

## OCULAR ASPECTS OF HYPERTHYROIDISM WITH SPECIAL REFERENCE TO OCULAR MYOPATHY

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### ABSTRACT

#### BACKGROUND

Hyperthyroidism can result in ocular manifestations even before systemic signs and symptoms develop. It is seen more in females and severe forms are more common in males. Early detection of ocular involvement can prevent vision threatening complications and troublesome discomforts affecting quality of vision. This clinical study highlights the importance of detailed ocular examination in hyperthyroidism.

#### MATERIALS AND METHODS

Fifty consecutive patients with ocular signs of hyperthyroidism were evaluated and followed up for an average period of 1 year. Detailed ocular examination included exophthalmometric measurements, ocular movements and Worth four-dot test. T<sub>3</sub>, T<sub>4</sub>, TSH, CT scan and antimicrosomal antibodies and antithyroglobulin antibodies were done along with routine investigations. Study Design- Prospective cohort study.

#### RESULTS

Statistical analysis did not reveal any correlation between the level of serum T<sub>3</sub> and severity of ocular findings. Majority of the cases were euthyroid with moderate ocular myopathy having multiple muscle involvement. Inferior rectus was affected most.

#### CONCLUSION

The ocular signs of hyperthyroidism in the present study seem to be mild. The severe eye changes like corneal involvement and optic nerve changes were less common.

#### KEYWORDS

Graves Disease, Hyperthyroidism, Thyroid Myopathy.

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#### BACKGROUND

The ocular aspects of endocrine disorder are of interest alike to ophthalmologist and the physician as ocular symptoms maybe the first manifestation of many endocrine disorders such as diabetes, Graves disease, myxedema and pituitary disorders. Ocular changes are also seen in disorders of parathyroid and adrenal glands. Of these, eye manifestations are commonly seen in diabetes and thyroid disorders. In 1985, McKenzie defined Graves disease as a multisystem disorder consisting of one or more of three specific entities- hyperthyroidism and diffuse goiter, infiltrative dermopathy (pretibial myxedema) and infiltrative ophthalmopathy. In 1969, Werner and the American Thyroid Association proposed a classification of ocular change in thyroid eye diseases. This was modified in 1977 to include patients with greater than 23 mm of proptosis into class 3

disease regardless of their symptomatology. From a clinicians view point, a simplified classification of orbital involvement in thyroid disease can be divided into four categories. They include Graves disease (hyperthyroid ophthalmopathy), malignant exophthalmos, Graves ophthalmopathy and euthyroid ophthalmopathy.

#### Graves Disease

Typically, patients present with autoimmune hyperthyroidism associated with a congested orbit, conjunctival suffusion, retraction, lid lag and they complain of irritation and tearing. Independent of the mode of therapy used to treat hyperthyroid state in 95% of patients, the orbital state returns to normal and 5% develop a chronic ophthalmopathy.<sup>1,2,3,4</sup>

#### Malignant Exophthalmos

This is a rare state that usually develops immediately after an ablative procedure for thyrotoxicosis, radioactive iodine or surgery, in which the eyes become progressively exophthalmic very rapidly, threatening the integrity of anterior segments and the optic nerve. These individuals require either plasmapheresis with concomitant use of immunosuppressive agents or orbital decompression.<sup>5,6,7,8,9,10</sup>

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**Graves Ophthalmopathy**

Although, most commonly associated with Graves hyperthyroidism, ophthalmopathy may also occur in patients with primary hypothyroidism or Hashimoto’s thyroiditis and it is sometimes found in the absence of thyroid disease. Levels of thyroid stimulating immunoglobulins that are believed to cause thyrotoxicosis don’t correlate with the presence, absence or progression of ophthalmopathy.

