

Dazzling and sparkling eyes in ladies: boon or bane in ophthalmology

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Abstract

Aim of Study: To study the prevalence, demographic factors, clinical features, examination, diagnosis and treatment outcome of Thyroid Eye Disease (TED).

Introduction: Graves's disease (GD) is the commonest autoimmune disorder affecting the thyroid gland which involves soft tissues of periorbital space, extraocular muscles and orbit. TED can be sight threatening besides its cosmetic effects. The manifestations can be effectively investigated and judiciously treated with antithyroid drugs and corticosteroid and surgery.

Materials and Methods: This Prospective study was done on 60 consecutive patients with Graves disease, relevant history was taken, thorough ocular examinations and investigations were done. All patients with thyroid ophthalmopathy were under antithyroid treatment.

Result: Out of 60 hyperthyroid patients, 27 presented with Grave's Ophthalmopathy (GO), with female: male ratio of 8:1. 59.2% presented as moderate to severe GO, 37% mild, and only 1% had sight threatening GO. Upper lid retraction was the commonest presentation (100%) followed by proptosis (70.3%) and exposure keratitis (51.8%). Treatment given to patient based on current protocol was quite effective in maximum cases.

Keywords: Thyroid Eye Disease (TED), Grave's Ophthalmopathy (GO), Upper Lid Retraction, Proptosis

Introduction

Thyroid eye disease (TED) is an inflammatory orbital disease of autoimmune origin with the potential to cause severe functional, aesthetic and psychosocial effects.⁽¹⁾ As an important part of Graves disease (GD) which being a very common endocrine disorder where immune system of body produces antibody and targets against thyroid stimulating hormone receptor of thyrocytes and affects various other systems directly or indirectly. The autoimmune process of the disease affects the soft tissues of periorbital region as well as orbit leading to Thyroid ophthalmopathy. The most common extrathyroidal site of morbidity in GD is the eye.⁽²⁾ Close to 10-20% of patients develop eye problems in the months before becoming thyrotoxic, about 10-15% present with current or previous hypothyroidism.⁽³⁾ Smoking is the most important modifiable risk factor, although post radiation exposure for hyperthyroidism also attributes to progression of thyroid ophthalmoplegia. Genetic factors appear to play a role in TED, but specific contributions have yet to be elucidated.^(7,8) The estimated incidence of GO in the general population is 16 females and 3 males per 100,000 person years.⁽⁴⁾ There is a female predilection for TED with the female to male ratio being reported to be 9.3:1 in patients with mild ophthalmopathy, 3.2:1 in those with moderate ophthalmopathy, and 1.4:1 with severe ophthalmopathy,⁽⁴⁾ which indicates the increasing risk of TED in males with increasing severity. Thyroid eye disease, or Graves' ophthalmopathy, is a potentially vision-threatening autoimmune disease that manifests most commonly in hyperthyroid patients (77%) and less frequently in euthyroid (20%) and hypothyroid (3%) patients.⁽⁵⁾ TED

can precede or succeed the thyroid disease, usually within 18 months of each other in the majority of the patients.⁽⁶⁾

Aim

This study discusses the prevalence, demographic factors clinical features, examination, diagnosis and treatment outcome of TED, in a tertiary health care center in western Odisha.

Materials and Methods

A Prospective study was done on 60 consecutive patients with Graves's disease presenting to department of Medicine and then referred to the eye OPD to rule out TED. Detailed history was taken emphasizing parameters such as age, sex, occupation, smoking, affected family members, other autoimmune disease. Best corrected distance and near vision, color vision, exophthalmometry, anterior segment examination and dilated posterior segment examination by indirect ophthalmoscope of all patients were done. Those found to have symptoms and clinical signs of TED were investigated for biochemical tests including serum Triiodothyronine (T3), free thyroxine (T4), Serum TSH, thyrotropic receptor antibodies (TRAB). Visual field test, B-scan, X-Ray Orbit, CT-Scan Orbit, MRI were done in patients with orbital involvement. Then symptomatic treatment and specific treatment was given as inpatient and outpatient basis, photographic documentation of relief of symptoms was done.

