumatology clinic. 100 patients had relevant eye complaints. The demographic features, clinical presentations, pattern and modes of treatment of eye involvement were registered .

Results: 59 % were females. Mean age was 39.26 years and the mean duration of systemic disease was 41 months. Mean duration of eye disease was 30 months. Behcet's disease was the most common identifiable cause of uveitis (24%) followed by JIA (6%) and VKH (5%). Idiopathic anterior uveitis was the most common uveitic entity, 32% of cases. Forteen percent needed intraocular steroid injections. Topical and systemic steroids were added in 58%, synthetic or biological DMARDs in 14%, and surgery in 14%of the patients.

Conclusions: Ocular complications are common among rheumatic patients. Awareness of the possibility of serious eye involvement should always be kept in mind. Routine ophthalmological evaluation of patients with any rheumatic disease is mandatory & should be stressed upon in all recommendations in rheumatology.

INTRODUCTION

Uveitis describes a group of intraocular inflammatory disorders. The uvea comprises the iris, ciliary body, and choroid. Uveitis may affect other tissues in the eye, however, including the retina (uveoretinitis), retinal blood

vessels (retinal vasculitis), the vitreous (vitritis), and the optic nerve (papillitis). So uveitis is anatomically classified in anterior, intermediate, posterior and panuveitis. **(Guly and Forrester, 2010)** . The cause of uveitis may be autoimmune, infection related, drug induced, traumatic, or associated with malignancy (when it is known as the masquerade syndrome). About half of cases are idiopathic and are presumed to be autoimmune. **(Rothova et al., 1992)**.

Immune-mediated ocular inflammation causes severe debilitation and visual loss .**(Durrani et al., 2004).**

Unfortunately , not all patients with rheumatological diseases follow up their condition with a rheumalogist, moreover , the eye is often overlooked by many rheumatologists.

Almost all the anatomical parts of the eye could be a target for an immunological reaction depending upon the underlying etiological disease. **(Nussenblatt et al., 2004).**Inflammation of ocular structures can lead to secondary complications including cataract, glaucoma, and optic atrophy. **(Nussenblatt et al., 2004).**

Many ocular complications are indicators of active systemic disease process and some of them are markers of severe and potentially life-threatening systemic involvement. **(Choudhary et al.,2014) .**

A patient with RA who develops peripheral ulcerative keratitis, often associated with scleritis, is at risk of a sight as well as life threatening vasculitis and this finding heralds the need for further immunosuppressive measures for control of a severely active systemic disease. **(Mohsenin and Huang , 2012. Foster et al., 1984)**. The pattern and prevalence of uveitis is largely influenced by a multitude of factors, including ethnic, genetic, environmental factors, referral and reporting bias**. Henderly et al., 1987. McCannel et al.,1999. Merrill et al., 1997. Kotake et al., 1997. Hamade et al., 1997. Birnbaum et al., 2011) .**

Although there are some epidemiological studies on uveitis from different geographic areas and populations, data from Africa is generally scarce and from North Africa is almost lacking. Such data will have significant clinical and research applications and would help plan appropriate treatment protocols on community bases.

In this study, we analyze the causes of uveitis in a tertiary rheumatology referral center in North Egypt in patients reporting eye problems during routine review of systems over the period from January 2014 to December 2014.

Patients and methods:

This cross sectional study was carried out on data from consecutive patients who were seen in a tertiary referral rheumatology clinic in Alexandria Main University Hospital, Alexandria, Egypt in 2014. Information regarding age, sex, and race was recorded. Details on ocular and systemic complaints, examination, and investigations were recorded for all patients. Ocular examination included slit lamp examination, tonometry, fundus biomicroscopy, and indirect ophthalmoscopy. Ultrasonography, optical coherence tomography, and fundus fluorescein angiography were ordered when needed.

A total of 1500 patients were recruited to this study, of which 100 patients had relevant eye complaints. Patients with infectious origin of uveitis were excluded from the study. They were classified according to the type of the underlying disease. All patients were questioned about systemic disease duration, age at onset, duration and pattern of eye involvement (unilateral or bilateral, course : acute , chronic or recurrent) , type and dose of medications (topical , systemic or both), eye complications, and the need for surgery. Local eye examination was performed to determine the type and location of eye affection (anterior or posterior segment, active or not, associated corneal or retinal involvement). Data analysis was performed using (SPSS Inc, Chicago, USA), and P value ≤ 0.05 was considered to be statistically significant.

