Original Article

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Clinical Study of Thyroid Orbitopathy

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Abstract

Aim: To study the age, sex, causal distribution, incidence and various modes of presentation of Thyroid Orbitopathy.

Methods: 40 patients with a diagnosis of Thyroid Orbitopathy seen between October 2016 - October 2018 were included in this study. A complete ophthalmic examination including visual acuity, ocular motility, exophthalmometry, intraocular pressure, slit lamp examination and fundoscopy was done.

Results: Among 40 patients with Thyroid Orbitopathy, 28 (70%) were females and 12 (30%) were males. Mean age of the patients was years 41.82 years (range 18-67). The female: male ratio was 2.3:1. 28 patients (70%) had Grave's hyperthyroidism, 8 patients (20%) had euthyroidism and 4 patients (10%) were hypothyroid. 80% of the patients had bilateral involvement. The most common ocular signs were eyelid retraction (80%), periorbital oedema (62.5), proptosis (60%) and chemosis (60%). Involvement of extraocular muscles in the descending order of frequency was inferior rectus (70%), medial rectus (50%), superior rectus (27.5%) and lateral rectus (15%).

Coclusion: Eyelid retraction was the most common clinical sign of Thyroid Orbitopathy in our patients. On orbital computed tomography (CT) scanning inferior rectus was the most commonly involved muscle. Lower eyelid retraction should be included in the diagnostic criteria in Asian patients.

Keywords: Thyroid Orbitopathy; Hyperthyroidis; Eyelid retraction; Periorbital oedema; computed tomography (CT) scanning

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Introduction

Thyroid eye disease (TED), also called Graves' orbitopathy (GO) is a potentially sight threatening ocular disease, mostly occurring in patients with hyperthyroidism or a history of hyperthyroidism due to Graves' disease (GD). However, it can occur in patients with euthyroid or hypothyroid chronic autoimmune thyroiditis as well and about 5-10% of patients with TED are euthyroid at presentation [1]. A prevalence of 34.7% has been reported in the in the Asian population and 28% prevalence has been reported in Indian studies among the Graves' disease patients [2,3]. Females are more commonly affected than males. However, for severe disease, this ratio reverses and severe thyroid eye disease is approximately 4 times more common in males than females [4].

The ocular changes associated with thyroid disease were first published by Graves' in 1835 and by Von Basedow in 1840. They noted swelling of tissues around the eyes in patients with hyperthyroidism but in 1786 Parry described a condition of goiter and eye protrusion [5].

The most significant pathological findings in TAO include glycosaminoglycan (GAG) deposition (accompanied by swelling resulting from the hydrophilic capacity of these macromolecules), fibrosis affecting the extraocular muscles, and adipogenesis in the orbit [6,7,8,9]. GD is an autoimmune disorder where loss of immunological

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tolerance to the thyroid-stimulating hormone receptor (TSH-R) is pivotal to the appearance of the specific antibodies [10,11].

It may occur before, with, or after the onset of overt thyroid disease and usually has a slow onset over several months. Clinical symptoms and signs are usually mild, consisting of ocular irritation with redness and tearing, stare due to lid retraction and exophthalmos, and periorbital swelling. Approximately 28% of GO cases are severe, with restricted motility leading to diplopia, exposure keratopathy, and optic neuropathy [12], 13. Management should consist of a coordinated, multidisciplinary, medical and surgical approach based on nature of the disease and its effect on the orbital and ocular structures. It is usually directed by abating or controlling the active phase of the disease, prevention of ocular and psychophysical damage, redressing ocular motor abnormality, and improving the cosmetic disfigurement 5. The current therapeutic options are corticosteroids, external beam radiation and steroid–sparing immunosuppressive agents for reducing the inflammation during active phase, and surgery for correcting the residual abnormalities secondary to fibrosis in the inactive phase of the disease. These interventions are aimed at the consequences of the disease rather than targeting its cause 14. Unfortunately, these treatments do not prevent or reverse the pathological changes in the orbital tissues [15].

Materials and Methods

This is a prospective study conducted over a period of 2 years (October 2016- October 2018). All the patients who were diagnosed with Thyroid orbitopathy at Narayana Medical College and Hospital, Nellore were included in this study. All the cases with similar presentation not proved to be Thyroid Orbitopathy and patients who did not report for the follow–up were excluded from the study. Information about age, occupation, family history, ocular symptoms and associated systemic diseases were obtained.

A comprehensive ophthalmic examination was performed in a standardized way for all patients. Best corrected visual acuity was documented by Snellen chart. Intraocular pressure (IOP) was measured by applanation tonometer in the primary position and with upward gaze. Eyelid, conjunctiva and ocular motility were assessed. Tear status was evaluated with Schirmer test and tear break-up time. We considered Schirmer < 10 mm and tear break-up time < 10 seconds as tear film dysfunction. The degree of proptosis was measured by the Hertelexophthalmometer. Proptosis was defined as the measurement of protrusion of the globe > 20 mm from the lateral orbital rim in either eye or any discrepancy in the degree of protrusion of the 2 eyes by > 2mm. Fundus examination was done for the evaluation of disc and retina.

