Original Research Article

Clinical features of thyroid-associated ophthalmopathy in a tertiary care teaching hospital

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Abstract

Introduction: Thyroid-associated ophthalmopathy is a complex orbital inflammatory disease, which can be sight threatening, debilitating and disfiguring. Thyroid eye disease is more severe in patients with thyroid dysfunction than in those with euthyroid status. **Material and Methods:** Study Design: This is a prospective and observational study conducted at Department of Ophthalmology. The patients included in the study their demographic data was recorded along with the serum levels of T3, T4, TSH at the time of diagnosis and examination. All the patients detailed ocular examination was carried out with the help of torch light, and slit lamp for anterior segment evaluation, direct ophthalmoscopy for posterior segment evaluation, indirect ophthalmoscopy whenever necessary. Proptosis was measured with the help of Hurtles exophthalmometer and graded as mild-moderate (less than 3 mm) and severe (more than 3 mm). **Result:** A total of 70 patients were examined. Of the 70 cases, male preponderance was noted.The age group 41-60 years had the highest incidence of thyroid orbitopathy, the patients were arbitrarily divided into four groups and least one less than 20 years of age group. Among 70 patients, 13 (18.5%) were hyperthyroid, 54 (77.1%) were hypothyroid, and 6 (8.5%) patients were euthyroid. Most of the patients came with complaint itching of (30.0%). The second most common symptom was foreign body sensation (24.2%). In hyperthyroid lid, retraction was more common (84.6%). In hypothyroid lid, edema was more common (16.6%). Frequency of dry eye syndrome in patients with TD was present; 29 (26.4%) patients had dry eye disease. Among 70 patients, proptosis was present in 3 patients had proptosis. Most of the patients were myopic. **Conclusion:** The present study examined the thyroid-associated ophthalmopathy in a tertiary care teaching hospital. Our results would be helpful in early diagnosis and proper management of thyroid-associated ophthalmopathy.

Keywords: Thyroid-associated orbitopathy, Euthyroid, Hyperthyroid, Hypothyroid

Introduction

Thyroid-associated ophthalmopathy or Thyroid-associated orbitopathy (TAO), frequently termed Graves ophthalmopathy, is part of an autoimmune process that can affect the orbital and periorbital tissue, the thyroid gland, and, rarely, the pretibial skin or digits (thyroid acropachy). [1] This condition is the most common autoimmune disease of the orbit. [2] Although the use of the term thyroid ophthalmopathy is pervasive, the disease process is actually an orbitopathy in which the orbital and periocular soft tissues are primarily affected with secondary effects on the eye. [3] Thyroid-associated orbitopathy is usually self-limiting and associated with Graves disease. In a minority of cases, this condition complicates Hashimoto thyroiditis. Cases have also been reported in hypothyroidism. [4] A retrospective, cross-sectional study of 461 German patients with thyroid-associated orbitopathy found a 4.3% prevalence of euthyroid/hypothyroid and a 95.7% prevalence of hyperthyroid. [5]Thyroid-associated orbitopathy may precede, coincide, or follow the systemic complications of dysthyroidism. Risk factors for thyroid-associated orbitopathy include increased age of onset, duration ofgraves hyperthyroidism, and smoking. [6] The ocular manifestations of thyroid-associated orbitopathy include eyelid retraction, proptosis, chemosis, periorbital edema, and altered ocular motility with significant functional, social, and cosmetic consequences. Of affected patients, 20% indicate the ocular morbidity of this condition is more troublesome than the systemic complications of dysthyroidism. [7] The annual incidence rate of thyroid-associated orbitopathy has been estimated at 16 cases per 100,000 women and 2.9 cases per 100,000 men in one rural Minnesota community. [8] There appears to be a female preponderance, with women are affected 2-6 times more frequently than men; however, severe cases occur more often in men than in women. [9] In addition, most patients are aged 30-50 years, with severe cases appearing to be more frequent in those older than 50 years. [10]Early diagnosis and appropriate monitoring of thyroid-associated orbitopathy may decrease corneal exposure and compressive optic neuropathy. Although most cases of thyroid-associated orbitopathy do not result in visual loss, this condition can cause vision-threatening exposure keratopathy, troublesome diplopia, and compressive optic neuropathy. Therefore, although the prognosis is generally favorable for patients with this condition, and most patients do not require surgical intervention, all clinicians should be able to recognize thyroid-associated orbitopathy.

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Material and Methods

Study Design: This is a prospective and observational study conducted at Department of Ophthalmology.

Inclusion criteria

All the Age groups with either gender subjects who were diagnosed with thyroid disease or those thyroid eye diseases with euthyroid

status with thyroid hormone profile at the time of diagnosis and at the time of examination visiting Ophthalmology OPD, and who gave consent for this study are included.

