Distribution of Antithyroid Peroxidase Antibody in Patients with Clinically Suspected Thyroid Dysfunction

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Abstract

Background: Thyroid peroxide had been characterized as an integral membrane hemoprotein catalyzes thyroglobulin iodination as well as the coupling of the di-iodotyrosine residues in the thyroglobulin molecule to form thyroxine. The prevalence of Thyroid peroxide autoantibody varies in different types of thyroid gland diseases and is positive in 5-15% of healthy individuals higher in elderly, but mostly in low titers.

Objective: The study was conducted to evaluate the relation between anti- Thyroid peroxide antibody and T3, T4, and TSH as thyroid function parameters in thyroid disease patients.

Patients and Methods: In 526 individuals suspected of having thyroid disease, from January 2011 to October 2011 in Al-Yarmouk Teaching Hospital. Measurement of anti-Thyroid peroxide antibody (ELISA) and T3, T4, and TSH (RIA) was done.

Results: Hyperthyroid patients constitute about 287 patients (54.56%) of total sample while 176 patients (33.46%) were hypothyroid and 63 individuals (11.98%) were euthroid.392 individuals (74.52% of the patients) were females while 134 (25.48%) were males. Our results confirm that 137 (26.05%) of the patients were Thyroid peroxide positive. 100 female patients (72.99%) and 37 male patients (27.01%). Levels of T3, T4, and TSH in individuals with negative and positive anti- Thyroid peroxide antibody were statically insignificant.

Conclusion: A correlation between TSH, T4 andT3 levels and abnormal anti-Thyroid peroxide antibodies was not proved.

Key words: Anti Thyroid peroxide, Thyroid dysfunction, Autoimmune diseases.

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Introduction

The thyroid gland produce thyroid hormones (thyroxin "T4" and triiodothyronine "T3" which regulates rate of metabolism and has effect on growth and rate of function of different systems in the body (1,2). The thyroid gland controls body production and utilization of energy, sensitivity of body to other hormones, making proteins, and also production of calcitonin hormone that plays a role in calcium homeostasis (3,4). Thyroxin (T4) is synthesized by the follicular cells from free tyrosine

and thyroglobulin (TGL). Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by thyroid peroxidase (TPO) enzyme, and linked to sites 3' and 5' of benzene ring of tyrosine residues on TG, and also on free tyrosine. The follicular cells reabsorb TGL and proteolytically cleave the iodinated tyrosines from TG upon stimulation by the thyroid-stimulating hormone (TSH) to form T4 and T3 then released into the blood. Deiodinase enzymes convert T4 to T3. Thyroid hormone that is secreted from the gland is about 90% T4 and about 10% T3.(5-11). The TSH, released by the anterior pituitary gland regulates production of thyroxin and triiodothyronine. Thyroid and thyrotropes form a negative feedback loop: T4 in high levels suppresses TSH production, and vice versa. The production of TSH is modulated by thyrotropin-releasing hormone (TRH) and blunted by somatostatin (SRIH), rising glucocorticoids levels of and sex hormones (estrogen and testosterone), and it is excessively high blood iodide concentration (12).

Thyroid peroxidase (TPO) is an integral membrane hemoprotein (M.W is about 100 kDa) which catalyzes thyroglobulin (TGL) iodination as well as coupling of two di-iodotyrosine residues in the TGL molecule to form thyroxine (13). The TPO antibodies assay sensitivity and specificity relies heavily on the purity and quality of the test antigen and in particular on the test antigen and on test absence of TGL contaminant (14). Prevalence of TPO autoantibody is 70-99% in Hashimoto thyroiditis and Grave's disease, while it is 40-70% in Primary myxedema, Post-partum thyroiditis, Endocrine orbitopathy, and is 5-25% in Simple goiter and Thyroid cancer, and very rare in Subacute thyroiditis (de-Quervain). TPO autoantibody may be found in organ – specific autoimmune disease, including type 1 diabetes mellitus; pernicious anemia, Addison's disease; polyglandular endocrine failure syndromes etc . TPO antibodies activates complements and are thought to be significantly involved in thyroid dysfunction. In Healthy individuals, it is 5-15% higher in elderly, but mostly in low titers (15).

