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Frequency and Pattern of Ocular Manifestations Among Adults with Thyroid Disorders at a Tertiary Care Hospital in Kohat, Pakistan

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Abstract: Background: Thyroid dysfunction may affect the eyelids, ocular surface, extraocular muscles, orbital fat, intraocular pressure, optic nerve, and visual function. Although ocular morbidity has been reported among patients with thyroid disorders in Pakistan, data based on standardized ophthalmological and endocrine assessment remain limited. **Objective:** This study aimed to determine the frequency and pattern of ocular manifestations among adults with thyroid disorders and to identify clinical and biochemical predictors of ocular involvement at a tertiary care hospital in Pakistan. **Methods:** A prospective observational study was conducted in 291 consecutive adults with biochemically confirmed overt hyperthyroidism, overt hypothyroidism, subclinical thyroid dysfunction, or euthyroid autoimmune thyroid disease. Participants underwent structured symptom assessment, best-corrected visual acuity testing, slit-lamp examination, tear-film evaluation, intraocular pressure measurement, Hertel exophthalmometry, ocular motility assessment, dilated fundus examination, and orbital imaging when clinically indicated. Definite thyroid eye disease was graded for activity and severity. Multivariable logistic regression was performed to identify independent predictors of any ocular manifestation. **Results:** Among 291 participants, 166 had at least one ocular manifestation, corresponding to a frequency of 57.0% (95% confidence interval, 51.3% to 62.6%). Hyperthyroidism was present in 125 participants and was associated with the greatest ocular burden. The most frequent findings were watering, ocular dryness or burning, foreign body sensation, lid retraction, lid lag, periorbital edema, conjunctival injection, and proptosis. Definite thyroid eye disease was identified in 98 participants (33.7%); 61 had mild disease, 32 had moderate-to-severe disease, and 5 had sight-threatening disease. Hyperthyroidism, TSH-receptor antibody positivity, current smoking, uncontrolled thyroid function, and thyroid disease duration longer than three years were independent predictors of ocular manifestations. **Conclusion:** Ocular manifestations were common across the spectrum of thyroid disorders and were most frequent among participants with hyperthyroidism. Patients with uncontrolled thyroid function, smoking exposure, TSH-receptor antibody positivity, and longer disease duration may benefit from closer multidisciplinary monitoring. Optimization of thyroid pharmacotherapy, assessment of treatment response and adherence, and timely ophthalmological referral may help facilitate earlier recognition and management of active and sight-threatening thyroid eye disease.

Keywords: thyroid eye disease; Graves orbitopathy; ocular manifestations; proptosis; dry eye; thyroid dysfunction; Pakistan

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INTRODUCTION

Thyroid disorders are common endocrine conditions and include overt and subclinical hyperthyroidism, overt and subclinical hypothyroidism, autoimmune thyroiditis, multinodular goiter, and euthyroid autoimmune thyroid disease. Ocular involvement may result from autoimmune inflammation of orbital tissues, altered sympathetic activity, exposure-related ocular surface disease, eyelid and lacrimal gland dysfunction, or metabolic effects associated with thyroid hormone excess or deficiency. Contemporary multidisciplinary guidance emphasizes that ocular involvement should be interpreted in the context of thyroid status, autoimmune activity, and the overall clinical phenotype [1].

Thyroid eye disease (TED), also termed Graves orbitopathy or thyroid-associated orbitopathy, is the most characteristic ophthalmic complication of autoimmune thyroid disease. It is driven by immune-mediated activation of orbital fibroblasts, expansion of extraocular muscles and orbital fat, and accumulation of hydrophilic glycosaminoglycans [1]. Clinical manifestations range from dryness, tearing, photophobia, eyelid retraction, lid lag, and soft-tissue congestion to proptosis, restrictive strabismus, diplopia, exposure keratopathy, elevated intraocular pressure, and dysthyroid optic neuropathy [2]. Although TED most commonly occurs in association with Graves hyperthyroidism, it may also occur in patients who are hypothyroid or euthyroid in the setting of autoimmune thyroid disease [1].

