ORIGINAL ARTICLE

Prevalence of Ocular Manifestations in Thyroid Disorder Patients in A tertiary Hospital of Karachi

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Abstract:

Objectives: To determine the frequency of various ocular manifestations in thyroid dysfunction and to assess their correlation with thyroid function test parameters.

Methods: A cross-sectional study was conducted at the National Institute of Diabetes & Endocrinology, Ear, Nose, Throat (ENT), and Eye outpatient department (OPD) between 2020 and 2023. All patients above 18 years of age diagnosed with thyroid dysfunction and referred to the Eye department from endocrine or ENT OPD were included in the study. An ophthalmologist did detailed clinical examination of the eyes as per the European Group on Graves' Orbitopathy (EUGOGO) recommendations. Data analysis was done on SPSS version 23.

Results: A total of 441 thyroid patients were included in the study. The majority of them 378 (85.7%) were females aged between 20 to 40 years 266 (60.3%). Ocular manifestations were present in 252 (57.1%), where the most prevalent symptom was watering 154 (61.11%), followed by foreign body sensation 63 (25%). Prevalent lid signs were lid retraction and lid lag (97.06%). It was found that ocular manifestations were significantly correlated to the levels of STSH, FT3, and FT4 (P-value 0.018, <0.001, and 0.001, R-value -0.120 -0.317 and 0.054, respectively).

Conclusion: It is imperative that prospective clinical health professionals should be acquainted with all the information related to the clinical manifestations of thyroid eye disease for better management. *Al-Shifa Journal of Ophthalmology 2025; 21(3): 174-183.*

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Introduction:

The thyroid gland is a butterfly-shaped endocrine organ, comprising two lobes connected by an isthmus, and is anatomically positioned in the neck below the laryngeal prominence [)]. Under the regulatory influence of thyrotropin (TSH), it synthesizes, stores, and secretes the hormones tetraiodothyronine (thyroxine or T4) and triiodothyronine (T3) [2]. Thyroid disorders represent the second most prevalent endocrine diseases worldwide [3], affecting approximately 3% to 21% of the population, with a particularly high incidence among females of reproductive age and the elderly [4, 5]. Several factors, including age, smoking, and thyroid antibody status, influence the dynamic relationship between TSH levels and thyroid hormone production. [6] Moreover, variables such as sex, age, ethnicity, and

geographical determinants, especially iodine intake, substantially impact the prevalence and presentation of thyroid disorders [7].

Thyroid hormones exert effects on all major organ systems, and maintaining their adequate levels is essential for optimal physiological functioning. Patients with thyroid disorders such as thyrotoxicosis, hypothyroidism, and thyroiditis as well as euthyroid individuals with positive thyroid antibody status, may present with a wide range of ocular symptoms and signs. These may include proptosis of the eyeball, eyelid retraction, corneal ulcers, and potential injury to the extraocular muscles and optic nerve [8].

The clinical features of Graves' ophthalmopathy constitute one of the most recognizable manifestations of Graves' disease (GD). [9] Thyrotoxicosis, including Graves' disease, affects a significant portion of the global population.[10] A hallmark sign of Graves' ophthalmopathy is proptosis. [11]Thyroid eye disease is an autoimmune disorder [12] and represents a common extra-thyroidal manifestation of GD [13], with severity ranging from mild and self-limiting disease to severe cases resulting in irreversible blindness. It is the most frequently occurring disorder affecting the orbit, present in approximately 25% to 40% of patients with Graves' disease, depending on whether eyelid signs are excluded or included in the assessment criteria. [14]

Accordingly, it is evident that thyroid disorders can induce a variety of ocular complications. Early identification and management are crucial, as timely intervention may prevent the development of severe ocular sequelae and blindness in individuals with thyroid dysfunction. Therefore, this study aims to evaluate the frequency of different ocular manifestations in patients with thyroid dysfunction and to assess their correlation with thyroid function test parameters.

