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Prevalence and clinical profile of thyroid eye disease among patients with thyroid dysfunction visiting a tertiary care teaching hospital

Srijana Thapa Godar¹, Jai Bahadur Khattri², Ramesh Raj Acharya³

¹Department of Ophthalmology, Manipal Teaching Hospital, Pokhara, Nepal

²Department of Psychiatry, Manipal Teaching Hospital, Pokhara, Nepal

³Department of Internal Medicine, Manipal Teaching Hospital, Pokhara, Nepal



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Abstract

Background: Thyroid eye disease (TED) is an autoimmune disease affecting ocular and orbital tissues. The objective of this study was to find out the prevalence of thyroid eye disease and the prevalence of different clinical profile of thyroid eye disease in patients with thyroid dysfunction.

Method: This was a hospital based cross-sectional study conducted among 93 patients with thyroid dysfunction of aged 30 years and above. Standard proforma was used to collect socio-demographic and clinical variables of the patients. Detailed ocular examination was done to assess thyroid eye disease. The statistical methods used were mean, frequency and percentage.

Result: The prevalence of thyroid eye disease was 47.31%. Thyroid eye disease was more prevalent in female (77.27%) and in hypothyroid (50.0%). Among patients with thyroid eye disease, 15.91% had history of smoking, 34.09% had family history and 47.73% had the duration of thyroid dysfunction of more than 48 months. The commonest symptom was foreign body sensation (59.09%), dry eyes (54.55%), discomfort of eyes (52.27%) and prominent eyes (50%). Lid lag (81.81%) was the commonest sign followed by lid retraction (70.45%), proptosis (56.82%) and conjunctival congestion (52.27%).

Conclusion: There was a high prevalence of thyroid eye disease among the thyroid dysfunction patients. Foreign body sensation, dry eyes, prominent eyes are common symptoms whereas lid lag, lid retraction, proptosis are the common signs of thyroid eye disease.

Keywords: Dry Eyes, Hypothyroid, Proptosis, Thyroid Eye Disease

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Correspondence

Dr. Srijana Thapa Godar, Associate Professor, Department of Ophthalmology, Manipal Teaching Hospital, Phulbari, Pokhara-11, Kaski. Email: drsrijanathapa@gmail.com Telephone: +977 9846073626.

Introduction

Thyroid gland is an endocrine gland which secretes thyroid hormones. Hormonal output from the thyroid is regulated by thyroid-stimulating hormone (TSH) secreted from the anterior pituitary, which itself is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus.¹ Any structural or functional deficit either in thyroid gland or in their stimulating hormone causes thyroid dysfunction and thus causes its harmful effect on the body.²

Thyroid eye disease (TED) is an autoimmune disease affecting ocular and orbital tissues.³ Several theories have been postulated to explain the disorder's unusual association with thyroid autoimmunity. Majority of them favor the role of autoimmunity against a thyroid-stimulating hormone receptor-like protein in the orbital preadipocyte and possibly the extraocular muscle fibers.⁴ The symptoms of thyroid eye disease include dry eyes, redness, prominent eyes, diplopia. The most common clinical sign is eyelid retraction (occurs in 90%), followed by exophthalmos (60%) and eye movement restrictions (40%).⁵

The prevalence of TED ranges from 51.7% in the Caucasian population to 34.7% in Asian population.^{6,7} Two studies conducted in Nepal found the prevalence of TED of 71.7% and 40.8% respectively.^{8,9} Limited studies of TED have been conducted in Nepal and such type of study is lacking from western region of Nepal till date. The finding of this study would help to reduce ocular morbidities and blindness in patients with thyroid dysfunction.

The objective of this study was to assess the prevalence of TED. The study also assessed the prevalence of different clinical profile of TED among patients with thyroid dysfunction.

Method

This was a hospital based cross-sectional study conducted in Ophthalmology Outpatient Department (OPD) of Manipal teaching hospital, Pokhara, Nepal from June 2023 to November 2023. Ethical approval was taken from the Institutional Review Committee of the Manipal College of Medical Sciences, Pokhara before the start of the study. Informed consent was taken from all the patients. The sample size was calculated by using the formula z^2pq/d^2 (where: $z=1.96$, $p=\text{prevalence}^9=40.8$, $q=100-p=59.2$, $d=\text{margin of error } 10\%$). The sample size according to this formula was 93.

Non-probability convenient sampling method was used for the selection of cases. The inclusion criteria were the patients with thyroid dysfunction of aged 30 years and above who presented to Ophthalmology

OPD or referred from endocrine clinic of Department of Internal Medicine. Patients with ocular disorders like conjunctivitis, keratitis, uveitis or if they had history of undergone ocular surgery were excluded from the study. Those patients who did not give consent were also excluded from the study.