**Euthyroid Graves Ophthalmopathy**

The occurrence of infiltrative ophthalmopathy in the absence of hyperthyroidism has been termed euthyroid Graves ophthalmopathy and is much less common than Graves ophthalmopathy.<sup>11,12,13,14,15,16</sup>

Two major theories exist concerning the underlying immunological mechanism of Graves ophthalmopathy. One theory considers ophthalmopathy to be a distinct autoimmune disease unrelated to Graves disease. The other theory consider ophthalmopathy to be an autoimmune condition linked to Graves disease by antigenic determinants common to orbital and thyroid tissue. The exact nature of the autoimmune disorder is not clear, although both humoral and cell mediated mechanisms maybe involved.

Thyroid ophthalmopathy is the most common cause of diplopia in middle-aged elderly patients. If the symptoms are intermittent or episodic, it is important to confirm the correct diagnosis, such condition as myasthenia can coexist with thyroid disease. Moreover, many intermittent thyroid diplopia problems resolve spontaneously; patients with early thyroid disease or an acute onset of double vision often improve with steroid treatment. Therapy for thyroid optic neuropathy is controversial, some investigators advocate steroids, others radiation and some immediate orbital decompression. There is almost universal agreement, however, that most of these patients with marked vision decrease required rapid intervention.<sup>10,17,18,19,20,21,22,23,24</sup>

More than 75% of thyroid ophthalmopathy patients have either a history of systemic thyroid disease or relatively characteristic eye findings making these ocular diagnosis straight forward. The tests are done in the following sequence until a positive result is obtained. Suspicious clinical findings and a positive systemic test are almost always sufficient to substantiate the diagnosis of thyroid eye disease. In addition to the history and physical findings discussed previously, a number of ocular tests and orbital scans are useful. These studies include the forced duction test, ultrasonography, CT with computer reformation and MRI. Currently, T1 weighted (orbital fat is bright) MRI produces better anatomic detail without radiation exposure.<sup>25,26,27,28</sup>

In this study, 50 consecutive patients were evaluated with ocular signs of hyperthyroidism at the Regional Institute of Ophthalmology, Government Ophthalmic Hospital, Trivandrum. Patients were evaluated clinically with the use of Hertel’s exophthalmometer and special investigations serum T<sub>3</sub> T<sub>4</sub> and TSH levels were done. Antimicrosomal and antithyroglobulin antibody and CT scan were done in special cases. All patients were treated with systemic antithyroid

drugs. Some cases with ocular muscle involvement and optic nerve involvement were treated with systemic steroids, which responded dramatically. In nonresponsive cases, azathioprine was given and a satisfactory improvement obtained.

**Objectives**

1. To study the various ocular manifestations of hyperthyroidism and severity of ocular muscle involvement in Graves disease.
2. To study the relation of optic neuropathy and ocular myopathy.
3. To study the relation between serum T<sub>3</sub>, T<sub>4</sub>, TSH level to ocular Myopathy in Graves disease.

**MATERIALS AND METHODS**

Study was conducted at the Regional Institute of Ophthalmology Medical College, Trivandrum, and Department of Endocrinology Medical College, Trivandrum. The study was in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration.

Fifty consecutive patients with ocular signs of hyperthyroidism were evaluated. They were followed up for an average period of 1 year (range from 4 months to 1<sup>1</sup>/<sub>2</sub> years). Detailed ocular examination and exophthalmometric measurements using Hertel’s exophthalmometer are taken at each visit. A detailed examination of ocular movements was done and Worth’s four-dot test done at each visit to detect diplopia.

Routine investigation and special investigations for assessment of thyroid gland including T<sub>3</sub>, T<sub>4</sub>, TSH were done. In some of the cases, CT scan was taken. In suspected cases of euthyroid Graves disease, antimicrosomal antibodies and antithyroglobulin antibodies was done.

**Inclusion Criteria**

1. Patients between 10 years and 60 years were taken.
2. Ocular signs of hyperthyroidism should be present.
3. Both sexes were included.

