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Research Article

PREVALENCE OF ANTI-THYROID PEROXIDASE ANTIBODY (ATPO) IN PATIENTS WITH THYROID DISORDERS-A HOSPITAL BASED RETROSPECTIVE STUDY

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A B S T R A C T

Introduction: The prevalence of auto immune disorders especially that of thyroid gland has been increasing nowadays. Antibodies directed against thyroid peroxidase are an important cause of autoimmune thyroid diseases. **Objective:** To determine the thyroid hormone status and prevalence of antithyroid peroxidase antibodies in patients referred for evaluation of thyroid function from January 2013 to December 2015. **Design:** Retrospective study. **Setting:** The results of the patients who attended the Nuclear Medicine department, Government Medical College, Kozhikode, Kerala from January 2013 to December 2015 were analyzed. **Results:** Among the 1197 individuals, 794 (66.3%) were euthyroid, 116 hyperthyroid (9.7%) and 287 (24.0%) hypothyroid. Anti thyroperoxidase antibody was elevated in 49.12% of patients, out of which 66.3% were euthyroid, 9.7%hyperthyroid and 24% hypothyroid. Prevalence of antithyro peroxidase antibodies in euthyroid, hypothyroid and hyperthyroid was42.4%, 69.7% and 44% respectively. Among the antibody positive individuals, subclinical hypothyroidism was the most common abnormality detected (53.78%).**Conclusion**: Nearly 49% of subjects under evaluation for various thyroid disorders in a tertiary care hospital population showed the presence of elevated antithyro peroxidase antibody. Autoimmune thyroiditis should be considered as a major health problem and antithyro peroxidase antibody could be a useful tool in its evaluation.

INTRODUCTION

Thyroid disorders are the most common among all endocrine diseases in India[1].Availability of highly sensitive and specific assays has made detection of thyroid disorders extensive[2].Auto immune thyroid disorders are one of the common organ specific autoimmune disorders. About 2% to 4% of women and up to 1% of men are affected with autoimmune thyroid disorders worldwide and the prevalence increases with advanced age[3].It is commonly seen in women when compared to men[4].

Circulating antibodies against various thyroid antigens results in immunological alterations in thyroid follicular cells[5]. Thyroid peroxidase (TPO), Thyroglobulin (Tg) and Thyroid Stimulating Hormone (TSH) receptor are the most important antigens. Of these, Antithyro peroxidase antibodies (anti-TPO) are considered to have more pathogenic importance than other antibodies, as they fix complements & may directly damage the thyroid cells[6].Thyroid peroxidase is a poorly glycosylated membrane bound protein that contains a heme group. This is the main enzyme involved in thyroid hormone synthesis in several steps, including iodination of thyroxine residues, and the coupling of iodotyrosine residues[7].

Serum anti TPO concentrations may be high in about 10% of normal adults with an immune prevalence in older adults (up to 30%). The concentrations also are high in most patients (up to 15%) with Grave's disease and in more than 90% of patients with chronic auto immune thyroiditis and 15% of patients with thyroid carcinoma[8].Most patients with auto immune thyroid disease have high serum anti-TPO antibody concentrations than serum anti Tg antibody. Patients may have high serum Anti Tg antibody levels with normal Anti TPO concentration only rarely. Thus measurement of Anti TPO antibody is a more sensitive test for thyroid autoimmunity and hence should be a part of routine diagnostic tests for identification of the spectrum of disease[7].

There have been only few studies on the prevalence of anti TPO antibody positivity in our population, especially in Kerala. As far as our knowledge, there have been no studies inquiring into both the prevalence of anti TPO antibody positivity and the assessment of various thyroid function abnormalities in them. Government Medical College,

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Kozhikode being an apex tertiary care hospital caters to the health care needs of nearly 6 districts of northern and middle Kerala. We investigated the prevalence of thyroid function test abnormalities and the presence of anti TPO antibody as an autoimmune thyroid diseases (AITD) marker in this hospital population referred for evaluation of thyroid disease, thus representing the general population better.

MATERIALS AND METHOD

This retrospective study consisted of 1197 subjects who were referred to the Department of Nuclear Medicine, Government Medical College, Kozhikode for evaluation of thyroid function & Anti TPO antibody level estimation. People who were already receiving thyroxine tablets or other anti-thyroid therapies were excluded from the study. Demographic details, medical history and clinical examination details were collected from their treatment records.