Evidence from Pakistan has demonstrated clinically relevant ocular involvement among patients with thyroid disorders. In a Karachi study of 111 patients with thyroid dysfunction, dry eye, eyelid puffiness, staring appearance, reduced visual acuity, and ocular pain were frequently reported [3]. A Karachi study published in 2023 reported thyroid eye disease in 26.81% of 220 patients with autoimmune thyroid disease, demonstrating a substantial burden of ophthalmic involvement in this population [4]. Cross-sectional imaging can support the diagnosis of TED, with characteristic findings including extraocular-muscle enlargement with tendon sparing, orbital fat expansion, superior ophthalmic vein dilatation, and apical crowding [5].

Available Pakistani studies have differed in case selection, definitions, thyroid-status distribution, and the extent of formal ophthalmological assessment. Earlier work included broad thyroid-disorder cohorts with variable ocular definitions [3], whereas imaging-based work focused on patients with established orbitopathy and therefore represented a more selected clinical population [5]. Published Pakistani studies have used differing patient populations, diagnostic definitions, and ophthalmological assessment protocols, which limits direct comparison of the reported frequencies of ocular involvement [3,4].

Ocular symptoms may receive less attention when clinical care is focused primarily on systemic manifestations of thyroid dysfunction. Conversely, nonspecific symptoms such as dryness or watering may be incorrectly attributed to TED when characteristic eyelid, motility, proptosis, or orbital findings are absent. A standardized assessment using predefined diagnostic criteria can help distinguish definite TED from nonspecific ocular morbidity and identify patients who require urgent ophthalmological or orbital evaluation [1].

The primary aim of this study was to determine the frequency of at least one ocular manifestation among adults with thyroid disorders. Secondary aims were to characterize the pattern of ocular symptoms and signs, determine the frequency and severity of definite TED, compare ocular involvement across thyroid-function categories, and identify clinical and biochemical predictors of ocular manifestations.

MATERIALS AND METHODS

Study design and setting

A prospective observational study was conducted at Al-Shifa Trust Eye Hospital, Kohat, Pakistan, over a 12-month period from January 2024 to December 2024. Adults with biochemically confirmed thyroid disorders presenting to the ophthalmology service or referred for ophthalmological assessment were enrolled consecutively [6].

Study population

Adults with a confirmed thyroid disorder presenting

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to the ophthalmology service or referred for ophthalmological assessment were screened for eligibility. Thyroid diagnoses were established on the basis of thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), thyroid antibodies when indicated, and the diagnosis documented by the treating physician.

Inclusion criteria

Patients were eligible if they were aged 18 years or older, had biochemically confirmed overt or subclinical hyperthyroidism, overt or subclinical hypothyroidism, or euthyroid autoimmune thyroid disease, were able to undergo the required ophthalmological examination.

Exclusion criteria

Patients were excluded if they had undergone previous orbital decompression, strabismus surgery, or eyelid surgery for TED; had an orbital tumor, orbital trauma, idiopathic orbital inflammation, or another cause of proptosis; had active ocular infection, severe corneal opacity, advanced glaucoma, retinal disease that independently explained visual loss, or a cranial nerve palsy unrelated to thyroid disease; or were unable to complete the essential examination. Diabetes mellitus was not an absolute exclusion criterion; however, diabetic retinal findings were recorded separately and were not attributed to thyroid disease.

Sampling technique

A non-probability consecutive sampling technique was used. Eligible patients were approached at their first study visit, before major alteration of thyroid or orbital treatment whenever clinically feasible.

Sample-size calculation

A Pakistani study published in 2023 reported thyroid eye disease in 26.81% of patients with autoimmune thyroid disease [4]. Using an anticipated frequency of 26.81%, a 95% confidence level, and an absolute precision of 6%, the calculated minimum sample size was approximately 210 participants. After allowing approximately 10% for incomplete examinations or missing data, the minimum target was approximately 231 participants. A total of 291 participants were ultimately included in the study.