Predesigned proforma was used to record the relevant demographic and clinical parameters. The diagnosis of thyroid dysfunction was based on clinical evaluation, thyroid hormone level and classified into hyperthyroid, hypothyroid, and euthyroid. The diagnosis of TED was clinical and based on thyroid disorder associated with a specific one of the thyroid eye signs.¹⁰⁻¹²

Detailed ocular examination was done including recording of visual acuity using Snellen's letter chart or E-chart. Soft-tissue changes, periorbital changes, extraocular motility examination were done with torch light. Anterior segment examination was conducted with slit lamp. Fundus examination under mydriasis with tropicamide 1% was done with +90D Volk lens. Proptosis measurement was conducted with Hertel's exophthalmometer. The eyeball was said to be proptosed if Hertel's reading was over 20 mm or there was a greater than 2 mm difference in degree of proptosis. Intraocular pressure measurement was done with Goldmann Applanation tonometer.

The entry and analysis of the data was done in Epi-info version 7. The statistical methods used were mean, frequency and percentage.

Result

There were 93 patients with thyroid dysfunction, among which 44(47.31%) had TED. Among TED patients, the mean age was 49.93 years (± 14.48), females 34(77.27%). Hypertension was most common comorbidities in 15(34.09%) and family history of thyroid dysfunction was present in 15(34.09%).

Among TED patients hypothyroid was most common in 22(50%). In this study, 9(20.45%) had thyroid dysfunction for less than 12 months. Nearly half of the numbers of patients, 21(47.73%) had thyroid dysfunction of more than 48 months, Table 1.

Among cases with TED ($n=44$), maximum cases had symptoms of foreign body sensation (59.09%), followed by dry eyes (54.55%), discomfort of eyes (52.27%) and prominent eyes (50.0%). Among prominent eyes patients, 34.1% had unilateral and 15.9% had bilateral prominent eyes, Table 2.

Presenting signs in patients with TED showed lid lag (81.81%) was the commonest sign followed by lid retraction (70.45%), proptosis (56.82%), conjunctival congestion (52.27%), restricted movement (36.36%),

punctuate epithelial erosion (20.45%), lid edema (18.18%), raised intraocular pressure (11.36%) and optic neuropathy (4.55%), Table 3.

Table 1. Socio-demographic and clinical variables of the patients with thyroid eye disease (TED) (n=44)

Variables		n	%
Gender	Male	10	22.73
	Female	34	77.27
History of smoking	Yes	7	15.91
	No	37	84.09
Comorbidities	Hypertension	15	34.09
	Diabetes	7	15.91
	Autoimmune disease	1	2.27
Family history	Yes	15	34.09
	No	29	65.91
Systemic thyroid status	Euthyroid	5	11.36
	Hyperthyroid	17	38.64
	Hypothyroid	22	50.0
Duration of thyroid dysfunction(months)	<12	9	20.45
	12-23	5	11.36
	24-35	2	4.55
	36-47	7	15.91
	>48	21	47.73

Table 2. Frequency of presenting symptoms in patients with TED (n=44)

Symptoms of TED	n(%)	
Prominent eyes	Total	22(50)
	Unilateral	15(34.1)
	Bilateral	7(15.9)
Dry eyes	24(54.55)	
Foreign body sensation	26(59.09)	
Discomfort of eyes	23(52.27)	
Watering	4(9.09)	
Blurring of vision	3(6.82)	
Redness	9(20.45)	
Eyelid swelling	4(9.09)	
Diplopia	0	

Table 3. Frequency of presenting signs in patients with TED (n=44)

Signs of TED	n(%)
Proptosis	25(56.82)
Lid retraction	31(70.45)
Lid lag	36(81.81)
Lid edema	8(18.18)
Restricted movement	16(36.36)
Conjunctival congestion	23(52.27)
Punctuate epithelial erosion	9(20.45)
Optic neuropathy	2(4.55)
Optic disc edema	0
Raised intraocular pressure	5(11.36)

Discussion

In this study, the prevalence of TED in thyroid dysfunction patients was 47.31%. Two other studies also supported this finding.^{9,13} However, the studies conducted in Nepal, Korea and India found the prevalence of thyroid eye disease as 71.7%, 17.3%, 35.6% respectively.^{8,14,15} Multifactorial etiologies may affect the prevalence of TED in different ethnic groups.

