# Prevalence of Thyroid Eye Disease Among Thyroid Disorder Patients

Dr Abinaya Ramakrishna<sup>1</sup>, Dr Panimalar A Veeramani<sup>2</sup>, Dr.Akash R<sup>3</sup>

<sup>1</sup> Junior Resident, Department of Ophthalmology, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

<sup>2</sup> Associate professor, Department of Ophthalmology, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

<sup>3</sup> Junior Resident, Department of Ophthalmology, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

## Abstract:

Aim

To assess the prevalence of Thyroid Eye Disease among thyroid disorder patients.

Introduction

Thyroid Eye Disease (TED) is a debilitating autoimmune disorder seen in hyperthyroid, hypothyroid and euthyroid patients. The global prevalence of TED is estimated to be 16 per 100,000 women and 2.9 per 100,000 men in the general population. Common symptoms include dry eyes, eyelid retraction, excessive watering, conjunctival redness and swelling, retro-orbital pain and blurred vision. This study aims to assess the prevalence of TED among dysthyroid patients attending Saveetha Medical College and Hospital, Chennai. Methodolody

The purpose of this study is to find the prevalence of TED among dysthyroid patients attending Saveetha Medical College and Hospital, Chennai during the months of July and August. A detailed history of each patient was taken after which a series of tests were conducted to identify and classify the severity of TED. This was done using NOSPECS (no signs, only signs, soft tissue involvement, proptosis, extraocular muscle involvement, corneal involvement, sight loss) classification. Schirmers test was performed to assess the prevalence of dry eyes among TED patients.

Result

122 patients consisting of 87 females and 35 males were included in this study. 43% (53 patients) were found to have Thyroid Eye Disease. There was no significant difference in prevalence between male and female subjects (43.6% and 42.8% respectively). The presence of TED was far greater in hyperthyroid than in hypothyroid patients. 44 out of 53 patients with TED were hyperthyroid (83%), 7 were hypothyroid (13.2%), and 2 patients were euthyroid (3.7%). Schirmers test conducted on each patient revealed that 12% of the TED patients suffered from dry eyes. NCT test conducted to find the intraocular pressure in TED patients revealed no significant results. Conclusion

The high prevalence of TED seen in dysthyroid patients in this study calls for increased awareness regarding ocular manifestations in thyroid disorders. Patients should be encouraged to undergo regular checkups to ensure normal functioning of eyes and to prevent progression of the disease.

Keywords: Thyroid eye disease, NOSPECS classification, hyperthyroid, hypothyroid, euthyroid

# INTRODUCTION

Thyroid Eye Disease (or Graves 'Opthalmopathy) is a condition caused by inflammation and enlargement of extraoccular muscles, de novo adipogenesis and interstitial edema [1]. CT indicates that most TED patients have a mixture of both extraocular muscle enlargement and orbital fat expansion [1,17].TED can be debilitating as it can cause optic nerve damage, ocular hypertension, Diplopia and glaucoma. Quality of life can be greatly compromised even in mild cases of TED [2].

90% of TED patients are known to be hyperthyroid, 5% are hypothyroid and 5% are euthyroid patients [3]. In the USA, the incidence of TED was 16 per 100,000 population per year in females and 2.9 per 100,000/year in males [3]. Surprisingly this ratio reverses in severe TED in which a female to male ratio of 1:4 is seen [4] [9]. About 60% of hyperthyroid patients eventually develop TED [5].

Risk factors of TED consists of middle age, female gender and smoking [6]. Smokers with Graves 'disease are approximately 2 times more likely to develop TED and heavy smokers are 8 times more likely [7].

Common symptoms of thyroid eye disease includes dry eyes, excessive watering, eye lid swelling, eye lid retraction, proptosis, conjunctival or eyelid redness and swelling, blurred vision and retro orbital pain [8].

A meta-analysis on the 'prevalence of TED in Graves 'disease patients 'conducted across 33 articles found that the pooled prevalence of TED in 22,384 Graves 'disease patients was 40% [9].

A study conducted in multiethnic Malaysian patients with Graves' disease, a similar rate of 34.7% patients had Thyroid Eye Disease [10].

There is a lack of research conducted regarding the prevalence of TED in Asian countries, especially India. This makes our study crucial in determining the prevalence TED among Indian dysthyroid patients. It also aids in comparing results obtained in our study with global statistics and research conducted in different parts of the part.