**Exclusion Criteria**

1. Patients less than 10 and more than 60 years were excluded.
2. Patients with the other thyroid disorders like Hashimoto’s thyroiditis and myxedema were excluded.
3. Patients with other causes of proptosis and ocular myopathy were excluded.

**RESULTS**

Sl. No.	Age (Years)	Number of Patients	Percentage
1.	10-20	2	4
2.	21-30	5	10
3.	31-40	17	34
4.	41-50	15	30
5.	51-60	11	22
	<b>Total</b>	<b>50</b>	<b>100</b>

*Table 1. Age Wise Distribution of Patients*

Sl. No.	Sex	Number of Patients	Percentage
1.	Female	33	66
2.	Male	17	34

**Table 2. Sex Wise Distribution of Patients**

T <sub>3</sub> Level ng/dL	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
0-100	0	0	2	1	0	0
101-200	2	0	3	5	1	2
201-300	2	0	2	3	0	0
301-400	0	0	0	4	0	0
401-500	1	2	0	2	0	0
501-600	0	0	0	2	0	0
>600	1	0	1	2	0	0
Not done	1	2	4	4	0	0

**Table 3. Relationship between ST<sub>3</sub> Level and Signs**

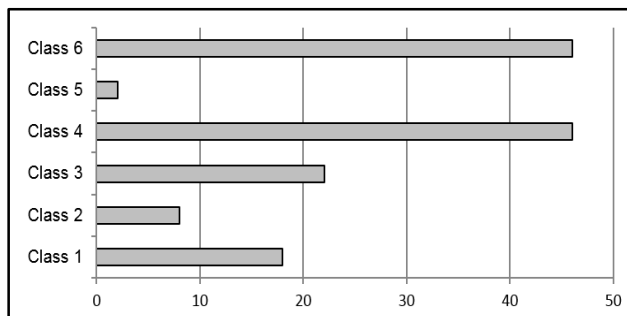
There is no definite correlation between ST<sub>3</sub> level and severity of ocular involvement.

S.T <sub>3</sub> Level ng/dL	Number of Cases	Percentage
0-70 (<N)	3	7.69
70-210 (N)	14	35.89
>210 (>N)	22	56.4
Not done	11	

**Table 4. Correlation between ST<sub>3</sub> Level and Ocular Involvement**

S.T <sub>4</sub> Level µg/dL	Number of Cases	Percentage
<3	1	2.6
3-13	15	39
>13	22	57
Not done	12	

**Table 5. Correlation between ST<sub>4</sub> Level and Ocular Involvement**



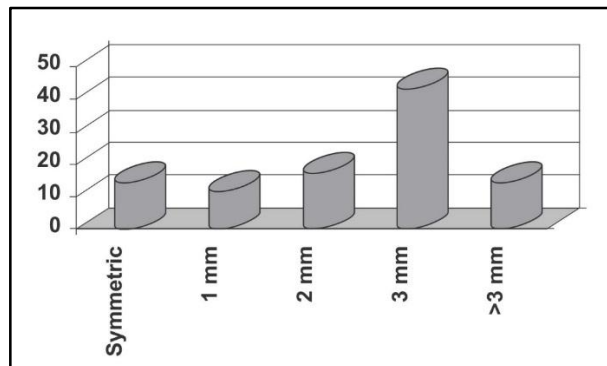
**Graph 1. Bar Diagram Showing Ocular Myopathy in Different Classes**

	Number of Cases	Percentage
No proptosis	15	30
Mild (21-23 mm)	20	57.1
Moderate (24-27 mm)	12	34.2
Severe (>27 mm)	3	8.5
Total number of proptosis cases	35	70

**Table 6. Relationship between Degree of Proptosis and Hyperthyroidism**

Difference between Two Eyes in mm	Number of Cases	Percentage
Symmetric	5	14.2
1 mm	4	11.4
2 mm	6	17.1
3 mm	15	42.8
>3 mm	5	14.28
Total proptosis cases	35	100

