ORIGINAL **PROF-1144**

HYPERTHYROIDISM;
MODE OF OPHTHALMIC MANIFESTATIONS

DR. MUHAMMAD SULTAN, MBBS, FCPS
Associate Professor
Head of Department Ophthalmology
Punjab Medical College/Allied Hospital/DhQ
Faisalabad.

DR. MUHAMMAD ALI QAISAR, MBBS
RMO, Allied Hospital
Faisalabad.

DR. M. SAEED AKHTAR
MBBS, M.Sc, Nuclear Medicine
Principal Medical Officer
Punjab Institute of Nuclear Medicine (PINUM)
Faisalabad.

ABSTRACT ... Objective: Thyroid eye disease presents a special challenge to the ophthalmologists with pathogenetic enigma & therapeutic dilemma. The objective of the study is to determine the frequency of mode of ophthalmic manifestation of thyrotoxicosis, rating of all components of "NOSPECS" classification system and to determine the relative magnitude of low & high index orbitopathies. **Design:** Cross sectional study. Setting: The department of ophthalmology Allied Hospital / Punjab Medical College (PMC) & Punjab Institute of Nuclear medicine (PINUM) Faisalabad. **Period:** From 1st Apr 2004 to 31st March.2005. **Material & Methods:** 100 patients of all age & sex, after having diagnosed as thyrotoxic on the basis of positive laboratory investigations were subjected to a planned ocular examination according to the given protocol. An ophthalmopathy index scoring system was adopted to tabulate the results. **Results:** Among 100 thyrotoxic patients, 72 were female & 28 were male with male to female ratio 1:26. The over all mean age was 36.59 ±13.81 years with 77 % of cases lying between 21-50 year of age. Orbitopathy was found in 74 % of thyrotoxic patients with relative distribution of eyelid retraction 56 %, soft tissue involvement 38 %, Proptoses 16%, restrictive myopathy 11%, corneal involvement 13 % and sight loss due to optic neuropathy 7 %. There is more occurrence of low index orbitopathy 83 % as compared to high index orbitopathy i.e 17 %. **Conclusion:** The occurrence of dysthyroid orbitopathy is not essentially present in all hyper thyroid patients. Only 3 out of 4 develop it. The frequency of manifestation of various eye lesions in descending order is eyelid retraction, soft tissue involvement, Proptosis, corneal involvement, myopathy & vision loss. Low index orbitopathy is more common & males are at more risk of developing orbitopathy than females.

Key words: Orbitopathy, Thyrotoxicosis, Ophthalmopathy, Dysthyroid, Hyperthyroid.

INTRODUCTION

As early as the 12th century, a Muslim scholar Sayyed Ismail Al Jurgani described the relationship of exophthalmos with goiter[1]. In 1786, Mr. Parry[2] and in 1835, Grave[3] recorded the complete description. A variety of terms have been used to describe the constellation of eye findings that occur in patients with thyroid disease. Since the orbit is primary site of involvement and the patient may be euthyroid, the term dysthyroid orbitopathy is preferred. Although most of the patients having orbitopathy are hyperthyroid yet they may be hypo or euthyroid. Similarly not essentially all hyperthyroids develop orbitopathy, some do not ever. Also there is no correlation between the severity of ophthalmopathy & thyroid dysfunction. Actually dysthyriod orbitopathy is a distinct autoimmune disorder separable from hyperthyriodism. In general many hyperthyroids have some detectable ophthalmopathy and majority of patients with ophthalmopathy have some subtle or overt dysthyroidsm indicating multifactorial causes and close relationship between the two but with independent unique features. "NOSPECS" is a system of classification of dysthyroid orbitopathy in which the first letter of each class in the grading system speaks the mnemonic NOSPECS as follows [4].

N	No Physical sign
O	Only sign
S	Soft tissue involvement
P	Proptosis
E	Extra ocular muscle involvement
C	Corneal involvement
S	Sight loss caused by optic nerve damage

Soft tissue class is further elaborated with mnemonic "RELIEF" i.e. Resistance to retropulsion , Edema of conjunctiva, Lacrimal gland enlargement, Injection of conjunctiva, Edema of lids & Fullness of lids. "NOS". are taken as low index while "PECS" are taken as high index of severity [5].

MATERIAL AND METHODS

One hundred laboratory diagnosed thyrotoxic patients were selected between 1st Apr 2004 to 31st Mar 2005 from a pool of patients coming to PINUM for their laboratory screening for thyoriod. Patients with lid contractures resulting from trauma, chemical & thermal burns, corneal ulcers and opacities, glaucoma and orbital tumors were excluded. These 100 thyrotoxic patients were subjected to the planned ocular examination and clinical testing at Department of Ophthalmology at Allied Hospital PMC FSD for a cross sectional study. Sample technique was non probability (purposive). The examination protocol included VA testing by snallen's test type, color vision with ISCHIHARA cards, direct and indirect pupillary light reflexes, extra ocular muscle movement including FDT, Lid movement for Darlymple's. Von Grafe's, Kocher's, Griffith's, Rosenbach's, Stellwag's, Joffroy's, Sainton's and Gifford's sign. Squint was examined by Hirshberg and Krimsky test, fundi with direct and I/D, IOP and differential IOP with Perkin's Tonometer, Anterior Segment with slit lamp, Exophthalmometery with Hertel's exophthalmometer, visual field analysis with Hamphery Field Analyzer and B-Scan was performed for extra ocular muscle mass. Data was collected and ophthalmopathy index scoring system of "NOSPECS" scoring was adopted for rating.

