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# **Relationship of Anti-Thyroid Peroxidase Antibody and Thyroid Function Test**

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## Abstract

**Background:** Anti-thyroid peroxidase antibodies (anti-TPO antibody) attack thyroid peroxidase enzyme that involved in the synthesis of thyroid hormones, named thyroid autoimmune disease leads to hypothyroidism or hyperthyroidism. **Objective:** assess the relationship between anti-TPO antibody and thyroid function test (T4, T3, and TSH) in thyroid patients. **Methods:** *The first study:* In 2425 people suspected of thyroid disease, referred to Yazd Central Medical Laboratory by physicians for 2 years, and anti-TPO antibody, T3, T4, and TSH concentrations were measured. *The second study:* conducted in 160 patients who demonstrated abnormal thyroid function tests were performed at Grand City Clinic, Hospital Services, and Kantipur dental college for 18 months since Baisakh 2072. **Results:** *The first study:* 2135 patients (88.04%) were female and 290 (11.96%) were male. The levels T3, T4, and TSH in individuals with normal and elevated anti-TPO antibody titers were significantly different ( $P < 0.0001$ ). A correlation was detected between TSH and T4 levels and an abnormal anti-TPO antibody ( $P = 0.002$ ). *The second study:* 126 patients (78.8%) were female and 34 (21.2%) were male. anti-TPO antibody test showed positive in 102/160 (63.8%) cases. **Conclusion:** The result confirms the relationship between anti-TPO antibody and thyroid function testing, which negatively affects thyroid function.

## Introduction

The thyroid is an endocrine gland found in the anterior part of the neck at vertebral levels C5 to T1, it located between the infrahyoid muscles, the larynx, and the trachea, and divide into two lobes, right and left lobe connected by the isthmus (1).

The thyroid is one of the largest of the endocrine glands where it is normally weighing 15 to 20 grams in adults. the thyroid secretes several hormones mainly thyroxine (T4) About 93% and triiodo-thyronine (T3) About 7%, almost all T4 is eventually converted into T3 in the tissues so that both have an important function is increase the metabolic rate of the body. T4 and T3 stimulate by thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland. the thyroid also secretes calcitonin, which plays an important role in the metabolism of the calcium (2).

The thyroid gland is cells are arranged into globular structures, called follicles, are the thyroid gland's structural and functional units, every follicle is surrounded by reticular fibers and a capillary vascular network that allows easy entry of thyroid hormones into the circulation. The follicular cells are synthesized, release, and store their product outside of their cytoplasm, In the follicle lumen as a gelatinous substance, known as a colloid, is composed of thyroglobulin (3).

T3 and T4 require a rare element (iodine) for bioactivity, Iodide enters the thyroid primarily through a  $\text{Na}^+\text{-K}^+$  ATPase-dependent thyroidal  $\text{I}^-$  transporter that controlled by TSH. heme-containing peroxidase is important to oxidize  $\text{I}^-$  to a higher valence state (only in the thyroid), A compulsory step in  $\text{I}^-$  organization, and biosynthesis of the thyroid hormone. and occurs at the luminal surface of the follicular cell. Thyroglobulin (Tgb) is synthesized in the basal portion of the cell and moves to the lumen, it is a large iodinated. Thyroglobulin is composed of two large subunits. Approximately 70% of iodide in thyroglobulin is found in inactive precursors, moniodotyrosine (MIT) and diiodotyrosine (DIT), while 30% is found in residues of iodotyrosine, T4, and T3. The coupling of two DIT molecules to form T4—or of an MIT and DIT to form T3—occurs within the thyroglobulin molecule. Thyroid hormones, stored in the colloid in the follicular space, are released from thyroglobulin by hydrolysis inside the thyroid cell. A periph-

eral deiodinase in target tissues such as pituitary, kidney, and liver selectively removes I<sup>-</sup> from the 5' position of T<sub>4</sub> to make T<sub>3</sub>, which is a much more active molecule. In this sense, T<sub>4</sub> can be thought of as a prohormone, though it does have some intrinsic activity (4).

So, when anti-TPO antibody bound to peroxidase that found in the thyroid lead into decrease oxidize I<sup>-</sup> to a higher valence state, this state is called Thyroid auto-immune disease.

### **Aim of the study**

To find the relationship between serum levels of anti-TPO antibody and the abnormal thyroid hormones test and function.