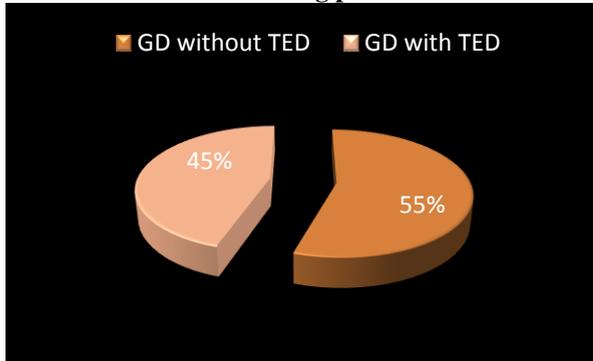
Result

Out of 60 hyperthyroid patients, 27 were evaluated with clinical features of TED and diagnosed as Thyroid

Ophthalmopathy as shown in Pie Chart 1, of which 24 were females and 3 were males.

Female to male ratio being 8:1 described in Pie Chart 2.

Pie Chart 1: % showing patients with TED



Pie Chart 2: Male: Female ratio

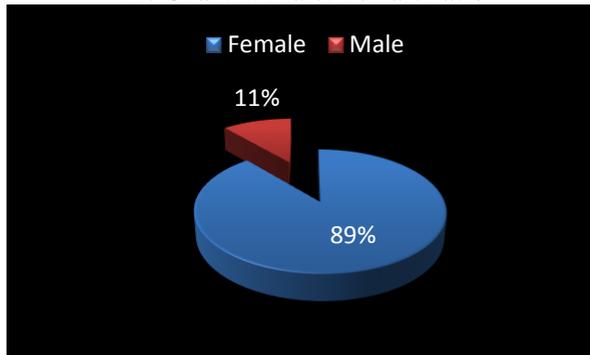


Fig. 1: Unilateral Proptosis



Fig. 2: Bilateral Proptosis

Patients usually presented with symptoms like proptosis unilateral and bilateral as in Fig. 1 and Fig. 2, dryness of cornea leading to exposure keratitis,

lacrimation, lid edema, upper eyelid retraction, restricted movements, ocular pain on pressure, diminution of vision and at times field loss as in Fig. 3 and Fig. 4. As described in Table 1, out of all, upper lid retraction was the most common presentation (100%) followed by proptosis (70.3%) and exposure keratitis (51.8%), lid edema was found in 18.5% of patients, lacrimation in 11.1%, diplopia, pain on pressure 7.4% each and diminished vision in 14.8% cases, restricted ocular movement in 11.1% cases other unusual symptoms included, dyschromatopsia, proptosis on upward gaze and field loss. Bilaterality of symptoms was seen in 25 patients showing symptoms accounting to 92.5%.