T3,T4, TSH and Anti-TPO antibodies were measured using enzyme immunoassay. ELISA kits for TSH, T3, T4, were obtained from Adaltis Italia, Italy. Anti TPO antibodies were measured using enzyme linked Hycor Biomedical Autostat™ II Anti TPO Kit. All the reagents in the kit were standardized for the direct determination of thyroid hormones in human serum or plasma.

Normal ranges for the assays were as follows

T3: 0.8 -2 ng/ml
T4: 55-135ng/ml
TSH: 0.2-4.05µIU/ml
Upper limit for the normal range of Anti TPO antibody was <30IU/ml.

Data and statistical analysis

All data were statistically analyzed by using SPSS version18 .A p value of 0.05 or less was considered to be statistically significant.

RESULTS

A total of 1197 individuals suspected of having thyroid disease were sent for anti TPO antibody estimation to the Department of Nuclear Medicine, Government Medical College, Kozhikode during the 3 year period (Jan 2013-Dec 2015). The median age of the study group was 35 years (Range 3.5-85years). Majority (81%) of the patients belonged to the age group of 20-59 years. Out of the 1197 individuals, 983 (82.1%) were females and 213 (17.9%) were males. Among 983 female subjects, 82% were of 20 to 59 years age. (Table 1)

Thyroid hormone status

Among the 1197 individuals, 794 (66.3%) were euthyroid, 116 were hyperthyroid (9.7%) and 287 (24.0%) hypothyroid. Median ages for euthyroid, hyperthyroid and hypothyroid are 35, 37.5 and 35 years respectively (pvalue: 0.021).16.2% cases had subclinical hypothyroidism and 7.8% had clinical hypothyroidism in the study population. Overall prevalence of thyrotoxicosis was 9.7% (116/1197) out of which 5.4% had clinical thyrotoxicosis & 4.2% subclinical thyrotoxicosis. (Table 1)

Anti-TPO antibody status

Out of 1197 patients, 588 individuals were positive for anti TPO antibody, and 609 persons were negative (49.12% & 50.88% respectively).35.4% showed strong antibody positivity (>90 IU/mL) (Table 1). There is no significant difference in the age distribution between anti TPO antibody positive and negative patients (Median age 36 and 34 respectively; p value: 0.56).Most anti TPO antibody positive individuals were in the age group of 20-59 years (50.3%), followed by age less than 20 years; but this difference is statistically insignificant(p value :0.165) (Fig 1). Among the anti-TPO positive individuals, 83.7% (492/588) were females and 16.3% (96/588) were males.

Among the 588 anti TPO positive individuals, 337 (57.3%) were euthyroid and 251 (42.7%) had some form of thyroid dysfunction (pvalue: 0.000) (Fig 2).Out of the 251 patients with anti TPO positivity and thyroid dysfunction, 65 (25.89%) have clinical hypothyroidism & 135 (53.78%) have subclinical hypothyroidism and 32(12.74%) have overt thyrotoxicosis,19 (7.56%) have subclinical thyrotoxicosis (p value: 0.197). Thus among anti TPO positive non-euthyroid subjects, 79.7% are in hypothyroid range and 20.3% are in hyperthyroid range. (Table 2)

Among the hyper thyroid individuals, 51 (44%) showed anti TPO positivity. Among euthyroid cases, 42.4% showed the antibody positivity. 69.7% (200/287) of hypothyroid individuals showed elevated anti TPO antibody titre.69.89 % (65/93) cases of clinical hypothyroidism and 69.6 %(135/194) cases of subclinical hypothyroidism showed antibody positivity (Table 2).69% of cases with TSH more than 4.5µIU/ml were positive for the antibody. Data regarding presence or absence of goiter was available only in 859 patients. Of these 859 patients, 341 had goiter (39.7%).Of the patients with goiter, 58.06 % (198/341) were anti TPO antibody positive and 41.93 % were negative (p value: 0.00014).Out of the anti TPO positive patients, 13.4 % had a family history of thyroid diseases which was not statistically significant. (p value:0.365) (Table 2)

Table 1 showing the distribution of age, gender, goitre, anti TPO antibody positivity and thyroid function in the study population