Patients and Methods

In the current study 526 cases suspected clinically as thyroid disease referred to the teaching medical laboratories of Al-Yarmouk Teaching Hospital from January 2011 to October 2011. Measurement of anti-TPO antibody (ELISA), T3, T4, and TSH (RIA) were done. The cases were grouped according to biochemical analysis into three levels: Low, Normal and High.

The thyroid activity was assessed, depending on TSH level and categorized as hypothyroidism, hyperthyroidism and euthyroid. Triiodothyronin (T3), thyroxin (T4), thyrotrophic stimulating hormone (TSH) and antithyroid peroxidase antibody (TPO) were determined in the sera of all patients with thyroid diseases. Determinations in the following ranges were considered normal: T3 =0.95-2.5 nmol/L, T4 =60-120 nmol/L, TSH =0.25-5.0 µIU/mL. The following ranges established with the Anti-TPO test kit: Anti-TPO (IU/ml) Normal: < 50, Borderline: 50–75, Elevated: > 75. An elevated level is considered a positive result to a normal range with serum samples from healthy blood donors .

Data were entered and analyzed using the available software packages of Statistical Packages for Social Sciences-Version 22 (SPSS-22). Data were presented as frequency and percentages

with use of Pearson Chi-square test as test of significance with P value equal or less than 0.05 as level of significance.

Results

In our study, there were 526 patients clinically suspected thyroid dysfunction, their different levels of TSH, T4 and T3 revealed that; first, TSH is low in 287 patients (54.56%) and elevated in 176 patients (33.46%), while was within normal range in 63 individuals (11.98%). Second, T4 results are grouped into 3 levels: low, high and normal which included 154 (29.28%), 321 (61.03%) and 51(9.69%) patients respectively. Lastly, T3 evaluation showed the distribution of patients into 3 groups: low included 87 patients (16.54%), high 232 (44.11%) and normal 207 (39.35%) patients. Hence, 287 patients showed the biochemical diagnosis of hyperthyroidism, this is corresponding to a total prevalence of (54.56%), 176 of patients were hypothyroid (33.46%), and the remaining 63 individuals (11.98%) were normal thyroid.

Clinically suspected thyroid dysfunction patients were classified according to gender as follows, 392 patients are females (74.52%).while 134 patients are males (25.48%). Sex distribution in each group reveals that, from 287 patients with hyperthyroidism, there are 197 females (68.64%), and 90 males (31.36%). Regarding hypothyroid patients, 142 (80.68%) patients out of 176 are females, and 34 (19.32%) are male patients. Moreover, from a total of 63 individuals with normal thyroid function, 53 (84.13%) were female and 10 (15.87%) were male Differences in the distribution of TSH values according to sex were statistically insignificant (P=0.3). While the distributions of T4, and T3 were statistically significant (P=0.004, P=0.006, respectively).

Figure 1 shows distribution of anti-TPO antibody in the sera of patients in the study. Anti-TPO antibody was positive in 137 of patients (26.05%) and negative in 389 of patients (73.95%).

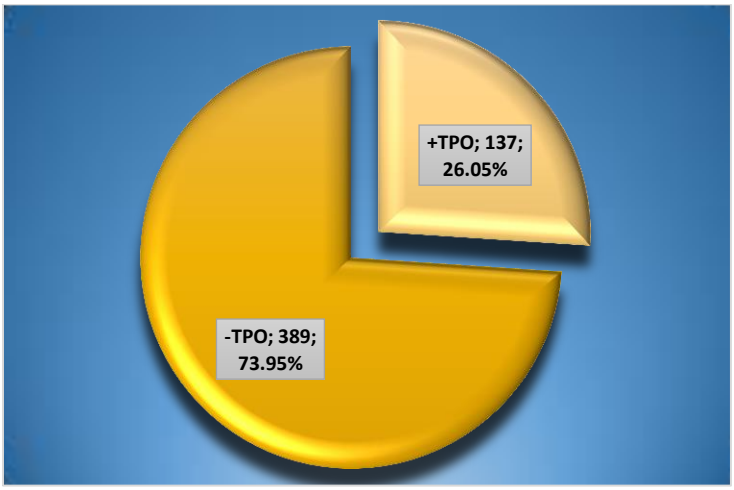

Figure (1) : The distribution of TPO antibody in thyroid dysfunction patients.