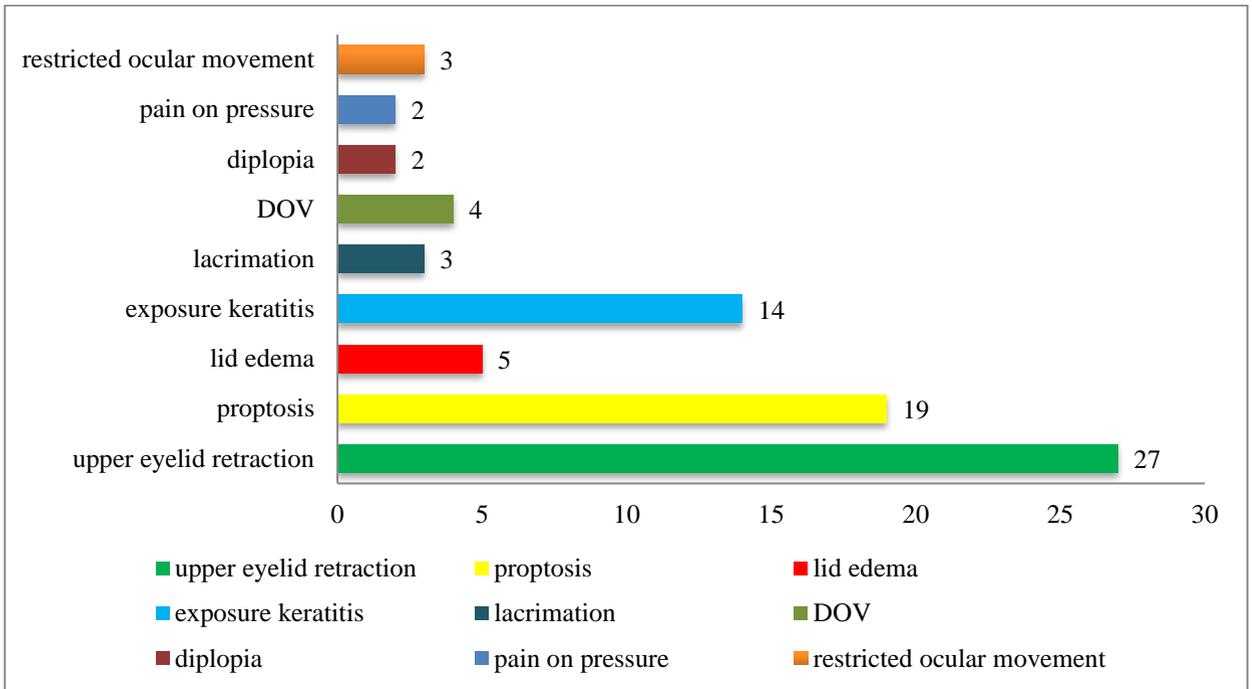
Fig. 3: Upper eyelid retraction and Lid edema



Fig. 4: EOM involvement

Table 1: Symptoms of TED among patients

Symptoms	No. of cases	% in Patient
Upper eyelid retraction	27	100
Proptosis	19	70.3
Lid edema	5	18.5
Exposure keratitis	14	51.8
Lacrimation	3	11.1
Diminution of vision and vision loss	4	14.8
Diplopia	2	7.4
Pain on pressure	2	7.4
Restricted ocular movement	3	11.1



The lid signs can be seen as a result of Lid retraction, Lid Lag, Globe Lag, Proptosis, Restrictive extraocular Myopathy. In this study various signs of TED has been found and documented in Table 2 below. Among the lid signs Dalrymple sign, Fig. 5 was found in almost all cases suffering from TED, followed by Kocher’s sign (70.3%) Fig. 6 and Von Graefe’s sign (59.2%). Facial signs like Joffroy’s sign were seen in 12 cases (44.4%) and Sainton’s sign in 3 cases (11.1%). Restricted Extraocular Myopathy was seen in many patients as palsy of EOM aka Ballet sign in 25.9% and convergence weakness in 18.5% (Mobius sign) Fig. 7 and weakness of fixation on lateral gaze aka Suker’s sign in 14.8%. Proptosis is seen in 24 cases (88.8%) commonly known as Naffziger’s sign Fig. 8. Different pupillary reactions like Knies’s sign i.e. unequal dilatation of pupils were seen in 25.9% cases, whereas on applying weak Adrenalin Lowy’s sign was seen in 11.1% and Cowen’s sign were elicited in 7.4% of all TED patients.