Methodology:

A cross-sectional study was conducted at the National Institute of Diabetes & Endocrinology, Ear, Nose, Throat (ENT), and Eye outpatient department (OPD) between 2020 and 2023 following ethical approval by the institution's review board under approval number IRB-1045/DUHS/Approval/2020. Based on prior studies indicating a 35.6% prevalence of thyroid eye disease [15], and applying a 95% confidence interval, the required sample size was calculated to be 353 using OpenEpi version 3.0. After accounting for a 20% attrition rate, the final sample size was adjusted to 425. Through convenient sampling technique, 425 patients were recruited through non-probability sampling to enhance representativeness and data reliability.

Inclusion criteria comprised all individuals aged 18 years or older with a diagnosis of thyroid dysfunction including hyperthyroidism, hypothyroidism, or euthyroid Graves' ophthalmopathy, who had been referred to the Eye department from the Endocrine or ENT OPD. Exclusion criteria involved individuals younger than 18 years, patients with a history of ocular trauma, and those with chronic systemic illnesses such as diabetes or pre-existing ocular diseases.

Following informed consent, demographic data including age, gender, educational level, marital status, and comorbidities were collected. Comprehensive ophthalmological evaluations were performed by an ophthalmologist in accordance with the European Group on Graves' Orbitopathy (EUGOGO) guidelines. Clinical findings were categorized according to the Clinical Activity Score (CAS) as recommended by EUGOGO [16], comprising seven clinical indicators: spontaneous retrobulbar pain, pain on attempted vertical gaze, eyelid erythema, conjunctival hyperemia, eyelid edema, conjunctival chemosis, and swollen caruncle. Each positive finding scored one point, generating a total CAS ranging from

0 to 7. A CAS of 3 or more indicated active disease, whereas scores below 3 denoted inactive disease, facilitating accurate classification of disease activity.

Thyroid dysfunctions were categorized into hyperthyroidism, hypothyroidism, and euthyroid states with positive antibodies. Diagnosis was confirmed based on serum levels of thyroid-stimulating hormone (TSH), free T3, and T4, interpreted by an endocrinologist and an ENT specialist.

During ocular assessment, the ophthalmologist obtained patient histories encompassing smoking habits, family history of thyroid disease, periocular pain, ocular movement pain, foreign body sensation, epiphora, photophobia, and diplopia. Examination included assessments of visual acuity, extraocular motility, intraocular pressure, eyelid signs such as lid retraction, lid lag, and lagophthalmos, as well as slit lamp biomicroscopy, fundoscopy, and proptosis measurement. Visual acuity was assessed using a Snellen chart. Extraocular motility was evaluated using a torchlight across nine cardinal gazes, noting any restrictions.

Intraocular pressure was measured via Goldmann Applanation tonometry attached to a slit lamp. Upper eyelid retraction was measured in millimeters using a ruler, observing the scleral show above the upper limbus in primary gaze. Retraction under 2 mm was categorized as mild, whereas 2 mm or more was classified as moderate to severe thyroid eye disease per EUGOGO recommendations. Lid lag was assessed as the persistence of the upper lid above its normal position during downward gaze. Lagophthalmos, defined as incomplete eyelid closure, was also evaluated.

Detailed slit lamp examination identified signs of eyelid erythema and swelling, conjunctival redness, and chemosis. Corneal integrity was examined post-fluorescein staining to detect punctate keratopathy, exposure keratopathy, corneal ulcers, and tear film deficiencies. Pupillary reflexes were tested using a torchlight, and fundoscopy was performed with slit lamp biomicroscopy and a 90D lens to assess optic nerve involvement.

Color vision testing with Ishihara charts was conducted in patients suspected of optic neuropathy. Proptosis was measured in millimeters using a plastic ruler aligned from the lateral orbital rim to the corneal apex, held parallel to the floor. Proptosis measurements exceeding normal racial and gender-specific values by less than 3 mm were classified as mild, while values of 3 mm or more were categorized as moderate to severe, according to EUGOGO standards (~18 mm for Asians, ~20 mm for Caucasians, and ~22 mm for African Americans).