## METHODOLOGY

A cross-sectional study was conducted on the prevalence of thyroid eye disease among dysthyroid patients who visited the Department of General Medicine, General Surgery and Ophthalmology in Saveetha Medical College, Chennai. The study was performed during a period of 3 months from July to September 2021.

A total of 122 patients were included in the study after confirming their thyroid status based on previous lab reports. 87 patients were females and 35 patients were males. Among these patients, 88 were hyperthyroid, 23 were hypothyroid, and 11 patients were euthyroid. All patients were above the age of 20 and their informed consent was taken before including them in the study. Each patients had confirmed their thyroid status using blood reports and were on regular medication for their condition. They also followed up frequently to avoid any complications.

Each participant was first asked about their demographic details, past medical and surgical history. NOSPECS classification(No signs/only signs/soft tissue involvement/proptosis/extraoccular muscle involvement/corneal involvement/ sight loss-optic nerve involvement) was used to identify the presence and classify the severity of TED [11]. Additionally, each patient underwent various tests such as Slit lamp examination, fundus examination, visual acuity, colour vision, acceptance, schirmers test and non-contact tonometry. Patients with at least one sign and symptom was considered to have thyroid eye disease.

NOSPECS classification score		
Score	Findings	
0	No signs or symptoms	
1	Only signs	
2	Soft tissue involvement with symptoms and signs	
3	Proptosis (>20mm)	
4	Extraocular muscle involvement	
5	Corneal involvement	
6	Sight loss	

Schirmer's test was performed to evaluate the aqueous tear production which is reduced in dry eyes, a common sign of TED. Using a strip of filter paper (what an 41 filter paper-35mmx5mm), a 5mm fold is made on one end and placed over the lateral third of the lower lid. Patient is then asked to keep their eyes closed for 5 minutes [12]. This test was performed without using anesthesia. A wetting of less than 10mm of the strip was considered as indicating dry eyes.

Non-contact Tonometry (NCT) is test performed to find the intraocular pressure (IOP) in which the instrument blows a brief puff of air at the cornea (hence also known as puff test). The tonometer records the IOP from the change in the light reflected off the cornea as it is indented by the air puff.

# RESULT

Of the 122 patients included in the study, 43.4% of the patients presented with thyroid eye disease (53 patients). 38 patients among them were female and 15 were males. There was no difference in the prevalence of TED between males and females [38/87 in females (43.6%), 15/35 in males (42.8%)] (Table1).

	Total number of patients	Patients with TED	Patients without TED	% of TED patients
Females	87	38	49	43.6%
Males	35	15	20	42.8%

Among hyperthyroid patients, 50% of the patients had TED (44/88 patients). However, a comparatively reduced prevalence was seen in hypothyroid with 30.4% having TED (7/23 patients) and only 18.1% in euthyroid patients (2/11 patients) (table2).

Table 2	2
---------	---

	Total number of patients	Patients with TED	Patients without TED	% of TED patients
Hyperthyroid	88	44	44	50%
Hypothyroid	23	7	16	30.4%
Euthyroid	11	2	9	18.1%

The presence of TED was far greater in hyperthyroid than in hypothyroid and euthyroid patients. 44 patients with TED were hyperthyroid (83%), 7 were hypothyroid (13.2%), a 2 were euthyroid (3.7%). (fig. 1)

Table 1



(Fig.1)

88.6% of the patients were classified under class 1 of TED (47/53 patients). In these patients, eyelid retraction was the most common sign seen.7.5% of the patients presented with class 2 TED with edema of conjunctiva and lids (4/53). Proptosis was seen in 3.8% of the patients and were classified under class 3 of TED (2/53 patients).

NOSPECS score	Hyperthyroid	Hypothyroid	Euthyroid
No signs -0	44	16	9
Only signs- 1	42	3	2
Soft tissue involvement- 2	3	1	0
Proptosis- 3	2	0	0
Extraocular muscle involvement-4	0	0	0
Corneal involvement- 5	0	0	0
Sight loss- 6	0	0	0

Table 3

This reveals that all the subjects included in the study had no severe ocular complications due to TED since none of the patients in the study had a nospecs score of above 3. None of the subjects suffered from optive nerve damage, sight loss or any corneal involvement. Proptosis (score 3) was only seen in hyperthyroid patients. Euthyroid patients with TED only had signs of TED (score 1) with no soft tissue involvement.

This may be a result of regular hospital visits and eye checkups followed by the subjects involved in the study.

Schirmer's test was performed on each patient without using anaesthesia and showed that 12% of the patients with TED had dry eyes with results ranging from 8 to 10mm.





