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Hashimoto's Thyroiditis among Patients with Thyroid Diseases in Sulaimani City: A Cross-Sectional Study

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ABSTRACT: This study aimed to measure the prevalence of Hashimoto's Thyroiditis among patients with thyroid diseases in Sulaimani city and to observe some features of this autoimmune disorder. Hashimoto's Thyroiditis, also known as Hashimoto's disease, is an essential cause of Hypothyroidism. Blood samples were collected from 203 patients suffering from thyroid disease in Sulaimani endocrine center and Bakshin Private Hospital in Sulaimani city from December 2018 to March 2019. Serum levels of thyroid hormones, anti-thyroid peroxidase antibodies, anti-thyroglobulin antibodies, and anti-thyroid-stimulating hormone receptor antibodies were determined using Cobas e411 Immunoanalyzer; moreover, data about gender, age, and family history of thyroid disease were recorded. The prevalence of Hashimoto's Thyroiditis among all thyroid patients was 62% (n=126/203), while Graves' disease was 15.3% (n=31/203); thus, autoimmune diseases represent 77.3% (157/203) of thyroid diseases. Hypothyroidism is diagnosed in 155/203 (76.4%) thyroid diseases, while the remaining 23.6% were patients with hyperthyroidism. The demographic data revealed that 88.9% (n=112/126) of Hashimoto's Thyroiditis are females, while 11.1 % (n=14/126) are males. The peak incidence of Hashimoto's Thyroiditis is in the age group 36-45 years; a family history of thyroid diseases was recorded in 64.3% of Hashimoto's patients. The correlation coefficient between anti-thyroid peroxidase antibodies and the ages of Hashimoto's Thyroiditis patients is 0.21938. Hashimoto's Thyroiditis is the main thyroid disorder in Sulaimani city among patients with thyroid diseases, Hypothyroidism, and autoimmune thyroid disorders; both seropositive and seronegative anti-thyroid peroxidase antibodies are recorded among Hashimoto's Thyroiditis patients. Family history of thyroid disorders and females of childbearing age are possible risk factors for developing Hashimoto's Thyroiditis. There is no significant correlation between anti-thyroid peroxidase antibodies concentrations and ages of Hashimoto's Thyroiditis patients, but these antibodies are much higher in Hashimoto's females than in Hashimoto's Thyroiditis males

Keywords: Hashimotos' thyroiditis, anti-thyroid peroxidase, autoantibody, Hypothyroidism.

1. Introduction

Hashimoto's Thyroiditis (H.T.) is a common chronic autoimmune disease of the thyroid gland (Zaletel, 2011). H.T. causes impairment in the production of thyroid hormones triiodothyronine (T3) and tetraiodothyronine (T4). This impairment in hormone production is due to an autoimmune reaction against the thyroid gland, which is in part manifested by making autoantibodies against thyroid peroxidase enzyme, the anti-thyroid peroxidase (anti-TPO) antibodies, and against thyroglobulin, the anti-thyroglobulin (anti-Tg) antibodies, leading to the gradual decline in thyroid function and eventually an underactive thyroid (Zaletel, 2007). In addition to inadequate iodine intake, H.T. is an essential cause of asymptomatic Hypothyroidism (Katagiri et al.,2017).

Most patients (90%) with H.T. have elevated levels of anti-TPO Abs, while serum levels of T.G. antibody concentrations rise in 20 to 50 percent of these patients (Fröhlich et al.,2017). H.T. has diverse clinical features like weight gain, constipation, cold intolerance, periorbital myxedema, depression, and bradycardia; the

patient may also experience fatigue, weakness, and puffy face; infants might suffer mental retardation (Wiersinga 2014).The diagnosis of H.T. is usually made by detecting a positive test for anti-TPO Abs in patients with suggestive clinical features; however, some Hashimoto's patients are seronegative; in these patients, laboratory features of Hypothyroidism are manifested by an increase in thyroid stimulating hormone (TSH) and decrease in T4 and T3 with positive anti-Tg Abs (Pyzik et al.,2015).

2. Material and Methods

2.1Sample collection

In this study, we randomly selected 203 patients consulting two main thyroid diseases referral healthcare facilities in Sulaimani, Sulaimani Endocrine Center and Bakshin Private Hospital, from December 2018 to March 2019; specialists diagnosed patients with thyroid diseases.

