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T3, T4, TSH, Anti-TPO, and Anti-TG Autoantibodies Distribution in Autoimmune Thyroid Patients with Chlamydia Trachomatis Infection

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Abstract

Autoimmune thyroid disorders (AITDs) include a variety of inflammatory conditions affecting the thyroid gland, with Graves' disease (GD) and Hashimoto's thyroiditis (HT) being the most commonly seen types. Autoimmune thyroid illnesses often include the existence of antibodies against thyroid peroxidase (TPO), thyroglobulin (Tg), and thyroid stimulating hormone receptor (TSHR). We specifically targeted recently diagnosed adult patients with Graves' disease (GD), Hashimoto's thyroiditis (HT), and those with normal thyroid function as controls. The study looked at and compared different groups' levels of anti-TG antibodies, anti-TPO antibodies, and anti-chlamydia antibodies in the blood, as well as several clinical and biochemical markers, such as thyroid function tests. We analyzed data from a cohort of 60 patients diagnosed with Hashimoto's thyroiditis (HT), 60 patients diagnosed with Graves' disease (GD), and 60 healthy individuals serving as controls. The study found a strong link between having anti-TPO Abs and having Hashimoto's hypothyroidism (63.3%) and Graves' hyperthyroidism (86.7%). In the groups without anti-TPO Abs, Hashimoto's hypothyroidism was found in 36.7% of people and Graves' hyperthyroidism was found in 13.3% (P<0.03). Anti-thyroid peroxidase antibodies (anti-TPO Abs) are found in 86.7% of people with Graves' disease, which is more than the 63.3% of people with Hashimoto's disease who have these antibodies. There is no significant link between the percentage of people who have anti-TG antibodies and either Hashimoto's hypothyroidism (96.7%) or Graves hyperthyroidism (90%), according to the study. The significance level was set at P = 0.143. This is in comparison to the percentage of negativity in Hashimoto's hypothyroidism (3.3%) and Graves's hyperthyroidism (10.0%). The study showed how the groups were spread out based on the presence of Chlamydia trachomatis IgG antibodies. Chlamydia trachomatis IgG antibodies were much more common in people with Hashimoto's hypothyroidism (42) and Graves hyperthyroidism (26) than in the control group (0) (P<0.01)..

Keywords: *Graves' Disease, Hashimotos Disease, Hyperthyroidism, Hypothyroidism, Chlamydia*

INTRODUCTION

Autoimmune thyroiditis (AIT) is the most prevalent autoimmune illness that specifically targets the endocrine system [1]. Graves' disease and Hashimoto's thyroiditis are two autoimmune disorders that affect the thyroid gland. The diagnosis of Graves' disease is often made by identifying the presence of autoantibodies in the bloodstream that activate the TSH receptor (TRAb), leading to the development of hyperthyroidism and goiter. The development of AITD is influenced by a complex interplay of genetic and environmental factors, which together contribute to its convoluted etiology. Autoimmune thyroid disease (AITD) is a multifaceted condition characterized by the immune system erroneously targeting the thyroid antigens as a result of certain hereditary factors, with environmental variables playing a role in influencing this phenomenon. The thyroid gland is the main site of autoimmune responses, occurring most often. Although AITDs are acknowledged as autoimmune illnesses that primarily affect certain organs, the precise trigger for these autoimmune reactions remains unknown [2 – 3]. Hashimoto's illness is primarily characterized by the presence of thyroid peroxidase (TPO) and thyroglobulin (Tg) as autoantigens. Nevertheless, around 70% of persons with Graves' illness also exhibit the presence of these antibodies (TPO-Ab and Tg-Ab). Like with Graves' disease, where the thyroid-stimulating hormone receptor (TSHR) is the primary autoantigen, a tiny proportion of people with Hashimoto's disease also have these antibodies [4]. A considerable amount of extragenetic variables have been linked to AITD, and these factors may be categorized as either infectious or noninfectious causes. The assessment of infectious factors has mostly been conducted retrospectively, particularly by the quantification of antibodies against

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microorganisms. This technique has been especially used to evaluate the presence of Y. enterocolitica, H. pylori, B. burgdorferi, Hepatitis C virus (HCV), Hantavirus, Saccharomyces, T. gondii, human immunodeficiency virus (HIV), and the gut microbiota [5-6].