Results:

A total of 100 patients (169 eyes) were included. The mean age at onset of uveitis was 39.26 (range 7-70) years, and the male-to-female ratio was 0.69. In our study, all patients were native Egyptians mainly from North Egypt governorates. Ocular involvement was unilateral in 31 patients. The mean duration of systemic disease was 41 months and 30 months for eye disease. The demographic data and patterns of eye involvement are demonstrated in table 1 and figures 1 and 2 respectively.

Anterior uveitis (AU) was most common (27%), followed by panuveitis (20%), posterior uveitis (28%), and intermediate uveitis (3%). Other forms of ocular immune disorders visiting the clinic included ocular cicatricial pemphigoid and Sjogren's syndrome detected in 4 patients.

The most common causes of uveitis regardless of the anatomical forms were Behçet disease (BD) (24%), juvenile idiopathic arthritis (JIA) associated uveitis (6%), Vogt-Koyanagi-Harada (VKH) syndrome (5%) and sarcoidosis (4%). Retinal vasculitis was found in 20% of the patients. The most common complications were cataract (21.6%), ocular hypertension (12%) and macular edema (5.6%).

We reported one patient with each; psoriatic arthritis, primary anti-phospholipid syndrome (PAPS), mixed connective tissue disease (MCTD), granulomatous uveitis, 1ry Sjogren's syndrome, systemic sclerosis, and one with combined Wegner granulomatosis and SLE. Diseases with corresponding pattern of eye affection are demonstrated in table 2. Eighty two per cent of patients had the rheumatic disease and eye affection simultaneously, 16% of patients had the ocular involvement following their systemic disease diagnosis, and of note, was the fact that the onset of eye involvement after systemic disease onset was long & reached up to 180 months in 16 % of patients. Eye involvement before systemic disease occurred in 2 patients, both with RA (24 and 12 months before RA onset respectively).

Table 3 shows the mode of treatment of eye affection. Most patients needed combined therapy; intra-ocular, topical as well as systemic steroids together with other synthetic or biological DMARDs.

Discussion :

The magnitude of eye problems associating rheumatic diseases is not well estimated in some populations and data concerning its pattern is highly deficient. **(Durrani et al., 2004. Kotake et al., 1997.)** . Uveitis can occur either as a co-manifestation of various autoimmune disorders, an extra-articular manifestation of these diseases or it can arise as a purely idiopathic ocular inflammation. It can affect any part of the eye from the cornea and sclera anteriorly to the retina and uveal tract posteriorly, and its occurrence determines the need for more aggressive immunosuppressive therapy. **(Guly and Forrester, 2010. Durrani et al., 2004. Kotake et al., 1997.Hamade et al., 1997.)** The incidence, severity, and disease course of uveitis will vary depending upon the natural history of the underlying systemic disease and the extent of the inflammatory process. In our study, the most common anatomic diagnosis was anterior uveitis. Behcet's disease was the most common identifiable cause of uveitis followed by JIA associated uveitis and VKH. Idiopathic AU was the most common uveitic entity.

An effect of referral and selection bias should be considered when looking into similar data, as most uveitis studies are published from tertiary referral centers causing perhaps an over representation of more complicated severe forms of pan or posterior uveitis. Our study is perhaps affected by inclusion bias as the study population is drawn from an outpatient department.

Regarding the pattern & associations of uveitis reported from other countries, it was noted that in a review of existing medical records of 5970 patients evaluated by the Uveitis Service at the University of Illinois at Chicago between 1973 and 2007 with a diagnosis of chronic anterior uveitis (CAU) ; 31% carried a diagnosis of CAU, idiopathic disease was diagnosed in 54% of patients, ocular sarcoidosis in 14% , Fuchs heterochromic iridocyclitis (FHI) in 12% and JIA in 6% of patients . **(Birnbaum et al., 2011)**

The frequency of diagnosis of idiopathic CAU decreased over time, with no significant change for sarcoidosis, FHI or JIA. An increase in frequency of diagnosis was observed for HLA-B27-related disease and uveitis related to multiple sclerosis and inflammatory bowel disease. It was concluded that the relative frequency of idiopathic disease has decreased over the past 35 years at their center. This may be related to an increase in the diagnosis of CAU associated with HLAB27 positivity, inflammatory bowel disease (including family history) and multiple sclerosis.

