



AN OCULAR PERCEPTIVE OF THYROID DISORDERS AND ASSOCIATED FACTORS- A CLINICAL PROSPECTIVE STUDY.

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INTRODUCTION

Thyroid eye disease (TED) also called Graves Orbitopathy, is an autoimmune complex orbital inflammatory disease, which can be sight-threatening, debilitating, and disfiguring. Thyroid disorders, particularly those involving autoimmune etiology such as Graves' disease, represent a significant public health concern due to their multifactorial impact on patient well-being, particularly through ocular manifestations that can lead to substantial morbidity. The relationship between thyroid dysfunction and ocular health has been well- documented, with thyroid eye disease (TED) being the most notable ocular complication^{1,2}. Additionally, the research will explore the biochemical parameters associated with thyroid dysfunction, ultimately aiming to understand how these factors influence ocular health in individuals with thyroid disorders³⁻⁵. The significance of this study lies in its potential to augment the current body of knowledge regarding the ocular implications of thyroid disorders and its practical application in clinical practice. By identifying specific risk factors and ocular manifestations associated with thyroid dysfunction, clinicians can improve screening protocols and management strategies for affected individuals. Furthermore, this research could foster a more integrated approach to treating patients with thyroid disorders, where ocular health is prioritized alongside endocrine treatment. Such insights are essential for both enhancing patient outcomes and guiding evidence-based clinical practices in endocrinology and ophthalmology⁶⁻⁸.

AIM:

- To estimate various ocular manifestations of thyroid disorders.

OBJECTIVES:

- The primary objective is to estimate various ophthalmic manifestations of thyroid disorders.
- To evaluate the status of thyroid in patients with thyroid eye disorders.
- To evaluate the associated risk factors in thyroid disorders.
- To analyze the IOP variations in patients with thyroid disorders.

METHODOLOGY:

- **TYPE OF STUDY:** A Prospective hospital-based study.
- **SAMPLE SIZE:** 50 confirmed cases of thyroid disorder with ocular manifestations based on convenience sampling method.
- **STUDY SETTING:** This study is conducted in the Department of Ophthalmology, ACSR Government General Hospital, Nellore.

DURATION OF STUDY: 6 months from the approval of institutional ethical committee

INCLUSION CRITERIA:

- Patients aged 11 -65 years.
- Patients with proptosis due to thyroid eye disease.
- Patients with lid signs.
- Patient with ocular surface disorders.
- Patients with comorbidities such as diabetes, hypertension, smoking, dyslipidemia.
- Patients who give informed written consent.

EXCLUSION CRITERIA:

- Patients with proptosis due to causes other than thyroid.

Study method:

Patients with known cases of hypo/hyperthyroidism who presented to the Ophthalmology Department received a thorough examination, including a detailed history of the disease's onset, duration of thyroid disorder, and rate of progression, as well as a history of smoking and ocular symptoms such as pain, redness, foreign body sensation, photophobia, defective vision, and double vision. Visual acuity, anterior segment slit lamp examination, pupillary reactions, extraocular movements, differential intraocular pressure measurement, Hertels Exophthalmometry, Schimers test, tear breakup time, visual fields, color vision, diplopia charting, fundus examination, and forced duction test were all part of the complete ophthalmology workup.

The study was started after obtaining Institutional ethical approval. The purpose and procedure of the study was explained to the participants in their local language. The participants were explained that the data collected in this study will be used only for research purposes. The participants were explained about the freedom of withdrawal from the study at any time without penalty or loss of benefits. The confidentiality of the data collected from the enrolled participants was maintained in all the phases of the study. The study participants who required medical attention during the period of intervention was given appropriate medical care. Patient information sheet and informed written consent was obtained from the patients before initiating the study. The collected data was checked for completeness before entering into the Microsoft excel spread sheet. The validation of the data was checked at regular intervals. Data analysis was performed with an intention to treat approach using Statistical Package for Social Sciences (SPSS IBM) 25. The quantitative data was expressed in frequency and percentage. Data has been subjected to Chi-square test and p-values calculated.

Results:**TABLE 1- GENDER DISTRIBUTION AMONG STUDY PARTICIPANTS.**

S.No	GENDER	FREQUENCY	PERCENTAGE
1	Male	23	46%
2	Female	27	54%
	Total	50	100%

TABLE 2-AGE DISTRIBUTION AMONG STUDY POPULATIONS.

S.No	AGE(YRS)	Male		Female		TOTAL	
		N	%	N	%	N	%
1	11-20	2	8.7	1	3.8	3	6
2	21-30	3	13	3	11.1	6	12
3	31-40	5	21.8	8	29.6	13	26
4	41-50	8	34.8	8	29.6	16	32
5	51-60	3	13	4	14.8	7	14
6	>61	2	8.7	3	11.1	5	10
	TOTAL	23	100	27	100	50	100

TABLE 3-SYSTEMIC ASSOCIATIONS OF THE PARTICIPANTS.

