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STUDY OF CLINICAL PROFILE OF THYROID OPHTHALMOPATHY

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ABSTRACT

Background: Graves ophthalmopathy is the most common extra thyroidal manifestation of graves disease. In extremely rare instances, it is also seen in hypothyroid or euthyroid patients with chronic autoimmune thyroiditis.

Aim & Objective: To study the clinical profile of Thyroid ophthalmopathy at tertiary care hospital. The main objective of this study was to know the occurrence of thyroid ophthalmopathy in hyperthyroid and hypothyroid patients, to study the clinical profile and thyroid status, to know the clinical scoring of thyroid ophthalmopathy, to study the severity of ophthalmopathy and its correlation with TFT's and Thyroid antibodies and to know the radiological features of thyroid ophthalmopathy and its correlation with clinical features.

Methodology: Present study was a Crosssectional Observational study. Study was conducted at outpatient department and all wards at Dr DY Patil Medical College and Hospital, DY Patil Vidyapeeth, Pimpri, Pune.

Results: Majority of cases were hyperthyroid (70%) and minor being hypothyroid (30%). Majority 65% were females and 35% were males. Among hypothyroid cases (n=30),

symptoms seen were 26.6% had fatigue, 20% had dry skin, 20% had constipation,13.3% had weight gain, 10% had cold intolerance and 10% had hoarsness of voice. And those among hyperthyroid cases 45.7% had weightloss, 25.7% had tremors, 18.5% had palpitations, 10% had heat intolerance. 40% cases had eye symptoms, among total 100 patients 18% ha dretrobulbardiscomfort,11%had lacrimation, 8% had photophobia, and 3% had milddiplopia. Among eye signs 25% had eyelid retraction, 8% had extra ocular muscle dysfunction, 7% had eyelid oedema. Thyroid antibody (TPO) in hyperthyroid was positive in 70% and among hypothyroid 73.3% were positive. On MRI orbit in hyperthyroid cases 48.5% had positive findings and all hypothyroid cases had normal study report.69%of exopthalmometry findings were normal and 31% were proptosis. 96.7% had bilateral proptosis and 3.2% had unilateral proptosis. No SPECS classification showed that 40 cases had soft tissue involvement, 31 hadproptosis, 31 had eye muscle involvement. Ophthalmopathy was seen among 57.1% among hyperthyroid cases (40 cases). And 0% among hypothyroid cases. ($p<0.001$) shows statistical significance. Present study showed that among 40 cases having ophthalmopathy 36 had TPO positive and 4 were negative. On MRI those having ophthalmopathy (n=40) 77.5% had extra ocular muscle enlargement,7.5% had increase in retroocular fat. Antithyroid treatment was given in 70% cases those were hyperthyroid and thyroxine was given to hypothyroid cases 30%.100%were given dark glasses, 95% lubricating drops and 30% were given steroids.

Conclusion: Thyroid ophthalmopathy is an autoimmune disease which can cause vision loss and reduced quality of life. Thyroid eye disease is more common in females than males and hyperthyroidism being commonest cause of thyroid eye disease in our setup. Developments in understanding of the pathophysiology of Thyroid ophthalmopathy led to a fundamental change in the management. Systemic thyroid disease should be managed in all thyroid patients. Hyperthyroidism and disease activity are risk factors for severe and sight threatening disease and hence close follow-up and prompt detection and management with adequate antithyroid drugs is required especially in newly diagnosed hyperthyroid patients.

Keywords: Thyroid, hyperthyroid, thyroxine, Thyroidantibody(TPO), lacrimation

INTRODUCTION

In Graves Ophthalmopathy, ophthalmic abnormalities reflect its multifactorial clinical expression and the uncertainties underlying its pathogenesis, natural history and treatment.

