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Evaluation Of Ocular Surface Changes In Thyroid Eye Disease

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I. Introduction

Dry eye disease (DED), also known as keratoconjunctivitis sicca (KCS), is a prevalent ocular condition characterized by tear film instability due to either reduced tear production or increased evaporation. This leads to damage of the interpalpebral ocular surface and manifests as ocular discomfort. DED is commonly observed in the general population, especially among individuals aged 65 to 84, with its prevalence increasing after the age of 59. Inflammatory changes in the lacrimal glands and ocular surface are central to its pathophysiology. Among patients with thyroid eye disease (TED), DED is notably frequent, with reported prevalence ranging from 23% to 96%. TED, a systemic autoimmune disorder, presents with features such as conjunctival hyperemia, eyelid retraction, and proptosis, all of which contribute to tear film instability through mechanical and immunological mechanisms.

The association between TED and DED is multifactorial and complex. Mechanical factors like widened palpebral fissures and exophthalmos lead to increased tear evaporation and corneal exposure, while immunological factors such as altered tear composition and lacrimal gland dysfunction exacerbate the condition. Studies have shown that individuals with Hashimoto's and Graves' disease report high rates of dry eye symptoms. Additionally, middle age, smoking, and female gender are recognized risk factors. The inflammatory cascade in TED not only affects the ocular surface but may also impair aqueous tear production. Immunohistochemical evidence suggests that TSH receptors in the lacrimal gland may serve as targets for autoantibodies, further implicating glandular involvement in DED. Confocal microscopy findings support this with increased keratocyte activation and reduced corneal nerve density.

Meibomian gland dysfunction (MGD), often secondary to inadequate blinking due to proptosis and eyelid retraction, further contributes to tear film instability in TED patients. Low serum free thyroxine levels and altered expression of thyroid hormone receptor β-1 in the lacrimal gland are additional contributors to reduced tear production. These pathophysiologic mechanisms result in ocular surface symptoms in up to 85% of TED patients, necessitating thorough evaluation. TED progresses through an active inflammatory phase followed by a static fibrotic phase, as depicted by Rundle's curve. The interplay of proptosis, lid retraction, and exposure leads to increased tear osmolarity and evaporation, underscoring the need for deeper investigation into the mechanisms linking TED and DED to improve diagnostic and therapeutic strategies.

II. Aims And Objectives

1. To assess the ocular surface in patients of thyroid disease.
2. To correlate ocular findings of thyroid disease patients with duration of the disease.

III. Materials And Methods

This study was conducted at Himalayan Institute of Medical Sciences (HIMS), Swami Ram Himalayan University, Dehradun over a period of 1 year from November 2022 to October 2023, after taking written informed consent (Annexure 1a.). Thyroid disease patients attending the out-patient department in HIMS were selected as per inclusion and exclusion criteria. All the selected patients were thoroughly evaluated for Schirmer's I test, tear film break-up time (TBUT) and ocular surface disease index score (OSDI score) was calculated for every patient.

Study Design
Observational Study

Sample size and Sampling method:

By using a convenient sample technique, the study included a minimum of 152 patients. The following formula was used to determine the minimum necessary sample size.

Formula for sample size: $n = \frac{Z2\alpha/2\ p(1-p)}{d2}$

- Z α/2 = 1.96 at 5% level of significance **(19)**
- p = prevalence (65.2%)
- d = 10% of absolute precision

Selection of Subjects:

Inclusion Criteria:

1. Thyroid disease patients (hypothyroidism and hyperthyroidism) who came to the Ophthalmology, Medicine and Endocrinology OPD at Himalayan Institute of Medical Sciences, Dehradun.
2. Patients in the age group 18 – 60 years

Exclusion criteria:

1. Patients on systemic medications such as antihistamines, tricyclic antidepressants, oral contraceptives and other medications which are known to cause dry eye.
2. Contact lens users
3. Patients who have undergone any ocular surgery (Laser-assisted in situ keratomileusis or any other intraocular surgery etc).
4. Patients having local ocular pathologies like meibomitis, blepharitis, ectropion or entropion, nasolacrimal duct block etc or any other systemic conditions apart from thyroid disease known to cause dry eye.
5. Glaucoma patients and carcinoma patients.
6. Uncooperative patients
7. Patients not willing to give consent.