Clinical and endocrine assessment

A structured questionnaire recorded age, sex, residence, socioeconomic status, smoking, passive smoke exposure, thyroid diagnosis and duration, medication use, history of radioactive iodine treatment or thyroid surgery, treatment adherence, symptom control, autoimmune comorbidity, and family history. Height and weight were measured. Thyroid status was categorized as overt hyperthyroidism, overt hypothyroidism, subclinical dysfunction, or euthyroid autoimmune thyroid disease. Serum TSH, FT4, and FT3 were measured within four weeks of the ophthalmological examination to assess biochemical control at the time of ocular assessment. TSH-receptor antibodies or thyroid-stimulating immunoglobulin, anti-thyroid peroxidase antibodies, and anti-thyroglobulin antibodies were recorded when available.

Ocular symptom assessment

Participants were asked about watering, dryness, burning, foreign body sensation or grittiness, photophobia, redness, eyelid swelling, orbital pressure or pain, pain with eye movement, visual loss, diplopia, altered color vision, and changes in ocular appearance. Symptom onset, progression, laterality, and interference with reading, driving, work, and activities of daily living were recorded.

Ophthalmological examination

Best-corrected visual acuity (BCVA) was assessed separately in each eye and expressed as the logarithm of the minimum angle of resolution. Pupillary reactions and the presence of a relative afferent pupillary defect were evaluated. Ishihara plates were used for color vision testing. Eyelid position, margin-reflex distance, eyelid retraction, lid lag, edema, and erythema were documented. Slit-lamp examination assessed conjunctival injection, chemosis, corneal staining, exposure keratopathy, and the anterior chamber.

Ocular surface assessment

When feasible, participants completed the Ocular Surface Disease Index questionnaire, a validated instrument for quantifying ocular-surface symptoms and their functional impact [7]. Tear-film breakup time, Schirmer testing without anesthetic, corneal fluorescein staining, and meibomian gland dysfunction were assessed using a standardized protocol. Dry eye disease was diagnosed when compatible symptoms were accompanied by at least one abnormal objective test.

Proptosis, motility and diplopia

Hertel exophthalmometry was performed using the same instrument whenever possible. Locally appropriate normative values, clinically evident asymmetry, and radiological confirmation when available were used to define proptosis. Ocular alignment, ductions, versions, restrictive motility, and the pattern of diplopia were evaluated. Among participants with definite TED, diplopia was graded using the Gorman scale.

Intraocular pressure and posterior segment

When clinically indicated, intraocular pressure was measured in primary gaze and upgaze. Dilated fundus examination documented the optic disc, macula,

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retinal vessels, and other posterior-segment pathology. Optic disc edema or pallor, choroidal folds, retinal vascular occlusion, and unrelated retinal disease were recorded separately.

Definition and grading of definite thyroid eye disease

Definite TED required a compatible thyroid or autoimmune background together with characteristic eyelid, soft-tissue, proptosis, extraocular muscle, corneal, or optic nerve findings after exclusion of alternative orbital disease. Disease activity was assessed using the seven-item Clinical Activity Score, with a score of at least 3 indicating active disease at the initial assessment [8]. Severity was categorized as mild, moderate-to-severe, or sight-threatening according to contemporary EUGOGO clinical criteria [2]. Sight-threatening diseases included dysthyroid optic neuropathy or severe corneal breakdown.

Orbital imaging

Computed tomography or magnetic resonance imaging of the orbits was obtained when there was diagnostic uncertainty, unilateral or markedly asymmetric proptosis, suspected dysthyroid optic neuropathy, reduced color vision, a relative afferent pupillary defect, unexplained visual loss, severe motility restriction, or a need for surgical planning [1]. Imaging variables included proptosis, extraocular muscle enlargement, tendon sparing, orbital fat expansion, superior ophthalmic vein enlargement, apical crowding, and alternative orbital pathology [5].

Primary and secondary outcomes

The primary outcome was the presence of at least one ocular manifestation considered related or potentially related to thyroid dysfunction. Secondary outcomes included definite TED, active disease, severity category, individual ocular symptoms and signs, ocular surface disease, diplopia, proptosis, exposure keratopathy, elevated intraocular pressure, and dysthyroid optic neuropathy.

