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An Observational Descriptive Cross-Sectional Study of 200 Iraqi Adult Patients with Ankylosing Spondylitis: Analysis of Ocular Manifestations

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Abstract
Objective: To analyze the ocular findings in adult patients with ankylosing spondylitis.**Patients and methods:** A cross sectional study was conducted on (200) ankylosing spondylitis (AS) patients diagnosed according to the modified New York criteria for ankylosing spondylitis. Demographic and clinical data were collected and all patients were examined by same ophthalmologist for ocular findings.**Results:** The mean age of patients was (35.2 ± 8.6) years with male to female ratio (13.3:1), and mean disease duration was (10.9 ± 6.7) years. Family history of AS was positive in (26%) of patients. HLA-B27 was obtained in (69.5%) of the total number of the patients. Among those patients in whom HLA-B27 test was obtained, (43.2%) had positive HLA-B27. Enthesitis was found in (48%) of patients, and (63.5%) had peripheral arthritis. Ocular manifestations were found in (21.5%) of the patients in the form of anterior uveitis (14.5%), conjunctivitis (3%), ocular dryness (2%), and cataract (2%). Ocular manifestations had significant association with enthesitis, peripheral arthritis, HLA-B27 positivity and positive family history of AS ($p<0.05$), but not with age, sex, disease duration and disease activity ($p > 0.05$).**Conclusions:** Prevalence of ocular manifestations in adult Iraqi patients with AS was (21.5%). The commonest form was anterior uveitis. Other forms included conjunctivitis, ocular dryness, and cataract. Ocular manifestations had significant association only with enthesitis, peripheral arthritis, HLA-B27 positivity and positive family history of AS. This may suggest that early screening for ocular features in AS is important for early diagnosis and treatment.
Keywords: Ankylosing spondylitis, Ocular manifestations, Anterior Uveitis, Conjunctivitis, Ocular dryness, Cataract.

1. Introduction

Ankylosing Spondylitis (AS) is a chronic, progressive inflammatory disease that affects primarily the axial skeleton and less frequently the peripheral joints as well as other extra-articular organs such as the eyes, and cardiovascular system [1].

The prevalence of ankylosing spondylitis is closely parallel to the prevalence of human leukocyte antigen-B27 (HLA-B27) [2], which is estimated to be (0.55 %) of the general population, with a male to female ratio (3:1) [3]. The estimated prevalence of AS in Iraq is (0.13%) [4, 5].

Ocular manifestations are the most common extra-articular manifestations in AS. Acute anterior uveitis is an acute inflammation of the anterior segment of the eye, patients with AS have a (25-30) % chance of developing uveitis during the course of their disease, it is more common in HLA B27 positive than HLA B27 negative patients [6].

Keratoconjunctivitis sicca (KCS) can occur in patients with AS [7, 8]. Symptoms of KCS include dryness, ocular irritation, foreign body sensation, photophobia, and rarely pain. Diagnosis of KCS is made by an abnormal Schirmer test demonstrating decreased tear production (typically < 5 mm of wetting at 5 minutes in eye) and by demonstrating damage to the ocular surface using rose bengal staining [9].

Scleritis is a painful and potentially sight threatening condition, usually presents with red eyes associated with deep boring pain. An association between scleritis with AS and other seronegative spondyloarthropathies has been reported [10]. Conjunctivitis is characterized by redness, itching, and burning sensation. Conjunctivitis has been reported to occur in patients with AS [11].

There was a case report of retinal vasculitis in a patient with AS. Retinal vasculitis presents as painless reduction in visual acuity, visual floaters, scotomas, decreased ability to distinguish colors, and metamorphopsia [12].

2. Patient and Method

2.1 **Study design and participants:** A cross-sectional study was conducted at the Rheumatology Unit in Baghdad Teaching Hospital, a tertiary referral center in Iraq, from June 2013 to July 2014. A total of 200 Iraqi patients were enrolled in the study, all of them were fulfilling the modified New York criteria for ankylosing spondylitis [13].Patient were excluded from the study if they had: Hypertension, diabetes mellitus, overlap with

other autoimmune disease, patients received or currently on steroids or sulphasalazine or anti-TNF alpha drugs, and those with infection or trauma to eye. This study was approved by the appropriate ethical committees of Medical Faculty in Baghdad Teaching Hospital. All patients gave their written informed consent before enrolling for the study.