MATERIALS AND METHODS

Between August 2022 and April 2023, 300 Iraqi patients with thyroid dysfunction were chosen randomly from the Al-Jawda private laboratory in the governorate of Baghdad. The sample was split into 60 healthy controls and 120 patients with autoimmune thyroiditis and non-autoimmune thyroiditis. The current study was conducted on newly diagnosed HT and GD patients who were referred to endocrine healthcare facilities in the Baghdad governorate between August 2022 and April 2023. The successive sample method was used to constantly enlist people who were at least 25 years old. The control group included euthyroid healthy adults who had been referred for checkup tests. Their family or personal history of autoimmune thyroid illness was negative. Based on age, sex, and BMI, case groups and the control group were matched. The inclusion criteria were GD or HT with a recent diagnosis. Participants were given blood samples between 8 and 9 AM after a 12-hour fast. Serum samples were collected, and until testing, they were kept at -70 °C. T3, T4, TSH, Anti-TPO, Anti-TG, and Anti-Chlamydia trachomatis IgG tests were assessed in individuals with GD and HT as well as in the control group. A human leptin ELISA Kit was used to assess leptin in both the patient group and the control group. Using immunochemiluminescent tests, the diagnostic product Roche Cobas e411 automated analyzer assessed T4, T3, and TSH. With the aid of commercially available kits, immunochemiluminescent assays were used to assess anti-thyroid peroxidase and anti-thyroglobulin. We carried out study procedures according to the (national or organizational) research committee's ethical guidelines. We also adhered to the ideas of the Helsinki Declaration of 1964 and its modifications. All participants gave their informed consent.

The research variable was described using descriptive statistics, including frequency, percentage, mean, and standard deviation. A unidirectional analysis of variance (ANOVA) test was used to assess the disparity in means of a quantitative variable among the three research cohorts consisting of patients with GD, HT, and a healthy control group. Furthermore, a post-hoc analysis was conducted using the Bonferroni correction to compare pairs of data. We used odds ratios (OR) to analyze the association between categorical characteristics and the study group. The correlation between the numerical variable and the correlation was assessed using Pearson's correlation coefficient. The statistical significance was determined at a significance level of $P<0.05$.

RESULTS AND DISCUSSION

Distribution Of Studied Groups According to Percentage of Normal and Abnormal T3(ng/ml) Levels.

Table (1) shows the distribution of Studied groups according to the percentage of abnormal T3 percent (53.3%) in Hashimotos patients' groups in comparison with control groups (0.0%), and the percentage of abnormal T3 percent (36.7%) in Graves patients groups in compare with control groups (0.0%), odds ratio (OR) test is used to measure of association between T3 with Hashimotos patients and T3 with Graves patients.

Table 1.Distribution of Studied groups according to percentage of normal and abnormal T3(ng/ml) levels.

Study groups		T3(ng/ml) Percentage		OR	95%CI
		Normal	Abnormal		
Control (n=60)	No.	60	0		
	%	100.0%	0.0%		
Hashimotos (n=60)	No.	28	32	2.143**	(1.635 - 2.808)
	%	46.7%	53.3%		
Graves (n=60)	No.	38	22	1.579**	(1.302 – 1.914)
	%	63.3%	36.7%		

The current study, as in Table (1), showed a decrease in the T3 hormone in Hashimoto's patients and an increase in Grave's patients. Table (1) shows the distribution of Hashimoto's patients and Graves who have a disorder in the level of the T3 hormone. The findings of this research align with well-established scientific evidence that demonstrates a reduction in the T3 hormone levels in individuals with Hashimoto's disease due to a malfunction in the thyroid gland, leading to insufficient production of thyroid hormones [7]. Hypothyroidism is a condition characterized by an inadequate supply of thyroid hormones to the body's tissues. Autoimmune thyroiditis, sometimes called Hashimoto's thyroiditis, is the predominant cause in regions with adequate iodine levels.

Hashimoto's thyroiditis is a result of the autoimmune destruction of thyroid tissue, which causes inflammation of the thyroid gland and a decrease in the synthesis of thyroid hormones. Due to its autoimmune nature, this ailment often coexists with other immune-related disorders and is generally characterized by antithyroid antibodies in the bloodstream [8-9-10.]

The findings of the present research align with established scientific evidence that demonstrates elevated levels of T3 hormone in individuals with Graves' disease due to impaired thyroid gland function, leading to an excessive release of thyroid hormones [7]. Hyperthyroidism is a condition characterized by the excessive production of thyroid hormones, which may be attributed to several disorders. Thyrotoxicosis is a medical disorder marked by abnormally high levels of thyroid hormones. Grave's disease is the predominant etiology of hyperthyroidism (thyrotoxicosis) in the population. Grave's disease is an autoimmune disorder characterized by the production of antibodies that specifically target the TSH receptors in the thyroid gland. This leads to excessive production of T3 and T4 hormones. Hyperthyroidism often presents with symptoms that are correlated with low levels of TSH and high levels of T3 and T4 hormones [11].

