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Corneal Endothelial Changes with Different Rheumatic Diseases and Correlation with Disease Activity

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ABSTRACT

Background: Rheumatoid arthritis [RA], systemic lupus erythematosus [SLE] and ankylosing spondylitis [AS] are chronic inflammatory diseases associated with progressive joint destruction, functional disability, reduced health-related quality of life, systemic complications, premature mortality, and a high economic burden.

Aim of the work: The aim of this study is to evaluate the corneal endothelial changes that occur in ankylosing spondylitis, systemic lupus erythematosus, and rheumatoid arthritis.

Patients and Methods: A cross-sectional study of 90 patients [thirty with RA, thirty with SLE, thirty with AS] and thirty healthy control patients. The study was conducted at the outpatient clinics of the rheumatology and rehabilitation department of Al-Azhar University hospitals. All patients were subjected to personal history, general and local examination, and laboratory tests to confirm diagnosis. They were then examined by specular microscope [Nidek CEM-530] to evaluate corneal cell morphology.

Results: In RA patients, significant differences were found between RA and control groups regarding central corneal thickness and cell variation [CV]. No significant difference was found regarding cell density and hexagonality [HEX]. In SLE patients, significant differences were found between the SLE and control groups regarding central corneal thickness and cell density. No significant difference was found between the SLE and control groups regarding cell variation [CV] and hexagonality [HEX]. In AS patients, significant differences were found between them and control group regarding central corneal thickness, cell density, cell variation [CV], and hexagonality [HEX].

Conclusion: Rheumatoid arthritis [RA], systemic lupus erythematosus [SLE] and ankylosing spondylitis [AS] have a slight effect on cell density [CD], central corneal thickness [CCT], cell size, and cell shape permanently.

Keywords: Autoimmune; Systemic lupus erythematosus; Ankylosing spondylitis; Cornea.

INTRODUCTION

The corneal endothelium, single hexagonal-cells, have a vital role in maintaining clear vision [1], and regulating corneal hydration through active ion-transport. Changes in this hydration cause inflammation of the cornea and loss of clarity [2].

Rheumatoid arthritis [RA] is a systemic auto-immune disease that can directly or indirectly affect the eye. These effects include dry eye syndrome, episcleritis, scleritis, or peripheral ulcerative keratitis [PUK] [3].

Ankylosing spondylitis [AS] is a chronic inflammatory disease of the axial spine that can present with variable clinical signs and symptoms. Chronic back pain and progressive spinal stiffness are the most common symptoms of this condition. A typical feature of the disease is the involvement of the vertebral joints, sacroiliac joints [SI joints], peripheral joints as well as the fingers and toes [3].

Systemic lupus erythematosus [SLE] is a complex connective tissue disease that affects multiple organ systems. The ocular symptoms of SLE vary and are influenced by the systemic activity of the disease [4].

Recent studies have focused on determining the effects of some connective tissue diseases such as RA, SLE and AS on corneal bio-mechanical parameters [5].

Ocular involvement is usually kerato-conjunctivitis sicca, while retinal and choroidal involvement can lead to vision loss. Filiform keratitis and ulcers can develop as a result of keratoconjunctivitis sicca. Rare cases of peripheral ulcerative keratitis, interstitial keratitis and dysfunctional corneal endothelial cells have been reported in patients with SLE or RA [6].

This study was designed to evaluate the corneal endothelial changes which occur in ankylosing spondylitis, systemic lupus erythematosus and Rheumatoid arthritis.

PATIENTS AND METHODS

A cross sectional study was carried out on 120 patients [thirty RA patients [5 male and 25 female] with mean age [43.5 ± 9.95], thirty SLE patients [3 male and 27 female] with mean age [39.3 ± 13.0], thirty AS patients [24 male and 6 female] with mean age [37.80 ± 3.63] and thirty health control patients [10 male and 20 female] with mean age [41.80 ± 7.29].

Inclusion Criteria

Age of 25-45 years old**,** Rheumatoid Arthritis patients were diagnosed according to 2010 ACR/ EULAR Diagnostic Criteria for RA. Systemic lupus erythematosus patients were diagnosed according to 2012 SLICC classification criteria of SLE. Ankylosing spondylitis patients were diagnosed according to 2009 ASAS classification criteria for axial spondyloarthritis. The study was conducted at outpatient clinics of rheumatology and rehabilitation department of Al-Azhar University hospitals.