Quality assurance

Investigators were trained in use of the case-report form and standardized examination definitions. The same exophthalmometer and tonometer were used whenever possible. Ten percent of study records were reviewed against source documents. Difficult cases were reviewed jointly by an ophthalmologist and an endocrinologist, and orbital imaging was interpreted by a radiologist experienced in orbital imaging.

Statistical analysis

Data was analyzed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean with standard deviation or median with interquartile range, as appropriate, while categorical variables were presented as frequencies and percentages. Group comparisons were performed using the chi-square test or Fisher exact test for categorical variables and the independent-samples t test, analysis of variance, Mann-Whitney U test, or Kruskal-Wallis test for continuous variables, as appropriate. Variables considered clinically relevant or showing a univariable p value below 0.20 were entered into a multivariable logistic regression model. For analyses involving TSH-receptor antibody status, complete-case analysis was performed, and participants without available antibody results were excluded from the respective analysis. Adjusted odds ratios with 95% confidence intervals were reported. A two-sided p value below 0.05 was considered statistically significant.

Ethical considerations

The study protocol was reviewed by the relevant Institutional Review Board/Ethics Committee, which granted a waiver of full ethical review. Participant confidentiality was maintained throughout the study, and all data were coded, de-identified, and stored securely with access restricted to the research team. The study was conducted in accordance with applicable institutional ethical requirements and the principles of the Declaration of Helsinki.

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RESULT

Participant characteristics

A total of 315 potentially eligible patients were screened. Twenty-four were excluded because of previous orbital surgery, non-thyroid orbital disease, dense media opacity, advanced glaucoma, incomplete thyroid testing, or inability to complete the essential examination. The final analysis included 291 participants. Mean age was 39.8 ± 12.1 years, and 236 participants (81.1%) were female. Median duration of thyroid disease was 3.0 years (interquartile range, 1.2 to 6.0 years). Hyperthyroidism was present in 125 participants, hypothyroidism in 134, euthyroid autoimmune thyroid disease in 18, and subclinical thyroid dysfunction in 14.

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Table 1. Demographic and thyroid-related characteristics

Characteristic	Value, n = 291
Age, years, mean ± SD	39.8 ± 12.1
Female sex, n (%)	236 (81.1)
Urban residence, n (%)	194 (66.7)
Current smoker, n (%)	29 (10.0)
Thyroid disease duration, years, median (IQR)	3.0 (1.2 to 6.0)
Overt hyperthyroidism, n (%)	125 (43.0)
Overt hypothyroidism, n (%)	134 (46.0)
Euthyroid autoimmune thyroid disease, n (%)	18 (6.2)
Subclinical thyroid dysfunction, n (%)	14 (4.8)
Graves disease, n (%)	107 (36.8)
Hashimoto thyroiditis, n (%)	93 (32.0)
Biochemically uncontrolled thyroid status, n (%)	119 (40.9)
TSH-receptor antibody positive among tested, n/N (%)	96/181 (53.0)
Previous radioactive iodine treatment, n (%)	31 (10.7)
Previous thyroid surgery, n (%)	22 (7.6)

Frequency of ocular manifestations

At least one ocular manifestation was present in 166 of 291 participants, giving a frequency of 57.0% (95% confidence interval, 51.3% to 62.6%). Ocular involvement was most frequent in overt hyperthyroidism, affecting 96 of 125 participants (76.8%). It was present in 54 of 134 participants with hypothyroidism (40.3%), 10 of 18 participants with euthyroid autoimmune thyroid disease (55.6%), and 6 of 14 participants with subclinical thyroid dysfunction (42.9%), $p < 0.001$.

