

Relationship Between Anti-Thyroid Peroxidase Antibody and Thyroid Function Tests

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Abstract: Anti-thyroid peroxidase antibody (anti-TPO) is a member of thyroid autoantibodies is important in inducing and also diagnosing autoimmune thyroid diseases. Thyroid autoimmunity can cause several forms of thyroiditis and abnormal thyroid functions, ranging from hypothyroidism to hyperthyroidism. Evaluation of the relationship between serum levels of anti-TPO and thyroid hormones (T3, T4 and TSH) was aimed. In 2425 persons suspected of thyroid disease and referred to Yazd central medical laboratory by physicians during 2 years, the concentrations of serum anti-TPO and also serum T3, T4 and TSH were measured using ELISA and RIA methods, respectively. Most of the patients (53.53%) were between 20 to 39 years old. Females comprised 88.04% (2135 patients) and the remaining 290 patients (11.96%) were male. The differences between patients who had normal anti-TPO and those who had more than normal anti-TPO in different levels of T3, T4 and TSH were significant ($p < 0.0001$). The correlation between TSH and T4 in patients who had abnormal anti-TPO were significant ($r = 0.107$, $P = 0.04$, $r = -0.160$, $p = 0.002$, respectively). Anti-TPO is a good marker for patients with autoimmune hypothyroidism who have high levels of TSH or less than normal T3 or T4 and there is a significant correlation between anti-TPO and both TSH and T4.

Key words: Autoimmune • Anti-TPO • Thyroid disease

INTRODUCTION

Autoimmune thyroid disease is a common organ-specific autoimmune disorder, seen mostly in women 30-50 years old [1]. About 2 to 4% of women and up to 1% of men are affected worldwide and the prevalence rate increases with advancing age [2]. Thyroid autoimmunity can cause several forms of thyroid disorders, including Graves' disease, Hashimoto's thyroiditis, atrophic autoimmune thyroiditis, hypothyroidism, postpartum thyroiditis and thyroid-associated ophthalmopathy. Of all these diseases, Hashimoto thyroiditis and Graves' disease are the most common types and share many features immunologically [3, 4]. Anti-thyroid peroxidase antibody (anti-TPO) is important in diagnosing autoimmune thyroid disease and for judging treatment efficacy [5]. Anti-TPO is also found in sera of about 10% of normal adults, with an increasing prevalence (up to 30%) in older adults [4]. Anti-TPO antibodies are more likely to be of pathogenetic importance than other antibodies for several reasons. They fix complement and may directly damage thyroid cells [6]. Serum anti-TPO antibody concentrations are positively correlated with the activity of chronic autoimmune thyroiditis [7]. More patients with thyroiditis have high serum anti-TPO than anti-Tg antibody concentrations [8]. Anti-TPO antibodies are cytotoxic *in vitro*, as detected by antibody-dependent cell cytotoxicity tests [9]

and thus are likely to be involved in the development of hypothyroidism [10].

Anti-TPO antibodies may exaggerate or perpetuate thyroid injury, but probably do not initiate it and this issue is not settled as yet [4]. Therefore, the evaluation of serum anti-TPO levels with respect to serum concentration of thyroid hormones would help in elucidating its probable pathogenetic role in induction of hypo- or hyperthyroidism.

MATERIALS AND METHODS

In this cross-sectional research, 2425 persons suspected of thyroid disease and referred by endocrinologist to central (reference) laboratory of Yazd Shahid Sadoughi University of medical sciences during 2 years (1382-1383), were studied by drawing 10 mL of blood and separating its serum, which was kept frozen at -80°C and we measured anti-TPO weekly by using enzyme-linked immunosorbent assay (ELISA) method (kit purchased from Radim Co, Italy). The serum TSH, T3 and T4 were also measured using radioimmunoassay (RIA) method (kit purchased from Kavoshyar Co, Iran). The normal ranges for these tests were: $\text{T4} = 4.5\text{-}11 \text{ ug dL}^{-1}$, $\text{T3} = 70\text{-}204 \text{ ng dL}^{-1}$, $\text{TSH} = 0.3\text{-}4 \text{ mIU L}^{-1}$, anti-TPO $< 100 \text{ IU mL}^{-1}$. The age and sex of the patients were also recorded. Statistical data were analyzed using chi-square and Pearson correlation tests.

Table 1: The frequency distribution of Anti-TPO levels according to age

Age	Anti-TPO					
	Normal		More than normal		Total	
	Number	Percent	Number	Percent	Number	Percent
0-19	501	20.66	204	8.41	705	29.07
20-39	792	32.66	506	20.87	1298	53.53
40-59	224	9.24	142	5.86	366	15.09
60-79	42	1.73	14	0.57	56	2.32
Total	1559	64.26	866	35.69	2425	100

Table 2: The frequency distribution of Anti-TPO Levels according to sex

Sex	Anti-TPO					
	Normal		More than normal		Total	
	Number	Percent	Number	Percent	Number	Percent
Male	196	67.5	94	32.5	290	100
Female	1363	63.8	772	36.2	2135	100

Table 3: The frequency distribution of Anti-TPO levels according to TSH concentration

TSH	Anti-TPO					
	Normal		More than normal		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

Table 4: The frequency distribution of Anti-TPO levels according to T4 concentration

T4	Anti-TPO					
	Normal		More than normal		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 <0.0001

A p-value of 0.05 or less was taken to indicate a significant difference.