Exclusion criteria

Dry eye, history of trauma, any ocular surface lesion, corneal opacity, malignancy, infection and history of Eye operation.

Ethical Considerations

The aim of the study was explained to each participate before collection of data. Verbal and written consent was obtained from those who welcome to participate in the study.

Methods

General examination: General condition, vital signs [pulse, blood pressure, respiratory rate and temperature], pallor, jaundice, cyanosis, skin [nodule, rash], lymph nodes, BMI, abdominal, chest and heart, head and neck and neurological examination.

Locomotor examination: includes combined inspection and palpation of all joints for swelling, tenderness, warmth and limitation of range of motion. Joint examination was applied to any symptomatic joint or where an abnormality has been identified by the GALS examination.

DAS28 score: DAS28 was used to measure disease activity in patients with rheumatoid arthritis.

SLEDIA: SLEDIA was used to measure degree of disease activity in SLE patient.

ASDAS: was used to measure disease activity in patients with ankylosing spondylitis.

Nidek CEM-530 specular microscope examination: Was used to measure central

corneal thickness [CCT], cell density [CD], hexagonality [HEX] and cell variation [CV].

Statistical Analysis

Data was analyzed using Statistical Package for Social Sciences software [SPSS, IBM]. Continuous data was expressed as mean ± standard deviation while categorical data as numbers and percentage. Mann-Whitney U Test was used to compare means of different groups. A statistical value <0.05 was considered as significant.

RESULTS

A Significant difference was found between the three studied groups [RA, SLE, AS] and control group regarding central corneal thickness [Table 1].

A significant difference was found between the SLE and AS groups and control group regarding cell density. No significant difference was found between the RA group and control group regarding cell density [CD] [Table 2].

A significant difference was found between the AS and control groups regarding hexagonality [HEX]. No significant difference was found between the RA and SLE groups and control group regarding cell density [Table 3].

A significant difference was found between the AS and RA studied groups and control group regarding cell variation [CV]. No significant difference was found between the SLE group and control group regarding cell variation [CV] [Table 4].

Table [1]: Comparison between RA,SLE and AS group and control group regarding central corneal thickness[CCT]

Corneal thickness	Group [1] RA group [n.= 30]		Group [4] Control group [n.= 30]		Mann-Whitney U Test	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	510.20	38.84	533.60	23.92	2.943	**0.003**
Left eye	508.17	32.17	535.20	24.44	3.448	**0.001**
Corneal thickness	**Group [2] SLE group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	512.20	16.85	533.60	23.92	3.693	**<0.001**
Left eye	515.90	21.97	535.20	24.44	2.977	**0.003**
Corneal thickness	**Group [3] AS group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	502.50	22.22	533.60	23.92	4.40	**<0.001**
Left eye	505.20	24.93	535.20	24.44	3.87	**<0.001**

Table [2]: Comparisons between RA, SLE and AS group and control group regarding cell density [CD]

Cell density [CD]	Group [1] RA group [n.= 30]		Group [4] Control group [n.= 30]		Mann-Whitney U Test	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	2700.48	370.77	2836.33	202.78	1.896	0.058
Left eye	2707.79	408.57	2780.20	223.74	1.410	0.158
Cell density [CD]	**Group [2] SLE group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	2428.50	325.86	2836.33	202.78	4.44	**<0.001**
Left eye	2512.10	366.58	2780.20	223.74	2.66	**0.008**
Cell density [CD]	**Group [3] AS group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	**±SD**	**Mean**	**±SD**	**Test value**	**P-value**
Right eye	2290.70	430.23	2836.33	202.78	5.149	**<0.001**
Left eye	2386.30	388.84	2780.20	223.74	4.573	**<0.001**

Table [3]: Comparisons between RA, SLE and AS group and control group regarding hexagonality [HEX]

Hexagonality [HEX]	Group [1] RA group [n.= 30]		Group [4] Control group [n.= 30]		Mann-Whitney U Test	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	65.21	7.68	65.67	4.92	0.320	0.749
Left eye	64.43	7.05	65.67	5.22	0.015	0.988
Hexagonality [HEX]	**Group [2] SLE group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	67.30	6.53	65.67	4.92	0.715	0.475
Left eye	65.10	6.13	65.67	5.22	1.072	0.284
Hexagonality [HEX]	**Group [3] AS group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	61.20	3.91	65.67	4.92	3.709	**<0.001**
Left eye	60.80	4.31	65.67	5.22	4.698	**<0.001**