Table 2. Frequency of ocular symptoms and signs

Manifestation	n	% of 291
Any ocular manifestation	166	57.0
Watering or epiphora	102	35.1
Dryness or burning	92	31.6
Foreign body sensation or grittiness	78	26.8
Lid retraction	77	26.5
Lid lag	70	24.1
Periorbital or eyelid edema	70	24.1
Conjunctival injection	59	20.3
Proptosis	58	19.9
Photophobia	47	16.2
Orbital pressure or pain	42	14.4
Restricted extraocular movements	30	10.3
Diplopia	28	9.6
Chemosis	23	7.9
Reduced best-corrected visual acuity	22	7.6
Elevated intraocular pressure	19	6.5
Lagophthalmos	20	6.9
Exposure keratopathy	12	4.1
Dysthyroid optic neuropathy	5	1.7

Definite thyroid eye disease and severity

Definite TED was identified in 98 participants, representing 33.7% of the total cohort and 59.0% of participants with any ocular manifestation. Disease was bilateral in 82 participants (83.7%) and clinically asymmetric in 39 (39.8%). A Clinical Activity Score of at least 3 was recorded in 29 participants (29.6% of those with definite TED). Mild TED was present in 61 participants, moderate-to-severe TED in 32, and sight-threatening TED in 5. All five sight-threatening cases had findings compatible with dysthyroid optic neuropathy, and two also had severe exposure-related corneal disease.

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Table 3. Characteristics of definite thyroid eye disease

Characteristic	n = 98	%
Bilateral disease	82	83.7
Clinically asymmetric disease	39	39.8
Active disease, Clinical Activity Score ≥3	29	29.6
Mild severity	61	62.2
Moderate-to-severe severity	32	32.7
Sight-threatening severity	5	5.1
Proptosis	58	59.2
Lid retraction	77	78.6
Extraocular movement restriction	30	30.6
Diplopia	28	28.6
Exposure keratopathy	12	12.2
Dysthyroid optic neuropathy	5	5.1

Ocular surface and visual function

Ocular surface disease was diagnosed in 104 participants (35.7%). The mean Ocular Surface Disease Index score was higher among participants with active TED than among those with inactive disease (39.6 ± 15.8 vs 25.1 ± 13.4, $p < 0.001$). Mean tear-film breakup time was shorter in participants with definite TED than in those without definite disease (6.8 ± 2.7 vs 9.7 ± 3.4 seconds, $p < 0.001$). Reduced visual acuity was most commonly related to ocular surface disturbance, refractive error, cataract, or optic neuropathy. Five participants had reduced visual acuity accompanied by color desaturation, relative afferent pupillary defect, visual-field abnormality, and orbital-apex crowding compatible with dysthyroid optic neuropathy.

Table 4. Comparison by presence of any ocular manifestation

Variable	Ocular manifestation present, n = 166	Absent, n = 125	p value
Mean age, years	41.2 ± 12.0	37.9 ± 12.0	0.021
Female sex, n (%)	138 (83.1)	98 (78.4)	0.305
Current smoker, n (%)	24 (14.5)	5 (4.0)	0.003
Hyperthyroidism, n (%)	96 (57.8)	29 (23.2)	<0.001
Disease duration >3 years, n (%)	99 (59.6)	49 (39.2)	0.001
Uncontrolled thyroid status, n (%)	87 (52.4)	32 (25.6)	<0.001
TSH-receptor antibody positive among tested, n/N (%)	78/117 (66.7)	18/64 (28.1)	<0.001
Graves disease, n (%)	82 (49.4)	25 (20.0)	<0.001
Previous radioactive iodine treatment, n (%)	24 (14.5)	7 (5.6)	0.016

Predictors of ocular manifestations

The multivariable analysis involving TSH-receptor antibody status was performed using participants with available antibody results (n = 181). Hyperthyroidism, TSH-receptor antibody positivity, current smoking, biochemically uncontrolled thyroid status, and thyroid disease duration longer than three years remained independently associated with ocular manifestations. Sex and previous radioactive iodine treatment were not independently significant after adjustment for thyroid diagnosis, antibody status, smoking, and biochemical control. The model showed acceptable discrimination, with an area under the receiver operating characteristic curve of 0.81.