### **Materials and Methods**

*The first study:* In this cross-sectional study, 2425 cases, suspected of having thyroid disease by an endocrinologist, were included in the Central Laboratory of Yazd University of Medical Sciences for two years (1382 and 1383). Sera were stored at -80 ° C, the anti-TPO antibody was measured using an enzyme-linked immunosorbent assay (ELISA) method (Radim Co, Italy). The serum TSH, T<sub>3</sub>, and T<sub>4</sub> were measured using the radio-immunoassay (RIA) method (Kavushiar Company, Iran). Resolutions in the following ranges were considered normal: T<sub>4</sub> =4.5–11 ug/dL, T<sub>3</sub> =70-204 ng/dL, TSH=0.3-4 mIU/L, anti-TPO <100 IU/mL. Data on age and sex of the participants were also recorded. Statistical analyses were performed using the Chi-Square and Pearson correlation tests. P-values less than 0.05 were statistically significant (5).

*The second study:* The present study was conducted in grande city clinic and hospital services and Kantipur Dental college for 18 months since Baisakh 2072. Permission was obtained from the institutional review committee.

Free T3, Free T4, and TSH were measured using the VITROS reagent pack and VITROS calibrators on the VITROS ECI/ECIQ immunodiagnostic systems, the VITROS 3600 Immunodiagnostic system, and VITROS 5600 Integrated system, a directly labeled antibody, competitive immunoassay technique.

Test for Anti TPO antibodies was performed using enzyme-linked immunosorbent assay (ELISA- EuroDiagnostica). The ELISA is intended for the qualitative determination of IgG antibodies in human serum directed against TPO. The measuring range of Free T4 in the system is 0.07-6.99ng/ dl with an euthyroid reference interval of 0.78 2.19ng/dl.

The measuring range of Free T3 in the system is 0.50-22.8ng/ dl with an euthyroid reference interval of 2.77-5.27ng/dl. The measuring range of TSH in the system is 0.015-100uIU/ml with an euthyroid reference interval of 0.485-4.68uIU/ml.

The reference range for anti- TPO antibodies is negative if less than 10 IU/ml and positive if more than 10IU/ml.

Data entry was done in MS. Excel and analysis were done using SPSS16. Statistical analyses were performed using Chi-square and Pearson correlation test. A P-value of less than 0.05 was statistically significant (6).

## **Results**

*The first study:* A total of 2425 individuals including 2135 (88.04%) females and 290 (11.96%) males (53.53% between 20 to 39 years old) were evaluated, suspected of having thyroid disease. The frequency of people with normal anti-TPO antibody compared with elevated anti-TPO antibody titer varied significantly in different age groups ( $P < 0.0001$ ). Elevated levels of anti-TPO antibodies were found in 32.5% of men compared to 36.2% of women. The differences in anti-TPO antibody distribution according to TSH, T4, and T3 values were statistically significant ( $P < 0.0001$ ). (Table 1-3).

There was a positive correlation between TSH and high anti-TPO antibody values ( $r=0.107$ ,  $P=0.04$ ). Moreover, T4 and high anti-TPO antibodies were negatively associated ( $r=-0.160$ ,  $P=0.002$ ) (5).

*The second study:* A serum of 160 people was analyzed with abnormal thyroid function tests for TPO-antibody. Out of 160 individuals, 126 (78.8%) are female and 34 (21.2%) are male with a male to female ratio of 1: 2.9. A large number of patients in this study belonged to the age groups 20-39 years with an average age of 39.07, SD:  $\pm 12.84$ .

The frequency of different thyroid cases. Subclinical hypothyroidism ( $n=90$ ; 56.3%) was more common than overt hypothyroidism ( $n=29$ ; 18.0%), overt hypothyroidism ( $n=27$ ; 16.9%) and subclinical hyperthyroidism ( $n=14$ ; 8.8%).

In this study, the anti-TPO antibody test was positive in 102(63.8%) cases among which 86 (53.8%) were females and 16 (10%) were males. 49/90 cases of subclinical hypothyroidism and 25/29 cases of overt hypothyroidism with an elevated anti-TPO antibody. Similarly, there was an elevated anti-TPO antibody in 5/14 cases of subclinical hyperthyroidism and 22/27 cases of overt hyperthyroidism.

Association was tested using the association of Pearson between anti-TPO antibody and hypothyroidism and hyperthyroidism. There is a significant positive correlation (Chi-Square test=9.410, p value=0.001,  $r=0.281$  and p-value = 0.002) between subclinical hypothyroidism and overt hypothyroidism with an anti-TPO antibody test. Subclinical hyperthyroidism and overt hypothyroidism also showed a significant positive relationship (chi-square test =8.588, p value=0.005,  $r=0.458$  and P value=0.003) with an anti-TPO antibody test.