Distribution Of Studied Groups According To The Percentage Of Normal And Abnormal T4(nmol/l) Levels.

Table (2) shows the distribution of Studied groups according to the percentage of abnormal T4 percent (43.3%) in Hashimoto's patient groups in comparison with control groups (0.0%), and the percentage of abnormal T4 percent (50.0%) in Graves patients groups in compare with control groups (0.0%), odds ratio (OR) test is used to measure of association between T4 with Hashimoto's patients and T4 with Graves patients.

Table 2.Distribution of Studied groups according to percentage of normal and abnormal T4(nmol/l) levels.

Study groups		T4(nmol/l) percentage		OR	95%CI
		Normal	Abnormal		
Control (n=60)	No.	60	0		
	%	100.0%	0.0%		
Hashimotos (n=60)	No.	34	26	1.765**	(1.414 – 2.202)
	%	56.7%	43.3%		
Graves (n=60)	No.	30	30	2.000**	(1.553 – 2.202)
	%	50.0%	50.0%		

The current study, as in Table (2), showed a decrease in T4 hormone in Hashimoto's patients and an increase in Grave's patients. Table (2) shows the distribution of Hashimoto's patients and Graves who have a disorder in the level of the T3 hormone. The current study's results are consistent with existing scientific data that shows a decline in T4 hormone levels in persons with Hashimoto's illness. This decline is mostly due to reduced thyroid gland function, resulting in inadequate release of thyroid hormones. Hypothyroidism is defined as the inadequate synthesis of thyroid hormones.

These disorders are categorized as major, secondary, or tertiary based on the endocrine gland that causes the problem. Hypothyroidism is a primary ailment caused by an insufficient synthesis of thyroid hormones due to a malfunction of the thyroid gland [7].

The results of the current research align with established scientific evidence that demonstrates an elevated concentration of T4 hormone in individuals with Graves' illness due to excessive production of thyroid hormone, which may be attributed to many medical conditions. Thyrotoxicosis is a pathological condition characterized by excessively elevated amounts of thyroid hormones. Grave's disease is the main cause of hyperthyroidism (excessive thyroid activity) in the population. Grave's disease is an autoimmune disorder characterized by the creation of antibodies that particularly target the TSH receptors in the thyroid gland. This leads to excessive synthesis of T3 and T4 hormones.Hyperthyroidism is defined by decreased levels of TSH and elevated levels of T3 and T4, which are likely to result in the manifestation of signs and symptoms [11].

Distribution Of Studied Groups According to Percentage Of Normal And Abnormal TSH (µiu/ml) Levels.

Table (3) shows the distribution of Studied groups according to the percentage of abnormal TSH percent (90.0%) in Hashimotos patients' groups in comparison with control groups (0.0%), and the percentage of abnormal TSH percent (93.3%) in Graves patients' groups in compare with control groups (0.0%), odds ratio (OR) test is used to measure of association between T4 with Hashimotos patients and TSH with Graves patients.

Table 3. Distribution of Studied groups according to the percentage of normal and abnormal TSH (µIU/ml) levels.

Study groups		TSH (µIU/ml) Percentage		OR	95%CI
		Normal	Abnormal		
Control (n=60)	No.	60	0		
	%	100.0%	0.0%		

Hashimotos (n=60)	No.	6	54	10.000**	(4.681 – 21.364)
	%	10.0%	90.0%		
Graves (n=60)	No.	4	56	15.000**	(5.820 – 38.661)
	%	6.7%	93.3%		

