



**PREDICTION OF HASHIMOTO'S THYROIDITIS IN PATIENTS WITH OTHER
SYSTEMIC AUTOIMMUNE DISORDERS: A FIVE-YEAR STUDY**

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ABSTRACT

Background: Thyroid autoimmune diseases, are a universal public health problem, with a broad spectrum of disorders linked to the thyroid gland, which has a vast outcome on human well-being. The frequency of thyroid dysfunction differs in each population that can be recognized to environmental elements, ethnicity, sex, age, etc. Autoimmune thyroid disorders are a various group of organ-specific autoimmune diseases, of which the most frequent include Hashimoto's Thyroiditis, which is recognized by thyroid autoantibodies, especially anti-thyroid peroxidase (TPO antibody) and anti-thyroglobulin (TG antibody), since they are significant diagnostic markers of Hashimoto's thyroiditis. The aim of this retrospective study is to show the importance of anti-thyroid autoantibodies in the diagnosis of Hashimoto's Thyroiditis in patients with abnormal thyroid function test, moreover this study implicates the significance of anti-thyroid auto-antibodies in the screening of patients with autoimmune diseases, to predict the development of Hashimoto's thyroiditis. **Materials and Methods:** This retrospective study was conducted in the time period between May 2017 and May 2022, and included 1000 subjects, divided into two groups; the first group consists of 800 patients, of which females were 530 and males were 270 referred from Surgical, Medical and Endocrine clinics at King Hussein Medical Center (KHMC), having abnormal TSH and T4 levels with clinical features of thyroid disorders after excluding other causes, clinical data was collected using Electronic medical records. The second group consists of 200 euthyroid subjects of which females were 140 and males were 60, suffering from other autoimmune diseases, who were referred from rheumatology and endocrine clinics, they were tested for their TSH and T4 levels in relation to anti-thyroid auto-antibodies as an autoimmune routine checkup. **Results:** This retrospective study that included 1000 subjects, aged between 18 and 75 with a mean age of 34.8 ± 14.08 . Group 1 included 800 patients, of which females were 530 and males were 270, group 2 consists of 200 euthyroid subjects suffering from other autoimmune diseases, of which females were 140 and males were 60, were followed in the clinic for 5 years duration for their thyroid function and the anti-thyroid antibodies. In group 1 our study reported that 344 were hypothyroid and 136 had subclinical hypothyroidism, 240 were hyperthyroid and 80 had subclinical hyperthyroidism. Of the hypothyroid and subclinical hypothyroid patients (n=360, 75 %) were positive for anti-TPO and (n=302, 63%) were positive for anti-TG. Of the hyperthyroid and subclinical hyperthyroid patients (n=205, 64 %) were positive for anti-TPO and (n=185, 58%) were positive for anti-TG. In group 2 and at the end of the time period of our study, we found that the percentage of hypothyroidism and subclinical hypothyroidism was 18.5%, and the percentage of hyperthyroidism and subclinical hyperthyroidism was 10%, of which 70% and 65% patients developed anti-TPO prior to the onset of deranged thyroid function, respectively. **Conclusion:** Thyroid autoantibodies are significantly important in the diagnosis of thyroid autoimmune diseases in patients with abnormal thyroid function test, and in predicting the development of Hashimoto's Thyroiditis in euthyroid patients with other systemic autoimmune diseases.

INTRODUCTION

Thyroid autoimmune diseases, are a universal public health problem, with a broad spectrum of disorders linked to the thyroid gland, which has a vast outcome on human well-being.^[1] Thyroid autoimmune disease is used to identify a set of pathologies that has thyroid abnormal function and an autoimmune reaction against thyroid gland.^[2] The frequency of thyroid dysfunction

differs in each population that can be recognized to environmental elements, ethnicity, sex, age, etc. Thyroid diseases are mainly divided into hypothyroidism and hyperthyroidism that is additionally subdivided into obvious and subclinical disease.^[3]