Exclusion criteria

Patients without thyroid hormone profile or those who didn't give consent are not included in this study. Patients with thyroid disease and with age less than 10-year-old were excluded from the study.

Sampling method: The patients included in the study their demographic data was recorded along with the serum levels of T3, T4, TSH at the time of diagnosis and examination. All the patients detailed ocular examination was carried out with the help of torch light,and slit lamp for anterior segment evaluation, direct ophthalmoscopy for posterior segment evaluation, indirect ophthalmoscopy whenever necessary. Proptosis was measured with the help of Hurtles exophthalmometer and graded as mild-moderate (less than 3 mm) and severe (more than 3 mm). Simple ruler scale was used for evaluation of upper lid retraction and it was graded as mild-moderate (less than 2 mm) and severe (more than 2 mm). Schirmers test was used for the evaluation of dry eye disease and was considered negative if more than 10 mm of wetness of the Schirmers strip over 5 minutes.The present study also observed the presence of conjunctival chemosis, congestion, diplopia, restriction to extra ocular movements and intraocular pressure was measured by using Goldman's applanation tonometry technique.The extraocular motility (EOM) function was assessed by asking the patient to move their eyes in an H-shaped pattern while severity of EOM was defined as the presence of chemosis, lid edema.

Statistical analysis: Then data was entered on SPSS software and analysed by using chi square test and one way annova test was used to establish the significance of serum levels of T3, T4, TSH at the time of study and Pre T3, Pre T4 and Pre TSH at the time of diagnosis of thyroid disease with the
severity and the frequency of thyroid eye disease signs.

Results

A total of 70 patients were examined. Of the 70 cases, male preponderance was noted as shown in table 1.

Table 1: Sex distribution of patients

Sex	No. of patients	Percentage
Male	28	40
Female	42	60
Total	70	100

Table 2: Age distribution of patients

Age group	No. of patients	Percentage
<20	4	5.7
21-40	23	32.8
41-60	34	48.5
>61	9	12.8
Total	70	100

According to table 2, 41-60 years age group had the highest incidence of thyroid orbitopathy, the patients were arbitrarily divided into four groups and least one less than 20 years of age group.

Table 3: Ocular manifestations

Thyroid status	No. of patients	Percentage
Hyperthyroid	13	18.5
Hypothyroid	54	77.1
Euthyroid	3	8.5
Total	70	100

In table 3, among 70 patients, 13 (18.5%) were hyperthyroid, 54 (77.1%) were hypothyroid, and 6 (8.5%) patients were euthyroid.

Table 4: Severity of Thyroid-associated ophthalmopathy

Severity of TAO	No. of patients	Percentage
Mild	51	72.8
Moderate	16	22.8
Severe	3	4.2.
Total	70	100

Table 5: Symptoms of thyroid eye disease patients

Sign	No. of patients	Percentage
Itching	21	30
Foreign body sensation	17	24.2
Dry eye	9	12.8
Lid swelling	7	10
Redness	6	8.5
Difficulty in reading	5	7.1
Protrusion of eye	3	4.2
Diminution of vision	1	1.4
Watering	1	1.4

In table 4 shows the frequency of different symptoms among the study group. Most of the patients came with complaint itching of (30.0%). The second most common symptom was foreign body sensation (24.2%).

Table 6: Ocular Signs in hyperthyroidism patient

Sign	Hyperthyroid, N=13 (%)	Hypothyroid, N=54 (%)
Lid edema (Enroth's sign)	7 (53.8)	9 (16.6)
Lid retraction (Dalrymple sign)	11 (84.6)	-
Lid lag (Graefe's sign)	9 (69.2)	-
Conjunctival congestion	3 (23.0)	2 (3.7)
Corneal ulcer	2 (15.3)	1 (1.8)
Proptosis	3 (30.7)	-
Scleral show	7 (53.8)	-
Increased palpebral aperture	6 (46.1)	-
Restrictive myopathy	1 (7.6)	-
Refractive error	12 (92.3)	42 (77.7)
Increase IOP with optic disk and visual field change	1 (7.6)	-

In table 5 shows the different types of signs among these two groups. In hyperthyroid lid, retraction was more common (84.6%). In hypothyroid lid, edema was more common (16.6%). Frequency of dry eye syndrome in patients with TD was present; 29 (26.4%) patients had dry eye disease. Among 70 patients, proptosis was present in 3 patients had proptosis. Most of the patients were myopic.