RESULTS

Among 100 laboratory diagnosed hyperthyroid patients, 72 were female and 28 were male and male to female ratio was 1: 2.6 .The overall mean age was 36.59 ± 13.81 years. Among females it was found to be 37.35 ±13.35 years and in males it was 34.72 ± 14.93 years .The difference in age according to sex was found statistically non-significant P= 0.60 , t =0.86 (Table I).

Table-I. Age & Sex of Thyrotoxic Patients

Gender	Age Mean ±S.D	Age Range	Median Value
Female (n = 72)	37.35±13.35	12.00-70.00	40.00
Male (n = 28)	34.72±14.93	13.00-80.00	32.00
Total (n = 100)	36.59±13.81	12.00-80.00	37.00

It was observed that 77% of the cases were lying

between 21 to 50 years of age (Table II). This study shows 74 out of 100 patients (74 %) patients were found to have some sort of orbitopathy. Among them, 23 were male and 51 were female .In each sex the occurrence of orbitopathy was found to be independent of sex when tested by Chi-square test. P = 0.24, Chi-square = 1.34.

Table-II. Age Groups of Thyrotoxic Patients

Age Group	Male	Female	Total	% Age
Up to 20	03	09	12	12%
21-30	10	15	25	25%
31-40	06	21	27	27%
41-50	04	21	25	25%
51-60	03	04	07	07%
61 & More	02	02	04	04%
Total	28	72	100	

Table-III. Sex Specific Rates of Orbitopathy in 100 Thyrotoxic Patients

	Orbitopathy	No Orbitopathy	Total
Male	23(82%)	5(18%)	28
Female	51(71%)	21(29%)	72
Total	74(74%)	26(26%)	100
P = 0.24, Chi-square = 1.34			

The frequency of manifestations of eye lesions in patients of dysthyroid orbitopathy in descending order is: Eyelid retraction (56%) , Soft tissue involvement (38%), Proptosis (16%) , Restrictive myopathy (11%) , Optic neuropathy (7%) (Fig-1).

DISCUSSION

Orbitopathy rates were 74 % in this study while no orbitopathy was found in 26% (Table IV) and this is different to other studies which rates as high as 91.4 %[6]. However orbitopathy rates in Graves' disease were strangely low in the study of Carter JN who reported it to be 2% to 7%[7]. In our study carried out by Qamar Farooq in Pakistan[8], The orbitopathy rate was found 8% which is very close to our study. Sex distribution in patients showing dysthyroid orbitopathy, male to female ratio is 23:51 i.e 1:2.2 (Table III) which is close to other studies[6]. While in another study done by Wiersinga-WM and associates[9], male to female ratio of Graves' orbitopathy patients was found 1:3.

Table-VI. Rates of Components of NOSPECS.

Components of NOSPECS	Observed Rates	95% Confidence Interval%
N	26(26%)	11.7-44.9
O	56(56%)	36.7-74.0
S	38(38%)	20.9-57.4
P	16(16%)	5.3-33.4
E	11(11%)	2.6-27.0
C	13(11%)	3.6-29.7
S	7(7%)	1.0-21.4

N = No Physical sign or symptoms (Class 1)
O = Only sign (Class 2)
S = Soft tissue involvement (Class 3)
P = Proptosis of 3 mm or more (Class 4)
E = Extra ocular muscle involvement (Class 5)
C = Corneal involvement (Class 6)
S = Sight loss (Class 7)

Age distribution among thyrotoxic patients showing highest rate in 21-30 years (25%) , 31-40 years (27 %) and 41-50 years (25%) age groups in our study (Table II). Age range covering the maximum cases was 21-50 years (77%) (Table II). The mean age range was found 36.59±13.8 years in our study (Table I), which is exactly the same found in another study in Pakistan where it was 38.88 years[8]. The orbitopathy rates in 30-50 years age group in our study remained about 4:1 for females and males (Table II) and is thus comparable to other studies[10]. The occurrence of orbitopathy in each sex was independent of sex when tested by chi-square test (Table III). Kendler and his associates has also reported no significant difference in orbitopathy rates between

males and females in each sex[11].

