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Role of Immunity in Hashimoto's Thyroiditis diseases in Diyala province

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Abstract

This study used to evaluate the Effect of Some Cytokines (IL-5, IL-18, IL-23 and TGEB1) levels in Hashimoto's Thyroiditis diseases and the study was carried out between February and August 2023.The study groups in involved Group for Hashimoto's disease: 60 people with thyroid problems that have been clinically and 30 people who seemed healthy made up the control group. All participants had taken a venous blood samples and thyroid hormone levels (T3, T4 and TSH) as well as cytokine levels (IL-5, IL-18, IL-23 and TGEB1) were measured by Minivoids device and ELISA, respectively. The study shown ahigh levels of T3 and TSH with low levels for T4 in patients compare to healthy groups. There was a significant increase in Cytokines levels (IL-5, IL-18, IL-23 and TGEB1) in patients' group (14.423±2.549, 185.13±5.058, 85.07±6.701, 88.025±4.54) compare to healthy groups (8.581±0.529,161.38±4.341, 45.25±5.758, 69.666±5.168) respectively. Serum IL-5 levels have a positive associated with thyroxine (rs=0.428**, p<0.001), IL-18 levels have a positive associated TGFB1 (rs=0.258*, p<.046), IL-23 levels have a positive associated TGFB1 (rs=0.392**, p<0.002). The results suggest that cytokines (IL-5, IL-18, IL-23 and TGEB1) levels may show a role in the pathogenesis of HT.

Keywords: Thyroid hormone levels; Immunity; Cytokines; Hashimoto's Thyroiditis diseases and ELISA

1. Introduction

Hashimoto's thyroiditis (HT), a type of organ-specific autoimmune disease, is brought on by a lack of immunological tolerance to the thyroid gland (1) and this may occur due to Genetic and environmental factors (2). This causes lymphocytes to infiltrate the gland, destroying the thyroid's structure and producing autoantibodies (3,4). Fatigue, joint pain, hair loss, depression, and an enlarged thyroid gland (goiter) are some of the symptoms of Hashimoto's illness. As the thyroid gland deteriorates over time, hypothyroidism may occur, lowering blood thyroid hormone levels and possibly causing goiter in certain people (5). Thyroid hormone and thyroid-stimulating hormone (TSH) levels in the blood are often used to identify Hashimoto's illness. Hypothyroidism, commonly observed in Hashimoto's disease, can be indicated by an increased TSH level and a low number of thyroid hormones. However, tabs are also a useful indicator for the diagnosis of Hashimoto's thyroiditis autoimmunity (6).HT is an autoimmune disease and there are many factors that contribute to the etiopathogenesis of these diseases that includes genetic predisposition and environmental factors (7).

HT is found in genetically predisposing populations, and diagnoses can be determined through a combination of clinical evaluation, increased thyroid antibodies, B lymphocytes, diffuse immune system of mononuclear cells, decreased levels of free thyroxine (T4), and increased levels of thyroid-stimulating hormone (TSH) in serum. The presence of regulatory B cells in the pathology is not yet fully disclosed. Thyroid echo must often be supplemented by a biopsy to diagnose HT. T regulatory (Treg) modulation therapy and related clinical studies concentrating on cytokine treatments have shown

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positive effects. However, it is currently impossible to restore euthyroidism to high levels in patient follow-up studies, and cure is often only temporary (8).

Cytokines are signaling proteins that regulate the immune response and inflammation. They are released by immune cells such as T lymphocytes, macrophages, and dendritic cells. In Hashimoto's thyroiditis, the balance of pro-inflammatory and anti-inflammatory cytokines can significantly influence the severity and progression of the disease (9). Chemokines and cytokines as apart from Cellular and humoral immunity, have an important role in the development of HT and these diseases considered a Th1-mediated disease (10,11). cell-mediated immunity and thyrocyte death that may be occurs due to increase of Th1 lymphocytes activity and causes HT (12). Th2 cells can also cause thyroiditis by stimulate B cells and plasmatic cells, which generate antibodies against thyroid antigens, excessively (13). The pathogenesis of HT may be occupied by several cytokines, including IL17, IL- 23, IL- 28, and IL- 29 (14,15,16). The current study aimed to assay serum levels of FT3, FT4, TSH, and IL- 5, IL-18, IL-23 and TGEB1 in patients with HT. The current study also aimed to assay the correlations between all parameter's studies levels.

2. Methods

The study was conducted from February to August of 2024 and involved two main groups: Thirty in the control group and sixty Hashimoto's patients. Blood was drawn from patients and control and then transfer to sterile plain tubes to separated serum by centrifugation at 2500 rpm for a 10 minute. Serum divided in to tube, one used immediately to assay T3, T4 and TSH by Minividis Kit by Biomerieux SA/ France and the others tube stored at -20°C for cytokines assay later. ELISA was used to measure the blood levels of TGEB1, IL-5, IL-18, and IL-23 in accord with the manufacturer's instructions (sunlong, Gaina).