Fig. 6: Kocher’s Sign



Fig. 7: Mobius Sign & Enroth’s Sign



Fig. 5: Dalrymple Sign



Fig. 8: Naffziger’s Sign

Table 2: Signs of TED in patients

	Signs	No. of Patients	% in Patients
Lid Signs	Dalrymple Sign (upper lid retraction)	27	100
	Kocher Sign (increased lid retraction with visual fixation)	19	70.3
	Von Graefe Sign (upper lid lag on downward gaze)	16	59.2
	Vigouroux sign (lid swelling)	5	18.5
	Grave Sign (resistance to pulling down retracted upper lid)	8	29.6
	Stellwag Sign (infrequent and incomplete blinking)	12	44.4
	Boston's sign (jerky irregular movement of upper lid on downward gaze)	6	22.2
	Enroth's sign (puffy eyelids)	11	40.7
	Gifford's sign (difficulty lifting upper lid)	16	59.2
	Gellinek sign (increased pigmentation of lids)	2	7.4
	Rosenbach's sign (tremor of closed lids)	8	29.6
	Pochin sign (diminished blinking)	10	37.03
Facial Signs	Joffroy's sign (absent forehead wrinkles on up gaze)	12	44.4
	Sainton's sign (delayed forehead wrinkling on up gaze)	3	11.1
Restrictive Extraocular Myopathy	Mobius sign (weakness of convergence)	5	18.5
	Ballet sign (palsy of extraocular muscles)	7	25.9
	Suker sign (weakness of fixation on lateral gaze)	4	14.8
Ptosis	Naffziger's sign (ptosis from behind)	24	88.8
	Payne Trousseau sign (globe luxation)	5	18.5
Pupillary Signs	Lowy's sign (dilatation of pupil with weak adrenalin)	3	11.1
	Cowen's sign (jerky pupillary constriction to consensual light)	2	7.4
	Knies's sign (unequal dilatation of pupil)	7	25.9

All symptoms and signs were classified according to NOSPECS classification and then scored according to CAS, tabulated as below in Table 3 and shown in Fig. 9, 10, 11.

Table 3: NOSPECS classification and scoring among patients

Score	Grade	No. of cases	% of cases
0	No signs or symptoms	0	0
1	Only signs	5	18.5
2	Soft tissue involvement with symptoms and signs	22	81.4
0	Absent	0	0
a	Minimal	6	27.2
b	Moderate	8	36.3
c	Marked	8	36.3
3	Proptosis		
0	<23mm	3	11.1
a	23-24mm	9	33.3
b	25-27mm	10	37
c	>28mm	5	18.5
4	Extraocular muscle involvement		
0	Absent	16	59.2
a	Limitation of motion in extreme of gaze	4	14.8

b Evident restriction of movement	5	18.5
c Fixed eyeball	2	7.4
5 Cornea involvement		
0 Absent	7	25.9
a Stippling of cornea	11	40.7
b Ulceration	8	29.6
c Clouding	1	3.7
6 Sight loss		
0 Absent	0	
a 20/20-20/60	17	62.9
b 20/70-20/200	9	33.3
c <20/200	1	3.7



Fig. 9: Exposure Keratitis



Fig. 10: Soft Tissue involvement



Fig. 11: Proptosis

Then disease activity is assessed by Clinical Activity Score (CAS) which helps in predicting the outcome of immunosuppressive therapy, as immunosuppressant is believed to be useful in early active phase of the disease. The CAS in our study is tabulated below in Table 4.

Table 4: CAS of patients

	No. of cases	% of cases
Pain Painful, oppressive feeling on or behind the globe during last 2 weeks	2	7.4
Pain on attempted upside or down gaze during the last 4 weeks	2	7.4
Redness of the eye lid	7	25.9
Diffuse redness of the conjunctiva covering at least one quadrant	20	74
Swelling of eyelids	5	18.5
Chemosis	3	11.1
Swollen caruncle	2	7.4
Increase of proptosis >2mm during a period of 1-3months	19	70.3
Impaired function Decrease of eye movements in any direction >5° during a period of 1-3 months	2	7.4
Decrease of visual acuity of >1 line on the snellen chart(using a pin hole) during a period 1-3months	3	11.1

According to EUGOGO recommendations, the following assessments for patients with Graves ophthalmopathy (GO) in specialist centers (IV, C), as reported previously by Wiersinga et al⁽¹⁴⁾ were done and clinical Activity was measured based on the classical features of inflammation: clinical activity score (CAS) is the sum of all items present:^(15,16)

Spontaneous retrobulbar pain
Pain on attempted up or down gaze
Redness of the eyelids
Redness of the conjunctiva
Swelling of the eyelids
Inflammation of the caruncle and/or plica
Conjunctival edema

A CAS R3/7 indicates active GO: In our study 8 cases were clinically inactive (30%) of which 5 patients had CAS within 1-2, whereas 19 cases (70%) were categorized in CAS 4-7 and were treated accordingly.