An orbital autoimmune disease, Graves ophthalmopathy is the most common extra

thyroidal manifestation of graves disease. In extremely rare instances, it is also seen in hypothyroid or euthyroid patients with chronic autoimmune thyroiditis.[(1)] While it can be demonstrated by orbital imaging in nearly all, it is clinically evident in about 30-50% of patients with Graves disease. Mild eye disease is prevalent in most patients, while sight threatening ophthalmopathy is seen in approximately 5% of them. According to a study, the incidence of Graves ophthalmopathy was 16/100000 per year for females, much higher than 2.9/100000 per year for males. [(2)] If we were to assume the prevalence of Graves disease in about 1% of the general population, and that of Graves ophthalmopathy in about 40% of patients with Graves disease as clinically apparent, then the prevalence of ophthalmopathy is 0.4%, or about 27 million in the world. There are two peaks that show up with reference to age distribution in an incidence cohort at 40 to 44years and 60 to 64 years respectively in women; in men, it shows at 60 to 69 years.[(3)]

Thyroid ophthalmopathy is very rarely seen in patients with primary hypothyroidism. But the relatively high prevalence rates of 8.2 to 8.6% is attributed to increased awareness and improved diagnostic techniques.[(2)] Thyroid ophthalmopathy differs in its clinical manifestations of its two variants-hyperthyroidism ophthalmopathy and hypothyroidism ophthalmopathy.

With regard to its pathogenesis, evidence significantly points to an autoimmune one with predominant genetic and environmental influences, particularly smoking. Initially there is an infiltration by lymphocytes and macrophages of the orbital muscle, connective tissue, and adipose tissue. This engenders an oedema in the extracellular compartment of extraocular muscles and orbital fibro-adipose tissue from the deposition of hydrophilic glycosaminoglycans in response to cytokines produced by infiltrating immune cells and macrophages and by the fibroblast themselves. In addition, vascular endothelium and macrophages are also stimulated by cytokines to produce other immunomodulatory and inflammatory mediators, which leads to a recruitment of T cells into the orbit and recognition and presentation of antigen, and thus perpetuates the local inflammatory response. Early on in the evolution, a cell mediated (Th1) immune response appears prominent, but in later stages humoral immunity (Th2), or both are seen. [(1,3)] Among the several extraocular muscles that are usually affected is the levator palpebrae superior is, which may lead to restriction of

eye movements, lid lag, and incomplete eyelid closure. As a consequence, sight threatening corneal exposure becomes likely. Erythema, swelling of conjunctiva and eyelids, and compounded venous and lymphocytic congestion may also result due to acute inflammation.[1]

Thyroid ophthalmopathy proceeds through a congestive (inflammatory) stage where the eyes are red and painful. Remission within 1-3 years is likely and only about 10% of patients are seen to develop serious long term ocular problems. This is followed by a fibrotic stage where the eyes are white along with the likely presence of a painless motility defect.

With orbital imaging, one can typically see the enlargement of extra ocular muscles sparing the tendons and/or increased fat mass. The extra ocular muscles' enlargement occurs early and precedes the increase in fat mass. It is also important that one rule out the GO unrelated conditions like neoplasms and vascular diseases. The lack of radiation and the potential for more accurate measurements of retro orbital tissues for treatment monitoring are the advantages of MRI. In addition to this, MRI helps in identifying active disease owing to its sophisticated tissue characterization which allows for a qualitative tissue analysis.[5]

AIMS:-

- To study the clinical profile of Thyroid ophthalmopathy at tertiary care hospital.

OBJECTIVES:-

- To know the occurrence of thyroid ophthalmopathy in hyperthyroid and hypothyroid patients
- To study the clinical profile and thyroid status
- To know the clinical scoring of thyroid ophthalmopathy
- To study the severity of ophthalmopathy and its correlation with TFT's and Thyroid antibodies
- To know the radiological features of thyroid ophthalmopathy and its correlation with clinical features.

MATERIALS AND METHODS

Study design: Present study was a Cross sectional Observational study.