Despite the advances over the last 35 years, idiopathic disease still comprises at least 39% of patients with CAU each year. **(Birnbaum et al., 2011)**

In 2010 **Chan et al** publishedthe characteristics of uveitis in a Canadian referral centre performed between September 2004 and March 2006 including 285 patients (364 eyes) with anterior uveitis, intermediate uveitis, or panuveitis and concluded that according to the anatomical subtypes there were 313 anterior, 36 intermediate, and 15 panuveitis. Systemic associations included ankylosing spondylitis (11.3%), inflammatory bowel disease (6%), sarcoidosis (4.1%), and herpes infections (3.8%). An HLA-B27-related association was found in 86 patients (23.6%). Patients with uveitis-associated complications or back symptomatology were more likely to have a recurrence. Of note, patients with posterior uveitis were excluded from this study. **(Chan et al., 2010)**

Whereas the anatomical and etiological spectrum of uveitis in an urban multiethnic population from Barcelona, Spain performed between 1 January 2009 and 31 December 2012 after exclusion of after exogenous endophthalmitis, surgery-related, post-traumatic and toxic uveitis along with masquerade syndromes were investigated. From 1022 patients , 52% were AU, 23% posterior, 15% panuveitis and 9% intermediate uveitis. Etiologically, 26% were unclassifiable, 29% infectious, 25% associated with systemic immune diseases, and 20% corresponded to ocular-specific syndromes. Among classified causes, herpes virus (12%), toxoplasma (7%), BD (5%), HLA-B27-isolated AU (5%), ankylosing spondylitis (5%), tuberculosis-related uveitis (TRU)(5%), birdshot chorioretinopathy (3%) and sarcoidosis (3%) were the most frequent. Non-Spanish origin was recorded in 22%, with 47% of VKH and 36% of toxoplasma cases coming from South America, 10% of BD and 11% of TRU from Africa and 24% of TRU cases from Asia. A mean annual incidence of 51.91 cases/100 000 inhabitants was found for the referral population. **(Llorenç et al., 2015)**

The patterns uveitis reported from Singapore demonstrated that AU was the predominant form of uveitis seen and most cases were unilateral (79.5%) and idiopathic (50.4%). Common etiological causes included FHI (5.6%), ankylosing spondylitis (AS)-related AU (5.1%), herpes simplex virus (HSV) (4.7%), and herpes zoster virus (HZV) (4.5%). There were increasing trends in AS-related AU from 3.2% in 2008 to 6.5% in 2010, and psoriasis-associated AU from 1.7% in 2005 to 4.0% in 2008. **(Tan et al., 2013)**

Of the 42 patients with AU seen at a tertiary care eye hospital in south India, 14 (33.33 %) were HLA-B27-positive and the remaining 28 (66.66 %) HLA-B27-negative. Overall, 32 of the 42 had no causative association, three patients were diagnosed with JIA, two with ankylosing spondylitis, two were associated with systemic tuberculosis, two with sarcoidosis and one with VKH syndrome. **(Mathur and Biswas , 2012)**

Data derived from Tunis showed that a total of 424 patients (596 eyes) were included. The mean age at onset of uveitis was 36 years, and the male-to-female ratio was 0.66.Uveitis was unilateral in 56.4%. AU was most common (48%), followed by panuveitis (33.6%), posterior uveitis (13.3%), and intermediate uveitis (5%). The most common causes were BD (14.7%), toxoplasmosis (10.2%), VKH syndrome (3.7%) and sarcoidosis (3.3%). Retinal vasculitis was found in 20%. Behçet disease was the most common cause of chronic uveitis. The most common complications were cataract (21.6%), ocular hypertension (12%) and macular edema (5.6%). **(Chebil et al., 2013)**

Another recent study aimed to determine the pattern of childhood eye disorders in patients attending outpatient eye department of a rural eye hospital in central Ethiopia was published . It was concluded that the three most common causes of childhood ocular morbidity were conjunctivitis, ocular injuries and refractive errors. Though these disorders require attention for proper management or early referral and 735 children were included; the idea of autoimmune uveitis was not addressed in their work. **(Mehari ,2014)**

The same issue was raised in another study from Nigeria evaluating the reports of 286 children between January 2001 and December 2006 which concluded that the most common causes of childhood ocular morbidity were injuries, allergic conjunctivitis, infections and refractive errors omitting the fact that eye can be the window for detection of many systemic diseases. **(Onakpoya and Adeoye, 2009)**.

Since uveitic entities follow different patterns in different regions and are influenced by a variety of demographic factors, epidemiologic studies can help improve our understanding of such diseases and provide appropriate diagnosis and timely management. **(Nashtaei et al., 2011. Mohsenin and Huang , 2012. Choudhary et al.,2014**)

Conclusions:

Ocular complications are common among rheumatic patients in Egypt. Awareness of the possibility of serious eye involvement should always be kept in mind. Routine ophthalmological evaluation of all patients affected with any rheumatic disease is mandatory & should be stressed upon in all guidelines & recommendations in rheumatology. Following a universal classification system and having population-based studies from different countries, a more reliable data for comparison between different geographic areas can be provided.