Autoimmune thyroid disorders are the most frequent organ-specific autoimmune disorders and arise in 2 - 5%

of the general population with female predominance, which include Hashimoto Thyroiditis and Graves' Disease, that are the main causes of hypothyroidism and hyperthyroidism, respectively.^[4] Moreover, focal thyroiditis and subclinical and serum anti-thyroid antibodies could be present in 15% of euthyroid individuals,^[5] and in older adults with a prevalence of (up to 30%).^[6]

Hashimoto's Thyroiditis can cause apparent hypothyroidism, but greatest number of patients have subclinical hypothyroidism with increased TSH and normal thyroid hormone concentrations.^[7] It has been theorized that antibody production stimulates development to hypothyroidism as the higher concentrations of antibodies against TG and TPO contribute to deranged thyroid function tests.^[8] Damage of more than 90% of the thyroid gland causes hypothyroidism.^[6] Hypothyroidism patients manifests tiredness, increased weight, sensitivity to cold, concentrating difficulty, dry skin, hair and nails, muscle soreness, constipation and increased menstruation.^[7] Hypothyroidism is more common in patients having another autoimmune diseases.^[9]

Graves' disease is the most common cause of hyperthyroidism, with 30 and 50 years of age as the highest incidence with female predominance.^[10] The diagnosis of Graves' disease is based on typical clinical features of hyperthyroidism such as weight loss, heat intolerance, palpitations, fatigue, tremor, and diffuse goiter, with other particular clinical features of Graves' disease including pretibial myxoedema, exophthalmos, and acropachy. Serum investigations typically show inhibited thyroid-stimulating hormone (TSH; thyrotropin) and raised thyroid hormones.^[11]

Anti-TPO antibodies are formed against a transmembrane protein of thyrocytes play a part in the synthesis of thyroid hormones, as it has a pathogenic role in destructing thyroid cells through complement fixation.^[12,13] Anti-TG antibodies are formed against thyroglobulin, a thyroid hormone precursor.^[12] Anti-TPO antibodies and anti-TG antibodies are essential in diagnosing autoimmune thyroid disorders and evaluating treatment efficiency since they are existent in more than 90% of patients with Hashimoto's Thyroiditis and over 80% of patients with Graves' disease.^[14,15] The concentration of anti-TPO antibody in serum is directly linked with chronic autoimmune thyroiditis activity. Patients with Hashimoto's Thyroiditis tend to have increased serum anti-TPO compared to anti-thyroglobulin antibody (anti TG antibody) levels. Consequently, the assessment of serum anti-TPO antibody concentrations in correlation with serum level of thyroid hormones could help in clarifying its possible pathogenic part in development of thyroid disorders.^[14]

Anti-thyroid peroxidase (TPO) and anti- Anti-thyroglobulin (TG) antibodies are closely associated to

levels of thyroid stimulating hormone (TSH) and both unaccompanied or in combination can be used to expect consequent hypothyroidism or hyperthyroidism. It was reported in various studies that abnormal levels of anti-thyroid antibodies and TSH in euthyroid persons have been linked with existence of hypothyroidism in the forthcoming years.^[16,17]

Lately, autoantibodies have shown significant results as primary diagnostic indices in several diseases such as rheumatoid arthritis, celiac disease and cancer.^[18-20] Unluckily, thyroid autoantibodies are usually tested when there is abnormal thyroid hormones, particularly TSH and FT4. However their existence even before the TSH abnormality, which is the primary indicator, has not been taken in consideration.^[3]

The aim of this retrospective study is to show the importance of anti-thyroid auto-antibodies in the diagnosis of Hashimoto's Thyroiditis in patients with abnormal thyroid function test, moreover this study implicates the significance of anti-thyroid auto-antibodies in the screening of euthyroid population to predict the development of hypothyroidism and hyperthyroidism.

MATERIALS AND METHODS

This retrospective study was conducted in the time period between May 2017 and May 2022 and included 1000 subjects, divided into two groups; the first group 1 consists of 800 patients, of which females were 530 and males were 270 referred from Surgical, Medical and Endocrine clinics at KHMC, having abnormal TSH and T4 levels with clinical features of thyroid disorders after excluding other causes, clinical data was collected using Electrctronic medical records. The second group consists of 200 euthyroid subjects, of which females were 140 and males were 60, were followed up by testing their TSH and T4 levels in relation to anti-thyroid auto-antibodies.