Study area: Study was conducted at outpatient department and all wards at Dr DY Patil Medical College and Hospital, DY Patil Vidyapeeth, Pimpri, Pune.

Study setting: Outpatient department of Medicine of tertiary care hospital. Registration of patients was from August 2019. They were registered when admitted under Medicine department. At the time of registration, the patients with exclusion criteria were not enrolled for study.

Study period: August 2019-September 2021

Sample size: 100

Study participant: Patients having thyroid ophthalmopathy and inclusion criteria.

Inclusion criteria:

- Age>12years
- Both gender
- Willing to participate

Exclusion criteria:

- Ophthalmopathy other than thyroid dysfunction like due to infections, drug induced, other autoimmune diseases and malignancies.
- Not willing to participate

Sampling technique: Patients attending and getting admitted under Medicine department with ophthalmopathy due to thyroid dysfunction. 100 patients were studied.

Data analysis:

All data was collected and complied in Microsoft excel. All statistical analyses were performed by using IBMSPSS statistics Version 21.0 (SPSS Inc., Chicago, IL, USA) and open epi version 2.3.1. Descriptive statistics such as percentage (%), mean, range and standard deviation (SD) were used to describe the data. Chi square test was applied for qualitative data and student t test for quantitative type of data. A p value of <0.05 was regarded as statistically significant.

Ethics

Institute Ethical committee's approval was taken prior to the study.

OBSERVATIONS AND RESULTS

Table 1: Distribution of cases

Parameter	No. of cases	percentage
Hyperthyroid	70	70%
Hypothyroid	30	30%

Table 2: Gender distribution

Gender	No. of cases	Total percentage
Male	35	35%
Female	65	65%

Table 3: Age distribution

Age in years	No. of patients	Percentage
≤40	52	52%
41 to 50	32	32%
51 to 60	12	12%
>60	4	4%
Total	100	100%

Mean age was 43.04±6.99years.

Table 4: Eye symptoms

Complaints	Noofpatients	Percentage
Retrobulbardiscomfort	18	18%
Lacrimation	11	11%
Photophobia	8	8%
Milddiplopia	3	3%
Nosymptoms	60	60%

Table 5: Eye signs

Eye signs	No. of patients	Percentage
Eyelid retraction	25	25
Extraocular muscle dysfunction	8	8
Eyelido edema	7	7
No signs	60	60

Table 6: Exophthalmometry findings

Finding	No. of patients	Percentage
Normal (18-20mm)	69	69%
Proptosis (>20mm)	31	31%

Table 7: Laterality of Proptosis (n=31)

Laterality of proptosis	No. of patients	Percentage
Bilateral	30	96.7
Unilateral	1	3.2

Table 8: NOSPECS classification

Pathology	Noofpatients
No signs and symptoms	60
Only signs, no symptoms	0
Soft-tissue involvement	40
Proptosis	31
Eye muscle involvement	31
Corneal involvement	0
Sight loss	0

Table 9: Activity by clinical activity score (CAS)

CAS	No. of patients	Percentage
0-2	66	66%
3-7	34	34%

Table 10: Occurrence of ophthalmopathy in thyroid disease

Ophthalmopathy	Hyperthyroid	hypothyroid
Present	40	0
Absent	30	30
Percentage	57.1%	0%

Pvalue<0.0001

Table 11: TPO Antibody in patients with ophthalmopathy

TPO Antibody	Patients with ophthalmopathy	Percentage
Positive	36	90%
Negative	4	10%
Total	40	100%

Table 12: MRI findings in patients with ophthalmopathy (n=40)

MRI findings	No. of patients	percentage
Extraocular muscle enlargement	31	77.5
Increase in retro-ocular orbital fat	3	7.5
Normal study	6	15

Table 13: Severity of ophthalmopathy (n=40)

Parameter	No. of patients	Percentage
Mild GO	28	70
Moderate to severe GO	12	30
Sight threatening GO	0	0