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 19. Descriptive statistics for socio-demographic and clinical characteristics were calculated using means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Associations among variables were analyzed using the Chi-square test for parametric data and Spearman's correlation for non-parametric data. A P-value of less than 0.05 was considered statistically significant.

Results:

A total of 441 thyroid patients were included in the study. The majority of them 378 (85.7%) were females with an age range between 20 to 40 years of 266 (60.3%). No family history or smoking history was found among the recruited participants. Further, age was found to be significantly associated with ocular manifestations (P-value <0.001) (Table 1).

Table 1: Demographics of the participants and its association with the ocular manifestations (n=441)

Variables		N	% age	P-value
Gender	Males	63	14.3	0.099
	Females	378	85.7	
Age	20-40 years	266	60.3	0.000
	41-60 years	154	34.9	
	Above than 61 years	21	4.8	
Family History	Yes	0	0	
	No	441	100	
Smoking History	Yes	0	0	
	No	441	100	

Ocular manifestations were present in almost 252 (57.1%) of thyroid patients, with the majority of them 210 (49.2%) having visual acuity one to two lines less than 6/6 (6/9 or 6/12). Anterior and posterior eye segments were normal for all the patients, and optic neuropathy was also negative. Intraocular pressure (IOP) was also within normal ranges for all the patients. However, lid signs were present in 238 (54%) of patients, conjunctival redness in 35 (7.9%), and ulceration and exposure keratopathy in only 7(1.6%). Proptosis was not present in 343 (77.8%) of patients, extra extraocular movement was full in 392 (88.9%) of patients (Table 2).

Table 2: Ocular manifestations present among the participants (n=441)

Variables		N	%
Ocular manifestations	Present	252	57.1
	No present	189	42.9
Visual Acuity	Normal (6/6)	210	47.6
	One to two lines less than 6/6 (6/9 or 6/12)	217	49.2
	Four to six lines less than 6/6 (6/24 or 6/36)	14	3.2
Anterior Eye Segment	Normal	441	100
	Not normal	0	0
Posterior Eye Segment	Normal	441	100
	Not normal	0	0
Optic Neuropathy	Negative	441	100
	Positive	0	0
Intraocular Pressure	Normal	441	100
	Not normal	0	0
Lid Signs	Present	238	54
	Not Present	203	46
Conjunctival Signs	Clear	406	92.1
	redness	35	7.9
Corneal Signs	Clear	434	98.4
	Ulceration and exposure keratopathy	7	1.6
Proptosis	Not Present	343	77.8
	Present	98	22.2
Extraocular movement	Full	392	88.9
	Restricted Motility	42	9.5
	Strabismus	7	1.6

The major ocular manifestation present was watering 154 (61.11%), followed by foreign body sensation 63 (25%) and blurring 56 (22.22%) (Figure 1).

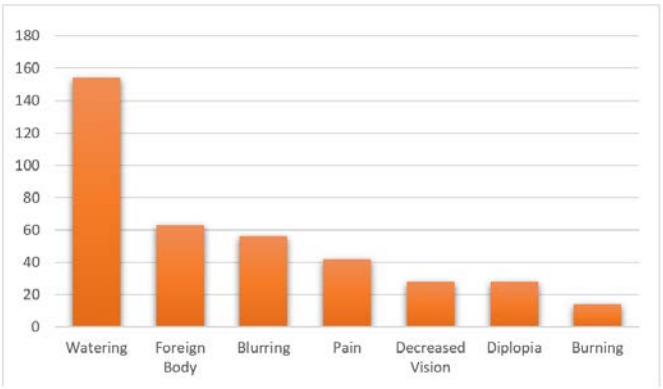

Figure 1: Ocular Manifestation present among the thyroid patients (n=385)