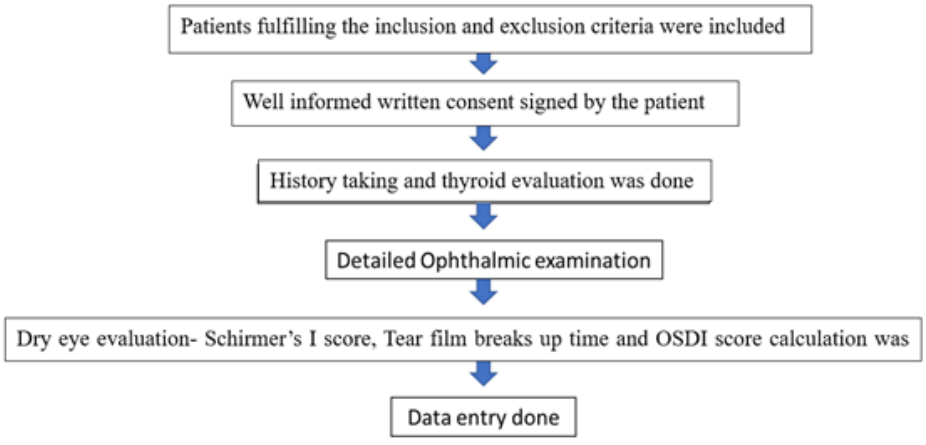
Study Tools:

1. Case reporting format
2. Thyroid stimulating hormone test kit
3. Ocular Surface Disease Index Sheet
4. Slit lamp examination
5. Sodium fluorescein strips (2%)
6. Proparacaine eye drops (0.5%)
7. Schirmer strips

Study Protocol:

A detailed history and thyroid status evaluation was done in all the patients. Every patient underwent a thorough ophthalmic examination of both eyes, which included a visual acuity assessment, pupillary reaction, slit-lamp examination, measurement of intraocular pressure using non-contact tonometry (NCT), fundus examination, and evaluation of ocular motility.

The Schirmer -I score and TBUT were calculated for all patients. The OSDI questionnaire was used to evaluate dry eye symptoms and OSDI score was calculated for each patient.



IV. Results

Age distribution

Age distribution (years)	Number (n)	Percent (%)
18-30	16	10.5
31-40	20	13.2
41-50	43	28.3
51-60	73	48.0
Total	152	100

Table 1: Distribution of patients as per age.

The mean age of the patients was 47.22 ± 10.65 years. Among total 152 patients, 16 (10.5%) patients were in the age group of 18-30 years, 20 (13.2%) patients were in the age group of 31-40 years, 43 (28.3%) patients were in the age group of 41-50 years, and 73 (48.0%) patients were in the age group of 51-60 years.

Gender distribution

Gender distribution	Number (n)	Percent (%)
Male	57	37.5
Female	95	62.5
Total	152	100

Table 2: Distribution of patients as per gender.

There were 57 (37.5%) male and 95 (62.5%) females among total 152 patients indicating female predominance.

Occupational distribution

Occupation	Number (n)	Percent (%)
Housewife	82	53.9
Shopkeeper	26	17.1
Farmer	13	8.6
Self-Employed	9	5.9
Teacher	8	5.3
Business	5	3.3
Student	5	3.3
Labourer	4	2.6
Total	152	100

Table 3: Distribution of patients as per occupation.

82(53.9%) patients were housewives, 26 (17.1%) patients were shopkeepers, 13 (8.6%) patients were farmers, 9 (5.9%) patients were self-employed, 8 (5.3%) patients were teachers, 5 (3.3%) patients were businessman, 5 (3.3%) patients were students, and 4 (2.6%) patients were laborers.

Distribution of patients as per thyroid status

Thyroid disease	Number (n)	Percent (%)
Hypothyroidism	103	67.8
Hyperthyroidism	49	32.2

Table 4: Distribution of patients as per thyroid status.

Hypothyroidism was seen in 103 (67.8%) patients whereas hyperthyroidism was seen in 49 (32.28%) patients.

Thyroid disease duration	Number (n)	Percent (%)
Duration<=10 Yrs	91	59.9
Duration>10 Yrs	61	40.1

Table 5: Distribution of patients as per thyroid disease duration.

The mean duration of illness was 9.32 ± 5.92 years. The duration of thyroid disease was <=10 years in 91 (59.9%) patients whereas >10 years in 61 (40.1%) patients.

TSH Level (mU/L)	Number (n)	Percent (%)
Low TSH	7	4.6
Normal TSH	51	33.6
High TSH	94	61.8
Total	152	100

Table 6: TSH Level.