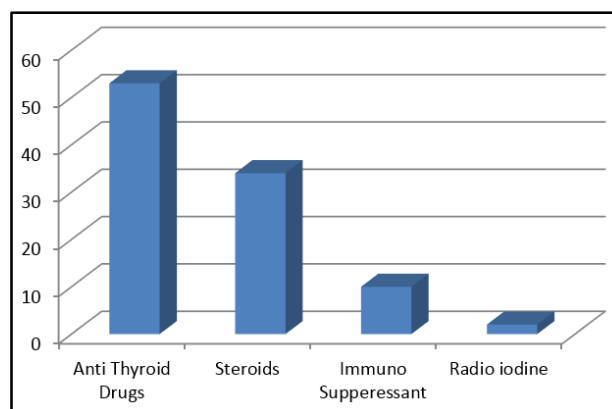
**Table 7. Difference in Exophthalmometric Readings between Two Eyes**



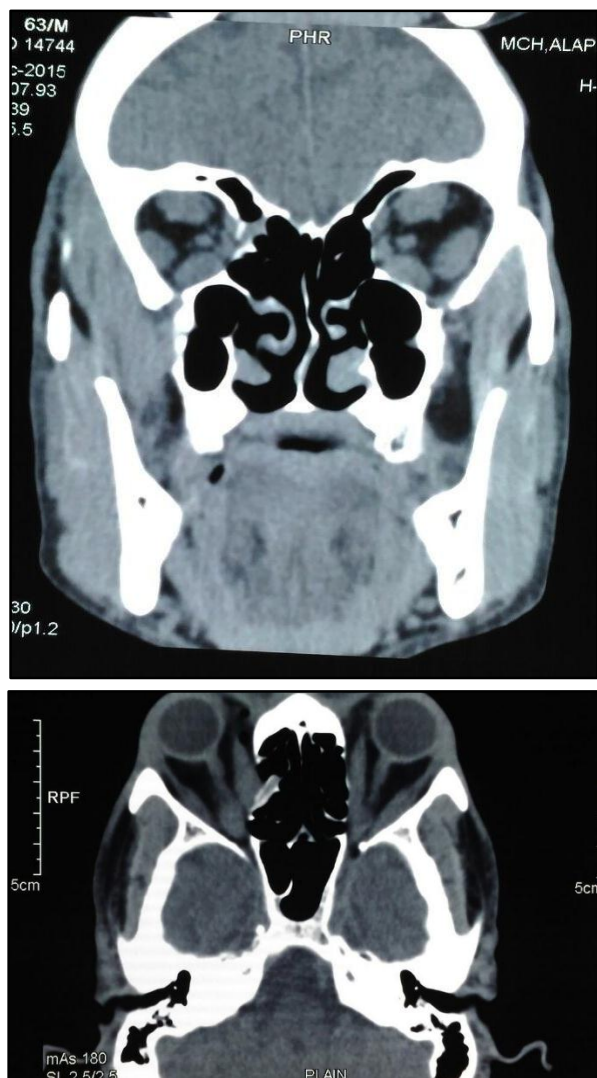
**Graph 2. Asymmetry of >3 mm between Two Eyes is Very Rare in Thyroid Exophthalmos**

	Mild	Moderate	Severe
0-70	0	1	0
70-210	3	4	3
211-300	2	1	0
301-400	2	1	0
401-500	2	0	0
501-600	1	1	0
>600	0	2	0
Not done	1	3	1
<b>Total</b>	<b>11</b>	<b>13</b>	<b>4</b>
<b>Percentage</b>	<b>39.28</b>	<b>46.42</b>	<b>14.28</b>

**Table 8. Correlation between Severity of Ocular Muscle Involvement and Hormone Level**



**Graph 3. Response of Patients to Various Modalities of Treatment**



**Figure 1 and Figure 2. Shows CT Scan Images Demonstrating Thickened Ocular Muscles**

## DISCUSSION

Hyperthyroidism is a very common condition in which eyes form a major target organ. Ocular signs can occur in individuals with raised thyroid hormone level and also in individuals with normal hormone level when the term Euthyroid Graves is generally used.

