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Research Article

Prevalence and risk factors of thyroid-associated ophthalmopathy among Indians

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ABSTRACT

Background: Thyroid-associated ophthalmopathy (TAO) is a part of an autoimmune process that can affect the orbital and periorbital tissue, the thyroid gland, and, rarely, the pretibial skin or digits. The aim of the present study was to determine the prevalence of TAO among Indian patients with thyroid dysfunction and the risk factors associated with TAO.
Methods: A cross-sectional study of thyroid eye disease was conducted on patients with thyroid dysfunction visiting the outpatient department of a tertiary care centre. Demographic data, past medical history, family history, and life-style data were collected from all patients. An ophthalmologist interviewed the patients and noted the presence of symptoms and signs relevant to thyroid eye disease.
Results: Out of a total of 100 patients, who were eligible for analysis, 80 were diagnosed with mild to moderate TAO and 20 were diagnosed with severe TAO. There were more male patients in patients with a severe course (50%) compared to those with a mild to moderate course (42.5%). More patients with a severe course were smokers compared to those with a mild to moderate course (chi-square test, p=0.021). More patients with a severe course had a higher clinical activity score (p=0.007).
Conclusions: We have confirmed that smoking is the strongest risk factor for development of a severe course of TAO in Indian patients. Thus, it is important for patients with Graves' disease to refrain from smoking.

Keywords: Thyroid associated ophthalmopathy, Hyperthyroidism, Smoking

INTRODUCTION

Thyroid-associated ophthalmopathy (TAO), frequently termed Graves ophthalmopathy, is part of an autoimmune process that can affect the orbital and periorbital tissue, the thyroid gland, and, rarely, the pretibial skin or digits.[1-3] Although the use of the term thyroid ophthalmopathy is pervasive, the disease process is actually an orbitopathy in which the orbital and periocular soft tissues are primarily affected with secondary effects on the eye. TAO may precede, coincide, or follow the systemic complications of dysthyroidism. The ocular manifestations of TAO include eyelid retraction, proptosis, chemosis, periorbital edema, and altered ocular motility with significant functional, social, and cosmetic consequences.

The annual incidence rate of TAO has been estimated at 16 cases per 100,000 women and 2.9 cases per 100,000 men.[4] There appears to be a female preponderance in which women are affected 2.5-6 times more frequently than men; however, severe cases occur more often in men than in women. In addition, most patients are aged 30-50 years, with severe cases appearing to be more frequent in those older than 50 years. Although most cases of TAO do not result in visual loss, this condition can cause

vision-threatening exposure keratopathy, troublesome diplopia, and compressive optic neuropathy. Therefore, although the prognosis is generally favorable for patients with this condition, and most patients do not require surgical intervention, all clinicians should be able to recognize TAO.[5,6] The aim of the present study was to determine the prevalence of TAO among Indian patients with thyroid dysfunction and the risk factors associated with TAO.

METHODS

A cross-sectional study of thyroid eye disease was conducted on patients with thyroid dysfunction visiting the outpatient department of a tertiary care centre. The study was performed during a one-year period from November, 2014 to November, 2015. All patients with thyroid dysfunction presenting to the hospital during the study period were identified and enumerated. The initial diagnosis was categorized as hyperthyroidism and hypothyroidism. Patients with thyroid gland malignancy and thyroid nodules were excluded.

All patients >18 years of age were informed of the study and invited to participate in the interview, which was conducted by an ophthalmologist. Demographic data, past medical history, family history, and life-style data were collected from all patients. An ophthalmologist interviewed the patients and noted the presence of symptoms relevant to thyroid eye disease using the VISA classification including vision, inflammatory, strabismus, and appearance categories.[7]

For the patients with eye symptoms, the ophthalmologist performed an ophthalmic examination. Patients with at least one symptom and one sign in any category in the VISA classification were considered to have thyroid eye disease. The diagnosis of TAO was based on the presence of typical clinical features of the disease, including eyelid retraction, proptosis, impaired motility, and increase in intraocular pressure on upward gaze, one or more enlarged extraocular muscles, and increased intraorbital fat on computed tomography scans. In this study, a mild course of TAO was defined as proptosis less than 21 mm with no or only intermittent diplopia without optic nerve involvement. Moderate TAO was defined as proptosis between 21 mm and 23 mm with intermittent diplopia and no optic nerve involvement.[8] Patients were judged to have a severe course of TAO if they had, in the worse eye, either motility impairment causing constant diplopia within 30 degrees by the binocular single visual field test and the Hess screen; or proptosis greater than 23 mm or with a difference between eyes of more than 5 mm by Hertel exophthalmometry, causing serious exposure keratopathy; or compressive optic neuropathy.

