

A DESCRIPTIVE CROSS-SECTIONAL STUDY ON THE ROLE OF ULTRASONIC B SCAN IN THYROID EYE DISEASE

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Abstract

Background: In this study, to evaluate the orbital content changes using ultrasonic B-scan in thyroid eye disease due to hyperthyroidism, assist in early detection of thyroid eye disease, assess the response of treatment in TED and progress of disease. **Materials and Methods:** A hospital-based descriptive cross-sectional study conducted among 45 patients- 90 eyes who presented with clinical signs and symptoms of thyroid eye disease due to hyperthyroidism, in Regional Institute of Government Ophthalmic Hospital, Chennai, for 1 year, after obtaining clearance from the institutional ethics committee, and written informed consent from the study participants. **Result:** The four recti muscles were significantly thicker. The mean of the sum of all four recti muscles in mild category was 15.7 mm in BE, moderate category was 20.5 mm in BE and severe category was 32 mm in BE. A severe form of TED was found to generally result in a higher exophthalmometric measurement of proptosis and eye muscle thickness (P value < 0.001). In thyroid eye disease, enlargement of the muscle belly with sparing of tendon insertion is the characteristic appearance in B-scan. Our result showed EOM enlargement to be the principal cause of proptosis. **Conclusion:** Difficult to distinguish the thickened muscle with high reflectivity from the surrounding orbital soft tissue. This can be avoided by decreasing the gain setting to get a better visualization of the muscle sheath.

INTRODUCTION

Thyroid Eye Disease (TED) also known as thyroid-associated orbitopathy and Graves ophthalmopathy is a self-limiting autoimmune inflammatory orbital disorder affecting orbital fat, extra-ocular muscle and lacrimal gland. It is the most common aetiology of both unilateral and bilateral proptosis in adults. The majority of TED about 90% is seen in Graves' disease (the most common form of hyperthyroidism), the remaining 5- 10% is seen in Hypothyroid and Euthyroid status, and 3% in Hashimoto's thyroiditis. TED affects women 5 times more commonly than men. Presentation is often seen in the 4th -5th decade, disease worsens as age increases. Smoking increases the risk and severity of TED by 7 times. The clinical diagnosis is based on the association of thyroid function status and ocular signs. The patient may develop a mild form of TED to a more severe form resulting in functional visual impairment and permanent

cosmetic disfigurement. Historical perspective of thyroid eye disease In 1802, G. Flajani, a skilled anatomist and surgeon showed the association between goitre and exophthalmos. C H Parry, in 1825, described hyperthyroidism but he didn't mention eye involvement. C. Von Basedow also described these clinical features in 1840. In the year 1843, Robert J. Graves described enlargement of the thyroid gland, palpitation, tachycardia and protrusion of the eyeball.

Biosynthesis and secretion of thyroid hormone

1. Regulate synthesis of thyroid hormone.
2. Synthesis and secretion of thyroglobulin
3. Iodide trapping
4. Oxidation of iodide
5. Transport of iodine into follicular cavity 6- Iodination of tyrosine
6. Coupling reactions
7. Storage of thyroid hormones. In blood, thyroid hormones are transported by
8. Thyroxine binding globulin (70%)

9. Thyroxine binding pre-albumin (10- 15%)
Albumin (20-25%)

Thyroid hormone functions

Every cell in the body is acted upon by the thyroid hormone. It increases the basal metabolic rate, affects the synthesis of protein, helps to regulate the growth of long bones, neural maturation, proper development and differentiation of all cells in the body, regulates the metabolism of fat, protein, and carbohydrate and helps in body heat generation.

ORBIT The two bony orbits are pear-shaped cavity lying between the anterior cranial fossa above and the maxillary sinus below.

Dimensions

1. Volume of orbit – 30 ml.
2. Depth of orbit – 40-45mm
3. Width of orbital base – 40mm
4. Height of orbital base – 35mm

Each bony orbit is formed by 7 bones: Frontal, ethmoid, lacrimal, palatine, maxilla, zygomatic and sphenoid. Each orbit has 4 walls

Medial wall

It is quadrilateral in shape and formed by the frontal process of the maxilla, lacrimal bone, the orbital plate of the ethmoidal bone and the body of the sphenoid.

Inferior wall (floor)

The floor of the orbit is a triangle in shape.