Characteristics	Overall (n=1197), n (%)
Age in years, median (range)	35.0 (3.5-85.0)
Female gender	983 (82.1)
Goitre[1]	341/859 (39.7%)
Family history of thyroid disorder	172 (14.4%)
Anti-TPO positivity	588 (49.1%)
• Strong anti-TPO positivity	424 (35.4)
• Weak anti-TPO positive	164 (13.7)
Thyroid status	
• Euthyroid	794 (66.3)
• Non-euthyroid	403 (33.7)
Thyrotoxicosis	116 (9.7)
• Clinical thyrotoxicosis	65 (5.4)
• Subclinical thyrotoxicosis	51 (4.3)
Hypothyroidism	287 (24.0)
• Clinical hypothyroidism	93 (7.8)
• Sub clinical hypothyroidism	194 (16.2)

Data regarding presence or absence of goiter was available only in 859 subjects.

Table 1 showing relation of anti TPO antibody with age, goitre, family history and thyroid function.

Characteristics	Anti-TPO positive (n=588) (%)	Anti-TPO negative (n=609) (%)	p-value
Age in years, median (range)	36.0 (6.0-85.0)	34.0 (3.5-82.0)	0.555[1]
Goitre (n=859)	198/430 (46.0)	143/429 (33.3)	**0.000**[1]
Family history of thyroid disorder	79 (13.4)	93 (15.3)	0.365
Thyroid status			
• Euthyroid	337 (57.3)	457 (75.0)	**0.000**
• Non-Euthyroid	251 (42.7)	152 (25.0)	
Hypothyroidism	200 (34.0)	87 (14.3)	
Clinical hypothyroidism	65 (32.5)	28 (32.2)	
Subclinical hypothyroidism	135 (67.5)	59 (67.8)	
Thyrotoxicosis	51 (8.7)	65 (10.7)	
Clinical thyrotoxicosis	32 (62.7)	33 (50.8)	
Subclinical thyrotoxicosis	19 (37.3)	32 (49.2)	

[1] Mann Whitney U test
[1]Chi- square test

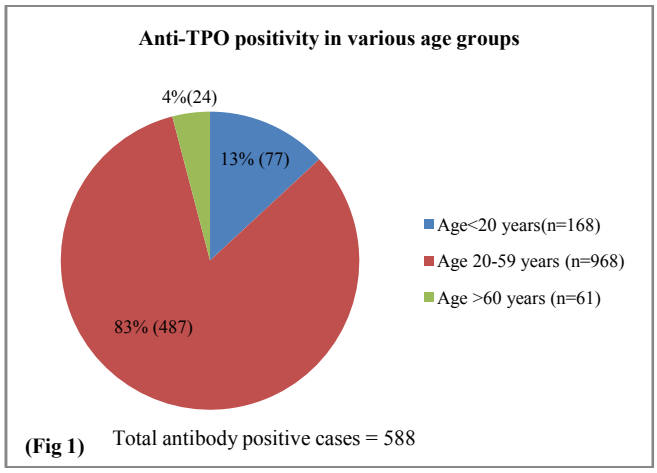

Figure 1 showing anti TPO positivity in various age groups.

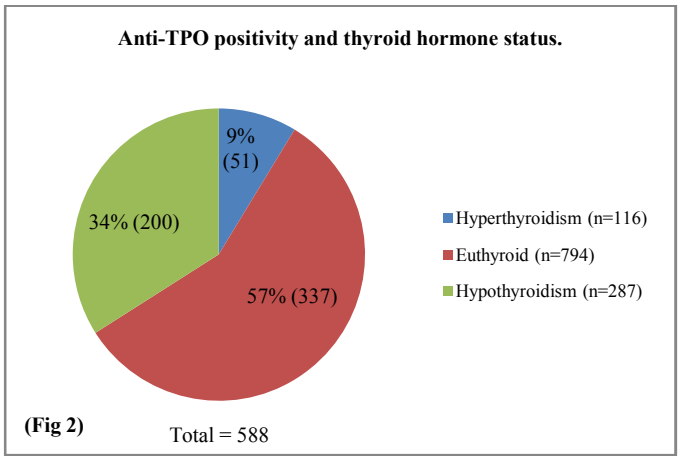

Figure 2 showing prevalence of anti TPO antibody in euthyroid, hypothyroid and hyperthyroid subjects.