Table 14: Ocular treatment

Ocular treatment	No. of patients	Percentage
Dark glasses	40	100%
Lubricating drops	38	95%
steroids	12	30%

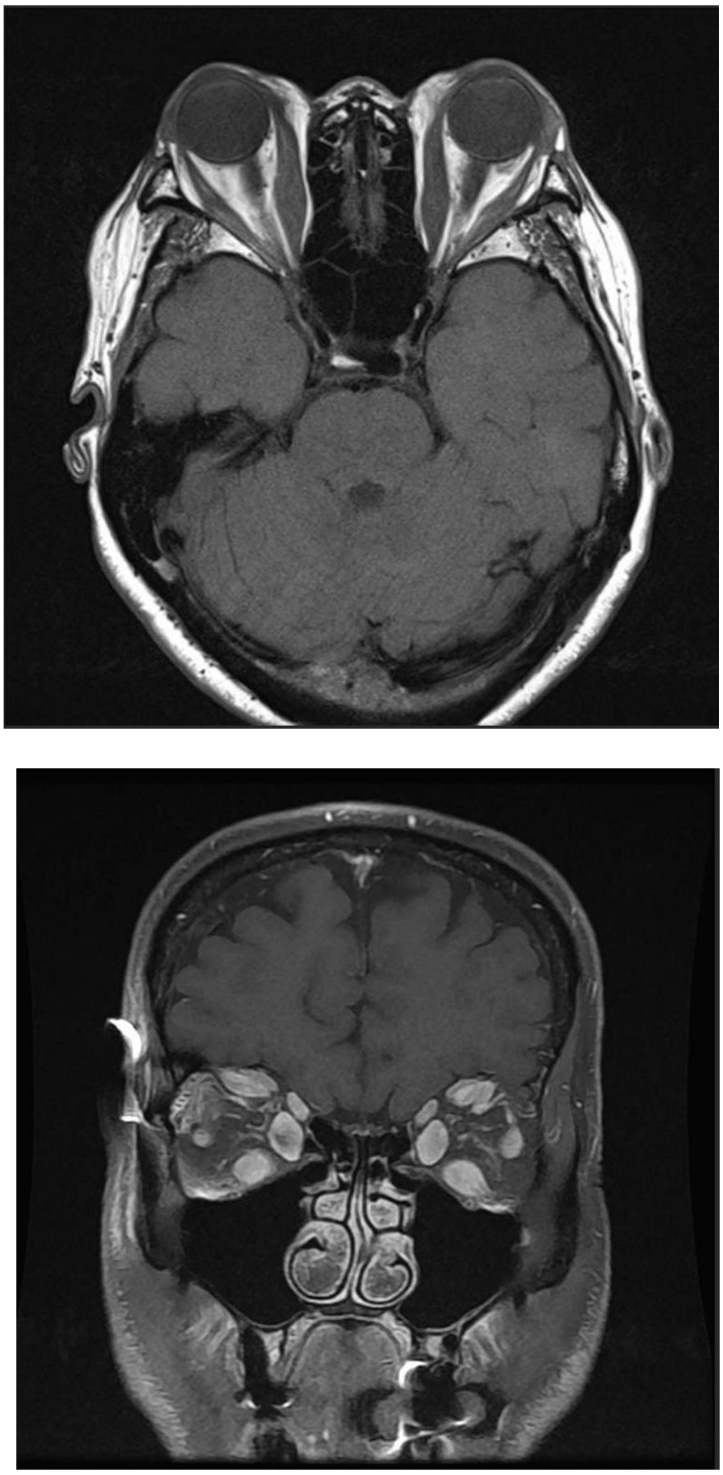

Figure 1 & 2: MRI ORBIT- Bilateral extra ocular muscles appears symmetrically thickened

Figure 3 & 4: Patient of thyroid orbitopathy with proptosis

DISCUSSION

Thyroid status

In our study, with respect to thyroid disorders, majority of them were hyperthyroid (70%) and 30% were hypothyroid.