Fig-1. Frequency of various eye lesions in patients of thyrotoxicosis

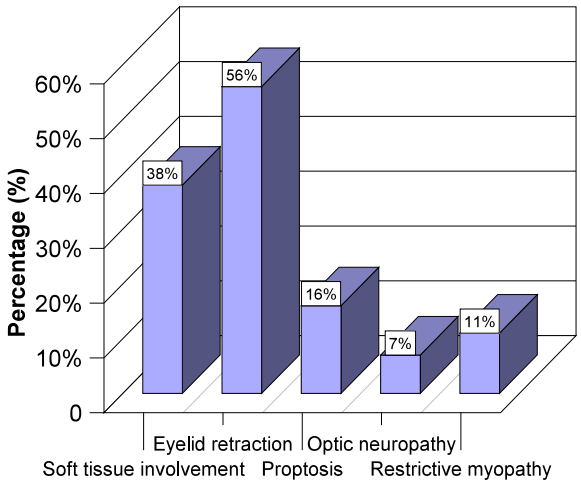
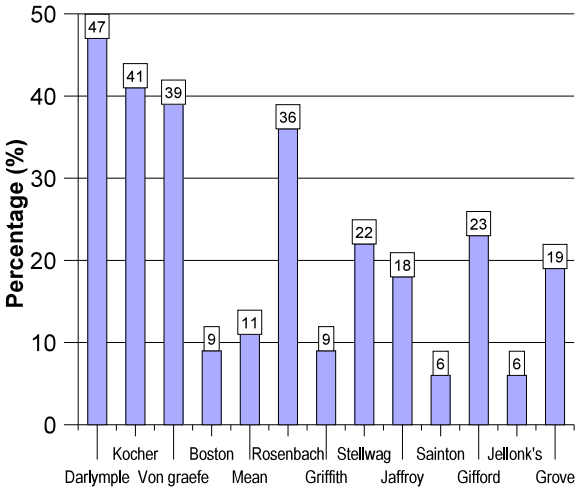


Fig-2. Relative frequency of lid signs in 100 thyrotoxic patients

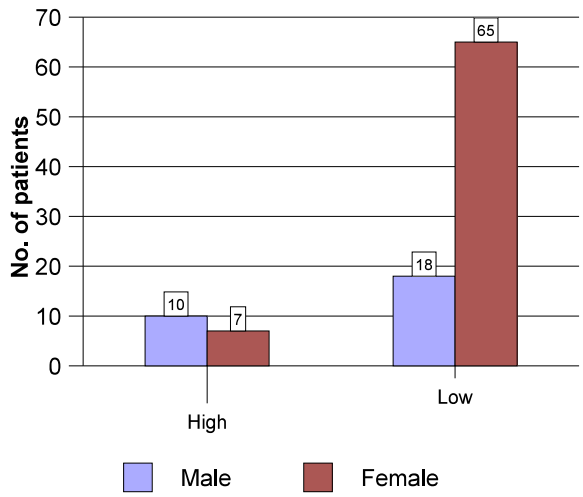


Lid retraction was the most common orbitopathy and occurred in 74% (Table IV) of the thyrotoxic patients. Bartley GB also published the same sign to be the most persistent[12], Kocher's, Darlymple's and von-Graefe's were the most frequently seen signs and were present in more than 30% of the thyrotoxic patients at the time of examination. 55% is reported in Bartley'study[12].

Unilateral or bilateral proptosis 20mm or more by Hurtel's exophthalmometer was seen in 16 thyrotoxic patients (16%). (Fig-1) Bartley-GB reported an extremely high rate (60%)[12] which was not seen in our study. Restrictive myopathy was found only in 11 %. All showed differential IOP rise of more than 6 mm in up gaze.

High index orbitopathy was more common among males 10 /17 (58.8%) as compared to females 7 / 17 (42.2%) (Fig-3) and commonly involves relatively higher age group i.e. above 40 years and this is comparable to the results of Perros-P and colleagues[13,8].

Fig-3. Index of orbitopathy



Signs of optic nerve compression were present in 7 out of 100 patients (7%) and this is comparable to other studies i.e 9.9 % in the study of Perros-P and associated published in April 1993[13] and 6 % in the study of Bartley-GB[12]. In a retrospective study of 89 patients with Graves' disease done by Barth- A and colleagues[14] , class 1 or greater was found in 34 % , proptosis more than 20mm in 8% and severe ophthalmopathy i.e. class 4 to 6 , in 7% of the patients before treatment with radio-iodine.

In a study carried out at RGH/PIMS Pakistan the high index orbitopathy rate was found 14% while low index orbitopathy rate was found 67%[8] while in our study, it was 17% and 83% respectively (Fig 3) which is very much similar.

CONCLUSION

All hyperthyroids do not devolp orbitopathy i.e the frequency rate of occurrence is 74 %. The frequency of manifestations of eye lesions in patients of thyrotoxicosis in descending order is:

1.	Eyelid retraction	56%
2.	Soft tissue involvement	38%
3.	Proptosis	16%
4.	Restrictive myopathy	11%
5.	Optic neuropathy	7%

The occurrence rate of dysthyroid orbitopathy in each sex appears to be independent of sex . Low index orbitopathy is more common than high index orbitopathy. Males are more at risk of developing orbitopathy than females.

It is recommended that multi centric studies, hospital and community based, may be carried out to:

A. Identify risk factors for development of thyrotoxicosis and for low and high index dysthyroid orbitopathy.

B. Identify early warning signs of both thyrotoxicosis and dysthyroid orbitopathy.

C. Measures to prevent this sight threatening condition.

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