DISCUSSION

Thyroid dysfunction is a common endocrine disorder seen in clinical practice. Prevalence of thyroid disease in a particular area depends on several important factors such as iodine intake, age, sex, genetic and environmental factors[9,10].In our study we have tried to estimate the thyroid function status and prevalence of anti TPO antibody positivity in patients referred for the evaluation of thyroid disorders.

In our study, overall anti TPO antibody positivity was 49.1 % (588/1197); 35.4 % (424/1197) showed strong antibody positivity (>90 IU/mL). Unnikrishnan *et al* (2013) conducted a study in 8 major cities in India in which 21.85% shows antibody positivity[11]. A survey by Amrita Institute of Medical Sciences, Kerala in 2009 showed that thyroid function abnormalities are present in 19.6% of adult population and about 9.5% of the subjects have anti-TPO antibodies[12]. In a pilot study conducted by Poulose *et al* (2012) in 125 asymptomatic young females in Thiruvananthapuram, Kerala reported that , 86 % of their subjects are anti TPO positive[13]. It is evident that the incidence of antibodies and hence autoimmune diseases are increasing in our population. Increasing exposure to thyroid disruptors, including industrial and agricultural contaminants and mutagens could be possibly be attributed to this increased autoimmunity[14]. NHANES III survey in the united states population during 1988-1994 had found a progressive increase with age in the percentage of people with positive anti TPO results [15]. Several studies have reported that there is an increased prevalence of anti TPO antibodies in the elderly especially in the 7th decade[9,16,17,18,19].In contrast, in our study maximum patients with anti TPO positivity was in the age group of 20-59 years followed ,by less than 20 years age. This difference in distribution was found to be statistically insignificant. This variation could be because the number of elderly subjects (61) was much less than the young subjects (1136) in our study.

It is well documented that anti TPO antibody positivity is more common in females[9,16,20,21]. Among the anti-TPO positive individuals, 83.7% were females in our study also.

Among the 588 Anti TPO positive individuals, 337 (57.3%) were euthyroid. Usha *et al* (2009) have suggested that about 16.7% of their adult subjects have anti-thyroid peroxidase (TPO) antibodies. In this same study of 971 subjects, when subjects with abnormal thyroid function were excluded, the prevalence of anti-TPO and anti-TG antibodies was 9.5% and 8.5%[22].The presence of anti-TPO antibody have been detected in 8% of children [23] and in 3.6-8.4% of apparently normal adults in other studies[24,25,26].Anti TPO antibodies could be a marker of ongoing subclinical autoimmune process and could be a pointer to impending development of thyroid dysfunction even in euthyroid patients. Hence such patients should be followed up regularly.

69.7% (200/287) of hypothyroid individuals showed elevated anti TPO antibody titre in our study. Nearly 70% cases of clinical hypothyroidism and 70% cases of subclinical hypothyroidism showed anti TPO antibody positivity. Arindam Bose *et al* (2015) reports the prevalence of anti TPO antibody as 79% and 87% in clinical and subclinical hypothyroidism respectively[27]. Whereas Jayasankar *et al* (2015) reports an anti-TPO prevalence of 80% and 50 % in clinical and subclinical hypothyroidism respectively[28].A hospital based study done on 300 subjects in rural Kerala by Thomas Cyriac *et al* (2015) demonstrates a prevalence of anti TPO antibody of 70 % in clinical and 69% in subclinical hypothyroidism which is well correlating with our study[29]. Association between the presence of anti-TPO antibodies and the development of autoimmune hypothyroidism has been studied by many authors and have shown positive correlation between the two[20,27,28,30]. The progression of subclinical hypothyroidism (borderline elevated TSH with normal thyroid hormone levels) to clinical hypothyroidism has been estimated

