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A Clinical Study of Ocular Manifestations in Various Autoimmune Diseases

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Abstract: ***Background: The wide variety of ocular manifestations associated with various autoimmune diseases are often overlooked, and their significance is underestimated. These manifestations range from minor disturbances to sight - threatening conditions that need immediate medical intervention. Aims & objective: To document the ocular manifestations seen in various Autoimmune diseases and to study the ocular complications associated with the systemic treatment in patients of autoimmune diseases. Methods and Material: Patients with confirmed diagnosis of Autoimmune diseases coming to the Ophthalmology OPD of Rajarajeswari Medical College and Hospital between January 2021 to July 2022. We included a total of 60 patients who satisfied the inclusion and exclusion criteria. It was a cross sectional observational study and the study protocol was had been cleared by the ethical committee of the institution prior to starting the study. Results: In the present study, All the study participants with dermatomyositis, Graves' disease, Myasthenia Gravis and RA were found to have Itching, Redness, Double vision and dryness respectively.93.8% and 55.6% of the study participants with SLE and Sjogren's were found to have Burning sensation and pricking sensation respectively. The association was found to be statistically significant between the ocular complaints of the study participants and the autoimmune disease status. Conclusions: Ocular symptoms can be the initial presentation of autoimmune disease so a complete evaluation is appropriate for cases without established autoimmune disease diagnosis. Once the autoimmune nature of the ocular disease is suspected, a multidisciplinary approach will prove to be the best option to manage autoimmune disease - associated ocular pathology***

Keywords: Auto- immune, Rheumatoid Arthritis, SLE, Sjogren's Syndrome, Myasthenia gravis, Grave's disease, Psoriasis, Dermatomyositis, Dry eyes, Keratitis, Uveitis, Conjunctivitis.

1. Introduction

Autoimmune diseases are increasing globally, from an estimated prevalence of 3.2% between 1965 and 1995 to 19.1 ± 43.1 reported in 2018 (1, 2). By 2026 the global diagnosis market size for autoimmune diseases, currently worth $4.1B, is estimated to reach $6.3B (3). Some reasons for this increase can be owed to genetic predisposition in an ageing population and improved diagnostic techniques. However, increasing prevalence has been more greatly influenced by environmental factors, thus suggesting a reason these issues can be reduced.

Autoimmune diseases result from the body's immune system attacking self - antigens (4) and are classified as either organ - specific or systemic depending on the target area within the body. Although there are over 80 known autoimmune diseases, the exact aetiology of many of these diseases is still unknown. Genetics and environmental factors are crucial in dictating disease susceptibility, prevalence and severity through the cellular immune system.

The wide variety of ocular manifestations associated with various autoimmune diseases are often overlooked, and their significance is underestimated. These manifestations range from minor disturbances to sight - threatening conditions that need immediate medical intervention. The eye is a delicate organ with a microenvironment sensitive to systemic changes within the body, which can also act as the first indicator of underlying autoimmune disease (5, 6). Ocular manifestations can also arise during active disease or years following diagnosis. Delaying treatment of these manifestations directly impacts a patient's quality of life, and in some cases, there is undoubtable risk for visual impairment.

Every section of the eye is a potential target for autoimmune - related complications. Ideally, an ocular examination should become a routine part of disease management to diagnose, investigate and treat any arising ocular symptoms on time. Furthermore, the importance of regular screening, even for those who are asymptomatic, should be emphasised due to the potential for acute, sight - threatening ocular complications, which are observed with several of the autoimmune diseases covered within this review.

In addition, polyautoimmunity or multiple autoimmune syndromes in a single patient is not uncommon, such as the association between rheumatoid arthritis, thyroiditis and type 1 diabetes mellitus (7). Such conditions increase the risk of systemic manifestations, including those affecting the eye.
With a global population seeing an increasing prevalence of autoimmune diseases, with additional risk of polyautoimmunity and an ageing population, we can only hypothesise the potential for accompanying ocular manifestations of these diseases also to increase. The present study aimed identify various ocular complications associated with autoimmune diseases and those at greatest risk so that particular care can be taken with screening and diagnosis.

2. Material and Methods

Patients with confirmed diagnosis of Autoimmune diseases coming to the Ophthalmology OPD of Rajarajeswari Medical College and Hospital between January 2021 to July 2022. We included a total of 60 patients who satisfied the eligibility criteria. It was a cross sectional observational study and the study protocol was had been cleared by the ethical committee of the institution prior to starting the study. Patients confirmed with diagnosis of Autoimmune diseases and willing to give consent were included in the study

Dry eyes due to other diseases like Steven - Johnson syndrome, ocular cicatricial pemphigoid, and chemical injuries. Patients with Diabetes mellitus, uveitis, scleritis, glaucoma due to causes other than Rheumatoid Arthritis or any other co - morbidities (ocular & systemic) wereexcluded.