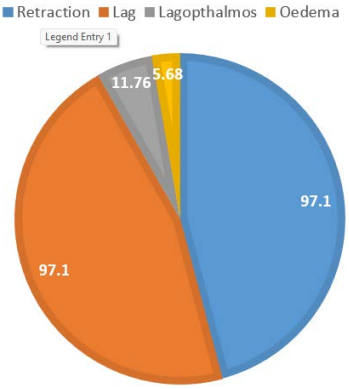

Figure 2: Lid Sign found among the Thyroid patients (n=238)

While lid retraction and lag were the most common signs, these signs are known to be nonspecific in early disease. Therefore, the proptosis was further stratified using EUGOGO severity scores. It was found that in most of the participants, proptosis was absent (77.8%). Of 22.2% of participants who had proptosis, most of them had mild proptosis in the right eye (11.1%) while moderate proptosis in the left eye (12.1%) (Figure 3).

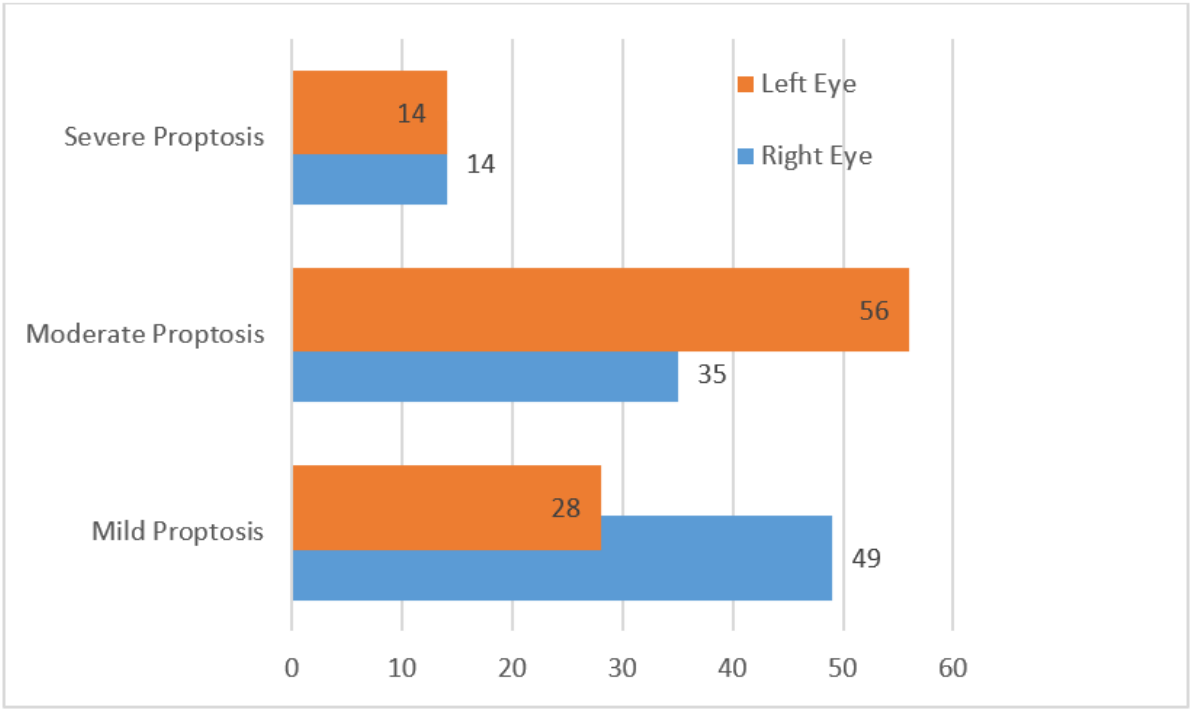

Figure 3: Proptosis severity found among the participants (n=98)

Thyroid patients were presented with a mean STSH of 5.33±15.113. The mean IOP was 13.17±2.594, with proptosis in the left and right eyes of 18.08±6.725 and 18.03±6.617, respectively (Table 3).