Various studies have been conducted to determine the incidence of thyroid disorders; as such, a study by Muralidhar A *et al* [(6)] showed high rate of hyperthyroidism at 46.23%, while hypothyroidism & euthyroid stood at 33.96% and 19. 81% respectively. Similar incidence rates were also represented in a study by Ackuaku-Dogbe EM *et al* [(7)]where 88.9% were hyperthyroid. Another study by Milind N. Naik *et al* [(8)] conformed to the same with hyperthyroidism at 43.3%, whereas 37.4% were euthyroid and 19.25% were hypothyroid.

Gender distribution

According to our study, cumulatively, females (65%) outweighed the males (35%) to a ratio of 1.7:1.

Distribution rates of thyroid disorders with respect to gender usually weighed in favour of women as can be seen in the studies by Muralidhar A *et al* [(6)]where majority were females at 52.83%, and by Prummel MF *et al* [(9)]where 77% were females. However, other studies reported a much lower female to male ratio of 2.1:1, with a mean age of 33years.[16]

Age distribution

More than half of them, about 52% were ≤40 years, whereas 32% slotted between 41 and 50years, 12% between 51 and 60 years, and about 4% were>60years

A majority of the studies on age distribution reported averages ranging between low to mid-40s-Muralidhar A *et al* [(6)], mean age=41.3±14.76 years; Ackuaku-DogbeEMetal[(7)], mean age=45.22±13.9 years; Milind N. Naik *et al*[(8)], mean age= 44.9years.

Eye symptoms

In our study about 40% of the cases had eye symptoms, and amongst all 18% had retrobulbar discomfort, 11% had lacrimation, 8% had photophobia, and 3% had mild diplopia.

According to a study by Muralidhar A *et al*[(6)] the most common presenting eye sign was prominent eyes in 65.1%, whereas redness of eyes was in 34.9%, retrobulbar pain in34.9%, diurnal variation in 34.9%, blurring of vision in 11.3%, as well as dry eye and epiphora. In an other study by Şahlı E *et al*[(10)], mostly half of Graves disease patients have symptoms of photophobia, dryness and stinging, epiphora and diplopia. Eckstein AK *et al* [(11)]from their findings stated that common symptoms related to exophthalmos or proptosis and consequent corneal exposure; they included photophobia, excessive

tearing, grittiness, and retro-orbital pain.

Eye signs

In our survey, about 40% presented eye signs. Of the common eye signs, 25% had eyelid retraction, 8% had extraocular muscle dysfunction, and 7% had eyelid oedema.

In the study by Şahlı E *et al* [10]eyelid retraction is the most common ocular finding followed by proptosis, extra-ocular muscle dysfunction, conjunctival hyperemia, eyelid edema, and chemosis. In the study by Ackuaku-Dogbe EM *et al* [7]eye lid retraction was near universal at 82.9%,whereas lid lags to odat 46.15%.

Thyroid antibody (TPO) in hyperthyroid and hypothyroid

As per our survey, positive rates of Thyroid antibody (TPO) in hyperthyroid was 70% and hypothyroid was 73.3%.

In the study by Agarwal A *et al* [12], of the 291 patients who were tested, a majority of 192 tested positive, while more than half of that, about 99tested negative.

Exophthalmometry findings

In our study about 69% of the patients had normal exophthalmometry findings and 31% had proptosis.

A mean exophthalmometry reading of 18.8 mm (SD±3.32, range 10.0-28.0) was reported by the study of Lim NC *et al*[15]

Laterality of Proptosis

Distribution of bilateral and unilateral proptosis in our survey was 96.7% and 3.2% respectively.

Bilateral presentations overshadowed unilateral ones in both the studies by Muralidhar A *et al* [6] at 81.1%.

No SPECS classification

According to No SPECS classification, 40 cases had soft tissue involvement, and 31 had both proptosis and eye muscle involvement.