The demographic and ocular chief complaints including the duration was recorded. The type of autoimmune disease, duration of the autoimmune diseases, ocular manifestations, drug usage for the said autoimmune diseases were also noted. Assessment of all patients with various autoimmune diseases was checked and evaluated with detailed ocular history and visual acuity tests. All the patients with autoimmune diseases were examined under slit lamp microscope for anterior segment evaluation. All the patients with confirmed autoimmune diseases were dilated and examined with Indirect Ophthalmoscope with +20D lens/ Direct Ophthalmoscope/ with +90D lens for posterior segment evaluation.

Ocular Examination –
Ocular examination was done to evaluate for the various ocular manifestation like dry eyes (KCS), scleritis, episcleritis, peripheral ulcerative keratitis, anterior uveitis and also for ocular complications of systemic treatment. It included best corrected visual acuity, testing for colour vision, Amsler's grid, detailed slit lamp examination of anterior segment, detailed fundus examination, refraction, intraocular pressure measurement and tests for dry eyes. Visual fields and B scan if necessary were performed.

Tear function tests /dry eye tests included tear break up time (TBUT), basal Schirmer's test, and vital staining using Rose Bengal and were performed in the same order. TBUT was measured as follows: fluorescein dye was instilled in to the lower fornix, patient was asked to blink several times, tear film was examined with a broad beam and cobalt blue filter, the time interval for the appearance of black spot in the fluorescein - stained film indicating the formation of dry areas was noted. TBUT < 10 seconds was considered abnormal.

Basal Schirmer's test was performed using Schirmer strips of 35mm in length and 5mm in width. After instilling local anaesthetic drops (proparacaine), the eyes were gently dried of excess tears. The Schirmer strip was folded 5mm from one end and inserted at the junction of the middle and outer third of the lower lid taking care not to touch the cornea. The patient was asked to keep the eyes gently closed. After 5 minutes the strip was removed and the amount of wetting from the fold measured. Value of < 10mm at the end of 5 minutes was considered abnormal.

Schirmer's test is a good measure for tear production TBUT is abnormal in tear deficiency and also in evaporative dry eye. Ocular surface staining with Rose Bengal is positive when there is damage to the ocular surface which results in death and devitalisation of epithelial cells, usually seen in mucin deficiency. Severe tear deficiency as well as evaporative dry eye can cause staining with Rose Bengal. Dry eye in RA, most commonly caused by tear deficiency (secondary Sjogren's syndrome) was graded based on Schirmer's test and according to the definition and classification given by subcommittee of International dry eye work shop (DEWS).

Table 1: Schirmer's Test values and severity of dry eyes.6

Grade	Schirmer's test value (mm)	Severity
0	>10	No Dry eyes
1	6 - 10	Mild
2	3 - 5	Moderate
3	≤2	Severe

Ocular Treatment
All Dry Eye Patients Received Topical Treatment with Tear Substitutes – Preservative Free Carboxy Methyl Cellulose (Cmc) Eye Drops 6 Times/ Day. Lubricating Eye Ointment Was Prescribed Twice Daily. Other Ocular Manifestations of Rheumatoid Arthritis Were Treated According To The Manifestation.

Systemic Treatment Was Advised In Severe Inflammatory Conditions Like Scleritis. In Cases of Ocular Complications With Systemic Treatment, The Drug Known To Cause The Ocular Complication Was Stopped.

Follow - up –
Follow - up examinations for assessment of ocular manifestations were done monthly for 3 months for dry eyes. At each follow- up any subjective assessment for any improvement in symptoms were asked, tear function tests including Schirmer's test (basal), TBUT and Rose Bengal staining were done. Patients with other ocular manifestations were also followed up.