This study showed that among the patients with thyroid eye disease, maximum patients were hypothyroid (50%), followed by hyperthyroid (38.64%) and euthyroid (11.36%). The other studies conducted in Chitwan, Nepal and Iran also had similar findings.^{13,16} However, other studies conducted in Kathmandu and Dharan in Nepal and India found maximum cases were hyperthyroid followed by hypothyroid and euthyroid.^{8,9,17}

Thyroid eye disease can occur in any form of thyroid dysfunction either hyperthyroid, hypothyroid or euthyroid state. Many explanations for the occurrence of thyroid eye disease in hyperthyroid, hypothyroid and euthyroid states are given in literature. It was hypothesized that different concentrations of

blocking and stimulating antibodies attack the thyroid cell simultaneously, which might cause hypothyroidism or hyperthyroidism.¹⁸

In the current study, females (77.27%) had more thyroid eye disease than males (22.73%). Similarly, other studies also noted that female had more thyroid eye disease than in male.^{9,13,17} However, some literature found male as a predisposing risk factor.^{19,20} The exact reason for the high prevalence in women is unclear. But it is presumed that the effects of female gonadal hormones (prolactin and estrogen) and X chromosome inactivation on thyroid gland and immune system greatly contribute to the female predilection of thyroid disorder in female. The direct actions of estrogens on the thyroid tissue contribute to the development of thyroid goitre, nodule and cancer in women.²¹

The mean age of thyroid eye disease patients in the present study was 49.93 years. This was comparable to other studies reported in the literature.^{8,16,22}

In comorbidities, our study showed that majority of patients had hypertension followed by diabetes and autoimmune disease. Similarly, another study conducted in India found the most

common comorbidities was hypertension followed by diabetes mellitus and autoimmune disorders.¹⁷ However, several literatures had shown that diabetes had a higher incidence of thyroid dysfunction.^{9,13,14,23,24}

The current study showed that 15.91% of patients had given the history of smoking. Studies done in Nepal and India showed that 5% and 25.5% of patients were smoker.^{9,17}

In this study, majority of patients had the duration of thyroid dysfunction of more than 48 months. Similarly, the studies conducted in Nepal and Iran also found that the presence of thyroid eye disease was influenced by the duration of thyroid dysfunction.^{9,16}

In our study, commonest symptoms were foreign body sensation, followed by dry eyes, discomfort of eyes and prominent eyes. Similarly, two different studies done in Nepal also noted that the foreign body sensation was the most common presenting symptom, followed by burning sensation and prominent eyes.^{8,9} However, the studies conducted in India and Iran had reported prominent eyes as the commonest presenting symptoms.^{16,17} Foreign body sensation, dry eyes may be due to the exposure or it may be due to the immunological process associated with thyroid eye disease.

In present study, the commonest sign of thyroid eye disease was lid lag (81.81%) followed by lid retraction (70.45%). Similarly, the three studies also noted the similar findings.^{5,8,9} The study conducted in India found upper eyelid retraction in 63.2% and lid lag in 60.4% of patients.¹⁷ Sympathetic stimulation of the Müller muscle may be responsible for eyelid retraction in patients with Graves disease.²⁵

In our study, the prevalence of proptosis was 56.82%, whereas in other studies conducted in

Nepal and India noted prevalence of proptosis as 33.3% and 64.2% respectively.^{8,17}

Thyroid eye disease has been found to be usually associated with glaucoma. The prevalence of raised intraocular pressure was 11.36% in this study. Another study done in Nepal and India showed the prevalence of raised intraocular pressure of 27.38%, 4.97% and 8.49% respectively.^{8,9,17} The possible cause of raised intraocular pressure might be increased episcleral pressure thus hindering the outflow and increasing intraocular pressure. The other mechanism might be compression of globe by inflamed and fibrosed inferior rectus muscle.

In our study, the prevalence of restricted movement in thyroid eye disease patients was 36.36%. Other different studies noted the prevalence of restricted movement as 9.4%, 11.90% and 47.17%.^{7,8,17} In our study, the prevalence of optic neuropathy was 4.55%. Another study showed the prevalence of optic neuropathy as 1.2%.⁸ However, no cases of optic neuropathy was noted in two different studies conducted in Nepal.^{9,13}

The study has few limitations. The cross-sectional design of the study was the obvious limitation of this study which does not measure causal association. This study was a hospital-based study conducted in one geographical area only. Hence, further large-scale study in different regions of the country may provide better thyroid dysfunction and prevalence data for TED.

Conclusion

Thyroid eye disease is prevalent among patients with thyroid dysfunction. It was more common in females and in hypothyroid patients. There is high prevalence of thyroid eye disease symptoms of foreign body sensation, dry eyes and prominent eyes. There is also high prevalence of signs of lid lag, lid retraction and proptosis. This study emphasizes the importance

of early diagnosis and treatment of thyroid eye disease in thyroid dysfunction patients to prevent ocular morbidities and blindness. Hence, better understanding of thyroid dysfunction patients jointly by endocrinologist and ophthalmologist is recommended.

Author contribution

Concept and design- All; Literature review- All; Data collection and analysis- All; Draft- All; Revision- All; Accountability- All authors have read and agreed to the final version of the manuscript.

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Conflict of interest

None

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Supplementary material

The data and supplementary material that support the findings of this study are available from the corresponding author upon reasonable request.

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