At a 95% confidence interval, the mean serum FT3, FT4, and TSH were  $1.99+0.572$ ,  $1.96+0.530$ , and  $2.49+0.869$ mIU/L (P-value  $<0.0001$ ) respectively(6).

**Table 1. Distribution of anti-TPO antibody according to TSH concentration**

Anti-TPO TSH	Normal		Elevated		Total	
	Number	Percent	Number	Percent	Number	Percent
Low	181	54.68	150	45.32	331	100
Normal	1223	73.76	435	26.24	1658	100
High	155	35.55	281	64.45	436	100

Chi-Square, P-value &lt;0.0001

**Table 2. Distribution of anti-TPO antibody according to T4 concentration**

Anti-TPO T4	Normal		Elevated		Total	
	Number	Percent	Number	Percent	Number	Percent
Low	26	32.5	54	67.5	80	100
Normal	1293	65.77	673	34.24	1966	100
High	240	63.33	139	36.68	379	100

Chi-Square, P-value &lt;0.0001

**Table 3. Distribution of anti-TPO antibody according to T3 concentration**

Anti-TPO T3	Normal		Elevated		Total	
	Number	Percent	Number	Percent	Number	Percent
Low	14	35.89	25	64.11	39	100
Normal	1367	64.39	756	35.61	2123	100
High	178	67.68	85	32.32	263	100

Chi-Square, P-value &lt;0.0001

## Discussion

*The first and second studies* showed patients with high anti-TPO antibodies or abnormal thyroid function tests were female more than a male. (In *the first study*, 58.42% of patients with high anti-TPO antibodies were 20-39 years old and 89.14% were female. and in *the second study*, among 160 individuals with abnormal thyroid function tests were analyzed for an anti-TPO antibody were 20-39 years with an average age of 39.07, SD:  $\pm 12.84$ . 126(78.8%) were females and 34(21.2%) were males with a male to female ratio of 1:2.9).

In a study by Ghoraishai et al, 88.04% had been females and 11.96% were males. Similarly, Shinto et al study also showed female predominance where 91 patients were females and 9 were males (6).

In *the first study*, the prevalence of anti-TPO antibody in women was about 7 times greater than men, Canaris et al reported that autoimmune thyroid diseases affect women 2 to 4 times more than men (5).

Table 1 reveals that in patients with high TSH concentration, 35.55% have normal anti-TPO antibody and 64.45% have abnormally high anti-TPO antibodies.

Bjoro et al found in a 20-year follow-up study that a positive anti-TPO antibody was highly correlated with thyroid dysfunction; the elevated TSH prevalence was almost 10 times higher in both females and males who had positive TPO antibodies compared with a negative anti-TPO antibody (5).

In *the second study*, subclinical hypothyroidism (56.3%) was more commonly seen than overt hyperthyroidism (18.0%), overt hypothyroidism (16.9%) and subclinical hyperthyroidism (8.8%).

*The second study* evaluated the level of anti-TPO antibody patients with abnormal thyroid function tests. In that study, an anti-TPO antibody was positive in 62.2% of hypothyroidism (49/90 subclinical cases and 25/29 cases of overt hypothyroidism). Likewise, 65.9% of cases of hyperthyroidism (5/14 subclinical hyperthyroidism and 22/27 overt hypothyroidism) showed elevated anti-TPO antibodies.

Kontiainen et al found lofty levels of anti-TPO antibody in 47% and 12% of samples with abnormal and normal levels of TSH, respectively. They have demonstrated that 61% of patients with hypothyroidism and 26% of hyperthyroidism have high levels of this antibody (5).

Table 2 showed that in patients with low T4, 32.5% of cases had a normal anti-TPO antibody, while 67.5% had abnormally high antibody titers ( $P < 0.0001$ ). According to Silva et al, the anti-TPO antibody is present in over 90% of patients with autoimmune hypothyroidism and Graves' disease. We have shown that there was a significant correlation between TSH or T4 concentration and a lofty anti-TPO antibody in the study population ( $P = 0.04$  and  $0.002$ , respectively) (5).



Table 1,2 and 3 Respectively showed when the Anti-TPO antibody is high, TSH was high in 64.45% and Low in 45.32% of patients, T4 was high in 36.68% and Low in 67.5% of patients, and T3 was high in 32.32% and Low in 64.11% of patients. that means a high level of anti-TPO antibody is strongly associated with hypothyroidism (5).

## **Conclusion**

The result confirms the relationship between the anti-TPO antibody and thyroid function test, which negatively affects the thyroid function. and test the anti-TPO antibody will help in the diagnosis of thyroid dysfunction disease. indicating the clinical and subclinical significance of this antibody.

## References

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