RESULTS

This retrospective study that included 1000 subjects, aged between 18 and 75 with a mean age of 34.8 ± 14.08 . Group 1 are 800 patients, of which females were 530 and males were 270. Group 2 consists of 200 euthyroid subjects, of which females were 140 and males were 60, who were suffering from other autoimmune diseases, the sex distribution of patients in group1 and group 2 is shown in table 1. In group 1 our study reported that 344 were hypothyroid and 136 subclinical hypothyroid, 240 were hyperthyroid and 80 subclinical hyperthyroid. Of the hypothyroid and subclinical hypothyroid patients (n=360, 75 %) were positive for anti-TPO and (n=302, 63%) were positive for anti-TG. Of the hyperthyroid and subclinical hyperthyroid patients (n=205, 64 %) were positive for anti-TPO and (n=185, 58%) were positive for anti-TG, the percentages of positive TPO and positive TG in patients with deranged thyroid function tests are shown in table 2. In patients with deranged thyroid function test, females who were

positive for anti-TPO antibodies account (n=497, 88%) and males account (n=68, 12%), while in anti-TG positive patients with deranged thyroid function test, females account (n=292, 60%) and males (n=195, 40%), the percentages of females and males who were positive for anti-TPO and anti-TG in patients with deranged function tests are shown in table 3.

In group 2, at the end of the time period of our study, we documented that (n=37, 18.5%) developed hypothyroidism and subclinical hypothyroidism, and (n=20, 10%) developed hyperthyroidism and subclinical hyperthyroidism. Also we found that in patients who developed hypothyroidism and subclinical hypothyroidism, (n= 26, 71%) were positive for anti-TPO and (n=23, 64%) were positive for anti-TG prior to their diagnosis of hypothyroidism and subclinical hypothyroidism. Also we recorded that (n=7, 20%) were positive for anti-TPO, and (n=6, 17 %) were positive for anti-TG, at or following the diagnosis of hypothyroidism and subclinical hypothyroidism. On the other hand we

found that (n=3, 9%) and (n=7, 19%) did not develop anti-TPO and anti- TG respectively during their follow up. While we reported (n=13, 65%) were positive for anti-TPO prior to the diagnosis of hyperthyroidism and subclinical hyperthyroidism, (n=5, 25%) were positive for anti-TPO at or following the diagnosis of hyperthyroidism and subclinical hyperthyroidism, On the other hand, we recoded (n=12, 59%) were positive for anti-TG prior to the diagnosis of hyperthyroidism and subclinical hyperthyroidism and (n=4, 18%) were positive for anti-TPO at or following the diagnosis of hyperthyroidism and subclinical hyperthyroidism, and (n=2, 10%) and (n=4, 23%) did not develop anti-TPO and anti- TG respectively during their follow up, the percentages of positive TPO and positive TG before, at or following the onset of deranged thyroid function tests versus never developing anti-TPO and anti-TG are shown in table 4. The percentages of positive TPO and positive TG in deranged thyroid function tests as a total despite timing of onset are shown in table 5.

Table 1: The sex distribution of patients in group1 and group 2.

	Number of patients	Females	Males
Group1	800	530	270
Group2	200	140	60

Table 2: The percentages of positive TPO and positive TG in patients with deranged thyroid function tests in group1.

	Number of patients	Positive anti-TPO	Positive anti-TG
Hypothyroidism	344	360 (75%)	302 (63%)
Subclinical Hypothyroidism	136		
Hyperthyroidism	240	205 (64%)	185 (56%)
Subclinical Hyperthyroidism	80		

Table 3: The percentages of Females and Males who were positive for anti-TPO and anti-TG in patients with deranged function tests. (group1).