It is formed by 3 bones:

- The orbital part of maxillary bone – medially
- Orbital surface of zygomatic bone – laterally
- Palatine bone – superiorly
- Lateral wall - It is the thickest and strongest wall, made up of zygomatic bone anteriorly and a greater wing of sphenoid posteriorly. The roof

The vault of the orbit is formed by the orbital plate of the frontal bone and the lesser wing of the sphenoid.

Orbital content

1/5th of the volume is occupied by the eyeball, levator palpebrae superioris, Muller muscles, extra-ocular muscles, orbital fat, orbital fascia, reticular tissue, lacrimal gland and lacrimal sac, vasselsan ophthalmic artery and its branches, infraorbital vessels, orbital branch of the middle meningeal artery, superior and inferior ophthalmic artery. Nerves – optic nerve, 3rd, 4th, 6th nerve, branches of V1 (lacrimal, frontal, nasociliary), branches of the maxillary division of 5th nerve (infraorbital and zygomatic nerve).

Thyrotoxicosis

Thyrotoxicosis (hyperthyroidism) is a condition in which there is excess secretion of thyroid hormones. The most common type of hyperthyroidism - Graves' disease is an autoimmune inflammatory disorder in which IgG Ab binds to the TSH receptor in the thyroid gland resulting in excess secretion of thyroid hormones.

Signs and symptoms

- Behavioural: Hyperactivity, irritability, restlessness, tremors.
- Excessive sweating, hunger, fatigability, heat intolerance, mood swings, insomnia, nervousness.
- Heart: palpitations, tachycardia, abnormal rhythm.
- Menstrual: irregular menstrual amenorrhea.
- Weight loss despite a good appetite, diarrhoea, loss of hair, warm skin, palmar erythema, loss of libido.
- Goitre- enlargement of the thyroid gland.
- Thyroid acropathy accounts for 1% - of clubbing of fingers.
- Pretibial myxedema accounts for 1-5% - of indurated thickened skin of the shin.

Risk factors for TAO

- Gender – male
- Age - older age group
- Cigarette smoking
- Systemic illness – diabetes
- Onset of disease – acute
- Imbalance in thyroid status initially
- Radioactive iodine exposure.
- Low selenium level

Pathogenesis

- It is an organ-specific autoimmune disorder
- Inflammation of orbital tissue occurs via stimulation of orbital fibroblast
- Orbital fibroblast expresses CD40 receptor and TSH receptor
- Interacts with T cells
- Results in the release of proinflammatory cells such as cytokines, IL-6,
- Leads to the synthesis and deposition of glycosaminoglycans and hyaluronic acid
- Results in osmotic imbibition of water
- Increase in the volume of orbital content mainly EOMs.

Orbital fibroblast

It originates from neural crest cells and can be differentiated into

1. Adipocytes
2. Myofibroblast.

Autoimmune response

1. Antigen dependent
 - Orbital fibroblast expresses IGF-1R and TSHR
 - Stimulation of these receptors results in the release of cytokines and deposition of GAGs in orbital tissue.
2. Antigen independent
 - Cytokines, chemokines, monocytes, NK cells, and granulocytes directly activate a cell-mediated immune response
 - Leads to the infiltration of inflammatory cells.

Clinical manifestations

TED may present in two stages

1. Active / Congestive / Inflammatory stage:
Characterized by signs of inflammation such as

enlargement of muscle, chemosis, conjunctival injection, and swelling of periorbital tissue. It typically waxes and wanes and is stable within 3 years in 90% of patients.

2. Quiescent/ Fibrotic stage: Follows resolution of active phase present as painless ocular motility defect due to fibrosis of muscle.

Aims and objectives

- To evaluate the orbital content changes in TED due to hyperthyroidism using B-scan ultrasonography.
- To assist in the early detection of thyroid eye disease using the B-scan
- To assess the response to treatment in TED
- To assess the progress of the disease using the B-scan.

MATERIALS AND METHODS

Ophthalmic Workup

All patients underwent complete ophthalmic workup which included best corrected visual acuity using Snellen's chart, intraocular pressure by Goldmann applanation tonometry, slit lamp biomicroscopy for anterior segment evaluation, colour vision and field of vision, diplopia charting, ocular motility test, Hertel's exophthalmometry for measurement of proptosis, and posterior segment examination using ophthalmoscopy. Based on clinical disease activity [EUGOGO classification], patients were categorized into a mild, moderate and severe forms of TED.