S.NO	VARIABLE	FREQUENCY	PERCENTAGE(%)
1	Diabetes	19	38
2	Smoking	6	12
3	Diabetes & smoking	11	22
4	Hypertension	8	16
5	Hyperlipidemia	6	12

TABLE-4 THYROID STATUS OF STUDY PARTICIPANTS

S.NO	THYROID STATUS	FREQUENCY	PERCENTAGE(%)
1	Hyperthyroid	32	64
2	Euthyroid	6	12
3	Hypothyroid	8	16
4	Subclinical Hypothyroidism	3	6
5	Subclinical Hyperthyroidism	1	2

TABLE-5 LATERALITY AMONG STUDY PARTICIPANTS.

S.NO	LATERALITY	FREQUENCY	PERCENTAGE
1	SYMMETRICAL	34	68
2	ASYMMETRICAL	16	32

TABLE 6-DISTRIBUTION OF SYMPTOMS AMONG STUDY PARTICIPANTS.

S.no	SYMPTOMS	FREQUENCY	PERCENTAGE(%)
1	Watering & Redness	23	46
2	Foreign body sensation	41	82
3	Burning sensation	38	76
4	Defective vision	19	38
5	Diplopia	6	12
6	Protrusion	20	40

TABLE 7-DISTRIBUTION OF SIGNS AMONG STUDY POPULATION.

S.NO	SIGNS	FREQUENCY	PERCENTAGE(%)
1	Lid signs	42	84
2	Proptosis	18	36
3	Dry eye	26	52
4	EOM Restriction	9	18
5	Corneal signs	2	4
6	Optic Nerve Involvement	3	6
7	Differential IOP	10	20

Association Between Thyroid status and Eye signs

Thyroid status	Lid signs	proptosis	Dry eye	EOM restriction	Corneal signs	Optic nerve involvement	Differential IOP
Hyperthyroid	30	15	20	6	1	2	6
Euthyroid	3	1	1	0	0	0	0
Hypothyroid	5	1	3	1	1	1	2
Subclinical hypo	3	1	1	1	0	0	1
Subclinical hyper	1	0	1	1	0	0	1

In the present study involving 50 participants, the distribution of various ocular signs across thyroid status categories was assessed. The majority of ocular manifestations were observed in patients with hyperthyroidism, with lid signs being the most common, present in 30 out of 32 hyperthyroid individuals (93.8%). Proptosis and dry eye were the next most frequent findings, seen in 15 (46.9%) and 20 (62.5%) hyperthyroid patients, respectively. Other manifestations such as EOM restriction, differential IOP, optic nerve involvement, and corneal signs were also noted predominantly among the hyperthyroid group, albeit at lower frequencies.

In contrast, ocular signs were less frequently observed among euthyroid, hypothyroid, and subclinical thyroid disorder groups. Euthyroid individuals exhibited minimal findings, with only isolated cases of lid signs, proptosis, and dry eye. The hypothyroid group demonstrated a slightly higher prevalence, particularly of dry eye (37.5%), along with occasional cases of corneal involvement and optic nerve changes. Notably, the subclinical hypothyroid and subclinical hyperthyroid groups, although small in number, did present with some ocular signs—primarily lid signs and dry eye—suggesting that even subclinical dysfunction may have ocular implications.

Association of Various Eye Signs with Thyroid Status using Chi-square test

Eye Sign	Chi-square (χ^2)	df	p-value (Chi-square)	Fisher's Exact p
Lid Signs	10.938	4	0.027	0.019
Proptosis	5.105	4	0.277	0.291
Dry Eye	6.430	4	0.169	0.131
EOM Restriction	6.527	4	0.163	0.230
Corneal Signs	1.986	4	0.738	0.595
Optic Nerve Involvement	1.241	4	0.871	1.000
Differential IOP	5.990	4	0.200	0.217

Among all ocular manifestations assessed, only lid signs demonstrated a statistically significant association with thyroid status. The Pearson Chi-square test yielded a value of $\chi^2 = 10.938$ (df = 4, p = 0.027), and the Fisher's Exact Test confirmed this result with an exact p-value of 0.019. This finding aligns with the well-established clinical observation that lid retraction, lid lag, and other lid-related changes are often the earliest and most common signs in thyroid-associated ophthalmopathy (TAO), particularly in hyperthyroid states.

Other ocular signs such as proptosis, dry eye, extraocular muscle (EOM) restriction, corneal signs, optic nerve involvement, and differential intraocular pressure (IOP) were observed more frequently in hyperthyroid individuals but did not show statistically significant associations with thyroid status.