Mean TSH value was 5.80 ± 3.32 mU/L. Normal TSH was seen in 51 (33.6%) patients. Low TSH was found in 7 (4.6%) patients and high TSH was recorded in 94 (61.8%) patients.

Ocular surface parameters

Distribution of patients as per TBUT:

TBUT (seconds)	Number (n)	Percent (%)
>10	127	83.6
8-10	14	9.2
5-7	6	3.9
<5	5	3.3
Total	152	100

Table 7: Distribution of patients as per TBUT.

The mean TBUT was 16.90 ± 5.75 seconds. Normal TBUT was seen in 127 eyes (83.6%), 14 eyes (9.2%) had TBUT between 8-10 seconds indicative of mild dry eye, 6 eyes (3.9%) had TBUT between 5-7 seconds indicative of moderate dry eye and 5 eyes (3.3%) had a TBUT <5 seconds indicative of severe dry eye.

Distribution of patients as per Schirmer-I score:

Schirmer (mm/5 min)	Number (n)	Percent (%)
>10	120	78.9
8-10	10	6.6
5-7	10	6.6
<5	12	7.9
Total	152	100

Table 8: Distribution of patients as per Schirmer-I score.

The mean Schirmer-I test result was 17.75 ± 8.52mm. 120 eyes (78.9%) had a Schirmer-I test result >10mm (Normal), 10 eyes (6.6%) had a Schirmer-I test result between 8-10 mm indicative of mild dry eye, 10 eyes (6.6%) had a Schirmer-I test result between 5-7 mm indicative of moderate dry eye and 12 eyes (7.9%) had a Schirmer-I test result <5mm indicative of severe dry eye

Ocular symptoms	Number(n)	Percentage(%)
Eyes that are sensitive to light	64	42.1
Eyes that feel gritty	92	60.5
Painful or sore eyes	62	40.8
Blurred vision	64	42.1
Poor vision	59	38.8

Table 9: Distribution of ocular symptoms in thyroid patients.

Out of 152 patients studied, ocular symptoms including sensitivity to light were found in 64 (42.1%) patients, gritty sensation in 92 (60.5%) patients, painful or sore eyes in 62 (40.8%) patients, blurred vision in 64 (42.1%) patients, and poor vision was found in 59 (38.8%) patients.

Vision related functions	Number(n)	Percent(%)
Problems with reading	67	44.1
Problems with driving at night	62	40.8
Problems with working on a computer	79	52
Problems with watching television	83	54.6

Table 10: Distribution of patients as per vision related functions.

Vision related functions including problems with reading were present in 67 (44.1%) patients, problems with driving at night were present in 62 (40.8%) patients, problems with working on a computer were present in 79 (52%) patients, and problems with watching television were present in 83 (54.6%) patients.

Environmental triggers	Number(n)	Percent(%)
Problems in windy condition	113	74.3
Problems in places with low humidity	131	86.2
Areas that are air conditioned	104	68.4

Table 11: Distribution of patients as per environmental triggers.

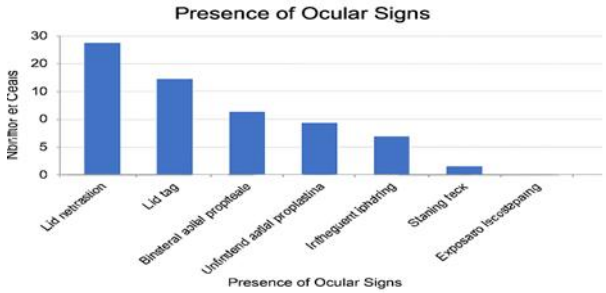
Environmental triggers including the problems in windy condition were present in 113 (74.3%) patients, problems in places with low humidity were present in 131 (86.2%) patients and areas that are air conditioned were present in 104 (68.4%) patients.

Distribution of patients as per OSDI score

OSDI SCORE	Number (N)	Percent (%)
0-12	118	77.6
13-22	11	7.2
23-32	8	5.3
33-100	15	9.9
Total	152	100

Table 12: Distribution of patients as per OSDI score.

The mean OSDI score was 12.54 ± 12.40. Normal OSDI score (0-12) was seen in 118 eyes (77.6%), 11 eyes (7.2%) had an OSDI score between 13-12 indicative of mild dry eye, 8 eyes (5.3%) had an OSDI score between 23-32 indicative of moderate dry eye and 15 eyes (9.9%) had an OSDI score between 33-100 indicative of severe dry eye.



Distribution of ocular signs in thyroid patients.