	Total number	Females	Males
Positive anti-TPO	565	497 (88%)	292 (60%)
Positive anti-TG	487	68 (12%)	195 (40%)

Table 4: The percentages of positive TPO and Positive TG before, at or following the onset of deranged thyroid function tests versus never developing anti-TPO and anti-TG (group2).

	Number of patients	Positive anti- TPO			Positive anti-TG		
		Prior	At or following	Never	Prior	At or following	Never
Hypothyroidism and Subclinical Hypothyroidism	37 (18.5%)	26 (70%)	7 (19%)	4 (11%)	23 (62%)	6 (16%)	8 (22%)
Hyperthyroidism and Subclinical Hyperthyroidism	20 (10%)	13 (65%)	5 (25%)	2 (10%)	12 (60%)	4 (20%)	4 (20%)

Table 5: The percentages of positive TPO and positive TG in deranged thyroid function tests as a total despite timing of onset (group2).

	Hypothyroidism and Subclinical Hypothyroidism N=37	Hyperthyroidism and Subclinical Hyperthyroidism N=20
Positive anti-TPO	N=33 (89%)	N=18 (90%)
Positive anti-TG	N=29 (78%)	N=16 (80%)

DISCUSSION

Anti-thyroid antibodies were known to have an effect on thyroid function and affect its hormone analysis. We have been theorized that anti-thyroid antibodies are commonly positive in persons with abnormal thyroid function test^[15] We had revealed that in group 1 anti-TPO and anti-TG antibodies are more frequently found in persons with abnormal TSH and T4 in comparison to those with normal TSH. Our study results reported that anti-TPO antibodies in patients who were hypothyroid or subclinical hypothyroid were positive in 75% and anti-TG antibodies were positive in 63%, while in patients who were hyperthyroid or subclinical hyperthyroid, anti-TPO antibodies found positive 64% and anti-TG antibodies found positive in 58%. Similar findings have been documented by Al Rabi among Saudi population in which TSH is more frequently disturbed when anti-TPO or anti-TG antibodies are positive^[21] and by Brown et al. who reported that positive anti-TPO is correlated with 60% increase in TSH, on the other hand they did not investigate anti-TG antibodies.^[22]

In our study, females patients in both groups were dominant constituting in group 1 (530) and in group 2 (140), while males in group 1 were (270) and in group 2 (60), similar to other studies one reported done by Siriwardhane T et al, and the other study in Pakistan by Hamid Nawaz Tipu, showed that females were more dominant than males.^[3,15]

Our study reported that in patients with deranged thyroid function test, females who were positive for anti-TPO antibodies accounted (n=497, 88%) and males accounted (n=68, 12%), while in anti-TG positive patients with deranged thyroid function test, females account (n=292, 60%) and males (n=195, 40%). Similarly, in a study conducted by AlRabi, a major relationship was identified between female gender and raised levels of anti-TPO. A higher proportion of females showed high levels of anti-TG, but it was not statistically significant.^[21]

Associations exist between development of Hashimoto's thyroiditis and the presence of other systemic autoimmune diseases, and this explained our findings in group 2 patients at the end of the time period of our study, in which we documented that the percentage of hypothyroidism and subclinical hypothyroidism was 18.5%, and the percentage of hyperthyroidism and subclinical hyperthyroidism was 10%, of which 70% and 65% patients developed anti-TPO prior to the onset of deranged thyroid function, respectively. Similar findings were reported by Siriwardhane T et al, who found that

73% of hypothyroid patients and 68.6% of hyperthyroid patients had anti-TPO prior to the onset of deranged thyroid function.^[3] This finding raised the value of adding anti-TPO in combination with thyroid function tests to predict the diagnosis of Hashimoto's thyroiditis; therefore patients with normal thyroid function and high antibodies titer would not be abandoned rather they can be followed up for treatment.

CONCLUSION

Thyroid autoantibodies are significantly important in the diagnosis of thyroid autoimmune diseases in patients with abnormal thyroid function test, and in predicting the development of Hashimoto's Thyroiditis in euthyroid patients with other systemic autoimmune diseases to minimize long-term morbidity.

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