Non contact tonometry (NCT) test conducted to assess the intraocular pressure of each patients revealed no significant findings. None of the patients included in the study suffered from ocular hypertension due to TED.

## DISCUSSION

In this study, 43.4% of the dysthyroid patients who were included in the study were found to have thyroid eye disease. This result coincides with the results of the meta-analysis study published in 2020 which calculated the pooled prevalence of TED in GD patients to be 40%. Asian countries had a higher pooled prevalence of 44%, followed by Europe with 38%, followed by North America with a prevalence of 27%. The slight increase in prevalence of TED among Asians may be due to the genetic predispositions, biochemical factors or increased prevalence of smokers [13]. However there has been controversy regarding the prevalence of TED in Asian countries compared to European countries. Some studies even suggest ethnic differences to be due to difference in smoking rates[2].

A study conducted in multiethnic Malaysian patients with Graves' disease, a similar rate of 34.7% patients had Thyroid Eye Disease [10]. However a decreased prevalence of TED among dysthyroid patients was seen in a study conducted in Korea in which 17.3% dysthyroid patients had TED[14].

In other British Studies, the prevalence of TED using NOSPECS was reported to be 51.7% in a Grave's disease cohort [16].

Our study found no significant difference in prevalence of TED between males and females. A similar study conducted in Korea also found similar results in which TED has equal prevalence in both males and females [14]. This may be because although TED is more common in younger women, studies have found that men and advancing age are at higher risk of severe disease [15]. It has also been seen that the mean age at onset of orbital disease was 44.4 years for women and 43.9 years for men, and at an average of 2.5 years from the onset of thyroid disorder[15].

Although any form of dysthyroidism can potentially cause TED, various studies have concluded that TED is most commonly seen in hyperthyroid patients. One such study found the global prevalence was 10.36% for hypothyroidism, 86.2% for hyperthyroidism and 7.9% for euthyroidism [16]. This study found similar results as 83% of the patients with TED were hyperthyroid ,13.2% were hypothyroid and 3.7% were euthyroid. 857

Smoking is considered as a major risk factor for TED. Ex-smokers have an increased risk compared to nonsmokers and a two fold increased risk of TED is evident in current smokers [17].

Along with assessing the severity of TED, this study also found the prevalence of dry eyes, a common sign in TED, in the study subjects. Studies found mechanical impairment of orbital muscles and immune mediated lacrimal gland dysfunction to be the cause of altered tear film seen in TED patients with Dry eyes. Ocular inflammation also contributes to this [18].

A value above 10mm is generally considered normal while performing schirmers test without anaesthesia. In this study we found 12% of the TED patients to have dry eyes without schirmers test results ranging from 8 to 10mm.

Increased intraocular pressure is a common manifestation of TED. Studies have shown a prevalence of 3.74% ocular hypertension and a 2.8% prevalence of glaucoma among TED patients [19]. The cause of elevated IOP is an increase in the episcleral venous pressure [20]. This study showed no significant result on conducted NCT test. This may be due to absence of patients with severe TED present in the study.

The low prevalence of severe TED in this study may be attributed to awareness of each patients regarding their thyroid condition for which they are on regular treatment. This study being hospital based is a limitation to the study. A population based study would be required to assess the prevalence of TED on a large scale in order to find the actual prevalence of severe forms of TED.

## CONCLUSION

This study revealed the prevalence of TED in dysthyroid patients to be 43.4%. This shows that TED is a common manifestation of thyroid disorders. However, none of the sunbjects included in the study had severe forms of TED. This may be due to their frequent visits to the hospital for eye checkups and regular treatment for their respective thyroid condition. This shows that disease can be arrested from progression if treated well and if eyes are assessed regularly.

Since it can be debilitating as the disease progresses, active screening should take place especially in patients with lower lid retraction and proptosis. Regular eye check ups must be advised to thyroid patients to ensure proper ocular function.

