

**ORIGINAL RESEARCH**

# Thyroid associated ophthalmopathy - A study comparing the clinical profile with hormonal status and orbital imaging

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**ABSTRACT**

This study aimed to investigate the epidemiological characteristics and clinical course of Ophthalmopathy associated with thyroid dysfunction, focusing on the correlation between hormonal status and clinical findings. The inclusion criteria encompassed thyrotoxicosis patients with eye signs, cases with diffuse goiter and eye signs, and cases with eye signs lacking evidence of thyroid dysfunction.

Conducted at RIO, GMCH, the study spanned from January to October 2023, involving a thorough ocular examination, including history-taking, extraocular examination, exophthalmometry, tonometry, fundus examination, and imaging studies. Follow-ups with the endocrinology department included T3, T4, TSH estimation, and TAB presence assessment.

The study drew insights from relevant departments and referenced existing literature, such as studies by Ofira Zloto, Alankrita Muralidhar, Bartley et al, and Sagili Vijaya Bhaskar Reddy. Notable findings included gender differences in thyroid eye disease presentation and prognosis, varying prevalence rates, and bimodal incidence peaks. Symptom distribution revealed discomfort/pain as the most common (30%), followed by lacrimation/photophobia (27%) and diplopia (20%). Eye involvement distribution indicated bilateral involvement in the majority of cases. The conclusion highlighted common occurrence between 30-50 years, a male-to-female ratio of 1:4, and ocular discomfort/pain as a prevalent complaint. Raised IOP, proptosis, and enlarged extraocular muscles (EOM) were noted, emphasizing the absence of a direct TH level correlation with TED course.

Ultrasonography proved valuable in detecting EOM enlargement without measurable proptosis.

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**INTRODUCTION**

Thyroid Associated Ophthalmopathy (TAO) is a potentially sight-threatening ocular disease mostly occurring in the patients with hyperthyroidism or a history of hyperthyroidism due to Graves' disease (GD). The prevalence of TAO among the patients with thyroid dysfunction ranges from 51.7% in the Caucasian population to 34.7% in the Asian population. (1) Thyroid eye disease (TED) is an autoimmune inflammatory disorder affecting orbital fat, extra-ocular muscles, and lacrimal gland, resulting in tissue expansion from glycosaminoglycan deposition and edema, and in some cases fibrosis from collagen production. (2,3)

Most individuals develop primarily fat expansion with eyelid retraction, proptosis, and ocular exposure. In a third of affected individuals, more serious manifestations may result from significant extraocular muscle involvement, including periorbital soft tissue erythema and edema, restricted ocular motility and double vision, and occasionally vision loss

from compressive optic neuropathy, CON (4)

This spectrum of ocular findings is graded as "disease severity."

The more severe form of TED follows a biphasic course, with a progressive or active phase lasting up to 18 months, followed by a stable or inactive phase. (5-7) Although TED is self-limited, it may cause permanent cosmetic disfigurement and functional visual impairment, and has been shown to impact quality of life more than chronic lung disease or diabetes mellitus (8).: Understanding the natural history of this disease helps in earlier diagnosis, in identifying those at risk for serious disease consequences, and in choosing appropriate therapy.

Primary risks factors for TED are environmental influences especially smoking but also prior pathogen exposures, stress and previous use of radioiodine in addition to a complex genetic component (9). Graves' ophthalmopathy affects women approximately 6 times more frequently than men. The peak rate occurs in age group 40-44 years and 60-64 years in women

and 45-49 years and 65-69 years in men (10)

Among patients with TED, about 90% have Graves hyperthyroidism, 6% are euthyroid, 3% have Hashimoto thyroiditis, and 1% have primary hypothyroidism. A close temporal relationship exists between the development of hyperthyroidism and the development of TED: in about 20% of patients, the diagnoses are made at the same time, and in about 60% of patients, the eye disease occurs within 1 year of onset of the thyroid disease. For patients who have no history of abnormal thyroid function or regulation at the time TED is diagnosed, the risk for development of thyroid disease is about 25% within 1 year and 50% within 5 years. Although hyperthyroidism is present or will develop in most patients with TED, only about 30% of patients with auto immune hyperthyroidism will develop TED. (11)

