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Research Article

HOSPITAL-BASED CLINICAL STUDY ON PREVALENCE OF TPO ANTIBODIES IN ASSOCIATION TO AUTOIMMUNE THYROID DISEASES IN TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: Autoimmune thyroid disease is one of the organs specific autoimmune disorders. The onset is much more common in women than in men. Worldwide, 2–4% of women and only 1% of men have affected and the rate increases with age. Thyroperoxidase (TPO) antibodies (Abs) level helps to diagnose autoimmune thyroid disease along with levels of thyroid stimulating hormone (TSH), Free Tri-iodotyrosine (Free T_3), and Free Thyroxin(Free T_4) and it helps in differentiation between subclinical and overt thyroidism. The core objective of clinical study was to evaluate prevalence of anti-TPO Abs in association to autoimmune thyroid disease in a tertiary care hospital – Punjab.

Methods: A cross-sectional study of random patient (n=200 patients) at a tertiary care hospital, Mohall – Punjab was carried out. All the patients fall in the age group 12–89 years. The parameters, which were used for the diagnosis of autoimmune thyroid disease, were anti-TPO level, Free T3 level, and Free T4 level. The patients were divided in different group on the basis of their age, gender, and their clinical conditions. The level of TPO Abs, TSH, Free T3, and Free T4 was noted for each patient. Electrochemiluminescence immunoassay method was used for determination of TPO Abs and other thyroid parameters. After a period of 16 weeks, subjects from different groups had great difference in their anti-TPO values in the autoimmune thyroid disease.

Results: TPO Abs positive is one of the most common associated with hypothyroidism which was 36.5%, among them 20.5% suffered from subclinical hypothyroidism, whereas other remaining suffered from clinical hypothyroidism, clinical hyperthyroidism, and other autoimmune disease.

Conclusion: TPO Abs level helps to diagnose autoimmune thyroid disease, along with this the level of TSH, Free T_3, and Free T_4 helps in differentiation between subclinical and overt thyroidism.

Keywords: Autoimmune, Anti-thyroperoxidase, Subclinical thyroidism, Overt thyroidism, Thyroid stimulating hormones, Free T3, Free T4.

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INTRODUCTION

The thyroid gland contains numerous follicles, which are composed of epithelial follicular cells and colloid, is an endocrine gland located in the neck region in front of the larynx and trachea [1]. It references in Western medicine first time in 1656, when it was thought that the main function of the thyroid gland was to lubricate the trachea [2]. The master gland, maintenance, and regulation of metabolic processes throughout the body and adverse effect on under and over production of hormones, synthesizes tri-iodotyrosine (T_3), tetra-iodotyrosine (T_4), and thyroid-stimulating hormones (TSH) and regulated by feedback inhibition mechanism of hypothalamus [3]. One of the major endocrine diseases is autoimmune thyroid disease (ATD) in which immune system produces antibodies (Abs) against body's own thyroid cells, that is, thyrocytes and causes inflammation of the gland [4].

The autoimmune endocrinal disease is characterized by the presence of high titers of Abs such as thyroperoxidase Abs (TPO) and thyroglobulin Abs produced by our own body system. These Abs damage the thyrocytes and causes inflammation of the thyroid gland. The onset is much more common in women, 2–4% women and only 1% of men are affected and this rate increases with the age [5,6].

Hereditary factors due to genetic alteration and environmental and endogenous factors such as advancing age, smoking, iodine overconsumption, adverse effects of medication, and hormonal changes (females) are key factors of Autoimmune thyroid disease [7,8].

The most common Abs measured in serum sample are thyroglobulin and TPO Abs [9]. Due to more specificity in the diagnosis of ATD, anti-TPO Abs are preferred along with results of TSH, Free T_3, and T_4. Free T_3 measurements support the differential diagnosis of thyroid disorders which are needed to distinguish different forms of hyperthyroidism and to identify patients with T_3 thyrotoxicosis [10,11]. The determination of Free T_4 is helpful for monitoring thyrosuppressive therapy [12,13]. Moreover, TSH is a very sensitive and specific parameter for assessing thyroid function and is particularly suitable for early detection or exclusion of disorders in the central regulating circuit between the hypothalamus, pituitary, and thyroid [14-17]. The TSH level varies in hypothyroidism and hyperthyroidism.