2.2 detection of laboratory findings

Serum thyroid-stimulating hormone (TSH), thyroxin (T4), free thyroxin (FT4), T3 triiodothyronine (T3), and free triiodothyronine (FT3), were measured by the automated immune analyzer Cobas e411 (Roche Diagnostics/Germany) using Cobas e411 chemoluminescence kits (TSH normal range 0.25 – 5 qI/ml), (T4 normal range 3.1_6.8 pmol/L) (FT4 normal values 12 – 22 pmol/L), (total T3 1.17 – 3.40 nmol/L), (FT3 3.1_6.8 pmol/L). Cobas e411 immune analyzer (Roche Diagnostics/Germany) was also used for measuring serum levels of anti-thyroid peroxidase antibodies (anti-TPO Abs, normal range <34 I.U./ml), anti-thyroglobulin antibodies (anti-Tg Abs, normal range <58.5 IU/ml), and anti-thyroid stimulating hormone receptor antibodies (anti-TSH Abs, 0.38 – 0.94 IU/ml) using chemoluminescence immunoassay kits (Roche-Germany). Gender, age, and family history were recorded for all patients in this study. For specimen collection, 5 ml of venous blood was obtained from each patient and collected in a clot activator tube for testing; specimen collection and laboratory testing were done in a private laboratory, the Dark laboratory, and each specimen was put in the centrifuge for 5 minutes at 2500 rpm for separating serum that is stored at – 20 °C till testing.

2.3. Ethics approval of research

Patients' rights and ethical approval statement describing: Institutional review boards or committees were not consulted for ethical approval of this research because all blood samples were collected from public and private clinical diagnostic laboratories officially recognized by the Kurdistan Regional Government of Iraq's ministry of health. The ministry requires all diagnostic laboratories in Iraq's Kurdistan Region of health guidelines to consider patient rights and ethical standards. All patients were willing to have their blood drawn orally after following all ethical guidelines. The name, age, gender, and history of patients and clients are entered into the lab database.

2.4 statistical analysis

Statistical analysis was conducted with Graph Pad Prism 6.0 (W.I., USA) software program; P-values <0.05 were considered statistically significant.

3. Results

A total of 203 untreated patients with thyroid diseases were enrolled in this study; the number of male patients was 30 while females were 173, and the range of their ages was 1-78 years old.

Depending on clinical features and the results of laboratory tests for serum thyroid hormone function and serum auto-antibodies , the endocrinologist determined the diagnosis of Hypothyroidism in 155/203 patients and hyperthyroidism in 48/203 patients. Among patients with Hypothyroidism, H.T. was diagnosed in 126 out of 155 (81.3%), while Graves' disease diagnosed in 31 out of 48 patients with hyperthyroidism, as shown in **figure 1.**

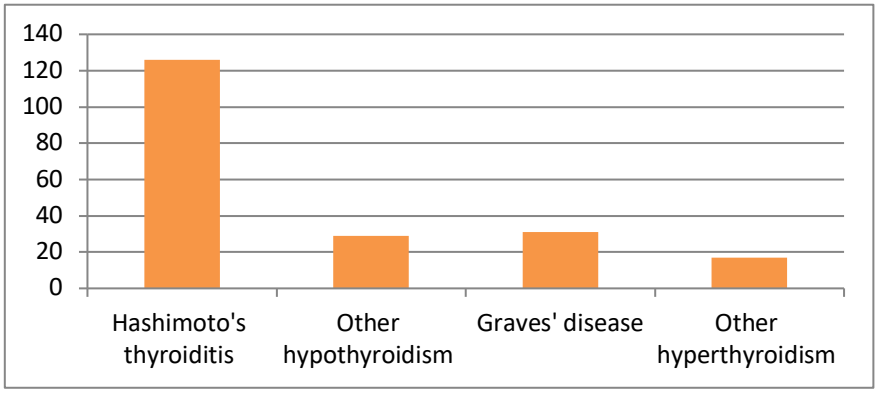

Figure 1. Prevalence of different thyroid disorders among patients in the study.

Of the 203 patients, 157 (77.3%) were diagnosed with autoimmune thyroid diseases. The frequency of H.T. was 126/203 (62%) of all patients, and it represents 126/157 (80.3%) of the patients with autoimmune diseases; the frequency of Graves' disease was 31/203 (15.3%), which represents 19.7% of the autoimmune diseases as described in table 1, the differences among frequencies were statistically significant, $p<0.05$.

Table 1. Frequency of autoimmune diseases among the study group.

Autoimmune thyroid diseases (%)	Non-immune thyroid disease (%)	P value
Hashimoto's thyroiditis 126 (62.0) Graves' disease 31 (15.3)	46 (22.7)	<0.05

Among 126 cases of Hashimoto's disease, just 14 (11.1%) patients were males while 112 (88.9%) patients were females, while for Graves' disease, 8/31 (25.8%) were males and 23 (74.2%) cases were females.

For the non-autoimmune thyroid diseases, just one male had hyperthyroidism while the other 16 hyperthyroid patients were females; in Hypothyroidism, 8 cases were male, and 22 cases were female, as shown in figure 2.