Apart from the routine hematological examinations, the patient was subjected to radiological investigations like ultrasound or CT scan or both as per the clinical requirement to assess the lesion as well as monitor its progression or regression. Serological investigations which include Thyroid profile was also done. Once the case was confirmed to be of thyroid orbitopathy, depending on the stage of clinical presentation, the patients were reassured and observed. All patients were referred to an endocrinologist for management of thyroid dysfunction and then they were followed for a period of 6 months. The first follow up was at the 1st week and then at 1st, 3rd and 6th months.

Results

A total of 40 patients were examined. The mean age of the patients was 41.82 years (range 18-67). Of the 40 cases analyzed, female preponderance was noted (Table 1).

Table 1: Sex distribution

Sex	No. of patients	Percentage
Males	12	30%
Females	28	70%
Total	40	100%

To analyze which age groups had the highest incidence of thyroid orbitopathy, the patients were arbitrarily divided into three groups; <25, 25-50, and >50. Maximum numbers of patients were present in the 25-50 years of age group (Table 2).

Table 2: Age distribution

Age Groups	No. of patients	Percentage
<25	04	10%
25-50	28	70%
>50	08	20%

Based upon the thyroid status of the patients, they were subdivided into three groups namely: Hyperthyroid, Euthyroid and Hypothyroid. 70% of the patients were hyperthyroid followed by euthyroid in 20% and then hypothyroid in 10% of

the patients (Table 3).

Table 3: Thyroid status

Category	No. of patients	Percentage
Hyperthyroid	28	70%
Euthyroid	08	20%
Hypothyroid	04	10%

The modes of presentations were analyzed. It was found that lid retraction was the most common mode of presentation. The data regarding the various modes are as follows (Table 4).

Table 4: Modes of presentation

Modes of Presentation	Numbers	Percentage
Lid retraction	32	80%
Periorbital swelling	25	62.5%
Proptosis	24	60%
Chemosis	24	60%
Congestion	18	45%
Dry eyes	05	12.5%
Diplopia	04	10%
Motility defects	04	10%

Next the laterality of orbitopathy was analyzed. The most common presentation was found to be Bilateral than unilateral (Table 5).

Table 5: Laterality status

Laterality	Numbers	Percentage
Bilateral	32	80%
Unilateral	08	20%
Right eye	06	15%
Left eye	02	5%

The incidence of involvement of the various recti muscles was also analyzed based upon ultrasonography and computed tomographic findings. It was found that inferior rectus was the commonest muscles involved followed by medial rectus, superior rectus –LPS complex and lateral rectus in descending order (Table 6).

Table 6: Muscle involvement

Muscle involved	Numbers	Percentage
Inferior rectus	28	70%
Medial rectus	20	50%
Superior rectus	11	27.5%
Lateral rectus	06	15%

Discussion

Thyroid associated orbitopathy (TAO) is a clinical manifestation of Grave's disease (GD), and autoimmune disorder that can affect the orbital and periorbital tissue, the thyroid gland, and rarely, the pretibial skin or digits (thyroid acropachy) [16,17, 18]. Among Malaysians and Indians, a prevalence of 34.7% and 28% has been reported, respectively [3,19]. An annual incidence of 16 cases/100000 for women and 2.9 cases for men has been documented in a population in the USA [20].

The prevalence and severity have, however, been observed to have declined in recent years [21,22]. This trend might be as a result of earlier diagnosis and treatment, enhanced attention of the ophthalmologists to the link between the initial ocular manifestations and thyroid dysfunction, and changes in smoking behavior [21].

TAO poses clinical and therapeutic challenges. The severity of the disease is mild to moderate and self-limiting in a majority of patients. It may precede, coincide, or follow the systemic manifestations of GD. Ocular manifestations range from mild symptoms to more significant findings including vision loss from compressive optic neuropathy [16, 17,20].

Therefore, this study was undertaken to study the clinical manifestations in 40 patients with thyroid orbitopathy.

Age Distribution

In our study, the mean age of the patients was 41.82 years. Mean age for the females was 40 years and for the males was 46.08 years. In JurateJankauskiene et al. study [23], the mean age of the patients was 42.7 years (range from 17 to 59 years). In Savku et al. study [24], mean age of the patients was 42.3 years (range 18-82 years). Mean age of the patients in JurateJankauskiene et al. [23] and Savku et al. [24] studies was slightly similar to our study. In L. Bartalena et al. study [25], the mean age of the patients was 47.4 years. In W. M. Wiersinga et al. study [26], the mean age of the patients was 45.5 years. Mean age of the patients in L. Bartalena et al. [25] and W. M. Wiersinga et al. [26] studies was slightly higher than our study.