We recommend extending this study to involve a large cohort of Egyptian patients with rheumatic diseases.

Table 1 : Demographic data of the patients.

Gender	No (%)
Female	59 (59)
Males	41 (41)
Age in yrs	
Min-max(Mean)	7-70 (39.26)
Disease duration (ms)	
Min-max (Mean)	0 -264 (41)
Eye disease duration (ms)	
Min-max (Mean)	0-180 (30)
Eye involvement in relation to disease onset	
Before	2 (2%)
After	16 (16%)
At the same time	82 (82%)

Table 2 Diseases with corresponding pattern of eye affection

Disease	No of patients	Anterior	Intermediate	Posterior	Panuveitis	Corneal	Retinal	Sogren's
AI	32	19	2	6	2	3	0	0
Behcet ds	24	2	1	11	9	0	1	0
RA	10	5	0	1	0	2	1	1
JIA	6	2	0	2	2	0	0	0
V K H	5							
AS	3	3	0	0	0	0	0	0
Sacroidosis	4	1	0	0	2	0	0	1
SLE/APS	4	0	0	4	0	0	0	0
SLE	3	0	0	0	1	0	2	0
OCP	2							
others	7	2	0	1	2	0	1	1
Total	100	34	3	25	18	5	5	3

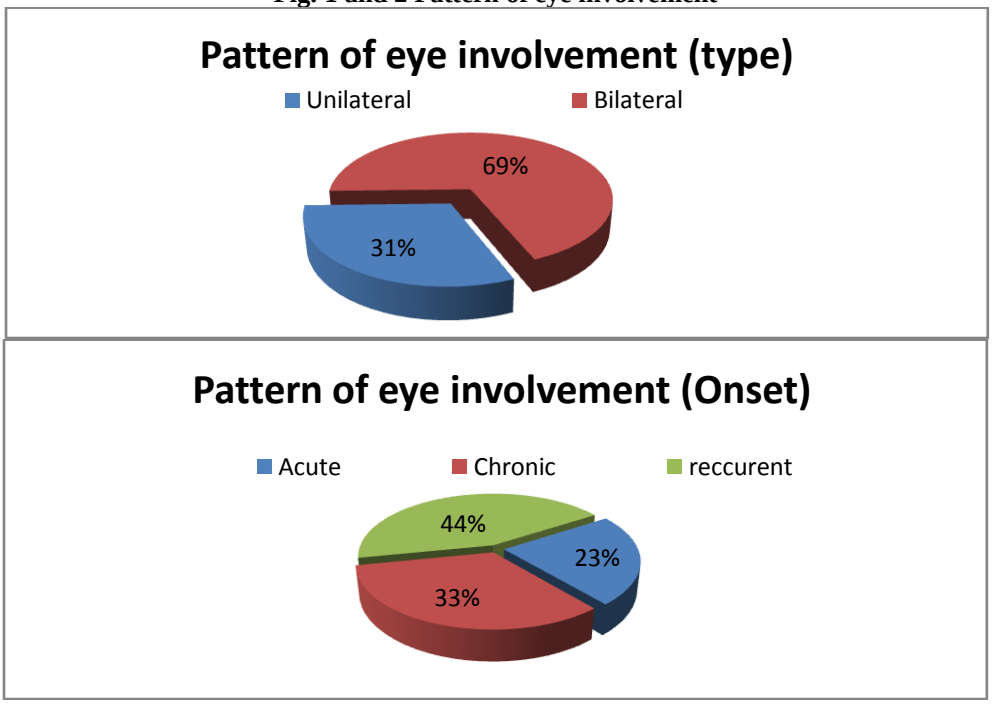
AI: autoimmune idiopathic uveitis, BD: Behcet's disease, RA: Rheumatoid arthritis, JIA: Juvenile idiopathic arthritis, VKH: Vogt-Koyanagi-Harada syndrome, AS: Ankylosing spondylitis, SLE: Systemic lupus erythematosus, APS: anti-phospholipid syndrome, OCP: Ocular cicatricialpemphigoid.

Table 3 : Type of treatment of eye diseases.

IO	Topical Only	sDMARDs	bDMARDs				Steroids	Surgery	Others
			14						
			Infliximab	Adalimumab	Etanercept	tried 2 biologics			
14	**58**	**44**	**7**	**4**	**2**	**1**	**57**	**14**	**5**

IO :intraoccular, sDMARD : synthetic disease modifying anti-rheumatic drugs, bDMARDs : biological disease modifying anti-rheumatic drugs

Fig. 1 and 2 Pattern of eye involvement



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