The severity classification of thyroid ophthalmopathy according to EUGOGO recommendations as described by Wiersinga et al,⁽¹⁴⁾ classified the disease into sight threatening, moderate to

severe and mild GO. Our study shows that only 1 case (3.7%) had sight threatening GO, 16 cases (59.2%) had mod-severe GO and 10 cases (37%) had mild GO.

Our study then investigated further with biochemical tests and imaging techniques which drew inference as follows in Table 5.

Table 5: Investigations done in TED patients

Investigations	No. of cases undergone investigation	No. of cases with findings suggestive of TED
Thyro 5	27	27 (100%)
CT Scan brain and orbits with contrast	16	10 (62.5%)
MRI brain and orbit	8	6 (75%)

All symptomatic patients were treated according to needful, and relief of symptoms was documented in Table 6 and Table 7.

Table 6: Medical management done in TED patients and Outcome

Medical Management	No. of cases treated	No. of cases resolved
Topical treatment for Exposure Keratitis CMC Hyaluronic acid +D- Panthenol Lacrigel(hypromellose)	20	16 (80%)
Antithyroid drugs	27	18 (66.6%)
Oral corticosteroids	16	13 (81.2%)
IV Methyl Prednisolone	5	4 (80%)

Table 7: surgical management of selective TED patients and Outcome

Surgical Management	No. of cases underwent	No. of cases with successful outcome
Tarsorrhaphy	6	4 (66.6%)
Orbital decompression surgery	2	1 (50%)

Discussion

In the present study, which was done in patients of Hyperthyroidism in western Odisha, the prevalence of thyroid ophthalmopathy in hyperthyroid patients is 45% as compared to a study performed in North India with 28% prevalence.⁽⁹⁾ The study was meticulously done with several diagnostic criteria and included patients affected with Thyroid Ophthalmopathy, the prevalence of which can be compared with many other studies in various ethnic groups with a wide range of prevalence from 8-56%.⁽¹⁰⁻¹³⁾

In our study, 70 percent were evaluated as clinically active according to CAS classification system. The study showed 59.2 percent as moderate to severe GO, 37 percent as mild GO and only 1 percent of all cases had sight threatening GO. Comparing it with the EUGOGO which described 152 European patients with GO where 28 per cent had severe and 33 per cent moderate disease.⁽¹⁷⁾

Upper lid retraction (100%), proptosis (70.3%), exposure keratitis (51.8%) and soft tissue involvement (81.4%) has been the leading presentations in our patients which had been the found to be consistent with most of the previous studies.⁽¹⁸⁾ Among lid signs Dalrymple sign was found in almost all cases suffering from TED, followed by Kocher's sign (70.3%) and Von Graefe's sign(59.2%). In a multi-ethnic Asian study, exophthalmos and lower lid retraction were the most common signs.⁽¹²⁾ Soft tissue inflammatory signs were

observed with greatest frequency (75%) in the EUGOGO study,⁽¹⁷⁾ comparable to that of our study.

All patients with thyroid ophthalmopathy were investigated and all cases suffering from TED were found to have deranged Thyroid Function Test, CT Scan Brain and Orbit was done in suspected cases of Exophthalmos and about 62.5% of patients who did the test were found to have thickened belly of EOM, proptosis radiologically and other features suggestive of TED. MRI Brain and Orbit was advised for 8patients out of which 6 cases (75%) had positive features. Patients were accordingly treated. All cases of TED were prescribed with anti-thyroid drugs according to the TSH values and about 66.6% of them had shown a great relief of symptoms, While 81.2% of those prescribed with Oral Corticosteroids and 80% of those prescribed with IV Methyl Prednisolone had tremendous relief of symptoms. Few cases were undertaken for lateral tarsorrhaphy and orbital decompression surgery with an outcome of 66.6% and 50% success respectively.

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