2.2 **Clinical, laboratory, and ophthalmological evaluation:**
Demographic data included: Age, gender, and family history of ankylosing spondylitis. Clinical data consisted of: symptoms of AS (presence of axial and peripheral involvement and enthesitis), duration of disease, presence of eye symptoms (pain, redness, photophobia, discharge, blurring of vision, dryness), medical history, history of previous and current treatment, and Bath ankylosing spondylitis disease activity index (BASDAI) score [14]. Laboratory investigation: patients were investigated for HLA-B27. All patients were examined by the same ophthalmologist for ocular manifestations of AS.

2.3 **Statistical analysis:** Statistical analyses were done using (SPSS version 21, 2014, IBM, US, software for windows in association with Microsoft Excel 2010. The database was examined for errors using range and logical data cleaning methods, and inconsistencies were remedied. Descriptive statistics were presented as mean and standard deviation (SD) for continuous variables and as numbers and percentages for categorical variables. Chi square test was carried out to detect differences in categorical variables and to find the significance of association between eye involvement and other variables. An association was considered statistically significant if its P value (level of significance) was less than 0.05.

3. Results

A total of 200 Iraqi patients with AS were enrolled in this study. The mean age of patients was 35.2 ± 8.6 (range: 18-66) years. Males were 186 (93%) and females were 14 (7%), with a male to female ratio of (13.3:1).

Family history of AS was positive in 52 patients (26%). The disease duration range was (1-30) years, with a mean of (10.9 ± 6.7) years. Forty six patients (23%) had a diseases duration of (1-5) years, 73(36.5%) patients with (6 – 10) years duration, and higher proportion (40.5%) of the patients had a disease duration of 10 years or more.

HLA-B27 was obtained in 139 patients represented (69.5%) of the total number of the patients. Among those patients, 60 (43.2%) patients had positive HLA-B27 and 79 patients (56.8%) had negative HLA-B27. Enthesitis was found in 96 (48%) patients, and peripheral involvement was found in 127 (63.5%) patients. The above findings are shown in table 1.

Ocular manifestations were present in 43 (21.5%) patients. Anterior uveitis (unilateral) was found in 29 (14.5%) patients, Conjunctivitis in 6 (3%), Ocular dryness in 4 (2%) patients, and unilateral and bilateral cataract in 2 (1%) patients for each as shown in table 2. All patients with ocular findings were symptomatic.

In Table 3, the association of ocular manifestations with the demographic and clinical characteristics of the group studied showed no significant association was found between ocular manifestations and each of the age group (P=0.75), sex (P=0.31), disease duration (P=0.23), and disease activity (P=0.16).

On the other hand, it had been found that ocular manifestations were significantly more frequent in patients with peripheral involvement (29.9%) than in those without peripheral involvement (6.8%), (P<0.001). Similarly, in patients with enthesitis, ocular manifestations were more frequent than in those without enthesitis, (34.4%) vs. (9.6%), respectively, (P<0.001).

Positive family history was significantly associated with ocular manifestations; it had been found that out of the 52 patients with positive family history, 22 (42.3%) had eye manifestations compared to 21 (14.2%) out of the 148 patients with negative family history (P<0.001). Regarding the HLA-B27, we found that prevalence of ocular manifestations was significantly higher in patients with positive HLA-B27 than those with negative HLA-B27; 28 (46.7%) vs. 11 (13.9%), respectively, (P<0.001).

Table 1 Demographic and clinical characteristics of the 200 AS patients studied.

Variable		No.	%
Age intervals	< 30	48	24.0
	30 - 39	89	44.5
	40 - 49	51	25.5
	≥ 50	12	6.0
	Mean ± SD	35.2 ± 8.6	-
	Range	18 - 66 yrs	-
Sex	Male	186	93.0
	Female	14	7.0
Family history	Positive	52	26.0
	Negative	148	74.0
HLA-B27	**Obtained**	**139**	**69.5**
	Not obtained	**61**	**30.5**
	Positive	60	43.2
	Negative	79	56.8
Disease duration	1 - 5 yrs	46	23.0
	6 - 10 yrs	73	36.5
	> 10 yrs	81	40.5
	Mean ± SD	10.9 ± 6.7	-
	Range	1 - 30 yrs	-
Enthesitis		96	48.0
Peripheral involvement		127	63.5

Table 2. Prevalence of ocular findings and types of eye lesions.

Ocular findings	No.	%
No ocular findings	157	78.5
Ocular findings	**43**	**21.5**
Anterior uveitis	29	14.5
Conjunctivitis	6	3
Ocular dryness	4	2
Unilateral cataract	2	1
Bilateral cataract	2	1

Table 3: Association of ocular manifestations with demographic and clinical characteristics of the AS patients studied.