Inclusion Criteria

- Age group above 15
- Both sex
- Thyroid eye disease due to hyperthyroidism

Exclusion Criteria

- Children below 15 years of age

- Other orbital diseases such as noninfective, inflammatory diseases like orbital pseudotumor, orbital myositis, and orbital tumours.

Objective assessment-ultrasonic B-scan

Contact non-invasive non-immersion A-B mode ultrasonic scan with 8-15 MHz was used in our study. It provided topographic information of extraocular muscle thickness and tendon status using a medium gain setting with the patient fixating in primary gaze/ approximately 10° towards the direction of muscle and transverse mode with the probe placed at the equator of the globe opposite to the muscle being examined. Tendon is considered enlarged if the ratio of the tendon to muscle belly width is greater than 0.5mm. Internal structure and reflectivity were evaluated in the anterior 1/3rd – 2/3rd of the muscle.

Statistical Methods

Data was entered in MS Excel and analysed using SPSS software. Results were presented as tables.

RESULTS

In our study out of 45 cases, most of them belong to 36 to 55 yrs. of age group. The Mean deviation of AGE distribution is 48.778. The standard deviation is 9.968.

In sex distribution Female preponderance is there, out of 45 cases 29 (64.44%) were female, remaining 16 (35.56%) were males. Regarding RISK FACTOR analysis 17 males and 4 females were having smoking and diabetes as RISK FACTOR. Among 17 cases, 13 (28.89%) were association with smoking, 4 cases (8.89%) having Diabetes, 4 females (8.89%) having Diabetes as RISK FACTOR.

Table 1: EUGOGO [European Group of Grave's Orbitopathy]

Laterality	No. of cases	Percentage
B/L	33	73.33
U/L – LE	6	13.33
U/L – RE	6	13.33
Total	45	100.00
<i>Laterality distribution</i>		
Clinical manifestations	No. of patients	Percentage
Lid retraction	45	100 %
Proptosis	45	100%
Soft tissue involvement	13	28.8%
Ocular movement restriction	12	26.6%
Diplopia	5	11%
Exposure keratopathy	2	4.4%
Optic neuropathy	-	-
Differential IOP	4	8.8%
<i>Clinical manifestation of thyroid eye disease</i>		
Severity	No. of cases	Percentage
Mild	17	37.78
Moderate	24	53.33
Severe	4	8.89
Total	45	100.00
Classification of disease based on the clinical activity of thyroideye disease according to EUGOGO [European Group of Grave's Orbitopathy]		

Table 2: Severity and status of insertion of tendon in TED

Tendon involvement		
Severity	Yes	No
Mild	0	17
Moderate	0	24
Severe	1	3
Total	1	44

Table 3: Disease severity and average thickness of recti muscles in TED

Muscle Thickness in mm	Mild	Standard deviation	Moderate	Standard deviation	Severe	Standard deviation
R-MR	3.876	0.464	4.95	1.10	9.1	0.95
L- MR	3.976	0.319	4.84	1.25	9.22	1.43
R- LR	3.58	0.54	4.56	1.04	7.27	0.39
L- LR	3.68	0.33	4.42	1.18	7.45	0.42
R- IR	3.46	0.52	4.05	0.85	5.57	0.25
L- IR	3.38	0.81	3.98	0.86	5.65	0.33
R-SR-LPS	4.80	0.47	7.34	0.56	10.1	0.95
L-SR-LPS	4.81	0.48	7.21	0.67	10.1	1.19
Sum of All 4 Recti Muscle RE	15.71	1.99	20.9	3.55	32.0	2.54
Sum of 4 All Recti Muscle LE	15.84	1.93	20.4	3.96	32.4	2.9