On the basis of laboratory results of anti-TPO Abs, TSH level, thyroid hormones level, we can differentiate between euthyroidism, subclinical thyroidism, and clinical or overt thyroidism. In case of euthyroidism, the level of anti-TPO Abs, TSH, Free T_3, and Free T_4 remains normal. In subclinical thyroidism, the level of Anti-TPO Abs and TSH increases but Free T_3 and Free T_4 remains normal. This is asymptomatic and only mild impairment occurs in the thyroid gland. If it remains, untreated, it will switch over to clinical thyroidism. Subclinical thyroidism is much more common than overt thyroidism, so early diagnosis and treatment may prevent the onset of overt thyroidism and its associated effects [18]. Level of anti-TPO Abs, TSH markedly increases, and thyroid hormones will increase or decrease according to hyperthyroidism or hypothyroidism, respectively, in overt thyroidism. Overt or clinical thyroidism is symptomatic and it may cause further complications such as depression and unexplained

weight gain. Hashimoto and Grave's thyroid disease is the most common examples of clinical thyroidism.

The study by Silva *et al*., conducted in 89 Brazilian women, has noted elevated anti-TPO levels in around 90% of the patients with autoimmune thyroiditis [19]. Lock *et al*. have highlighted the importance of considering anti-TPO antibody testing as an integral part of the clinical investigation for subclinical hypothyroidism [20]. In a study conducted during the period of 2007–2010 in Delhi, the percentage of TPO antibody-positive adults were found to be 13.3% [21]. Similarly, an apparent rise in prevalence was noted in the southern part of India. The corresponding prevalence of anti-TPO positivity noted in two different studies conducted in Kerala and Chennai was 16.7% and 25.81% [18,22]. A study by Jeena *et al*. has concluded on the usefulness of anti-TPO antibody estimation in establishing the etiological diagnosis of autoimmune thyroid diseases. The study has found that out of 47 hypothyroid subjects evaluated, 28 (60%) had an elevated TPO antibody titer [23]. This study is not sufficient because of limitation of the studies in the country and further research has been recommended by some authors to identifying the autoimmune thyroid disease and their changing patterns. The present clinical study was done to check prevalence of anti-TPO Abs in association with autoimmune thyroidism in a tertiary care hospital – Punjab region.

METHODS

The present clinical study was conducted in a tertiary care hospital, Mohali in Punjab region. This study was carried over a period of four months from January 2, 2017, to April 30, 2017.

Clinical data were collected from 200 random of males and females, of these 80 were males and 120 were female. Age range was 12–89 years for both males and females. UHID of the patient, level of anti-TPO antibody Titer, TSH level, Free T_3, and Free T_4 level was noted down. Then differentiation was done on the basis of age groups, gender basis, etc. For serum sample was collected in Yellow Top with SST gel. Electrochemiluminescence immunoassay method was used for testing.

Positive autoimmune thyroidism was ascertained when the anti-TPO antibody level was >35 U/L Table 1.

Table 1: Normal range of parameter

S. No	Name	Reference range
1	Anti-TPO Abs	5–35 IU/L.
2	TSH	0.27–4.20 uIU/ml
3	Free T_3	2.0–4.4 pg/ml
4	Free T_4	0.93–1.71 ng/dl

Anti-TPO Abs: Anti-thyroperoxidase antibodies, TSH: Thyroid-stimulating hormones, T_3: Tri-iodotyrosine, T_4: Tetra-iodotyrosine

Statistical analysis

Results of the study are presented as average, ranges, and percentage as per requirements. The values presented in the form of average and based on different age groups, presented in percentage form. Ranges given of all parameters included for study. All the data were calculated in Microsoft Excel 2010 and presented graphically.