Variable*		Ocular findings				P
		Yes		No		
		No.	%	No.	%	
Age	< 30	12	25.0	36	75.0	
	30 - 39	16	18.0	73	82.0	0.75
	40 - 49	12	23.5	39	76.5	NS
	≥ 50	3	25.0	9	75.0	
Sex	Male	38	20.4	148	79.6	0.31
	Female	5	35.7	9	64.3	NS
Disease duration	1 - 5 yrs	11	23.9	35	76.1	0.23
	6 - 10 yrs	11	15.1	62	84.9	NS
	> 10 yrs	21	25.9	60	74.1	
Disease activity	Mild	1	5.0	19	95.0	0.16
	Moderate	37	23.1	123	76.9	NS
	Severe	5	25.0	15	75.0	
Periphral involvement	Yes	38	29.9	89	70.1	<0.00
	No	5	6.8	68	93.2	1
Enthesitis	Yes	33	34.4	63	65.6	<0.00
	No	10	9.6	94	90.4	1
Family history	Positive	22	42.3	30	57.7	<0.00
	Negative	21	14.2	127	85.8	1
HLA-B27	Positive	28	46.7	32	53.3	<0.00
	Negativ	11	13.9	68	86.1	1

** Total number of patients was 200 in all variables except in HLA-B27, it was 139 (61 patients in whom the HLA-B27 was not obtained were excluded from the comparison with ocular findings).*

Discussion

Ankylosing spondylitis is the most prevalent and severe subtype of spondyloarthritis and ocular involvement are the most common extra-articular manifestations. The interdisciplinary team work of rheumatologists and ophthalmologists have been proved to be essential for the early diagnosis and treatment of ocular manifestations [15].

This cross sectional study is the first study in Iraq that analyzed the ocular findings in AS patients. It showed that ocular manifestations were prevalent in AS.

The prevalence of ocular finding was 21.5%, which was higher than the result of Ahmet et al [16] (11%). This disagreement may be explained by the larger number of patients enrolled in their study as well as the genetic factors. The exact mechanism of this ophthalmic manifestations are not entirely known, but the inflammatory process which characterizes the main rheumatic diseases seems to be responsible for this extraskeletal manifestation.

In the current study, Of these ocular findings: the prevalence of acute anterior uveitis was 14.5% which was similar to the result of Mihaela et al [17], but lower than the result of Zeboulon et al [18] (33.2%). This may be attributed to the larger number of patients, the longer follow up period, and genetic factors. Conjunctivitis was (3%), which was lower than the prevalence reported from AL-Arfaj which was (7%) [12]. This may be explained by the different genetic and environmental factors between the two population. Ocular dryness was (2%), this results had been supported by studies done by Brandt et al [9], and Kobak et al [8] which revealed an increase in the prevalence of dryness in patients with AS. The prevalence of cataract in this study was (2%) which was in agreement with other studies [19].

This study showed that the ocular manifestations had no significant association with age and sex. No data available supported the relation between the ocular manifestations of AS with age and sex except one study done by Sampaio-Barros et al [20] which found that the anterior uveitis was more common in male patients.

In addition, the present study showed no significant association between ocular manifestations and both of disease activity (BASDAI) and disease duration which was in agreement with a study done by Brophy et al [21], and Chen et al [22] respectively.

The presence of peripheral arthritis and enthesitis were significantly associated with ocular manifestations in this study. Singh et al [23] and Sampaino-Barros et al [20] reported similar conclusions.

Ocular manifestations were significantly associated with HLA-B27 positivity and positive family

history in this study which was in line with another study done by Mihaela et al. [3]

The main limitations of the study were the small sample of the patients and being cross sectional so cause and effect could not be determined. These can be solved by a larger sample and longer follow up study. However the strict inclusion and exclusion criteria and being the first study in Iraq that assessed the most common and important extraarticular manifestation of AS were strong points.

In conclusion, prevalence of ocular findings in a sample of Iraqi patients with AS was 21.5%.The ocular findings were as follow: anterior uveitis 14.5%, conjunctivitis 3%, ocular dryness 2%, unilateral and bilateral cataract 1% for each. There were significant association between ocular manifestations with enthesitis, peripheral arthritis, HLA-B27 and positive family history. There were no significant association between ocular manifestations with age, sex, disease duration, and disease activity.

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