Discussion

Thyroid eye disease can be an extremely distressing condition that affects both men and women, primarily in their formative years. Fortunately, our understanding of the disease process has increased dramatically of late, allowing for targeted treatments that have the potential to change the course of the disease. Here, discusses the epidemiology of TED, the anatomy involved, how it affects the eye and how to best diagnose it. [11]

Pathophysiology

The thyroid gland, located in the neck, is chiefly responsible for secreting thyroid hormones. These hormones are integrally involved in almost every process of the body, including regulation of the heart, lungs, brain and metabolism. If the thyroid produces too much of the hormone thyroxine, hyperthyroidism occurs. Hyperthyroidism leads to cell growth, both via the effects of the hormone and via the IGF-1 (insulin like growth factor) pathway, which is connected to the thyroid hormone receptor. Activation of these two pathways leads to growth of fat, muscle and fibrous cells, causing the characteristic clinical manifestations of thyroid eye disease. [12] In general, between 25 and 50 percent of patients with a thyroid problem (hyperor hypothyroidism) will go on to develop some form of TED, with roughly 5 percent having a moderate to severe form of the disease that can affect vision. Interestingly, once TED starts, it's a separate process from the initial thyroid abnormality, with very little interaction between the two. Specifically, once patients develop TED, having well-controlled thyroid hormone levels won't make the eye disease better, although having poorly-controlled thyroid hormone levels may make it worse. Though strides are constantly being made, it's still unclear exactly why patients with a thyroid-hormone abnormality develop the eye disease. [13]In our study, there was female preponderance. Out of 70 patients, 42(60%) were female and 28(40%) were male. This was similar to the results of Palikhe et al. who reported 80 (68.4%) patients were females and 37 (31.6%) were male. [14] In our study, females more commonly, and is seen in the 4^{th} and 5^{th} decades of life and commonly in females as cited by many previous studies. The mean age of presentation of the TED was 41.84 years in our study. This was similar to the results of Patel A et al. who reported median age as of 43 years and 39.7 years by Rajai et al. who documented 39.7 years as the median age. [15,16]In our study, TED can occur in any form of TD either hyper, hypo, or euthyroid state. In our study, out of 70 TED patients, 13(18.5%) were hyperthyroid and 54(77.1%) were hypothyroid. The study by Agnihotri P et al. showed that out of 84 TED patients, 63 (75%) were hyperthyroid, 14(16.7%) were hypothyroid, and 7(8.3%) were euthyroid. [17] A study reported by DeParis SW et al. at Mayo Clinic,Rochester,USA,has cited that 90% patients were hyperthyroid, 6% euthyroid, 1% had primary hyperthyroidism, and 3% had Hashimoto's thyroiditis. [18] In our study showed that eyelid retraction was present in 84.6% (n = 13) which was similar to results of Choudhari P.C et al. by 79.8%. [19] Another study by Sabita P et al. reported that lid retraction was present in 98% of the patients. [20] Similarly, lid lag was present in 70.6% (n = 17) of cases in our study while it was reported as 76.2% by Holthoff HP et al. and 43.33% by Chen Q et al. [21,22] This difference could be due to ethnic variation and also due to varying degree of disease severity. Restrictive extraocular myopathy was seen in only in 7.6% in patients with hyperthyroidism. This finding is similar to that found in the study by Sarfo-Kantanka et al. [23] In our study, corneal ulcer was seen in 15.3 % of cases of hyperthyroidism. The possible cause of increased intraocular pressure (IOP) and thus causing optic neuropathy might be increased episcleral pressure which hinders the outflow thus increasing IOP. The other mechanism of increased IOP might be compression of the globe by inflamed and fibrosed inferior rectus muscle.

Conclusion

Most of the patients who come for ophthalmic department with TAO are females belonging to 20 – 40 years of age. Though many of them had toxic thyroid symptoms and swelling, even enlargement of EOM on USG, 'B' scan orbit and CT scan the proptosis was mostly minimal. Many of them were on medical Treatment associated with proptosis for thyroid and required systemic steroids for arresting progression of ophthalmic disease. The most important reason for consulting ophthalmologists is to get a good cosmetic appearance since many of these patients have marked lid retraction, with even minimal proptosis, cause an ugly starring look either unilaterally or bilaterally.