RESULTS

From a total of 2425 persons suspected of thyroid disease, the most common (53.53%) age group was between 20 to 39 years old. The results for different age groups are shown in Table 1. The number of subjects with normal anti-TPO compared with those who had high anti-TPO is significantly different in various age groups ($p < 0.0001$). It can be seen in Table 2 that 290 (11.96%) persons were male and 2135 (88.04%) were female. High anti-TPO was found in 32.5% of

males and 36.2% of females referred to our lab. In other words, 89.14% of those who had abnormal anti-TPO were female. In patients who had high TSH, 35.55% showed normal anti-TPO but 64.44% had abnormal anti-TPO and the differences in various levels of TSH were significant ($p < 0.0001$) (Table 3). In 32.5% of the patients who had low T4 concentrations, tests revealed normal anti-TPO, but 67.5% of them had abnormal anti-TPO and the difference between low and high T4 concentrations with respect to anti-TPO level is significant ($p < 0.0001$) (Table 4). In patients who had low T3, 35.89% showed normal anti-TPO, but 64.10% had more than normal anti-TPO and the difference is again significant ($p < 0.0001$) (Table 5).

Table 5: The frequency distribution of Anti-TPO levels according to T3 concentration

T3	Anti-TPO					
	Normal		More than normal		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 <0.0001

Table 6: Correlation between Anti-TPO and TSH, T4 and T3

Hormones	Anti-TPO	
	Normal	More than normal
TSH	r=-0.02 p=0.451	r=0.107 p=0.04
T4	r=-1.79 p=0.451	r=-0.160 p=0.002
T3	r=-0.08 p=0.086	r=-0.068 p=0.197

r=Pearson correlation, p=p-value

As seen in Table 6, the correlation between TSH and high anti-TPO is positive and significant ($r=0.107$, $p=0.04$). The correlation between T4 and high anti-TPO is negative and significant ($r=-0.160$, $p=0.002$). However, the figure is not significant in the case of serum T3.

DISCUSSION

The results of our study show that 58.42% of patients with high anti-TPO were 20-39 years old and 89.14% were female (Tables 1 and 2). According to Swain *et al.*, [1] most (95%) of the patients with autoimmune thyroid disease are women, mainly in the 30-50 years old age.

It is seen in this study that the prevalence of anti-TPO in females is about 7 times more than males and Canaris *et al.*, [2] say that autoimmune thyroid diseases affect women 2 to 4 times more than men. A similar observation was found in a health survey in Norway, in which the prevalence of pathological anti-TPO was 13.9% in females and 2.8% in males. Of course, they set the cut-off value for anti-TPO to 200 IU mL⁻¹ instead of (as we set) 100 IU mL⁻¹ to be sure not to include those with weakly positive antibodies [11]. These findings are in accordance with higher rates of female involvement in other autoimmune diseases.

It is shown in Table 3 that in patients who have high TSH, 35.55% have normal anti-TPO but 64.45% have abnormally high anti-TPO and the differences between patients who have normal anti-TPO and patients with high anti-TPO are significant ($p<0.0001$). Vanderpump *et al.*, [12] reported that

the higher the serum level of TSH is above 2 mIU L⁻¹, the greater the prognostic significance for development of overt hypothyroidism in both anti-TPO positive and negative subjects. Bjoro *et al.*, [11] in a 20-years follow-up study found that positive anti-TPO were strongly correlated to thyroid dysfunction and the prevalence of elevated TSH was nearly 10-fold higher both in females and males with positive anti-TPO compared with subjects with negative anti-TPO. Kontiainen *et al.*, [13] found elevated levels of anti-TPO antibody in 47% of samples with abnormal and in 12% of samples with normal levels of TSH, indicating a meaningful difference ($p<0.001$) and also showed that 61% of patients with hypothyroidism and 26% with hyperthyroidism contained this antibody in their sera ($p<0.001$).

We showed (Table 4) that in patients with low T4, 32.5% had normal anti-TPO, but 67.5% had abnormally high anti-TPO and this difference is significant ($p<0.0001$). According to Silva *et al.*, [14] anti-TPO is found in over 90% of patients with autoimmune hypothyroidism and Graves' disease. We showed in Table 6 that there is a significant correlation between TSH or T4 and elevated anti-TPO (p -value=0.04, p -value= 0.002, respectively).

Clearly elevated anti-TPO values (>500 IU mL⁻¹), were found in one study in 59% of patients with thyroiditis but none of the controls or the patients with non-thyroidal illnesses [15], which demonstrated the significance of their evaluation as one of the most critical tests for those with thyroiditis.

Roti *et al.*, [16] studied 342 elderly subjects, 248 men and 94 men (mean age 80 years) in Italy and found that the prevalence of anti-TPO was 2.3% in the men and 10.2% in women. It shows that these antibodies are of importance also in aged individuals.

We conclude that anti-TPO assessment is a necessary test for patients who have high levels of TSH or low levels of T3 and T4, for diagnosis of autoimmune hypothyroidism and there is a significant positive correlation between anti-TPO and serum TSH, but a significant negative correlation between anti-TPO and serum T4, which suggests a direct pathogenetic role for anti-TPO in development of hypothyroidism.

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