Evaluation of anti-TPO according to sex Table 1 reveals that in the group with positive anti-TPO, 100(72.99%) are women, while men are 37(27.61%). Of these Patients negative for TPO: 292 (75.06%) are women and 97(24.94%) are men. Differences in the distribution of anti-TPO antibody according to sex were statistically insignificant (P=0.6).

Table (1): The distribution of anti-TPO antibody according to sex.

Gender	+TPO	%(n.137)	-TPO	%(n.389)	P value
Female	100	72.99	292	75.06	0.632
Male	37	27.01	97	24.94	

The differences in the distribution of anti-TPO antibody according to TSH (Table 2), T4 (Table 3), and T3 (Table 3) levels were analyzed. The percentages of positive anti-TPO results in various groups were comparable. On statistical analysis no differences were detected in the number of positive anti-TPO tests between groups with low and normal hormone levels or between groups with high and normal hormone levels (P>0.05).

In patients with low TSH, TPO positive results were in 72 patients (25.79%), while those with high TSH 46 patients (26.55%), and 19 individuals (30.16%) for normal TSH. Antibody results in regard to individuals with low level of T4 are positive in 44 (28.57%) patients from a total number of 154, while 82 (25.55%) are positive from a total of 321 patients with high T4.and 11 individuals (22.57%) for normal T4 (51 individuals). Serologically positive TPO patients with low T3, high T3 and normal T3 are (21.84%, 25.43% and 28.50% respectively).

Table (2): The distribution of anti-TPO antibody according to TSH levels.

TSH	+TPO	%	-TPO	%	Total	%	P value vs. Normal
Low	72	25.79	215	74.21	287	100	0.406
Normal	19	30.16	44	69.84	63	100	-
High	46	26.55	130	73.45	176	100	0.538

Table (3): The distribution of anti-TPO antibody according to T4 levels.

T4	+TPO	%	-TPO	%	Total	%	P value vs. Normal
Low	44	28.57	110	71.43	154	100	0.328
Normal	11	21.57	40	78.43	51	100	-
High	82	25.55	239	74.45	321	100	0.542

Table (4): The distribution of anti-TPO antibody according to T3 levels.

T3	+TPO	%	-TPO	%	Total	%	P value vs. Normal
Low	19	21.84	68	78.16	87	100	0.238
Normal	59	28.50	148	71.50	207	100	-
High	59	25.43	173	74.57	232	100	0.469

Discussion

In this study 526 patients with clinically suspected thyroid disease were evaluated for the relationship between anti-TPO antibody and thyroid function test parameters (TSH, T4 and T3). Hyperthyroid patients accounted for about

54.56% of total thyroid dysfunction patients while 33.46% were hypothyroid. Burglund reported a mean incidence for hyperthyroidism of 25.80 % and higher incidence was reported in Denmark during the Second World War (16) while toxicity incidence in Iraq in 1993 was 14% (17). Higher incidence of thyroid hyperactivity in this study reflects the variation of the incidence of toxic-nodular goiter in endemic and non–endemic goiterous regions, or the delay in diagnosis and treatment of multinodular goiter that ultimately converted to toxic-nodular goiter, Aghini–Lombardi reported higher "doubling" of prevalence of toxic-nodular goiter (18).

The distribution of patients with thyroid diseases according to sex, 74.52% of the patients were female while 25.48% were male; this is consisting with a study done by Kalk who showed higher incidence in females ranging from 5:1 to 10:1(19).