The current study, as in Table (3), showed an increase in TSH hormone in Hashimoto's patients and a decrease in Grave's patients. Table (3) shows the distribution and percentage of Hashimoto's patients and Graves who have a disorder in the level of the TSH hormone. The result of the current study is consistent with established scientific facts that indicate an increase in the level of the TSH hormone in Hashimoto's patients because of a defect in the functioning of the thyroid gland, which results in a lack of secretion of thyroid hormones. The current study's findings also coincide with existing scientific facts indicating a low level of TSH hormone in Graves patients due to a deficiency in thyroid gland functioning, which increases thyroid hormone release. Hyperthyroidism arises from excessive production and secretion of thyroid hormone (TH) by the thyroid gland [12]. Graves' disease (GD) is a kind of autoimmune illness that affects particular organs. It is characterised by the presence of autoantibodies (Ab) in the bloodstream that activate the thyroid-stimulating hormone receptor (TSH-R). This activation leads to the development of hyperthyroidism (overactive thyroid) and goitre (enlarged thyroid gland). TSH-R stimulating antibodies mostly belong to the IgG1 isotype and specifically target a non-continuous epitope inside the leucine-rich region of the TSH-R extracellular domain, which is approximately defined by certain amino acids [13-14]. Thyroid-stimulating immunoglobulin (TSI), commonly referred to as thyroid-stimulating antibody (TSAb), is the underlying cause of Graves' disease's lymphocytes mostly produce Thyroid-stimulating immunoglobulin inside the thyroid cells, however, it may also be synthesized in lymph nodes and bone marrow. T cells, after being sensitized by antigens in the thyroid gland, activate B lymphocytes. Thyroid-stimulating immunoglobulin attaches to the TSH receptor on the thyroid cell membrane and enhances the activity of the thyroid-stimulating hormone. It induces both the production of thyroid hormones and the enlargement of the thyroid gland, resulting in hyperthyroidism and thyromegaly [15].

Distribution of Studied Groups According to Anti-TPO Abs

Table (4) shows the distribution of studied groups according to Anti-TPO Abs. The percentage of Anti-TPO Abs positivity showed a highly significant correlation in Hashimoto's hypothyroidism (63.3%) and Graves hyperthyroidism (86.7%) at the ($P<0.03$) in comparison with the negativity percentage which been in Hashimoto's hypothyroidism (36.7%) and Graves hyperthyroidism (13.3%).

Table 4. Distribution of Studied groups according to Anti TPO Abs

Anti TPO Abs		Study groups Hashimotos	Graves	Total
Positive	No.	38	52	90
	%	63.3%	86.7%	75.0%
Negative	No.	22	8	30
	%	36.7%	13.3%	25.0%
Total	No.	60	60	120
	%	100.0%	100.0%	100.0%
Kappa Test		P=.003 (HS)		

The study revealed a strong correlation between the presence of Anti-TPO Abs and Hashimoto's hypothyroidism patients' group (63.3%) and Graves' hyperthyroidism patients' group (86.7%) at a statistically significant level (P<0.03), compared to the percentage of negativity observed in Hashimoto's hypothyroidism patients' group (36.7%) and Graves' hyperthyroidism patients' group (13.3%).

The research demonstrated a greater prevalence of anti-thyroid peroxidase antibodies (anti-TPO Abs) in individuals with Graves' disease (86.7%) compared to those with Hashimoto's disease (63.3%). The findings of this study align with previous scientific consensus, indicating that thyroid peroxidase antibodies (ATPO) serve as an indicator of autoimmune thyroid disease. These antibodies are present in almost all individuals with Hashimoto's thyroiditis and 50 – 70 % of individuals with hyperthyroidism caused by Graves' disease [16 -17].

Distribution of Studied Groups According to Anti TG Abs

Table (5) shows the distribution of Studied groups according to Anti TG Abs. The percentage of Anti TG Abs positivity showed no significant correlation in Hashimoto's hypothyroidism (96.7%) and Graves hyperthyroidism (90.0%) at the (P=0.143) is compared with the negativity percentage which been in Hashimoto hypothyroidism (3.3%) and Graves hyperthyroidism (10.0%).

Table 5. Distribution of Studied groups according to Anti TG Abs

Anti TG		Study groups		Total
		Hashimotos	Graves	
Positive	No.	58	54	112
	%	96.7%	90.0%	93.3%
Negative	No.	2	6	8
	%	3.3%	10.0%	6.7%
Total	No.	60	60	120
	%	100.0%	100.0%	100.0%
Kappa Test		P=.143 (NS)		

The study found that there is no significant correlation between the percentage of Anti TG Abs positivity in Hashimoto's hypothyroidism (96.7%) and Graves' hyperthyroidism (90.0%) at a significance level of P=0.143. This is in comparison to the percentage of negativity, which was 3.3% in Hashimoto's hypothyroidism and 10.0% in Graves' hyperthyroidism. The findings of this research align with prior scientific consensus, indicating that 69.9 % of individuals with Hashimoto's thyroiditis had antibodies against thyroglobulin [18].