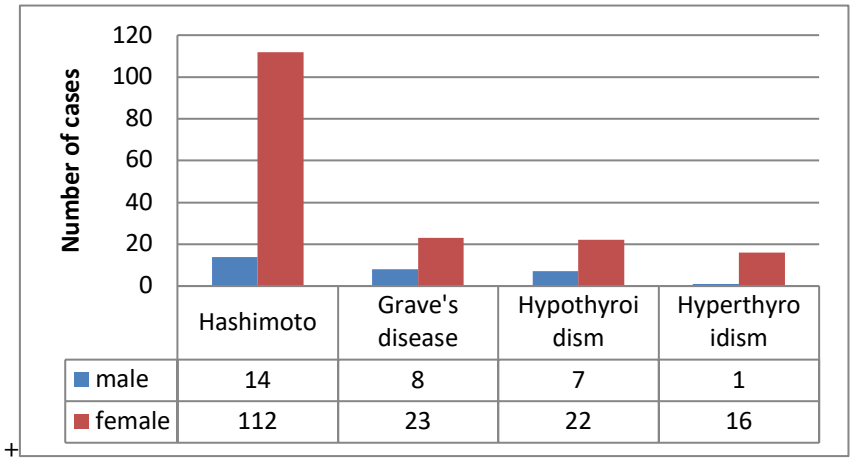

Figure 2. Gender distribution among patients in the study group.

In this study, patients' ages ranged from 1 to 78 years old, with a mean and standard division of 38.45 ± 54.44.The mean age of H.T. was 39.17 ±37.5; for other hypothyroidism patients, it was 39.76±26; for Grave's disease was 39.17 ±37.5, while for other hyperthyroidism patients were 33.05±25,(Table 2).

Table 2. Age distribution among Hashimoto's patients

Age	Frequency (%)
4-15	9
16-26	9
26-35	28
36-45	39
46-55	27
56-65	10
>66	4

The serum anti-TPO antibodies above the normal level were mainly detected in H.T. 42/126 (33.3%), while only 3 patients with Grave's disease are positive for anti-TPO Abs (3/31, 0.01 %); in hyperthyroidism anti-TPO, Ab is within normal except in one patient with elevated positive anti-TPO Ab; the non-immune hypothyroidism patients have normal range, (**Figure 3**).

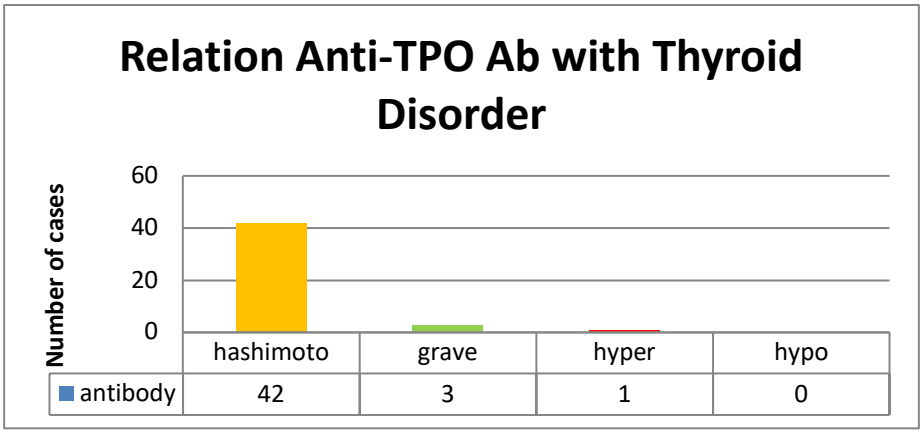

Figure 3. The frequency of positive anti-TPO Abs in thyroid disorders.

In the current study, most patients 81/126 with H.T. have a positive family history of thyroid disorder, as described in **figure (4).**

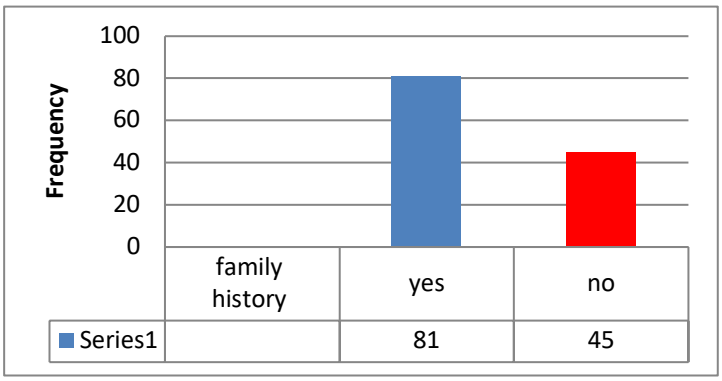

Figure 4. Family history of thyroid diseases among Hashimoto's thyroiditis patients.