3. Results

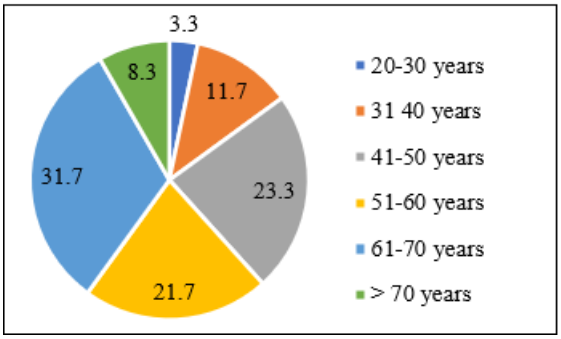

Figure 5: Distribution of the study participants according to their age group

Table 2: Distribution of the study participants according to their gender

Gender	Frequency N	Percentage %
Male	22	36.7
Female	38	63.3

Table 3: Distribution of the study participants according to their ocular complaints

Ocular Complaints	Frequency N	Percentage %
Burning sensation	15	25.0
Double Vision	3	5.0
Dryness	23	38.3
Grittiness	1	1.7
Itching	4	6.7
Pricking sensation	5	8.3
Redness	9	15.0

Table 4: Distribution of the study participants according to their treatment history of drugs

Treatment History of Drugs		Frequency N	Percentage %
Steroid, Hydrochloroquine, Methotrexate	< 1 year	10	16.4
	1 - 5 years	27	44.3
	6 - 10 years	10	16.4
	11 - 15 years	10	16.4
	> 15 years	3	5
MEAN + SD		6.22 + 6.65 years	

Table 5: Distribution of the study participants according to their autoimmune disease

AUTOIMMUNE DISEASE	Frequency N	Percentage %
DERMATOMYOSITIS	4	6.7
GRAVES DISEASE	5	8.3
MYASTHENIA GRAVIS	3	5.0
RA	23	38.3
SJOGREN'S	9	15.0
SLE	16	26.7

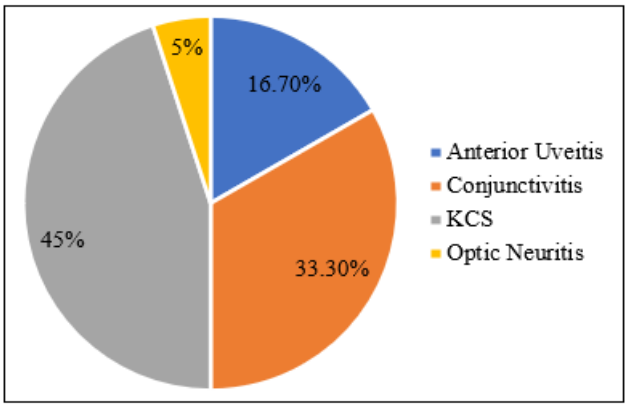

Figure 6: Distribution of the study participants according to ocular manifestation

Table 6: Visual Acuity and BCVA of the study participants

Visual Acuity and BCVA		Right Eye		Left Eye	
		N	%	N	%
Vision	6/12	9	15.0	9	15.0
	6/18	11	18.3	11	18.3
	6/24	5	8.3	5	8.3
	6/36	10	16.7	10	16.7
	6/6	11	18.3	11	18.3
	6/60	5	8.3	5	8.3
	6/9	8	13.3	8	13.3
	HMCF	1	1.7	1	1.7
BCVA	6/12	11	18.3	11	18.3
	6/18	3	5.0	3	5.0
	6/24	2	3.3	2	3.3
	6/36	2	3.3	2	3.3
	6/6	27	45.0	27	45.0
	6/60	2	3.3	2	3.3
	6/9	13	21.7	13	21.7

Table 7: Findings of ocular examination of the study participants

Findings of Ocular Examination		Right Eye		Left Eye	
		N	%	N	%
CV	NORMAL	60	100	60	100
EYELIDS	NORMAL	60	100	60	100
CONJUNCTIVA	CC+	16	26.7	16	26.7
	N	36	60.0	36	60.0
	Papillae +	8	13.3	8	13.3
CORNEA	KP+	3	5.0	3	5.0
	N	54	90.0	54	90.0
	SPK+	3	5.0	3	5.0
AC	Grade 3	1	1.7	1	1.7
	Irregular	1	1.7	1	1.7
	N	58	96.7	58	96.7
IRIS	NORMAL	60	100	60	100
PUPIL	NORMAL	57	95	57	95
	RAPD+	3	5.0	3	5.0
LENS	N	50	83.3	50	83.3
	SIMC	10	16.7	10	16.7
FUNDUS	Drusen +	8	13.3	8	13.3
	HCQ Retinopathy	1	1.7	1	1.7
	N	51	85.0	51	85.0