References

1. Heisel CJ, Riddering AL, Andrews CA, Kahana A. Serum vitamin D deficiency is an independent risk factor for thyroid eye disease. Ophthalmic PlastReconstr Surg. 2020;36:17-20
2. Diana T, Kahaly GJ. Thyroid stimulating hormone receptor antibodies in thyroid eye disease-methodology and clinical applications. Ophthalmic PlastReconstr Surg. 2018;34:S13-9.
3. Kahaly GJ, Riedl M, König J et al.Mycophenolate plus methyl prednisolone versus methylprednisolone alone in active, moderate- to-severe Graves' orbitopathy(MINGO):a randomi-sed,observer-masked,multicentre trial.Lancet Diabets Endo-crinol. 2018; 6:287-98.
4. Ye X, Bo X, Cui H, Lu B, Shao J, Wang J. Efficacy and safety of mycophenolate mofetil in patients with active moderate-to-severe Graves' orbitopathy. ClinEndocrinol (Oxf). 2017;86: 247-55.
5. Leszczynska A, Molins B, Fernandez E, Adan A, Ortiz-Perez S. Cytokine production in thyroid eye disease: in vitro effects of dexamethasone and IL-6 blockade with tocilizumab. Graefes Arch ClinExpOphthalmol. 2019;257:2307-14.

6. Perez-Moreiras JV,Gomez-Reino JJ, Maneiro JR et al. Efficacy of tocilizumab in patients with moderate-to-severe cortices-teroid-resistant Gravesorbitopathy: a randomized clinical trial. Am J Ophthalmol. 2018;195:181-90.
7. Salvi M, Vannucchi G, Curro N et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. J Clin Endocrinol Metab. 2015;100:422-31.
8. Stan MN, Garrity JA, Carranza Leon BG, Prabin T, Bradley EA, Bahn RS. Randomized controlled trial of rituximab in patients with Graves' orbitopathy. J Clin Endocrinol Metab. 2015; 100: 432-41.
9. Smith TJ, Kahaly GJ,Ezra DG et al.Teprotumumab for thyroid-associated ophthalmopathy.N Engl J Med. 2017;376: 1748-61.
10. Douglas RS. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: a focus on proptosis. Eye (Lond). 2019;33:183-90.
11. Hao HT,Wang Y,Wang X et al. Treatment of Graves' ophthalmopathy with an in-house phosphorus-32 source: initial clinical observations. ExpTher Med. 2017;14:2795-800.
12. Wu CY, Niziol LM, Musch DC, Kahana A. Thyroid related orbital decompression surgery: a multivariate analysis of risk factors and outcomes. Ophthal Plast Reconstr Surg. 2017;33(3): 189–95.
13. Mellington FE, Dayan CM, Dickinson AJ, Thyroid Eye Disease Amsterdam Declaration Implementation Group (TEAMeD), et al. Management of thyroid eye disease in the United Kingdom: a multicentre thyroid eye disease audit. Eye Disease Amsterdam Implementation Group UK. Orbit. 2017;36(3):159–69.
14. Nicosia L, Reverberi C, Agolli L et al. Orbital radiotherapy plus concomitant steroids in moderate-to-severe Graves' ophthalmopathy: good results after long-term follow-up. Int J Endocrinol Metab. 2019;17(1):e84427.
15. Patel A, Yang H, Douglas RS. A new era in the treatment of thyroid eye disease. AJO. 2019;208: 281–8.
16. Rajaii F, McCoy AN, Smith TJ. Cytokines are both villains and potential therapeutic targets in thyroid associated ophthalmop-athy. From bench to bedside.Expert Rev Ophthalmol. 2014; 9(3):227–34.
17. Agnihotri P, Choudhary P, Chandravanshi SCL. Clinical Study of Ocular Manifestations of Thyroid Disease in Tertiary Eye Care Center. Int J Sci Stud. 2019;7(4):46-52.
18. DeParis SW, Tian J, Rajaii F. Practice patterns in orbital decompression surgery among American Society of Ophthalmic Plastic and Reconstructive Surgery members. OphthalmolTher. 2019;8:541–8.
19. Choudhari PC, Usgaonkar U, Shrivastav D. Ophthalmic manifestations of thyroid disease and the association of serum levels of T3, T4 and TSH with thyroid eye disease. Trop J OphthalmolOtolaryngol.2019;4(8):468-477
20. Sabita P, Ajit T, Narayan SD, Kumar SA, Niranjan A. Ocular manifestations in thyroid eye disorder: a cross-sectional study from Nepal. Int J Clin Med. 2016;7(12):814-823.
21. Holthoff HP, Li Z, Fabbender J et al.Cyclic peptides for effective treatment in a long-term model of Graves disease and orbitopathy in female mice. Endocrinology. 2017;158(7):2376–90.
22. Chen Q. The expression of interleukin-15 and interleukin-17 in tears and orbital tissues of Gravesophthalmopathy patients. J Cell Biochem. 2019;120(4):6299–303.
23. Sarfo-Kantanka O, Sarfo FS, Ansah EO, Yorke E, Akpalu J, Nkum BC et al. Frequency and determinants of thyroid autoimmunity in Ghanaian type 2 diabetes patients: A case -control study. BMC Endocr Disord. 2017;17:2.

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