Table [4]: Comparisons between RA, SLE and AS group and control group regarding cell variation [CV]

Cell variation [CV]	Group [1] RA group [n.= 30]		Group [4] Control group [n.= 30]		Mann-Whitney U Test	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	31.82	4.82	27.73	2.98	2.991	**0.003**
Left eye	31.07	5.28	27.47	3.66	2.333	**0.020**
Cell variation [CV]	**Group [2] SLE group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	27.40	2.95	27.73	2.98	0.318	0.750
Left eye	27.80	2.72	27.47	3.66	0.225	0.822
Cell variation [CV]	**Group [3] AS group [n.= 30]**		**Group [4] Control group [n.= 30]**		**Mann-Whitney U Test**	
	Mean	±SD	Mean	±SD	Test value	P-value
Right eye	30.10	2.43	27.73	2.98	2.453	**0.014**
Left eye	30.70	3.12	27.47	3.66	2.798	**0.005**

DISCUSSION

The eye is an important indicator of rheumatologic disease. Various ocular signs and symptoms are characteristic of different rheumatologic diseases [7].

In this study, we aimed to evaluate the corneal changes which occur in ankylosing spondylitis, SLE and rheumatoid arthritis.

In the current study: Significant difference was found between the three studied groups [RA, SLE, AS] regarding central corneal thickness [CCT] in right and left eye compared to control group.

Consistent with our results, the study by **Özcura *et al.*** [8] reported that 54 patients with rheumatoid arthritis [104 eyes] and 21 control patients of the same age and gender [42 eyes] were included in the study. Mean central corneal thickness were thinner in rheumatoid arthritis than in control eyes.

Furthermore, the study by **Anayol *et al.*** [9] reported that significant differences in central thickness and corneal thickness measurements were smaller in RA patients than in the control group.

Compared to the study by **Eissa *et al.*** [10] who reported that the mean central corneal thickness [CCT] was statistically significant difference between the SLE group and the control group; Lupus patients with thinner mean central pachymetry. Another study of **Cabuk *et al.*** [11] reported that CCT was significantly decreased in the AS group compared to control group.

A recent study by **Gunes *et al.*** [12] examined corneal parameters and found that the mean CCT and corneal volume were significantly reduced in patients with AS.

In the current study, significant difference was found between the SLE and AS groups and control group regarding cell density. No significant difference was found between the RA group and control group regarding cell density.

In another study of **Villani *et al.*** [13], it was seen that total corneal densitometry was statistically higher in the RA group, although there was no evident opacity or infiltration. In addition, when subdivisions of the cornea were evaluated, a higher density was found in the RA group.

Compared to our results, the study by **Kaya *et al.*** [14] showed that there were no statistically significant differences in cell density between SLE group and control group.

The biomechanical properties of the cornea were studied in patients with SLE in **Yazici *et al.*** [15] examined Corneal parameters differed significantly between SLE and healthy controls. The CD was lower in the SLE group than in the control group.

Consistent with our results, **Guclu and Gurlu** [16] found a decrease in CD in patients with uveitis. Healthy volunteers had decreased CV and increased HEX values compared to uveitis patients. **Alfawaz *et al.*** [17] suggested that patients with unilateral uveitis had lower CD in the affected eye than in the contralateral eye without uveitis.

In addition to the previous results, we found that no significant differences were observed between the control group and the SLE and RA groups in terms of hexagonality. At the same time, a significant difference was found between the control group and the AS group in hexagonality, which was larger in the AS group than in the control group.

A previous study by **Alfawaz et al** [17] reported a decrease in Hex compared to the affected eye and suggested that this was due to direct contact between endothelial cells and ocular inflammatory cells or cytokines with the aqueous humor.

In this study, significant difference was found between the AS and RA studied groups compared to control group regarding cell variation [CV]. No significant difference was found between the SLE group compared to control group regarding cell variation [CV].

Guclu and Gurlu [16] who also found a significantly higher CV in uveitis in patients with AS. Similarly, a recent study by **Örnek and Örnek** [18] reported that CD was significantly lower and CV was significantly higher in the RA group than in healthy subjects

Conclusion: Rheumatoid arthritis [RA], systemic lupus erythematosus [SLE] and ankylosing spondylitis [AS] have slight effect on Cell density [CD], central corneal thickness [CCT], cell size and shape permanently. Specular microscopy is a simple and valuable tool for assessing the corneal mucosa of normal and diseased eyes.

Financial and Conflict of Interest: Nil

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