Table 8: Findings of ocular tests of the study participants

Ocular Tests		Right Eye		Left Eye	
		N	%	N	%
SCHIRMERS	1 - 10	25	41.7	26	43.3
	11 - 20	21	35.0	20	33.3
	21 - 30	9	15.0	9	15.0
	>30	5	8.3	5	8.3
MEAN + SD		14.52 + 9.55		14.70 + 9.79	
TBUT	1 - 10	25	41.7	26	43.3
	11 - 20	23	38.3	21	35.0
	21 - 30	11	18.3	12	20.0
	>30	1	1.7	1	1.7
MEAN + SD		13.07 + 8.42		13.20 + 8.36	

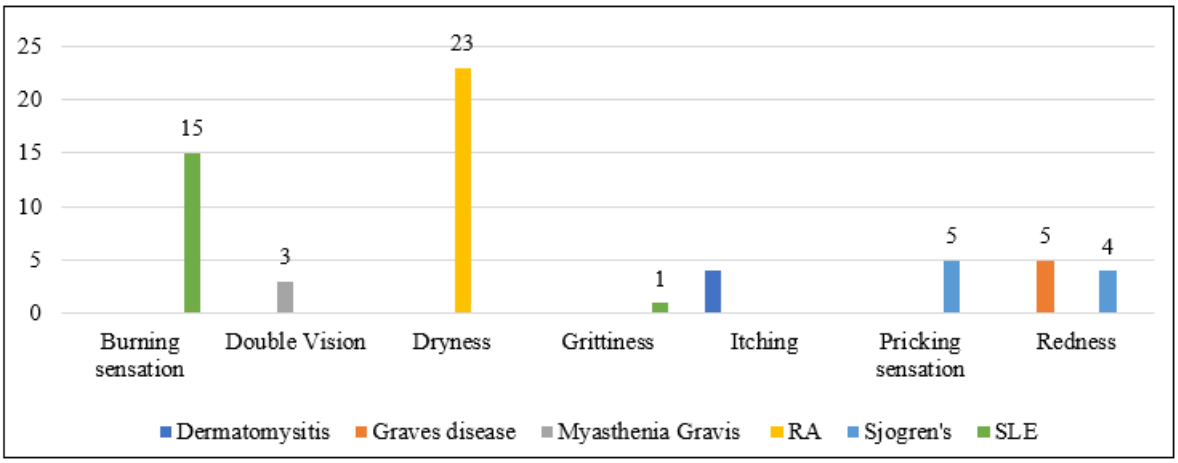

Figure 7: Association of ocular complaints with autoimmune disease status of the study participants

Table 9: Association of ocular manifestation with autoimmune disease status of the study participants

Ocular Manifestation	Autoimmune Disease Status					
	D - M	GD	MG	RA	Sjogren's	SLE
Anterior Uveitis	1 (26%)	2 (40%)	1 (33.3%)	1 (4.3%)	-	5 (31.3%)
Conjunctivitis	3 (74%)	2 (40%)	1 (33.3%)	1 (4.3%)	4 (44.4%)	9 (56.3%)
KCS	-	1 (20%)	-	20 (87%)	5 (55.6%)	1 (6.3%)
Optic Neuritis	-	-	1 (33.3%)	1 (4.3%)	-	1 (6.3%)