**The diagnosis of TED is made when 2 of the following 3 signs are present:**

1. Concurrent or recently treated immune-related thyroid dysfunction:
  - a. Graves hyperthyroidism
  - b. Hashimoto thyroiditis
  - c. Presence of circulating thyroid antibodies without a coexisting dysthyroid state (partial consideration given): thyroid-stimulating hormone- receptor (TSH-R) antibodies, thyroid-binding inhibitory immunoglobulins, thyroid-stimulating immunoglobulins, antimicrosomal antibodies
2. Typical ocular signs:
  - a) Chemosis and/or caruncular edema
  - b) Restrictive strabismus in atypical pattern
  - c) Unilateral or bilateral eyelid retraction with typical lateral flare
  - d) Unilateral or bilateral proptosis (in comparison with old photos of the patient)
  - e) Compressive optic neuropathy
  - f) Fluctuating eyelid edema and/or erythema
3. Radiographic evidence of TED: unilateral or bilateral fusiform enlargement any of the rectus muscles and/or the levator muscle complex (11)

Sometimes the patient may just present clinically with unilateral proptosis without any systemic manifestation of thyroid dysfunction. Or sometimes the patient might not be showing any severe signs and symptoms but may be progressing towards serious dysthyroid optic neuropathy. As proptosis a defensive mechanism of the eye to the underlying pathological changes, in some patients when the orbital septum is too thick or because of their anatomical structure they

might be an early prey to DON and might face a serious unwarranted vision loss. A on time CT Scan/ MRI can diagnose the subtle crowding at orbital apex and keep such complications at bay by preparing the ophthalmologist on time for adequate actions.

## MATERIALS AND METHODS

The study was conducted for a period of 10 months from January 2023 to October 2023. It was a prospective observational study conducted in Regional Institute of Ophthalmology, Gauhati Medical College and Hospital, Guwahati. A total of 50 patients were included in the study. A detailed history, local and systemic examinations including laboratory investigations were done in all cases fulfilling the criteria after taking informed consent from the patient and/or the attendant. Ophthalmic evaluation consists of the following:-

1. Elicitation of proper ocular history such as any photophobia. Lacrimation. or any history of Diplopodia etc.
2. Thorough external ocular examination under diffuse light and slit lamp.
3. Fluorescein/Rose Bengal staining of the cornea
4. IOP examination by Schiotz tonometer.
5. Exophthalmometry.
6. Forced duction test
7. Central visual field charting.
7. Color vision testing by Ishihara plates.
8. Fundus examination by Heine direct ophthalmoscope.
10. B-scan ultrasonography of orbit.

The results were statistically analysed

## DIAGNOSTIC CRITERIA

1. Unilateral or bilateral lid retraction with no alternative explanation.
2. Lid retraction and unilateral exophthalmos.
3. Bilateral exophthalmos.
4. Ophthalmoplegia associated with bilateral lid retraction or exophthalmos
5. USG evidence of extraocular muscle involvement.

## INCLUSION CRITERIA

1. Thyrotoxicosis patients with eye signs.
2. Cases with diffuse goitre with eye signs
3. Cases with eye signs but no evidence of thyroid dysfunction

## RESULTS AND OBSERVATIONS

50 patients with different signs and symptoms of thyroid Ophthalmopathy were examined in the study.

### DISTRIBUTION OF AGE-Table 1

| Age Group | Number Of Cases | Percentage |
|-----------|-----------------|------------|
| 10-20     | 4               | 13.33%     |
| 21-30     | 7               | 23.33%     |
| 31-40     | 9               | 30%        |
| 41-50     | 7               | 23.33%     |
| 51-60     | 2               | 6.66%      |
| >60       | 1               | 3.33%      |

|       |    |     |
|-------|----|-----|
| Total | 30 | 100 |
|-------|----|-----|

**DISTRIBUTION OF SEX-Table2**

| Sex     | No. Of cases | Percentage |
|---------|--------------|------------|
| MALES   | 6            | 20         |
| FEMALES | 24           | 80         |
| TOTAL   | 30           | 100        |

**DISTRIBUTION OF SYMPTOMS-Table3**

| Symptoms                | No. Of cases | Percentage |
|-------------------------|--------------|------------|
| Discomfort/pain         | 16           | 32         |
| Lacrimation/photophobia | 13           | 26         |
| Diplopia                | 8            | 16         |
| Blurredvision           | 4            | 8          |
| Decreasedvision         | 2            | 4          |
| Nosymptoms              | 7            | 14         |