## REFERENCES

- [1] Khong JJ, McNab AA, Ebeling PR, et al Pathogenesis of thyroid eye disease: review and update on molecular mechanisms British Journal of Ophthalmology 2016;100:142-150.
- [2] Tellez M, Cooper J, Edmonds C. Graves' ophthalmopathy in relation to cigarette smoking and ethnic origin. Clin Endocrinol (Oxf) 1992;36:291–294.
- [3] Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota. Trans Am Ophthalmol Soc. 1994;92:477-588
- [4] Perros P, Crombie AL, Matthews JN, Kendall-Taylor P. Age and gender influence the severity of thyroidassociated ophthalmopathy: a study of 101 patients attending a combined thyroid-eye clinic. Clin Endocrinol (Oxf) 1993;38:367–372. doi: 10.1111/j.1365-2265.1993.tb00516.x.
- [5] Soeters MR, van Zeijl CJ, Boelen A, Kloos R, Saeed P, Vriesendorp TM, Mourits MP. Optimal management of Graves orbitopathy: a multidisciplinary approach. Neth J Med. 2011;69:302–308.
- [6] Sikder S, Weinberg RS. Thyroid eye disease: pathogenesis and treatment. Ophthalmologica. 2010;224:199–203. doi: 10.1159/000260224.
- [7] Vestergaard, P. (2002) Smoking and thyroid disorders a meta-analysis. European Journal of Endocrinology, 146, 153–161.
- [8] A New Era in the Treatment of Thyroid Eye Disease Patel, A., Yang, H. and Douglas, R.S.
- [9] Chin YH, Ng CH, Lee MH, Koh JWH, Kiew J, Yang SP, Sundar G, Khoo CM. Prevalence of thyroid eye disease in Graves' disease: A meta-analysis and systematic review. Clin Endocrinol (Oxf). 2020 Oct;93(4):363-374. doi: 10.1111/cen.14296. Epub 2020 Aug 10. PMID: 32691849.
- [10] Lim SL, Lim AK, Mumtaz M, Hussein E, Wan Bebakar WM, Khir AS. Prevalence, risk factors, and clinical

features of thyroid-associated ophthalmopathy in multiethnic Malaysian patients with Graves' disease. Thyroid. 2008 Dec;18(12):1297-301. doi: 10.1089/thy.2008.0044. PMID: 19012471.

- [11] Wiersinga W, M, Smit T, van der Gaag R, Mounts M, Koomneef L: Clinical Presentation of Graves' Ophthalmopathy. Ophthalmic Res 1989;21:73-82. doi: 10.1159/000266782
- [12] Stevens S. Schirmer's test. Community Eye Health. 2011;24(76):45
- [13] Khalilzadeh O, Noshad S, Rashidi A, Amirzargar A. Graves' ophthalmopathy: a review of immunogenetics. Curr Genomics. 2011;12(8):564-575.
- [14] Woo KI, Kim YD, Lee SY. Prevalence and risk factors for thyroid eye disease among Korean dysthyroid patients. Korean J Ophthalmol. 2013 Dec;27(6):397-404. doi: 10.3341/kjo.2013.27.6.397. Epub 2013 Nov 15. PMID: 24311923; PMCID: PMC3849301.
- [15] Kendler DL, Lippa J, Rootman J. The initial clinical characteristics of Graves' orbitopathy vary with age and sex. Arch Ophthalmol. 1993;111(2):197-201.
- [16] Muñoz-Ortiz J, Sierra-Cote MC, Zapata-Bravo E, Valenzuela-Vallejo L, Marin-Noriega MA, Uribe-Reina P, Terreros-Dorado JP, Gómez-Suarez M, Arteaga-Rivera K, de-la-Torre A. Prevalence of hyperthyroidism, hypothyroidism, and euthyroidism in thyroid eye disease: a systematic review of the literature. Syst Rev. 2020 Sep 1;9(1):201. doi: 10.1186/s13643-020-01459-7. PMID: 32873324; PMCID: PMC7465839.
- [17] Manji N, Carr-Smith JD, Boelaert K, et al. Influences of age, gender, smoking, and family history on autoimmune thyroid disease phenotype. J Clin Endocrinol Metab. 2006;91:4873–4880.
- [18] Selter JH, Gire AI, Sikder S. The relationship between Graves' ophthalmopathy and dry eye syndrome. Clin Ophthalmol. 2014;9:57-62. Published 2014 Dec 31. doi:10.2147/OPTH.S7658
- [19] da Silva, F., de Lourdes Veronese Rodrigues, M., Akaishi, P. et al. Graves' orbitopathy: frequency of ocular hypertension and glaucoma. Eye 23, 957–959 (2009). https://doi.org/10.1038/eye.2008.155
- [20] Burch HB, Wartofsky L. Graves' ophthalmopathy: current concepts regarding pathogenesis and management. Endocr Rev. 1993;14(6):747–793. doi:10.1210/edrv-14-6-747

DOI: https://doi.org/10.15379/ijmst.v10i1.2672

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.