The results of this study revealed that the association between anti-TPO antibodies and the ages of Hashimoto's thyroiditis patients would not be considered statistically significant according to Spearman's Rho calculator of correlation coefficient (the value of rs is: 0.21938).

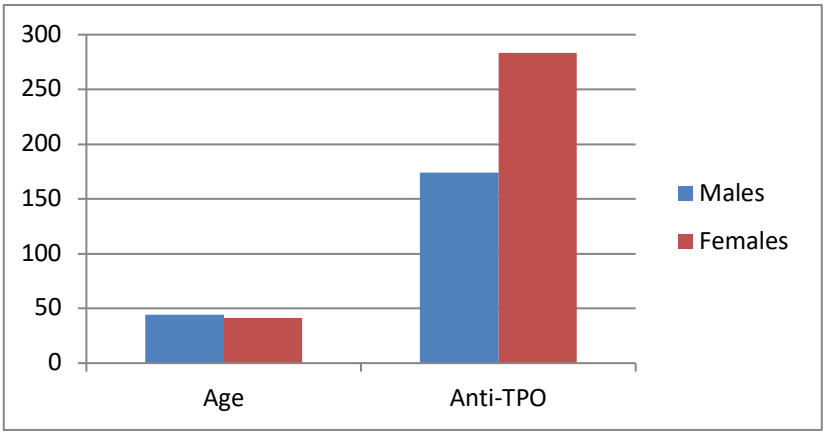

Figure 5. The mean age and anti-TPO antibodies among males and females patients with Hashimoto's Thyroiditis. The p-value is 0.016952.

The mean of H.T. males' ages (44.25 years) is slightly more than that of H.T. females (41.2 years), but the mean concentrations of anti-TPO antibodies are significantly higher (p-value <0.05) in H.T. females (283.5 IU/ml) than in males (173.8 IU/ml)(Figure .5).

4. Discussion

In the current study, H.T. was the most prevalent thyroid disease at three levels: among thyroid disorders (62%), among patients with Hypothyroidism (81.3), and among autoimmune diseases (80.3%); these results showed a much higher prevalence than those recorded in other regions of Iraq (Al-Hashimi 2014).

However, about 20 years ago, the reports of Sulaimani health authorities recorded that most of thyroid diseased people in Sulaimani city were suffering from hyperthyroidism rather than Hypothyroidism, but the current study showed that H.T. ranked number one among people with thyroid disorders in Sulaimani city and this increase in the prevalence of H.T. needs to be clarified. This high prevalence is the following that reported by (Staii *et al.*, 2010)worldwide, H.T. is the most prevalent cause of Hypothyroidism in regions with normal iodine intake (Kapil ,2007)

The results showed an obvious relationship between gender and autoimmune thyroid diseases, as most of the patients are females, and this was particularly noticed for H.T. It is well-known that females are more prone to develop autoimmune diseases than males; this might be due to skewed chromosome inactivation in females(Brix *et al.*,2005) or hormonal heterogeneity between males and females makes females more susceptible to autoimmune diseases as testosterone hormone has anti-inflammatory effect while estrogen hormone has a pro-inflammatory effect(Rubtsova *et al.*,2015)

Moreover, H.T. predominates in women of childbearing age, as indicated in our data; this is also mentioned in previous studies related to physiological changes during pregnancy to achieve the demands of gestational needs (Galofre *et al.*,2009; Smallridge *et al.*,2005).

Anti-TPO antibody is an important marker for the diagnosis of autoimmune thyroid diseases, especially in H.T., as the diagnosis of H.T. depends on combinations of clinical features and laboratory testing, including serum anti-TPO Abs, serum anti-Tg Abs, and determination of serum thyroid hormones concentrations. However, this study did not reveal that only nearly one-third of H.T. patients are positive for anti-TPO Abs and a higher percentage of H.T. patients are seronegative for anti-TPO Abs; these data follow that mentioned by Thushani S et al.. However, they also recorded elevated anti-TPO Abs in Graves' disease, which is against our results (Siriwardhane *et al.*,2019).

The results of this study showed that positive family history of thyroid disorder is a possible risk factor for developing H.T., as many H.T. patients had a positive family history of thyroid diseases; the inheritance of special HLA alleles might be related to this association (Paknys *et al.*,2009).

5. Conclusion

Hashimoto's Thyroiditis is the main thyroid disorder in Sulaimani city among patients with thyroid diseases, Hypothyroidism, and autoimmune thyroid disorders, both seropositive and seronegative anti-TPO antibodies are recorded among H.T. patients. Family history of thyroid disorders and females of childbearing age are possible risk factors for developing H.T. There is no significant correlation between anti-TPO antibodies concentrations and ages of H.T. patients, but these antibodies are much higher in H.T. females than in H.T. males.

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