**DISTRIBUTION OF EYE FINDINGS IN ORDER OF FREQUENCY-Table4**

| Ocular findings         | Number | Percentage |
|-------------------------|--------|------------|
| Eyelidretraction        | 41     | 82         |
| Exophthalmos            | 29     | 58         |
| Softtissueinvolvement   | 28     | 56         |
| LidLag                  | 21     | 42         |
| RestrictiveMyopathy     | 17     | 34         |
| DryEyes                 | 16     | 32         |
| Raised IOP              | 15     | 30         |
| Optic Nerve Involvement | 3      | 6          |
| Exposure Keratopathy    | 2      | 4          |



Image 1: Bilateral Lid retraction with



Image 2: unilateral lid retractionproptosis

**DISTRIBUTION OF OPHTHALMOPATHY IN RELATION TO THYROID STATUS-Table5**

| Thyroid status | No. Of cases | Percentage |
|----------------|--------------|------------|
| Hyperthyroid   | 42           | 84         |
| Hypothyroid    | 2            | 4          |
| Euthyroid      | 6            | 12         |
| Total          | 50           | 100        |

**DISTRIBUTION OF STAGE OF DISEASE-Table6****ACTIVE: Ophthalmopathy with pain/redness IN ACTIVE: Ophthalmopathy without pain/redness**

| Ophthalmopathy | No .Of cases | Percentage |
|----------------|--------------|------------|
| ACTIVE         | 28           | 56         |
| INACTIVE       | 22           | 44         |
| TOTAL          | 50           | 100        |



**Image 3: Bilateral Severe chemosis with sloughing corneal ulcer due to exposure Keratopathy**



**Image 4: Bilateral lid retraction with proptosis**

**RELATIONSHIP OF OPHTHALMOPATHY TO THYROID STATUS**

Of the 28 active cases 78.5% had high  $T_3$ , 89.2% had high  $T_4$  and 89.2% cases had suppressed TSH indicating hyperthyroid state. In 3 patients (10.7%) had low  $T_3$  but normal TSH probably indicating effect of antithyroid drug therapy. 10.7% had normal  $T_3$ ,

normal  $T_4$  and TSH indicating euthyroid Graves'. Of the inactive cases, 72.7% had high  $T_3$  and high  $T_4$  and 77.2% had suppressed TSH indicating hyperthyroidism. Of the 3 patients with low  $T_3$  and  $T_4$ , 2 had high TSH indicating hyperthyroidism, while 1 patient on antithyroid therapy had normal TSH indicating a drug effect.



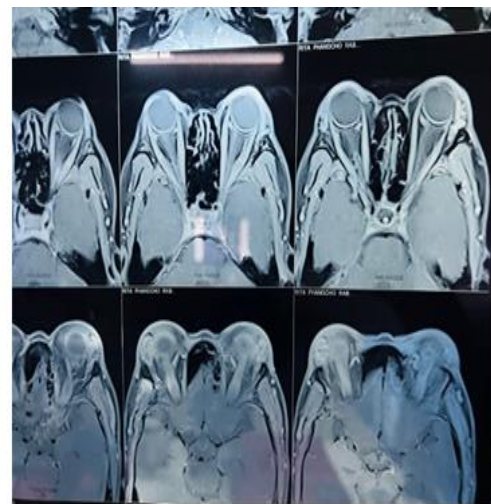
**Image 4: Orbital apex crowding due to EOM enlargement Image 5: soft tissue involvement.**

**DISTRIBUTION OF EXTRAOCULAR MUSCLE ENLARGEMENT AS EVIDENCED BY USGB SCAN /CTSCAN /MRI-Table 7**

| ENLARGED EOM      | NO. OF Cases | Percentage |
|-------------------|--------------|------------|
| With Proptosis    | 31           | 62         |
| Without Proptosis | 9            | 18         |
| Normal            | 10           | 20         |
| Total             | 50           | 100        |

**FREQUENCY OF INVOLVEMENT OF EXTRA OCULAR MUSCLE AS EVIDENCED BY CT SCAN/MRI**

| Extraocular Muscle | No. Of cases | Percentage |
|--------------------|--------------|------------|
| INFERIOR RECTUS    | 37           | 74         |
| MEDIAL RECTUS      | 28           | 56         |
| SUPERIOR RECTUS    | 13           | 26         |
| LATERAL RECTUS     | 11           | 22         |



**Image 6: inferior rectus muscle involvement in CT scan Image 7: EOM enlargement as seen in MRI**

**DISCUSSION**

In our study we found that majority of the affected patients were females 80% . To support our study, Ofira Zloto et al(2020) had found 71.21% affected females(12) . Henry et al too had found more affected females than males. (13)

In our study, we found only four cases in the age group of 10 to 20 years. One had mild proptosis and the other three had mild unilateral Lid Retraction with no other signs and symptoms.