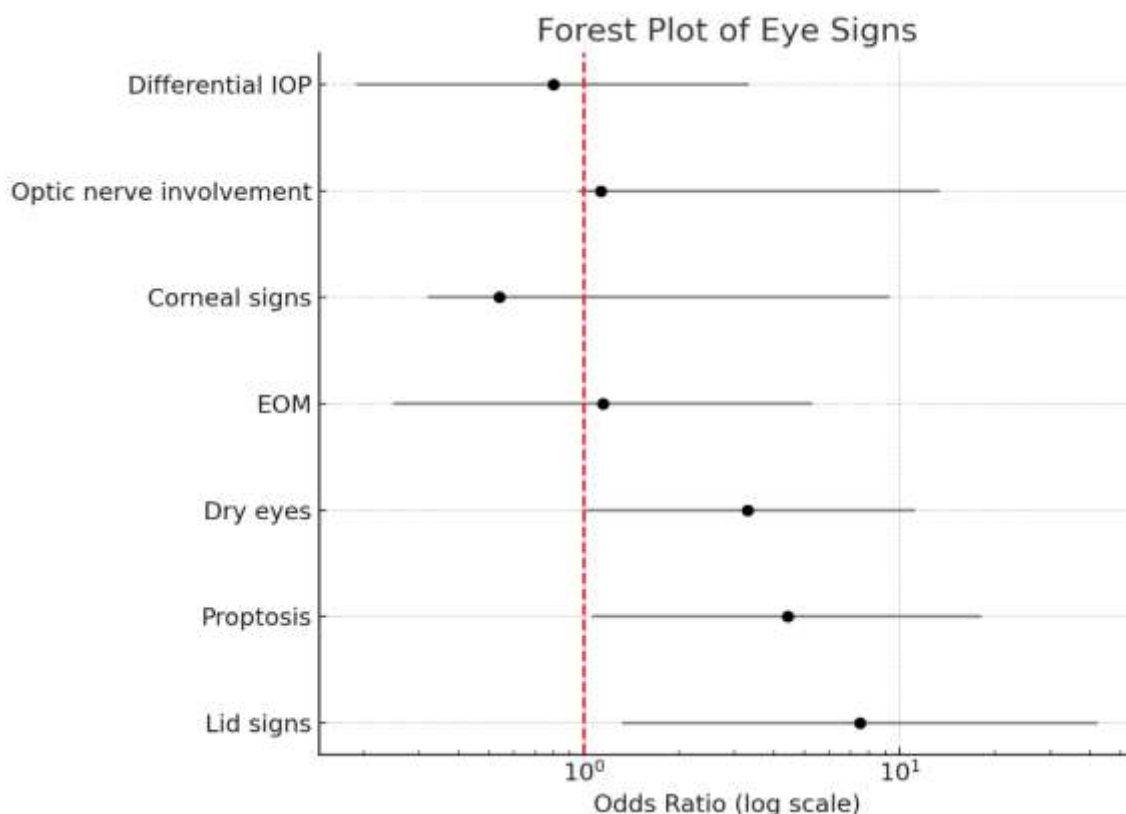
Association Between Thyroid Status and Ocular Manifestations Using Binary Logistic Regression (n

= 50)

Eye sign	Odds ratio	95% CI	P value
Lid signs	7.5	1.32-42.5	0.012
Proptosis	4.41	1.06-18.2	0.033
Dry eyes	3.3	0.99-11.2	0.048
EOM	1.15	0.25-5.3	0.85
Corneal signs	0.54	0.32-9.33	0.67
Optic nerve involvement	1.13	0.96-13.4	0.92
Differential IOP	0.80	0.19-3.34	0.76

The analysis revealed that lid signs were significantly associated with thyroid dysfunction, with an OR of 7.5 (95% CI: 1.32–42.5, $p = 0.012$), suggesting that individuals with thyroid abnormalities were over 7 times more likely to present with lid abnormalities compared to those without. Proptosis also showed a statistically significant association (OR: 4.41; 95% CI: 1.06–18.2, $p = 0.033$), indicating that thyroid disorders may considerably increase the risk of orbital involvement. Dry eyes showed a marginally significant association with thyroid status (OR: 3.3; 95% CI: 0.99–11.2, $p = 0.048$), hinting at a potential relationship that warrants further exploration.

Other ocular signs such as EOM restriction (OR: 1.15; $p = 0.85$), corneal signs (OR: 0.54; $p = 0.67$), optic nerve involvement (OR: 1.13; $p = 0.92$), and differential intraocular pressure (IOP) (OR: 0.80; $p = 0.76$) did not demonstrate statistically significant associations. Their wide confidence intervals further suggest considerable variability and a lack of strong association in this sample.