Table 5. Multivariable logistic regression for any ocular manifestation

Predictor	Adjusted odds ratio	95% confidence interval	p value
Overt hyperthyroidism	3.85	2.18 to 6.81	<0.001
Positive TSH-receptor antibody	3.12	1.65 to 5.90	<0.001
Current smoking	2.68	1.02 to 7.05	0.046
Uncontrolled thyroid status	2.25	1.31 to 3.86	0.003
Thyroid disease duration >3 years	1.84	1.08 to 3.14	0.025
Age >40 years	1.41	0.83 to 2.40	0.204
Female sex	1.28	0.67 to 2.45	0.456
Previous radioactive iodine treatment	1.36	0.55 to 3.36	0.502

Multivariable analysis was restricted to participants with available TSH-receptor antibody results.

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DISCUSSION

This study found that 57.0% of adults with thyroid disorders had at least one ocular manifestation. Watering, dryness or burning, foreign body sensation, lid retraction, lid lag, eyelid edema, conjunctival injection, and proptosis were the predominant findings. Definite thyroid eye disease was identified in 33.7% of the present cohort, compared with 26.81% reported in a previous Karachi study [4]. Differences in study populations, case definitions, referral patterns, and ophthalmological assessment methods may account for the variation between studies. These results indicated that ocular morbidity associated with thyroid disorders extended beyond clinically obvious proptosis and included a substantial ocular-surface component.

The frequency of ocular involvement differed across thyroid-function categories and was highest among participants with overt hyperthyroidism, consistent with the established association between Graves' disease and TED [2]. Ocular findings were also observed among participants with hypothyroidism and euthyroid autoimmune thyroid disease, emphasizing that TED was not restricted to biochemically hyperthyroid patients [1]. Patients with Hashimoto thyroiditis or euthyroid autoimmune thyroid disease who developed suggestive ocular features therefore required careful assessment for TED as well as exclusion of alternative orbital disease. Approximately one-third of the cohort had definite TED, whereas 57.0% had at least one ocular manifestation. This difference reflected the broader primary outcome, which included ocular-surface and other findings considered related or potentially related to thyroid dysfunction. Separating general ocular manifestations from definite TED reduced the risk of overdiagnosis and supported a more clinically meaningful interpretation of the findings. Symptoms alone were insufficient to establish orbital disease; evaluation of eyelid retraction, lagophthalmos, proptosis, restrictive motility, corneal exposure, and optic nerve function remained essential [1].

The severity distribution showed that most participants with definite TED had mild disease, whereas a smaller proportion had moderate-to-severe or sight-threatening disease. Contemporary EUGOGO referral data have likewise shown a shift toward presentation with less severe disease, possibly reflecting greater awareness and earlier specialist referral [9]. Regional cohorts may nevertheless differ substantially; a Saudi Arabian tertiary eye-hospital cohort reported a larger proportion of moderate-to-severe TED [10]. Dysthyroid optic neuropathy was uncommon but clinically important. Reduced visual acuity accompanied by color desaturation, a relative afferent pupillary defect, visual-field loss, or orbital-apex crowding required urgent multidisciplinary assessment because delayed treatment could result in irreversible visual loss [2].

Ocular surface disease was also a prominent component of observed morbidity. Lid retraction, proptosis, incomplete blinking, lagophthalmos, meibomian gland dysfunction, and inflammatory tear-film changes may all contribute to ocular-surface symptoms in TED. Previous observational work has demonstrated worse ocular-surface parameters in active than inactive disease [11]. Accordingly, the present study combined symptom assessment with objective tear-film testing rather than relying on symptoms alone.

Endocrine disorders often involve complex interactions between hormonal regulation, metabolic status, inflammation, and oxidative stress. Evidence from other endocrine conditions has shown that metabolic interventions may influence hormonal and oxidative-stress-related parameters [13], while ghrelin has been described as a multifunctional hormone involved in metabolic, immune, and stress-related signaling pathways [14]. Although these mechanisms are not specific to thyroid eye disease, they illustrate the broader systemic interactions that may influence the clinical expression and progression of endocrine disorders.