In our study, highest number of cases fell under the age group of 31 to 40 years followed by 41 to 50 years in a retrospective study conducted among thousand patients by Millindet al(2020) for a period of 10 years, found the average age at presentation to be 44.9 years(14). In another study conducted by Alankrita Muralidhar et al(2020) conducted amongst 106 TED patients the mean age was found to be 41.30 years. (15) Symptomatically we found that maximum number of patients ( 36%) had complained of ocular

discomfort that is grittiness or mild irritation, followed by lacrimation and photophobia (26%) which is almost similar to Yao Wang et al (2022) where they found most common ocular complain amongst TAO patients to be dry and grittiness or discomfort(77%), followed by excessive tearing (43%) (16)

Out of our total 50 cases, 16% cases complained of diplopia and our finding is nearly same with several other studies like Khurana et al (1992) - 13 33%(17). Kendler et al(1993)\* 20% and Bartley et al (1994)° 17%.(18,19)

Decrease vision is noted in 4% patients of our study which is supported by Kindler et al(1993) and Bartley et al (1994) and they found 6% and 2% of their cases having decreased vision (18,19)

In our study we found that lid retraction is most common sign followed by Exophthalmos, restrictive myopathy, lid lag, dry eye.

**IN COMPARISON TO OTHER STUDY (15, 20)**

| Symptoms                   | Alankrita Muralidhar et al, 2020 Aug | symptoms              | Dr Gangadhara Sundar et al, March 2015 |
|----------------------------|--------------------------------------|-----------------------|--|
| proptosis                  | 64.10%                               | proptosis             | 61.00%                                 |
| upper lid retraction       | 63.20%                               | upper lid retraction  | 62.10%                                 |
| epiphora                   | 50.90%                               | lig lag               | 57.50%                                 |
| grittiness                 | 43.40%                               | Acquired epiblepharon | 11.50%                                 |
| Diplopia                   | 23.60%                               | corneal erosions      | 29.30%                                 |
| optic neuropathy           | 3.70%                                |                       |  |
| exposure keratopathy       | 0.90%                                |                       |  |
| spontaneous globe luxation | 1.90%                                |                       |  |

Out of total 50 cases 56% were under active group and 44% were under active group. It was seen that irrespective of hormone level (T3, T4 & TSH); signs of thyroid eye disease were present in all the cases with mild and moderate to marked degree of the disease. SO. we observed that though thyrotoxicosis is the underling cause of thyroid eye disease there is no

direct relationship between the thyroid hormone levels (T3, T4 & TSH) and course of ophthalmopathy. Few other authors who support our findings are Alankrita Muralidhar et al (2020), Subramaniam et al(2023) (15,21)Adams DD. and Kennedy T.H. (1974), Lawton NF. and Fells P(1978) and Wall JR and Jovner D. M. (1982)(22 -25)

We have found that the most common involved extraocular muscle in our cases as evidenced by ultrasound was inferior rectus (74%). followed by

medial rectus(56%)superior rectus (26%) and lateral rectus (22%).

#### IN COMPARISON TO OTHER STUDIES ( 26 ,27 )

|                                  |                 |
|----------------------------------|-----------------|
| JuditDamjanovich et al,July 2000 | INF>MED>LAT>SUP |
| Rebecca S Bahn, 2003             | INF>MED>SUP>INF |

#### CONCLUSION

Thyroid Eye Disease (TED)frequently manifests in individuals aged between 30 to 50years,exhibiting a notable male-to-female ratio of1:4.Among the diverse array ofocularsymptoms associated with TED, ocular discomfort and pain emerge as the mostcommonlyreported complaints.

Interestingly, intraocular pressure (IOP) may be elevated, irrespective of the presence orabsence of measurable proptosis. Contrary to expectations, this study reveals that there isnoindirectcorrelation between thyroid hormone (TH)levels and the course ofTED.

This challenges conventional assumptions about the influence of TH on the progression ofthe disease. Furthermore, the utility of ultrasonography (USG) is underscored in detectingthe enlargement of extraocular muscles (EOM) even in the absence of discernibleproptosis, emphasizing the importance of advanced imaging techniques in thecomprehensive evaluation ofTED.

These findings collectively contribute to a nuanced understanding of the demographic,clinical, and diagnostic aspects of TED, paving the way for more tailored and informedapproaches to its management.

**Conflict of interest-**Nil

**Financial interest-**Nil

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