The above Forest plot illustrates the odds of developing specific ocular manifestations in hyperthyroid patients compared to those with other thyroid statuses (euthyroid, hypothyroid, subclinical), using binary logistic regression. Only **lid signs** and **possibly proptosis** show a meaningful association with hyperthyroid status.

Discussion :

The patient demographic analysis revealed a slight female preponderance, with 54% of participants being female and 46% male⁹. This aligns with the generally higher incidence of thyroid eye disease (TED) in females^{9,10}. However, some studies indicate that severe TED can show a reversal of this ratio, with males being overrepresented. The average age of presentation in our study, while not explicitly stated, falls within the 20-65 years inclusion criteria, with other studies reporting mean ages around 42.54 years or 49.93 years for TED patients^{11,12}

Regarding the distribution of thyroid status among participants, hyperthyroidism was the most common, observed in 64% of cases, followed by hypothyroidism (16%), Euthyroidism (12%), subclinical hypothyroidism (6%), and subclinical hyperthyroidism (2%). This finding contrasts with studies from Nepal and India that reported higher prevalence of TED in hypothyroid patients (50% and 69% respectively)^{9,13}. Conversely, Bartley et al. found hyperthyroidism in 90% of TED patients. It is well-established that TED can manifest in hyperthyroid, hypothyroid, or euthyroid states^{13,14}

The study also assessed laterality, finding that ocular manifestations were symmetrical in 68% of patients and asymmetrical in 32%³. This contrasts with general understanding that TED is most often bilateral and asymmetric, with only about 10% of cases being unilateral¹¹

Various comorbidities were identified among the study participants: 38% had diabetes, 22% had both diabetes and smoking, 16 % were hypertensive, and 12% had dyslipidemia and 12% were also found to be smokers. Smoking is a known significant risk factor for TED, increasing the risk by 7-8 times and reducing treatment effectiveness^{15,16}. Similarly, diabetes is also recognised as a risk factor for progressive and severe TED¹⁰. High cholesterol levels have also been identified as a risk factor for Graves' orbitopathy^{17,18}

Analysis of ocular symptoms revealed foreign body sensation (82%) and burning sensation (76%) as the most frequent complaints, followed by watering & redness (46%), protrusion (40%), defective vision (38%), and diplopia (12%)¹⁷. These findings are consistent with other studies that also report foreign body sensation and dry eyes as common symptoms¹⁷⁻¹⁹. Ocular pain and dry eye are frequently reported and significantly impact quality of life in TED patients. While diplopia was observed in 12% of our cases, other studies reported varying frequencies, from 0% in children to 17%. Defective vision, present in 38% of our cohort, is a significant symptom also noted in other studies, ranging from 1.2% to 10.1%²⁰

Regarding clinical signs, lid signs were the most common (84%), followed by dry eye (52%), proptosis (36%), extraocular muscle (EOM) restriction (18%), differential IOP (20%), optic nerve involvement (6%), and corneal signs (4%). This high prevalence of lid signs aligns with other research indicating lid retraction (82.4%) and lid lag (70.6%) as common findings, particularly in hyperthyroid patients^{10,18,21}. Proptosis, observed in 36% of our patients, is a hallmark of TED, with rates varying from 25% in children to 62.7% in young adults in other studies¹⁹. The prevalence of dry eye (52%) is within the reported range of 26.4% to 95% in TED patients. EOM restriction (18%) is also a recognized feature, with other studies reporting rates from 9.4% to 47.17%²⁰. The presence of differential IOP (20%) is noteworthy, as raised IOP can be influenced by increased episcleral pressure or compression of eye muscles. Though less common, severe manifestations like corneal involvement (4%) and optic nerve involvement (6%) were observed²². Corneal ulceration has been reported in up to 17.6% of hyperthyroid patients in another study. Optic nerve involvement is a serious complication, with prevalence around 4.55%, indicating potential sight-threatening TED^{16,20}

An important observation was that the majority of ocular manifestations were associated with hyperthyroid status. Specifically, hyperthyroid patients exhibited higher frequencies of lid signs, proptosis, dry eye, EOM restriction, corneal signs, optic nerve involvement, and differential IOP compared to other thyroid states. This underscores the active inflammatory nature often seen in hyperthyroid TED²³.

In conclusion, our study confirms the substantial ocular burden in patients with thyroid dysfunction. The findings largely resonate with existing literature regarding the prominent ocular signs and symptoms, the influence of gender, and the impact of risk factors like smoking and diabetes. The observed prevalence of manifestations in hyperthyroidism, as well as the laterality patterns, provide valuable insights, though some differences from global data highlight potential demographic or diagnostic variations. These results emphasize the critical need for early detection and a multidisciplinary approach involving endocrinologists and ophthalmologists to improve outcomes and quality of life for patients with TED

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