RESULTS AND DISCUSSION

Age-wise distribution

Two hundred patients were studied in this clinical study. The mean age of total population was 44.67±17.87 (mean±SD) years with range 12–89 years. The study was divided in four different groups on the basis of age factor.

Number of patients in age groups: Group-1, Group-2, Group-3, and Group-4 were 10, 62, 100, and 28, respectively, with percentage of 5%, 31%, 50%, and 14%. Table 2 shows differentiation of different age groups as per positivity of anti-TPO Abs and their percentage. The prevalence of TPO-Abs positivity in the total population was 1.5%, 10%, 20.5%, and 4.5% in the Group-1, Group-2, Group-3, and Group-4, respectively. During the study, it was observed that the patients within the age Group-3 (20.5%) were more prone to autoimmune thyroid disease. The advancing age and high TSH level could be a risk factor for ATD.

Swain *et al*. have reported that most of the patients with autoimmune thyroid disease were mainly belonging to the age group of 30–50 years [5]. In our study, age group of 35–65 years found the highest number antibody positivity which is very similar to the Swain *et al*. This study showed that TPO positivity increased with the aging of people. In aging, there might be an absence of thyroid cysts: Might possess beneficial influence on thyroid hormone synthesized by pooling thyroglobulin. In the absence of thyroid cyst will affect the production of thyroid hormone.

Out of 200 patients, 73 patients showed a positive titer for anti-TPO Abs. Hence, 36.5% patients suffered from autoimmune thyroid disease. The average anti-TPO Abs level in 73 patients was 258.67U/L and ranged from 37.62 to 660U/L Table 3. The average TSH level was 12.72 μIU/ml and ranged from 0.005 to 65.97 μIU/ml. In the study, we found the anti-TPO Abs level higher in Group-2 which is age group in 18–34 years.

Atluri *et al*. study found that anti-TPO Abs was more prevalent in the 20–40 age groups [24]. Sindhu *et al*. found the highest mean value of anti-TPO Abs in the 35–44 years age group in Kerala [25]. Our study and Atluri *et al*. finding are similar, however, Sundhu *et al*. finding are some difference. This difference finding maybe due to their sample size or may be how they differentiate their population group.

Table 2: Distribution of age groups

Age group	Average age mean±SD (years)	No. of patients	%of total	TPO positive (%)
Group – 1 (12–17 years)	14.4±2.31	10	5%	3 (1.5)
Group – 2 (18–34 years)	28.19±3.77	62	31%	20 (10)
Group – 3 (35-65 years)	49.51±9.04	100	50%	41 (20.5)
Group – 4 (>65 years)	74.67±6.04	28	14%	9 (4.5)
Total		200	100	73 (36)

Sample size(n)=200, SD: Standard deviation, TPO: Thyroperoxidase

Table 3: Mean value of TPO Abs, TSH, Free T3, and FreeT4 in various age groups

Age group	Anti-TPO Abs (u/ml)	TSH (μiu/ml)	Free T_3 (pg/ml)	Free T_4 (ng/ml)
Group – 1 (12–17 years)	327.93	28.09	2.41	0.99
Group – 2 (18–34 years)	281.08	10.68	3.23	1.27
Group – 3 (35–65 years)	255.45	14.02	2.81	1.10
Group – 4 (>65 years)	225.04	6.26	3.26	1.16

Anti-TPO Abs: Anti-thyroperoxidase antibodies, TSH: Thyroid-stimulating hormones, T_3: Tri-iodotyrosine ,T_4: Tetra-iodotyrosine

Gender-wise distribution

Out of 200 patients, 60% were female patients whereas 40% were male patients. The mean age of male patients was 46.5±19.9 years whereas for female patients mean age was 43.8±16.9 years.