Sex Distribution

In our study, there were 28 females and 12 males. Female to male ratio was 2.3:1. In JurateJankauskiene et al. study [23], female to male ratio was 2:1. In W. M. Wiersinga et al. study [26], female to male ratio was 2.75:1. In JurateJankauskiene et al. [23] and W. M. Wiersinga et al. [26] studies female to male ratio

was slightly similar to our study. In Qian Li et al. study [27], which was held in China, the incidence of male and female patients was roughly equal, with a female-to-male ratio of 1.09:1. In Ali Sadeghi et al. study [28] which was conducted in Iran, the female to male ratio was 1:1.7. This was against our study.

Thyroid Status

In our study, 28 patients (70%) were hyperthyroid, 8 patients (20%) were euthyroid, and 4 patients (10%) were hypothyroid. In Ogun and Adeleye et al. study [29], 78% of the patients were hyperthyroid, 11.8% were euthyroid, and only 9.8% of the patients were hypothyroid. In M.E. Razavi et al. study 30, the majority of the patients had hyperthyroidism (82%), euthyroidism was present in 10.8% of the patients, and only 3 % of the patients were hypothyroid. Ogun and Adeleye et al. [29] and M. E. Razavi et al. [30] studies were similar to our study.

Laterality Status

In our study, 32 patients (80%) had bilateral involvement while only 8 patients (20%) had unilateral involvement. In Qian Li et al. study [27], the majority of the patients presented with bilateral disease (85.54%). The unilateral disease was present in 14.46% of the patients. In Ali SadeghiTari et al. study [28], 88.3% of the patients had bilateral involvement. Unilateral eye disease was present in only 12 patients (11.65%). Qian Li et al. [27] and Ali SadeghiTari et al. [28] studies were similar to our study.

Clinical Features

In our study, the most common signs of TED in the descending order of frequency were:Lid retraction (80%), Periorbital edema (62.5%), Proptosis (60%), Chemosis (60%), Congestion (45%), Dry eye (12.5%), Motility defects (10%), Diplopia (10%).

In Bartley et al. study [31], he indicated that eyelid retraction was the most common sign of Grave's ophthalmopathy and being present at diagnosis in 75% of the patients. This study was similar to our study.

In Nigel C S Lim et al. study [32], the commonest sign on ophthalmic examination was eyelid retraction (62.1%), followed by proptosis (61%) and conjunctival injection (55.7%). This study was similar to our study. But there was less incidence of lid retraction, and more incidence of conjunctival congestion in their study wherein in our study lid retraction and conjunctival congestion were noted in 80% and 40% of the patients respectively.

Shueh Lin Lim et al. [33] stated that the occurrence rate of upper eyelid retraction was lower compared to American and European patients. This difference may be due to a number of possible factors. Asian orbits are smaller, so any enlargement of orbital contents will more likely push the globe forward. A relatively shallower orbit and a more obtuse angle between the longitudinal axes of the orbits could combine to give rise to the higher mean values for blacks than for whites [34].

Shueh Lin Lim et al. [33] studies concluded that lower lid retraction is a common feature in Asian patients with TAO and perhaps should form a part of the diagnostic criteria in the evaluation of TAO.

Muscle Involvement

In our study, the most commonly affected muscle in the descending order of frequency was, Inferior rectus (70%), Medial rectus (50%), Superior rectus (27.5%), Lateral rectus (15%).

In Ali Sadeghi Tari et al. study [28], the commonly affected muscles in the descending order of frequency were inferior rectus (68%), medial rectus (55%), superior rectus (38%), and lateral rectus (15%). W.M. Wiersinga et al. [26] study demonstrated enlargement of inferior rectus in 60%, medial rectus in 50%, superior rectus in 40% and lateral rectus in 22%. Ali Sadeghi Tari et al. [28] and W.M. Wiersinga et al. [26] studies were similar to our study

Conclusion

Thyroid eye disease (TED) is an extremely unpleasant, painful, cosmetically distressing and occasionally sight threatening condition. It can be manifested in all thyroid states and is the most frequent extra-thyroidal manifestation of Grave's disease. Non-severe TED requires only supportive measures, such as eye ointments, sunglasses and prisms. In contrast, severe TED requires aggressive treatment, either medical (high-dose glucocorticoids, orbital radiotherapy) or surgical (orbital decompression) [35,36].

Thyroid orbitopathy is a matter of important health concern among patients with thyroid disorder. Since TED occurred with a high prevalence in all thyroid states, a close collaboration between the endocrinologists and ophthalmologists along

with timely referrals of patients with any eye complaint is deemed necessary.

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