Table 3: Descriptive statistics of the study participants (n=441)

Variables	Normal Ranges	Mean	Standard Deviation
Serum TSH	0.4 to 4.0 mIU/L*	5.33	15.113
Free T4	0.9 to 2.3 ng/dL*	10.09	32.375
Free T3	0.13 to 0.45 ng/dL*	10.71	24.064
IOP	12-21 mm Hg	13.17	2.594
Proptosis Right Eye	23 mm for female 24 mm for male	18.03	6.617
Proptosis Left Eye		18.08	6.725

*According to the American Thyroid Association

It was found that ocular manifestations were significantly correlated to the levels of STSH, FT3, and FT4 (P-value 0.018, <0.001, and 0.001, r-value-0.120 -0.317 and 0.054, respectively) (Table 4).

Table 4: Association between the ocular manifestations and serum TSH, free T3 and T4 (n=441)

Variables		Spearman's rho	Pearson Correlation	Correlation Coefficient	Sig. (2-tailed)
General Symptoms	STSH	1.000	-0.133**	-0.120*	0.018
	FT3		0.073	-0.317**	0.000
	FT4		-0.183**	0.054	0.001
Visual Acuity	STSH	1.000	-0.107**	-0.133**	0.008
	FT3		0.222**	-0.171*	0.015
	FT4		0.069	0.079	0.158
Lid Signs	STSH	1.000	0.174**	-0.007	0.001
	FT3		-0.143*	0.209**	0.003
	FT4		0.097	-0.075	0.082
Proptosis range	STSH	1.000	-0.020	0.154**	0.002
	FT3		0.140*	0.034	0.047
	FT4		-0.240**	-0.203**	0.000
EOM	STSH	1.000	0.056	0.080	0.113
	FT3		-0.072	-0.001	0.306
	FT4		-0.092	-0.156**	0.005
*** Correlation is significant at the 0.01 level (2-tailed)*					
**Correlation is significant at the 0.05 level (2-tailed)*					

Discussion:

Ocular manifestations in patients with thyroid disorders arise due to autoimmune responses, typically associated with thyroid dysfunction. This condition is characterized by inflammatory processes and fibrotic alterations in the periocular tissues. [17] The present study aimed to assess the frequency of different ocular manifestations among thyroid disorder patients attending a tertiary care hospital in Karachi.

A total of 441 thyroid disorder patients were enrolled in the study. The majority (85.7%) were female, and 60.3% of the participants were aged between 20 and 40 years. Age demonstrated a significant association with ocular manifestations (P-value <0.001). Similarly, a study conducted in Nepal reported that thyroid eye disease predominantly affected females and individuals with hyperthyroidism[18], a finding consistent with prior research.[19, 20] Although the exact mechanism linking female gender to thyroid eye disease remains unclear, it is postulated that female gonadal hormones—specifically prolactin and estrogen—as well as the influence of the X chromosome on the thyroid gland, contribute to an enhanced autoimmune response, thereby increasing susceptibility among females. [21]

In this study, ocular manifestations were observed in approximately 57.1% of thyroid patients. This prevalence aligns with findings from studies in Nepal and other regions, where the reported prevalence rates were 44.27% and 51.7%, respectively. [18, 22] The most common ocular manifestation was watering (61.11%), followed by foreign body sensation (25%) and blurring of vision (22.22%). In contrast, the Nepalese study identified foreign body sensation as the predominant symptom [18], while another investigation highlighted burning sensations, ocular pain, and puffiness as the most frequent complaints. [15]