Out of 73 patients having positive TPO Abs, 22 were male and 51 were female patients Table 4. Prevalence of TPO Abs was 11% and 25.5%, respectively, in male and female population. In our observation, women were more as compared to the men suffering from autoimmune thyroid disease and the number of females was more as compared to the men in the data.

From above results, female shows more prevalence towards autoimmune thyroid diseases as the number of females are more as compared to male population and positivity of anti-TPO Abs is also more in female Table 5.

The prevalence of TPO-Ab positivity in the total population was 11.9, 14.9, and 13.6% in the young, middle age, and elderly, respectively [26]. Swain *et al*. have also found that the patients with autoimmune thyroid disease were more women than men [5]. These previous studies and our study verify the AITD is more prevalence in female than male National Health and Nutrition Examination Survey III reported that over 10% of adults were TPO-Ab or Tg-Ab positive, with a prevalence of 13% for TPO-Ab and 11.5% for Tg-Ab [27]. A study by Atieh Amouzegar *et al*. (2016) results about 5783 participants, of which 742 (12.8%) were TPO-Ab positive, with the higher prevalence among women than in men.

Differential study on the basis of type of Thyroid disease

Seventy-three patients out of 200 were shown positive titer for TPO Abs out of 73 positive TPO Abs patients following:

- Fourty-one patients were suffering from subclinical hypothyroidism having high TPO Abs and TSH level but normal Free T3 and T4 level
- Sixteen patients were suffering from clinical or overt hypothyroidism having high levels of TPO Abs, TSH, and low levels of free thyroid hormones
- Seven patients were suffering from clinical hyperthyroidism having high levels of TPO Abs, TSH and free thyroid hormones
- Nine patients showed high level of TPO Abs but normal level of TSH, Free T3, and Free T4. This seems to be having other autoimmune response toward thyroid Abs or may be due to some another reason. That is why, Only TPO Abs titer is high and rest parameters are normal.

Rest 127 out of 200 patients showed a normal TPO Abs level with normal TSH, Free T3, and Free T4 level. Hence, these patients considered under euthyroidism condition.

Percentage wise: 63.5% population were under euthyroidism condition, having normal parameters of thyroid profiles and TPO Abs. Out of 36.5% patients suffering from autoimmune thyroid disease, 20.5% were suffering from subclinical hypothyroidism, 8% from overt hypothyroidism, 3.5% were suffering from clinical hyperthyroidism, and 4.5% patients were suffering from the other autoimmune condition. Table 6 shows about a differential study on the basis of thyroid disease.

The mean level for TPO Ab, TSH, Free T_3 and, Free T_4 in Euthyroidism was 11.68 U/L, 3.894 µIU/ml, 2.82 pg/ml, and 1.27 ng/ml, respectively. In the case of subclinical hypothyroidism, the mean level of TPO Abs, TSH, Free T_3, and Free T_4 was 242.56 U/L, 11.46 µIU/ml, 2.88 pg/ml, and 1.12 ng/ml, respectively. In clinical hypothyroidism, the mean level is 348.33 U/L, 25.97 µIU/ml, 2.14 pg/ml, and 0.7 ng/ml, respectively, for TPO Abs, TSH, Free T_3, and Free T_4. The mean for clinical hyperthyroidism is 145.84, 3.63, 4.7, and 1.93, respectively. About 4.5% of patients were seemed to be having other autoimmune thyroid conditions having mean TPO Abs level 284.98 and 1.99, 3.47, and 1.36, respectively, for TSH, Free T_3, and Free T_4 level.

Around 20.5% of the total patients were suffering from subclinical hypothyroidism having high levels of TPO Abs and TSH with normal levels of free thyroid hormones. Gupta *et al*. found that 28.9% prevalence of subclinical hypothyroidism [28]. This difference may be due to the simple size, type of patient they observed and the parameters they applied for identifying disease. Anti-TPO is a more promising marker for ATD than other parameters. Others various research and study have explained that the prevalence of subclinical hypothyroidism is from 4% to 22% [29-32] which is similar to our finding of the study.