Statistical analysis

Categorical variables were compared using the chi-square test, a t-test was used for continuous variables, and continuous variables for multiple groups were compared using analysis of variance (ANOVA). Multivariable logistic regression analyses were carried out to evaluate the independent relationship of significant risk factors for thyroid eye disease. The SAS ver. 8 software package (SAS Inc., Cary, NC, USA) was used for statistical analyses. Odds for thyroid eye disease were presented with 95% confidence internals (CIs). A p-value of <0.05 was considered significant.

RESULTS

Total 100 patients were eligible for study. Out of a total of 100 patients who were eligible for analysis, 80 were diagnosed with mild to moderate TAO and 20 were diagnosed with severe TAO.

Table 1: comparison of demographic, clinical, and biochemical features between patients with mild to moderate courses and severe courses of thyroid-associated orbitopathy.

Characteristics	Mild to moderate course (n=80)	Severe course (n=20)	p Value
Age (yrs)	39±9.8	52±8.8	0.008
Male	34 (42.5%)	10 (50%)	NS
Initial fT4 level (> 3 ng/dl)	20 (25%)	5 (25%)	NS
Positive TBII	77 (96.25%)	18 (90%)	NS
Comorbidities			
Diabetes	9 (11.25%)	2 (10%)	NS
Hypertension	12 (15%)	3 (15%)	NS
History of smoking	13 (16.25%)	10 (50%)	0.021
Exophthalmos	18.4±2.5	20.1±3.4	0.026
Lid retraction	42 (52.5%)	12 (60%)	NS
Clinical activity score	1.2±1.1	2.7±2.1	0.007

NS= Non-significant.

Demographic, clinical, and biochemical features of mild to moderate TAO and severe TAO are compared in Table 1. There were older patients among those with severe courses than in the group with mild to moderate courses (*t*-test, $p = 0.008$). There were more male patients in patients with a severe course (50%) compared to those with a mild to moderate course (42.5%); however, this difference was not statistically significant.

The initial free T4 levels were high (above 3 ng/dL) in 25% of the mild to moderate group as well as severe group. The ratio of patients with positive TBII was similarly high in both groups; 96.25% in the mild to moderate group and 90.0% in the severe group. However, there was no statistical significance with respect to the number of patients with a high initial free T4 level (>3.0 ng/dL) and positive TBII (>10 U/L) between the two groups.

Comorbid illnesses like diabetes and hypertension were almost similar in both groups. More patients with a severe course were smokers compared to those with a mild to moderate course (chi-square test, $p=0.021$). More patients with a severe course had a higher clinical activity score ($p=0.007$). On multiple logistic regression analysis, smoking behaviour was found to be a risk factor for severe TAO with an odds ratio of 0.325. A history of diabetes and a positive TBII level also revealed odds ratios of 1.125 and 1.069, respectively; however, they were not statistically significant.

DISCUSSION

Several risk factors including old age, male gender, smoking, and abnormal thyroid function have been identified in several reports as possible predisposing factors for severe TAO. A positive relationship between age and ophthalmopathy has been identified.[9] Several cross-sectional and cohort studies have shown that smoking is an independent risk factor for severe ophthalmopathy.[10-14]

Prsent study showed that old age, diabetes, hypertension and smoking are strong risk factors for severe TAO. Risk factors, which were not statistically significant, are free T4 level, TBII, and TAO duration. Higher degree of exophthalmos and higher clinical activity scores were noted in severe TAO. Smoking was strong predictor of severe TAO in multiple logistic regression analysis. Many study showed that thyroid binding inhibitor immunoglobulin or thyroid-stimulating antibody are involved in the etiology of TAO.[15-17] In present study, TBII levels were positive in most of TAO patients (96.25% and 90.0% in mild-moderate TAO and severe TAO respectively).

CONCLUSION

Present study confirmed that smoking is a statistically strong risk factor for TAO and its complications. Thus smokers with TAO should be aggressively monitored and treated.

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