DISCUSSION

A total of 45 patients with TED due to hyperthyroidism were evaluated. The mean age group in this study was the 3rd – 4th decade of life with female predominance (64.4%). Our study was compared with a study done by Bartelena et al.^[1] which showed peak incidence in the 5th and 7th decades. The major risk factor for the development of the disease in our study was cigarette smoking (33.3%) followed by type 2 DM (17.6%). The increased severity of the disease was found in males (17.6%) who were having the above risk factors. Our study was correlating with a study done by Haage E et al.^[2] which showed cigarette smoking playing a major role in the occurrence of orbitopathy and also associated with disease severity and risk of progression of the disease. Our study was correlating with the study by Prummel et al.^[3] which showed diabetes having a 10 % association with TED. . Our study was compared with the study conducted by Bartley et al.^[4]. Bestcorrected visual acuity using Snellen's chart showed a 6/6 improvement of vision in 80.1% of patients. 13.3% of patients had vision 6/12-6/18 due to lens changes and 4.4% of patients with vision 6/24- 6/60 due to EK associated with a severe form of the disease. [Vision drop in 13.3 % of patients due to lens changes may not be due to the disease process and therefore not considered as a cause of ocular morbidity due to TED]. In this study group, 73.3% of patients had bilateral presentation whereas 26.7% of patients had a unilateral presentation. Our study was compared with the study conducted by Bartley et al.^[4] Bestcorrected visual acuity using Snellen's chart showed a 6/6 improvement of vision in 80.1% of patients. 13.3% of patients had vision 6/12-6/18 due to lens changes and 4.4% of patients with vision 6/24- 6/60 due to EK associated with a severe form of the disease. [Vision drop in 13.3 % of patients

due to lens changes may not be due to the disease process and therefore not considered as a cause of ocular morbidity due to TED]. The major clinical features observed in this study were proptosis with lid retraction (100%) followed by soft tissue involvement in the form of epibulbar hyperemia with chemosis and periorbital oedema in 13 patients(28.9%), extraocular muscle restriction in 12 patients (26.6%) with associated diplopia in 11% of patients, and differential IOP of more than 4 mmHg in 8.8% of patients and finally exposure keratopathy in 4.4 % of patients which was compared with the study by Bartley et al 1996.^[4] and Kendler et al 1993. In this study, patients were categorized into mild, moderate and severe forms based on the EUGOGO [European Group of Grave's Orbitopathy] classification of disease severity. 37.7% of patients belonged to the milder form, 53.3 % of patients to the moderate form, and 8.89 % of patients to the severe form of the disease. Our study was compared with the study conducted by Bartley et al.^[4] In this study among 45 cases of thyroid eye disease which were categorised into mild, moderate, and severe forms of the disease, using the B-scan, the muscle thickness of MR, LR, SR, and IR was measured and the result was obtained. In the present study, we found a significant correlation between the disease severity and average thickness of the extraocular muscle. Our observation study was compared with the study by Hans C Fledelius et al, Tina Zimmermann-Belsing et al, and Ulla Feldt-Rasmussen et al.^[5] which established a significant positive correlation between Hertle's value, the clinical activity of Grave's orbitopathy and horizontal recti muscle thickness.

In this study, among 45 patients with TED, it was found that 44 patients (99.9%) had muscle enlargement with tendon sparing and one patient

(1.1%) had muscle enlargement with involvement of tendon that comes under the severe form of TED. Our study was compared with a study by Guy J Ben Simon et al.^[6] that demonstrated tendon involvement (6.4%) on axial CT or MRI.^[7]

CONCLUSION

Ultrasonic B-scans help establish or confirm the diagnosis of thyroid ophthalmopathy. Although the disease presents bilaterally, it is usually asymmetric with marked changes in one eye and very subtle changes in the other eye. Echography reveals mild changes in the clinically undiagnosed orbit. Although marginally overlapping, all four recti muscles in each category were significantly thicker in the study group. The mean of the sum of all four recti muscles in the mild category was 15.7 mm in BE, the moderate category was 20.5mm in BE and the severe category was 32 mm in BE. A severe form of TED was found to generally result in a higher exophthalmometric measurement of proptosis and eye muscle thickness (P value < 0.001). In thyroid eye disease, enlargement of the muscle belly with sparing of tendon insertion is the characteristic appearance in B-scan. The internal reflectivity of thickened muscle showed medium – high reflectivity in mild to moderate form of the disease and low reflectivity in a severe form of disease using A-mode ultrasound and the internal structure was irregular. Our result showed EOM enlargement to be the principal cause of proptosis. From the study, we observed that it is

difficult to distinguish the thickened muscle with high reflectivity from the surrounding orbital soft tissue. This can be avoided by decreasing the gain setting to get a better visualization of the muscle sheath.

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Conflict of interest

There are no conflicts of interest.

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