Subclinical hypothyroidism is a common condition. The prevalence is 3–8%, increasing with age and being more common in women. After the sixth decade, the combined prevalence in both men and women is around 10%. About 80% of these patients have a serum TSH of <10 mIU/L, and 80% have anti-thyroid Abs [33]. In case of subclinical thyroidism patient does not show proper sign and symptoms, but there are mild increase levels of TSH and anti-TPO but within normal level of Free T_3 and Free T_4.

Subclinical hypothyroidism may progress to overt hypothyroidism in approximately 2–5% cases annually. Subclinical hypothyroidism is more common than overt condition so early diagnosis and treatment helps to prevent the onset of overt condition and its adverse effects on body systems [34]. Patients having high titers of anti TPO are more prone to changes in overt condition and it will be more symptomatic.

Table 4: Gender-wise distribution and TPO antibodies

Gender	No. of patients	Total (%)	TPO Ab+	% positivity
Male	80	40	22	11
Female	120	60	51	25.5
Total	200	100	73	36.5

Sample size (n)=200, TPO Abs: Thyroperoxidase antibodies

Table 5: Mean level of TPO Abs, TSH, Free T_3, and Free T_4 in male and female

Gender	Anti-TPO Abs (U/ml)	TSH (uIU/ml)	Free T_3 (ng/dl)	Free T_4 (pg/ml)
Male	258.82	13.14	3.16	1.20
Female	262.94	12.54	2.88	1.11

Anti-TPO Abs: Anti-thyroperoxidase antibodies, TSH: Thyroid-stimulating hormones, T_3: Tri-iodotyrosine ,T_4: Tetra-iodotyrosine

Table 6: Differential study on the basis of autoimmune thyroid disease condition

S. No	Clinical Condition	No. of patients n=200	% of patients	Mean TPO Abs level	Mean TSH level	Mean Free T3 level	Mean Free T_4 level
1	Euthyroidism	123	63.5%	11.68	3.894	2.82	1.27
2	Subclinical hypothyroidism	41	20.5%	242.56	11.46	2.88	1.12
3	Clinical/overt hypothyroidism	16	8%	348.33	25.97	2.14	0.7
4	Clinical hyperthyroidism	7	3.5%	145.84	3.63	4.7	1.93
5	Other autoimmune conditions	9	4.5%	284.98	1.99	3.47	1.36

Sample size(n)=200, Anti-TPO Abs: Anti-thyroperoxidase antibodies, TSH: Thyroid-stimulating hormones, T_3: Tri-iodotyrosine ,T_4: Tetra-iodotyrosine

CONCLUSION

In the current study, of 200 participants, 73 (36.5%) were TPO Abs positive, with higher prevalence among women (25.5%) than in men (11%). The prevalence of TPO-Abs positivity in the total population was 1.5%, 10%, 20.5%, and 4.5% in Group-1, Group-2, Group-3, and Group-4, respectively. About 63.5% population showed normal results of TPO Abs, TSH, Free T3, and Free T4, so they had euthyroidism conditions. About 20.5% suffered from subclinical hypothyroidism, 8% of patients suffered from clinical hypothyroidism, 3.5% suffered from clinical hyperthyroidism, and 4.5% patients had a high level of TPO Abs but normal levels of other thyroid parameters probably had some other clinical conditions or autoimmune diseases related to the thyroid gland. Gender, age, and elevated serum TSH were found to be risk factors for developing TPO Abs positivity.

The TPO Abs level helps in diagnoses the autoimmune thyroid disease along with the level of TSH, Free T3, and Free T4 and differentiation between subclinical and overt thyroidism.

AUTHORS CONTRIBUTION

The manuscript writing and data collection had performed by Singh J, research reviewed and edited by Prabhakar PK, and Manuscript editing, reviewed, finalized, and submitted for publication by Neupane N.

CONFLICT OF INTEREST

The authors affirm no conflict of interest.

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