In a study conducted by Prummel MF *et al* [9], majority of the patients (75%) had at least NOSPECS class 2 signs (upper eye lid swelling being more frequent than lower eye lid swelling), whereas 38% qualified for class 3 (proptosis) with 63% of the patients presenting values above the upper normal limit of 20 mm (2). With respect to the rest, class 4 signs (eye muscle involvement) were present in 49%, class 5 signs (corneal damage) in 16%, and class 6 signs (optic nerve involvement) in 21%. Mean NOSPECS were reported to be3.38$\pm$1.4 by SY Jang *et al*[14].

CASSCORE

Clinical activity score (CAS) in our patients turned out to be between a range of 0 and 2 in 66% and 3 and 7 in 34%.

Clinical activity scores greater than 4 was seen in 29.7% (141 cases) and a score of less than 3 in 70.3% (335 cases) of the patients according to the study by Milind N. Naik *et al*[8].

Ophthalmopathy

Ophthalmopathy was seen among 57.1% of the hyperthyroid cases (40 cases) and 0% among hypothyroid cases ($p<0.0001$ shows statistical significance). According to our study, of the 40 cases that displayed opthalmopathy, 90% (36 cases) were TPO positive while10%(4 cases) were negative.

Supporting the above results, a study by Hiromatsu [15]concluded that majority of ophthalmopathy affected patients were cases of hyperthyroidism, whereas the minimum were hypothyroid and euthyroid cases.

Severity of opthlamopathy

With regard to the severity of opthlamopathy (n=40), 70% showed mild GO, while 30 % moderate to severe GO.

In the study by Lim NC *et al* [13]of the Southeast Asian population, mild, moderate and severe disease were found to occur in 71.3%, 20.7%and 8.0%of the patients.

In another study of Indian Population by Bhaskar *et al* [18], it was found that mild cases constituted the majority at 83%, with 15% and 2% of the patients having moderate to severe and sight-threatening disease respectively.

MRI

On MRI orbit in hyperthyroid cases, 48.5% had positive findings, and all hypothyroid cases had normal study report. On MRI, those having opthalmopathy (n=40), 77.5% had extraocular muscle enlargement, while7.5% had increase in retro ocular fat.

Medical treatment

Antithyroid treatment was given in 70% cases those were hyperthyroid and thyroxine was given to hypothyroid cases (30%).

Ocular treatment

All of them were given dark glasses, 95% of them lubricating drops and about 30% were given steroids.

Study by Şahlı E *et al* [12] showed that oral steroids were found to be effective with high doses (60-100mg/day or higher prednisolone) and long duration(10-20weeks).

CONCLUSION

Thyroid ophthalmopathy is an autoimmune disease which can cause vision loss and reduced Quality of life Thyroid eye disease is more common in females than males and hyperthyroidism being commonest cause of thyroid eye disease in our setup.

Developments in understanding of the pathophysiology of Thyroid ophthalmo-pathy led to a fundamental change in the management. Serum markers will help in diagnosis, prognosis and response to management.

Patients with moderate to severe disease will require additional steroids or immuno modulation with anti-thyroid drugs.

Treatment with Intravenous glucocorticoids

have shown the best response with low side effects and hence play a major role in the management of moderate to severe disease. Ophthalmologists should be consulted in Thyroid ophthalmopathy diagnosis and management. A collegial relationship between the physician and ophthalmologist is needed in providing the most comprehensive care. A complete ophthalmic evaluation will help in differentiating ocular conditions like dry eye or allergies from Thyroid eye disease. The ophthalmologist will help in identifying active disease, manage ocular symptoms, and work with the physician to manage Thyroid eye disease. The molecular underpinnings of TED are now becoming clearer and after decades of suboptimal treatment, better targeted therapies now offer the hope for a change in its natural history.

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Conflict of Interest

The authors declare that they have no conflict of Interest

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