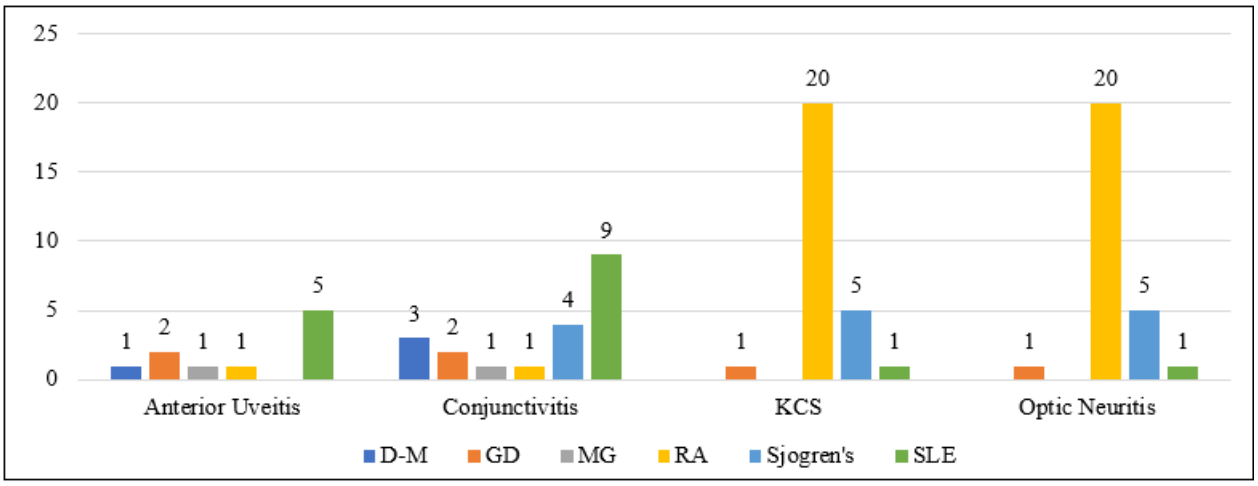

Figure 8: Association of ocular manifestation with autoimmune disease status of the study participants

4. Result and Observation

In the present study, the ocular complaints of the study participants were seen in the following order: Dryness (38.3%), Burning sensation (25%), Redness (15%), Pricking sensation (8.3%), Itching (6.7%), Double Vision (5%) and Grittiness (1.7%). In a study done by Uribe - Reina P et al., Thirty - five percent of the patients reported one or more ophthalmological symptoms, being dry eye (DE) sensation the most common (30.9%), followed by ocular pain (2.8%), red - eye (2.6%), and decreased visual acuity (VA) (2.6%).[9]

In the present study, All the study participants with dermatomyositis, Graves' disease, Myasthenia Gravis and RA were found to have Itching, Redness, Double vision and dryness respectively.93.8% and 55.6% of the study participants with SLE and Sjogren's were found to have Burning sensation and pricking sensation respectively. The association was found to be statistically significant between the ocular complaints of the study participants and the autoimmune disease status.

Considering the 4 most prevalent rheumatologic pathologies, we observe how dry eye, ocular pain, red eye, decreased VA, and photophobia were common in patients with these diagnoses.26% and 74% of the study participants with dermatomyositis were found to have Anterior uveitis and Conjunctivitis respectively. The study participants with Graves' disease were found to have symptoms of Anterior uveitis (40%) and Conjunctivitis (40%) respectively.

The study participants with Myasthenia gravis were found to have Anterior uveitis (33.3%), Conjunctivitis (33.3%) and optic neuritis (33.3%) respectively.87% of the study participants with RA were found to have KCS.55.6% of the study participants with Sjogren's were found to have KCS.56.3% and 31.3% of the study participants with SLE were found to have conjunctivitis and anterior uveitis respectively. The association was found to be statistically significant between the ocular manifestations of the study participants and the autoimmune disease status.[10]

5. Discussion

The present study included 60 study participants with clinical diagnosis of Autoimmune diseases attending the department of Ophthalmology, RRMCH, Bangalore to document the ocular manifestations seen in various Autoimmune diseases and to study the ocular complications associated with the systemic treatment in patients of autoimmune diseases.

In the present study, Majority of the study participants belonged to the age group 61 - 70 years (31.7%) of age. The mean age of the study participants was found to be 55.12 + 12.97. In a study done by Vignesh APP et al., the mean age of the patients was 43.85 ±21.54 years. In a study done by Uribe - Reina P et al., the mean age of our population was 54.61 ± 15.64 years. These findings are comparable with the findings of the present study.7 In the present study, Majority of the study participants were females 63.3% with males contributing for 36.7% of study participants. In the present study, RA was diagnosed in majority 38.3% of the study participants in the present study followed by SLE in 26.7% of the study participants. Sjogren's and Graves' disease was found in 15% and 8.3% of the study participants respectively. Myasthenia Gravis contributed to 5% of autoimmune disease burden in the present study.45% of the study participants were found to have KCS with conjunctivitis in 33.3% of the study participants. Anterior Uveitis was seen in 16.7% of the study participants with 5% of the study participants having ocular manifestation of optic neuritis. In a study done by Uribe - Reina P et al., the most common diagnoses were RA in 33.37% and Sjogren's in 19.93% of the study participants, which is comparable with the findings of the present study.8

In the present study, the visual acuity of the study participants is seen in the following order: 6/18 & 6/6 (18.3%) > 6/36 (16.7%) > 6/12 (15.0%) > 6/9 (13.3%) > 6/24 & 6/60 (8.3%).45% of the study participants were found to have 6/6 on BCVA with 21.7% having BCVA of 6/9. In a study done by Vignesh APP et al., Eighty - six percent (86%) of the patients had normal visual acuity. Fourteen percent of the patients had decreased visual acuity due to manifestations like sclerosing keratitis, scleritis and cataract.

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