The most frequently observed eyelid signs were lid retraction and lid lag (97.06%), with lagophthalmos identified in 11.76% of participants. Previous studies have reported lid retraction in 78% to 90% of thyroid eye disease cases. [21, 23] These discrepancies may reflect ethnic variations and differences in the severity of ocular involvement. Fan et al. identified eyelid retraction as the most common manifestation of Graves' ophthalmopathy, present in 75% of patients at diagnosis. [24] Furthermore, conjunctival redness was observed in 7.9% of patients, while corneal ulceration and exposure keratopathy were noted in only 1.6% of cases. Proptosis was absent in 77.8% of participants, and extraocular muscle movement was full in 88.9% of patients. Existing literature suggests that thyroid eye disease can present with ocular surface discomfort, reduced vision, diplopia, inflamed eyes, and proptosis. [25] In this study, 22.2% of patients exhibited proptosis, predominantly mild in the right eye (11.1%) and moderate in the left eye (12.1%). Although proptosis was relatively uncommon, previous studies emphasize its clinical significance due to its potential to cause vision loss and, in severe cases, mortality, with thyroid eye disease identified as the principal etiology. [26] Research further suggests that proptosis associated with thyroid eye disease predominantly affects middle-aged individuals and females [27, 28], findings that align with the current study where the majority were middle-aged females.

Additionally, significant correlations were found between ocular manifestations and serum levels of STSH, FT3, and FT4 (P-values 0.018, 0.000, and 0.001, respectively). Visual acuity, eyelid signs, degree of proptosis, and extraocular movements were all significantly associated with these thyroid function parameters, suggesting a higher prevalence of ocular manifestations among hyperthyroid patients. Literature supports that while ocular involvement is most common in hyperthyroid states, it can also occur in euthyroid and hypothyroid conditions. [25] Other studies have similarly reported a predominance of ocular

symptoms among hyperthyroid patients [29-31]. Furthermore, research indicates that thyroid-stimulating hormone receptor antibodies (TRAbs) play a role in the clinical activity and progression of thyroid eye disease toward Graves' ophthalmopathy. [32]

In conclusion, ocular manifestations in thyroid patients, particularly those with hyperthyroidism, can range from mild symptoms to severe forms such as Graves' ophthalmopathy or orbitopathy. Early diagnosis and timely intervention are crucial in preserving vision and ocular function. Therefore, the establishment of an integrated referral system between endocrinologists and ophthalmologists, coupled with routine ophthalmological evaluations, is essential for improving patient outcomes and preventing complications. Future strategies should emphasize early detection and minimally invasive therapeutic approaches to effectively manage thyroid eye disease.

Nevertheless, this study had certain limitations. The cross-sectional design restricts the generalizability of the findings to the broader population of thyroid eye disease patients, thus limiting the ability to make causal inferences.

This study offers several strengths that enhance its credibility, including its focus on a tertiary care setting in a developing country, a rigorously calculated large sample size, and standardized assessments based on EUGOGO guidelines, ensuring methodological consistency and comparability with international research. The use of comprehensive ophthalmic examinations by experienced specialists, exclusion of confounding conditions, and application of both parametric and non-parametric analyses further strengthen the validity and reliability of the findings.

However, certain limitations must be acknowledged. The cross-sectional design precludes causal inferences, and the single-center setting may restrict generalizability. Potential selection bias, absence of a control group, reliance on self-reported data, and lack of advanced imaging reduce the robustness of the outcomes. Moreover, subjective clinical assessments introduce the possibility of inter-observer variability, while the hospital-based nature and absence of long-term follow-up limit broader applicability and evaluation of disease progression.

Conclusion:

It is imperative for prospects that clinical health professionals should be acquainted with all the information related to the clinical manifestations of thyroid eye diseases. Additionally, endocrine specialists and consultants should also be aware of the relevant knowledge regarding the anatomy of the eye and the clinical presentation of thyroid eye diseases to better manage the ocular manifestations. This could help reverse the Graves' ophthalmopathy and further consequences through early identification of symptoms and efficient management. Routine ophthalmic screening of patients with thyroid dysfunction, particularly in endocrine clinics, should be implemented to enable early detection and timely intervention of ocular complications.

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