Out of total 152 thyroid disease patients examined, 29 (19%) patients had lid retraction, 21 (13%) patients had lid lag, 5 (3.2%) patients had bilateral axial proptosis, 3 (1.9%) patients had unilateral axial proptosis, 18 (11%) patients had bulbar conjunctival congestion, 10 (6.5%) patients had infrequent blinking, 7 (4.6%) patients had staring look. No patient had exposure keratopathy, relative afferent pupillary defect (RAPD), restriction of extraocular movements and disc edema suggestive of compressive optic neuropathy.

Correlation between ocular findings of thyroid disease patients with duration of the disease

TBUT and duration of disease	Value
Pearson's correlation coefficient	-0.028
P value	0.731

Table 14: Correlation between TBUT and duration of disease.

A negative correlation (r=-0.028) was observed between the TBUT and duration of thyroid disease (p=0.731).

Correlation between Schirmer score and duration of thyroid disease:

Schirmer score and disease duration	Value
Pearson's correlation coefficient	0.060
P value	0.466

Table 15: Correlation between Schirmer score and duration of thyroid disease.

A positive correlation (r=0.060) was observed between the Schirmer score and duration of thyroid disease (p=0.466).

Correlation between OSDI score and duration of thyroid disease:

OSDI score and disease duration	Value
Pearson's correlation coefficient	-0.187
P value	0.021

Table 16: Correlation between OSDI score and duration of thyroid disease.

A negative correlation (r=-0.187) was observed between the OSDI score and duration of thyroid disease (p=0.021).

V. Discussion

Thyroid eye disease (TED), a form of orbital inflammation, affects 45–85% of individuals with thyroid dysfunction and is frequently associated with dry eye disease (DED) and other ocular surface abnormalities. DED diagnosis relies on a combination of subjective questionnaires and objective tests that assess both tear quantity and quality. In the present study, Schirmer-I test, tear break-up time (TBUT), and the Ocular Surface Disease Index (OSDI) score were employed to evaluate DED. The mean age of participants was 47.22 ± 10.65 years, with the majority (48%) falling within the 51–60 age group. A female predominance was observed (62.5%), consistent with previous studies attributing this trend to hormonal and genetic factors influencing thyroid autoimmunity. Hypothyroidism was more prevalent (67.8%) than hyperthyroidism (32.28%) in the cohort, contrasting with some earlier studies that reported higher rates of hyperthyroidism.

Tear film instability was evident in TBUT and Schirmer-I test results. The mean TBUT was 16.90 ± 5.75 seconds, with 16.4% of eyes showing mild to severe dry eye. These findings align with prior research indicating reduced TBUT in thyroid dysfunction due to increased tear evaporation and lacrimal gland insufficiency. The mean Schirmer-I test result was 17.75 ± 8.52 mm, with 21.1% of eyes showing varying degrees of aqueous deficiency. Comparative studies have consistently demonstrated lower Schirmer scores in TED patients, particularly those with active disease. Factors such as exophthalmos, lagophthalmos, and eyelid retraction contribute to tear film instability, while autoantibodies targeting TSH receptors in the lacrimal gland further impair tear production. The role of mucins from goblet cells and corneal microvilli in maintaining tear film stability is also critical, and their dysfunction may exacerbate DED symptoms.

The mean OSDI score in this study was 12.54 ± 12.40, with 22.4% of eyes exhibiting mild to severe symptoms. These results are consistent with previous findings that TED patients report higher ocular discomfort than controls. Correlation analysis revealed a weak negative association between TBUT and disease duration, a slight positive correlation with Schirmer-I test, and a significant negative correlation between OSDI score and disease duration. These findings suggest that ocular surface symptoms may intensify over time in thyroid dysfunction. Given the high prevalence of DED in thyroid patients, especially women aged 40–60, routine thyroid profiling and proactive ocular surface evaluations are recommended to ensure timely diagnosis and management of TED-associated dry eye.

VI. Conclusion

In our study we conclude that the mean age of the patients was 47.22 ± 10 years and highest incidence of thyroid disease was reported in the age group of 51-60 years. An obvious female predominance was recorded in the study population. Hyperthyroidism was present in 32.2% patients whereas hypothyroidism was presented in 67.8% patients.

A significant negative correlation was observed between the OSDI score and duration of thyroid disease. TBUT, Schirmer test and OSDI score can be used effectively for assessment of dry eye disease in thyroid disease patients.

We recommend that patients with thyroid disease should have proactive evaluations of their ocular surfaces and dry eyes.