In cases with hyperthyroidism, 68.64% were females and 31.36% were males, while in hypothyroid patients 80.68% were females and 19.32% were male. These findings goes with findings reported by Furszyfer in Rocheste (20). However in an Arabic country (Saudi Arabia) Hardy found that toxic-goiter is proportionally more common in males than that in the west where the result in about 1 to 6 (21).

The distribution of anti-TPO antibody in the current study was positive in 26.05% of patients; this is a relatively high prevalence in comparison to studies in other countries (Netherlands(22), Germany "Berlin" (23), Northen Europ(24); 10%, China(20); 11%, South Germany(25); 14%, France(26); 17%, Taiwan(27); 21.8%, and Iran(28); 23.4%).

This wide range prevalence in various reports may be due to differences in ethnic groups, geographic area, iodine intake, methodology, and population size. Another explanation of the high incidence of anti TPO in present study may be the endemic goiter which is prevalent, in Iraq and thyroid dysfunction is an endemic disease especially in the north and middle zone (30, 31).

In patients with positive anti-TPO, females represent 72.99% compared to 27.01% in males. 95% of the patients with thyroid autoimmune disease were women, mainly 30-50 years old reported by Swain et al study, (32). Canaris et al mentioned that women affected 2-4 times than men with autoimmune thyroid diseases (33). Similar results were found in a health survey in Norway (34). Our results are consistent with these reports and these findings are in accordance with higher rate of female involvement in other autoimmune diseases. Sharifi reported that 38.2% of males and 40.4% of females had anti-TPO antibodies (35) which is somewhat lower than in the current study.

A higher prevalence of anti-TPO positivity was noticed in patients with normal TSH level (30.16%), but this is statistically not significant. A higher serum levels of TSH, particularly titers above2 mIU/L, correlated and had prognostic significance for development of overt hypothyroidism, considering both anti-TPO positive and negative subjects (36). Positive anti-TPO antibody was correlated strongly with thyroid dysfunction as rported by Bjoro et al with prevalence of elevated TSH as nearly as 10-fold higher both in females and males having positive in TPO antibody compared with negative anti-TPO antibody (34). A study by Kontiainen et al reported an elevated anti-TPO antibody levels in 47% and 12% of samples with

abnormal and normal levels of TSH, respectively in 61% of hypothyroidism patients and 26% of hyperthyroidism with high levels of this antibody (37).

The evaluation of T4 level revealed that higher frequency of anti TPO positive patients had been reported in patients with low T4 level (28.57%), which is statistically insignificant. However, Sundbeck G et al. revealed a direct relationship between TPO-Ab and thyrotropin (TSH) concentrations and an inverse relationship between TPO-Ab and free thyroxine (T4) concentrations was found, but no relationship between TPO-Ab and defined disorders (38). There was no significant correlation between TSH, T4 and T3 concentration and positive anti-TPO antibody in the studied population (P >0.05). This observation is in agreement with the published study of Mariotti S et al. who found no simple relationship between anti-TPO Ab levels and thyroid function (39).

An explanation of the non-significant difference in anti-TPO antibody in the present study is probably the dominance of endemic goiter which could be found here, in Iraq.

In conclusion Iraqi patients had a relatively high prevalence of anti-TPO antibody with suspected thyroid dysfunction. There was no significant difference in positivity of the anti-TPO antibody between patients with abnormal thyroid hormone levels and those whose hormone levels were within the normal range. Thyroid autoimmunity appears to be less important in our patients than in many other countries but this requires further evaluation in a wider population and by using more sensitive methods that can measure the concentration of anti-TPO antibodies.

Due to apparent importance of anti-TPO, a study for the follow up of subjects with positive or high anti-TPO antibody titer is recommended. The small sample size in this study restricted the establishment of the clinical utility of these antibody measurements hence further evaluation with a wider Iraqi population is required. The use of thyroid diagnostic tests is patient-specific and depends clinncally on the patient's clinically on thyroid disease, so more precise selection of patients with specific entities of thyroid disease is recommended to reach a significant correlation.

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