Hyperthyroidism, TSH-receptor antibody positivity, current smoking, uncontrolled thyroid status, and longer thyroid disease duration were independently associated with ocular manifestations. These findings were consistent with established modifiable and biological risk factors described in EUGOGO guidance, particularly smoking, thyroid dysfunction, and elevated TSH-receptor antibody levels [2]. Prospective longitudinal evidence has also demonstrated associations between TSH-receptor antibody measurements and TED activity or severity over time [12]. The present findings therefore supported smoking cessation, restoration and maintenance of biochemical euthyroidism, and targeted ophthalmological assessment of patients with higher-risk clinical and biochemical profiles.

From a clinical pharmacy perspective, these findings highlight the importance of optimizing pharmacotherapy and monitoring treatment response in patients with thyroid disorders who are at increased risk of ocular involvement. Persistent biochemical thyroid dysfunction may reflect inadequate treatment response, suboptimal adherence, inappropriate dosing, or the need for therapeutic reassessment. Medication review, reinforcement of adherence, monitoring of thyroid-function tests, identification of

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treatment-related problems, and timely referral for ophthalmological assessment may therefore contribute to multidisciplinary care. Collaboration among physicians, ophthalmologists, and clinical pharmacists may be particularly valuable in patients with uncontrolled thyroid function, smoking exposure, or other risk factors for thyroid eye disease [2].

This study had several limitations. As a single-center study, its findings may not be fully generalizable to the broader Pakistani population. Recruitment through tertiary-care outpatient services may also have influenced the clinical spectrum of participants. TSH-receptor antibody testing and orbital imaging were not available for every participant, and ocular-surface abnormalities were potentially influenced by environmental exposure, screen use, medications, age, and meibomian gland dysfunction. These limitations were mitigated by consecutive recruitment, predefined diagnostic criteria, specialist ophthalmological assessment, and separate reporting of general ocular manifestations and definite TED.

The findings had practical implications for routine thyroid care. Patients with thyroid dysfunction should be asked about ocular discomfort, watering, changes in appearance, diplopia, and visual loss. A focused examination should include visual acuity, pupillary responses, color vision when indicated, eyelid position, ocular motility, corneal exposure, and optic disc assessment. Patients with proptosis, diplopia, motility restriction, reduced color vision, a relative afferent pupillary defect, corneal breakdown, or progressive symptoms should be referred promptly for specialist ophthalmological or orbital assessment [1].

CONCLUSION

In this cohort, 57.0% of adults with thyroid disorders had at least one ocular manifestation and 33.7% had definite TED. Ocular involvement was independently associated with hyperthyroidism, TSH-receptor antibody positivity, current smoking, uncontrolled thyroid function, and longer duration of thyroid disease. A standardized multidisciplinary approach involving endocrinology, ophthalmology, and clinical pharmacy may improve optimization of thyroid therapy, early recognition of ocular involvement, and timely management of active and sight-threatening disease.

DECLARATIONS

Ethics approval and consent to participate: The study protocol was reviewed by the relevant Institutional Review Board/Ethics Committee, which granted a waiver of full ethical review. Participant confidentiality was maintained throughout the study, and all data were handled in accordance with applicable institutional and ethical standards.

Consent for publication: Not applicable. The manuscript does not contain identifiable individual patient information, images, or other personal data requiring separate consent for publication.

Availability of data and materials: The de-identified data generated and analysed during the current study are not publicly available because of institutional, ethical, and patient-confidentiality requirements. De-identified data may be made available from the corresponding author upon reasonable request, subject to institutional and ethical approval.

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Research integrity and transparency: The authors affirm that all numerical findings reported in this manuscript were derived from the enrolled clinical cohort and analysed according to the methodology described in the study. The authors take responsibility for the accuracy, completeness, and integrity of the reported data and analyses.

Use of artificial intelligence: Generative artificial intelligence tools were used solely to assist with language refinement, organization, and editorial improvement of the manuscript. Artificial intelligence was not used to generate, modify, or fabricate patient data, clinical outcomes, or statistical results. All scientific content, statistical findings, interpretations, references, and final manuscript text were critically reviewed and verified by the authors, who retain full responsibility for the accuracy and integrity of the work.

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