at 5% per year in a 4-year follow-up[31]. It has been suggested that the presence of thyroid peroxidase antibodies may serve as a marker of future thyroid failure[32]. Roos *et al* (2010) in their prospective study concluded that, association between the presence of TPO antibodies and increasing levels of TSH within the euthyroid range, strongly suggests that TSH levels, even though they are still in the accepted normal range would have been actually lower in the absence of anti TPO antibodies. They also mentioned that, the presence of TPO antibodies frequently sets a subject in a compensated state in which somewhat higher levels of TSH that was still in the normal reference range ,was necessary for the gland to produce enough thyroid hormone[21]. We also would like to emphasize that anti TPO antibodies could be useful to detect and manage subclinical hypothyroidism and thus enabling the physician to prevent long term effects of thyroid failure as well as provide an etiology to cases of hypothyroidism. In our study, 69% of cases with TSH more than 4.5µIU/ ml were positive for the antibody. This conforms to the TSH values reported by Robles osorio *et al* (>4.5 uIU/mL) and Zelaya *et al* (2.5-5.9 uIU/mL) in which there was maximum antibody positivity[2,20].In the presence of anti TPO antibody, subclinical hypothyroidism is known to be associated with a higher risk of developing overt hypothyroidism later in life [33]. We should also be cautious, that the use of anti ATPO antibody survey does not lead to detection of all individual with mild thyroid failure caused by autoimmunity as can be concluded from the percentage of those with hypothyroidism who had negative anti TPO in our study(14.3%) and other clinical studies[9].

Among the hyper thyroid individuals, 51 (44%) showed anti TPO positivity. While Kontiainen *et al* (2006) reported 26% and Ghoraishian *et al* (1994) reported that 37 %of their biochemically hyperthyroid samples contained anti TPO antibodies in their studies, our series shows an antibody positivity of 44% in hyperthyroid cases [30,34].

Of the patients with goiter, 58.06 %(198/341) were anti TPO antibody positive and 41.93 % were negative (p value: 0.00014). Hanushraj (2016) *et al* in their study demonstrated that 53.3 % of their patients with thyroid swelling were anti TPO antibody positive[35]. Whereas Poulose *et al* (2012) had 94 % of their subjects with thyromegaly had the antibody positive[13].

Out of the 251 patients with anti TPO positivity and thyroid dysfunction, subclinical hypothyroidism (53.78%; 135/251) was the most common thyroid abnormality detected, followed by clinical hypothyroidism (26%; 65/251). No literature could be identified investigating the most common thyroid dysfunction that was produced by the effect of anti TPO antibodies in a subject.

It is to be noted that, there have been only few studies on the prevalence of TPO antibody positivity in our population, especially in Kerala. Moreover, our study has evaluated a larger number of subjects compared to most other studies. Government Medical College, Kozhikode being a forefront tertiary care hospital caters to the health care needs of nearly 6 districts of northern and middle Kerala. Hence the subjects of our study have a more random background in terms of their environment, geographical area, socio economic status and lifestyle thus representing the population better.

One of the limitations of our study was that, this was focused on individuals referred with suspicion of some thyroid disease and hence does not represent the normal general population much. As this was a retrospective study, we could not follow up the course of disease in each patient, especially the anti TPO positive euthyroid and subclinical thyroid disease cases. Also investigations like USG neck to detect more cases of enlarged thyroid gland or nodules, and FNAC thyroid to confirm the autoimmune changes pathologically could not be done.

However, the increasing prevalence of anti TPO antibody positivity in the study population, inspite of Northern Kerala being an iodine sufficient coastal area provokes us to think whether surplus iodine could be inducing autoimmunity. This needs to be investigated further.

CONCLUSION

Nearly 49% of subjects under evaluation for various thyroid disorders in a tertiary care hospital population showed the presence of elevated antiTPO antibody, with a higher prevalence in females than males. In view of this high prevalence of anti TPO antibody positivity in the study subjects representing various groups of general population, geographical area, and socio economic status, autoimmune thyroiditis should be considered as a major health problem. Anti TPO antibodies could be useful to detect and manage subclinical thyroid dysfunction early, especially subclinical hypothyroidism. This will enable the physician to prevent long term effects of thyroid failure, as well as provide an etiology to many cases of primary hypothyroidism. All anti TPO antibody positive cases should be adequately followed up to detect the development of autoimmune thyroid diseases even if they are euthyroid in the initial evaluations. Anti TPO antibodies detected incidentally in patients with SLE, type I diabetes mellitus or mood disorders must alert the physician that there could be coexistent ongoing thyroid failure and should be investigated for the same. The possibility of surplus iodine triggering autoimmune thyroid disease in our community, particularly in India's post iodisation phase, needs to be studied further.

Footnotes

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