The frequency of antibodies was 60-80% in individuals with Hashimoto's thyroiditis (HT) and 50-60% in those with Graves' disease (GD). In a separate study, it was shown that 70-80% of patients with autoimmune thyroid diseases (AITD) had anti-Tg antibodies. Additionally, 30-40% of patients with Graves' disease (GD) and 10-15% of patients with non-thyroid immune disorders were found to have these antibodies [19].

Distribution of Studied groups according to Chlamydia trachomatis IgG Abs

Table (6) shows the distribution of Studied groups according to Chlamydia trachomatis IgG Abs. The percentage of Chlamydia trachomatis IgG Abs positivity showed a highly significant correlation in Hashimoto's hypothyroidism (42) and Graves hyperthyroidism (26) at the (P<0.01) in comparison with the positivity of the control group (0).

Table 6. Distribution of Studied groups according to Chlamydia trachomatis IgG

Study groups	Chlamydia trachomatis IgG			
	Positive	Negative	Test of Sig.	P-Value
Control (n=60)	0	60	MCP	P<0.01 (HS)
Hashimotos (n=60)	42	18		
Control (n=60)	0	60	MCP	P<0.01 (HS)
Graves (n=60)	26	34		

Autoimmune thyroid disorders include a group of conditions marked by aberrant functioning of the immune system inside the thyroid gland, leading to either an underactive or overactive thyroid. The complexity of thyroid gland autoimmunity is well-established. Microorganisms have been linked to the pathogenesis of Hashimoto's thyroiditis and Graves' disease. These variables may account for the heightened occurrence of autoimmune thyroid diseases. No suggestions have been proposed about the mechanisms by which these bacteria contribute to thyroid autoimmunity. Multiple studies have shown that thyroid disease is a significant public health issue. Autoimmune thyroid disease (AITD) can be triggered by various factors, such as genetic susceptibility, immune system dysregulation, inflammation, stress, and environmental factors. However, the exact cause of AITD remains unknown [20-21-22].Table (3) indicates a significant increase (P=0.001) in the presence of both C.trachomatis IgG antibodies among HT patients (42) compared to healthy individuals (0), as well as among Graves patients (24) compared to control groups (0). The findings demonstrate a

correlation between C.trachomatis infection and autoimmune disease, suggesting that the bacteria contributed to HT and GD in Iraqi patients. Although this analysis failed to clarify the consequences of C. trachomatis that might lead to thyroid autoimmunity, we still concur with the view. Animal models have shown that infections may act as triggers for Alzheimer's disease. In addition, infections may play a role in the stimulation and subsequent reproduction of autoreactive T cells

CONCLUSION

The thyroid gland is an intricate endocrine organ that exerts extensive influence and regulation on several organ systems and activities. The regulation of circulating hormones involves a complex interplay between the brain, pituitary gland, and thyroid gland. Abnormalities in thyroid hormone levels, whether too high or too low, may result in conditions such as hypo- and hyperthyroidism. These conditions can be caused by several factors, with the most prevalent ones being Hashimoto's thyroiditis (causing hypothyroidism) and Grave's disease (causing hyperthyroidism).

The laboratory is crucial in the management and identification of thyroid problems since it enables the detection of abnormalities via very sensitive TSH testing even before the manifestation of clinical signs and symptoms. The current guidelines for assessing thyroid function have evolved from using a comprehensive thyroid panel to adopt a more cost-effective and medically efficient approach centered on measuring TSH levels. The current study's findings indicate a clear association between C.trachomatis infection and the occurrence of Autoimmune thyroid disorders in Iraqi individualsInfection with some strains of C.trachomatis may increase the likelihood of developing autoimmune hypothyroidism. Moreover, it may lead to an elevation in thyroid antibodies and TSH, leading to a decline in thyroid hormone levels and exacerbation of the condition. Thus, it is advisable to undergo antibiotic treatment to eradicate the bacterial infection. Hence, it is justifiable to suggest including thyroid antibodies (anti-TPO and anti-Tg) in the thyroid function test panel and investigating the association between C.trachomatis infection and Graves' illness. Further research is advised to elucidate the molecular mechanism that links C.trachomatis infection to HT illness.

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Authors' Declaration

Conflicts of Interest: None.

We affirm that all the Figures and Tables in the text are our own work. In addition, any external figures and pictures used in the text have been obtained with the requisite permission for re-publication, which is provided with the manuscript.

Ethical Approval: The proposal received approval from the local ethics committee at the University of Middle Technical University.

Authors' Contribution Statement

Mohammed Ali Mohammed Al-Badri, Issam Jumaa Nasser, Mahdi, and Ali A.A. contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript.

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