In our study of 50 cases of hyperthyroidism, the maximal incidence was found between fourth and sixth decades of life. About 65% of cases belong to this age group. Nordyka and coworkers observed in a study of 880 patients that eye findings almost disappeared in the seventh and eighth decades.

The overall female/male ratio in systemic hyperthyroidism is 4:1; however, in thyroid eye disease, the ratio is less usually documented at approximately 2.5:1. In our study, about 66% were females with a female:male ratio of approximately 2:1.

There is no definite correlation between serum T3 level and severity of ocular signs in our study.

Euthyroid ophthalmopathy, which accounts for about 10 to 25 percent of patients with presumed thyroid eye disease. In our study, about 35% individuals belong to euthyroid Graves ophthalmopathy. Several studies have attempted to

identify correlations between thyroid function and ocular status. Liddle et al<sup>16</sup> suggested that a combination of Graves disease and Hashimoto's thyroiditis would account for the euthyroid state in most cases.

Exophthalmos is a characteristic finding in thyroid eye disease occurring in 34 to 93% of patients. The degree of proptosis can be measured using an exophthalmometer with readings over 21 mm or difference greater than 2 mm between eyes considered suggestive of orbital pathology. In our study of 50 cases of hyperthyroidism, proptosis was present in 70% of cases. Of these cases of proptosis, majority, i.e. about 57% are of mild degree (21-23) and severe proptosis >27 mm occurred in only 8.5% cases.

While some asymmetry in the degree of proptosis is not uncommon in thyroid eye disease, it is almost never greater than 7 mm and usually less than 3 mm. In our study, symmetric exophthalmos occurred in 14.2% cases and an asymmetry of more than 3 mm was seen in only 14.2% cases.

Visual loss is an important, but rare complication of thyroid eye disease and is usually due to optic neuropathy. The incidence of optic neuropathy in thyroid eye disease is approximately 5% and affected individuals usually do not have marked proptosis or optic nerve changes on ophthalmoscopy. Because, it often has an insidious onset and maybe associated with subtle findings, the cause of visual loss is frequently misdiagnosed. In our study of 50 cases of hyperthyroidism with eye involvement, only two cases (4%) showed optic nerve involvement. Both cases were associated with severe degree of ocular muscle involvement. Both cases resolved dramatically on giving steroids. Patients with thyroid optic neuropathy display enlarged extraocular muscles, which cause a demonstrable compression of the optic nerve at the orbital apex. Kennerdell and co-workers observed seven patients with optic neuropathy and noted enlarged apical extraocular muscles compressing the optic nerves in all.

In our study of 50 cases, ocular myopathy is seen in 28 cases, i.e. in 56% cases of which majority of the cases are of moderate degree. Multiple muscle involvement is more common than single muscle involvement. Most commonly the inferior rectus muscle is involved with a restriction of elevation in primary position. Forced duction test was positive in all cases.

The various treatment modalities are undertaken with prime importance given to medical management. In our study, we have given antithyroid drugs (T. NeoMercazole 5 mg thrice daily), systemic steroids and immunosuppressants.<sup>23,24,27,29,30</sup> In only one case, radioactive iodine was tried because the patient developed agranulocytosis on treatment with NeoMercazole. Systemic steroids are given in 34% cases, majority of which include patients with ocular muscle involvement and optic nerve involvement. In 10% cases, immunosuppressants (T. azathioprine 50 mg twice daily) was given.<sup>31,32,33,34,35</sup>

**CONCLUSION**

This study shows the female preponderance, symmetrical presentation in both eyes and lack of correlation between serum hormone level and severity of ocular signs.

To conclude, the ocular signs of hyperthyroidism in the present study seem to be generally mild. The severe eye changes like corneal involvement and optic nerve changes requiring active management with systemic steroids and immunosuppressants were less common.

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