Statistical analysis: To compare the means of the two groups, an independent sample t-test was employed. Pearson's test was utilized to do correlation analysis. It was deemed statistically significant when $P < 0.05$. Standard deviation ± mean is used to express the results.

3. Results

3.1. Biochemical Parameters (TSH, T4 and T3 Levels)

In this study, Patients with Hashimoto's Disease showed increased levels of T3(1.6252±0.6014 mIU/L) in contrast to the control group (1.2633±0.2399mIU/L) but patients with Hashimoto's Disease proved decreased levels of T4 (51.255±17.726nmol/L) in comparison to the control group (66.90±4.301 nmol/L). Compared to the normal group (2.2303±0.5655 nmol/L), patients with Hashimoto's Disease higher levels of TSH (13.825±9.022 nmol/L) as shown in table 1.

Table 1 Thyroid hormone levels in study groups

Parameter	Patients	Control	P. value
Number	60	30	
Sex(F/M)	41/19(45.5%, 21.1%)	17/13(18.8%,14.4%)	
T3	1.6252±0.6014	1.2633±0.2399	0.063
T4	51.255±17.726	66.90±4.301	0.091
TSH	13.825±9.022	2.2303±0.5655	<0.001

3.2. Cytokines levels in studied groups

The serum levels of IL-5, IL-18, IL-23 and TGEB1 in Hashimoto's Disease group have considerably greater in comparison to the control group, as shown in the table 2.

Table 2 Cytokines levels in studied groups

Parameter	Patients	Control	P. value
IL-5	14.423±2.549	8.581±0.529	0.062
IL-18	185.13±5.058	161.38±4.341	<0.001
IL-23	85.07±6.701	45.25±5.758	<0.001
TGEB1	88.025±4.54	69.666±5.168	<0.001

In this study and according to Pearson correlation analysis was showed the high a positive correlation levels of T4 hormones with IL-5 in HT patients ($r = 0.428^{**}$, $p = 0.001$), the study shown high a positive correlation IL-5 with IL-23 in HT patients ($r = 0.392^{**}$, $p = 0.002$), a high a positive correlation between IL-18 with TGFB1 in HT patients ($r = 0.258^{*}$, $p = 0.046$). The study also shown a high a negative correlation between IL-23 with TGFB1 in HT patients ($r = -0.274^{*}$, $p = 0.034$) as shown in table 3.

Table 3 Correlations between study parameters in Hashimoto's disease group

Correlations								
		T3	**T4**	**TSH**	**IL5**	**IL18**	**IL23**	**TGFB1**
T3	Pearson Correlation	1	0.008	-0.024	-0.006	-0.041	0.088	-0.115
	Sig. (2-tailed)		0.953	0.853	0.963	0.756	0.505	0.383
T4	Pearson Correlation	0.008	1	-0.117	0.428**	0.121	0.181	0.080
	Sig. (2-tailed)	0.953		0.372	<.001	0.358	0.165	0.543
TSH	Pearson Correlation	-0.024	-0.117	1	0.116	0.102	0.014	0.073
	Sig. (2-tailed)	0.853	0.372		0.378	0.436	0.914	0.579
IL5	Pearson Correlation	-0.006	0.428**	0.116	1	0.237	0.392**	0.078
	Sig. (2-tailed)	0.963	<.001	0.378		0.069	0.002	0.555
IL18	Pearson Correlation	-0.041	0.121	0.102	0.237	1	-0.151	0.258*
	Sig. (2-tailed)	0.756	0.358	0.436	0.069		0.251	0.046
IL23	Pearson Correlation	0.088	0.181	0.014	0.392**	-0.151	1	-0.274*
	Sig. (2-tailed)	0.505	0.165	0.914	0.002	0.251		0.034
TGFB1	Pearson Correlation	-0.115	0.080	0.073	0.078	0.258*	-0.274*	1
	Sig. (2-tailed)	0.383	0.543	0.579	0.555	0.046	0.034	
**. Correlation is significant at the 0.01 level (2-tailed).								
*. Correlation is significant at the 0.05 level (2-tailed).								

4. Discussion

The present study was designed to investigate role of some cytokines in Hashimoto's disease patients. We analyzed thyroid hormone levels (T3, T4, and TSH) and some cytokines levels (IL-5, IL-18, IL-23 and TGEB1) in patients. The thyroid gland may be affected by Hashimoto's disease, an autoimmune condition marked by lymphocytic congestion, gradual degradation, and fibrous replacement of the thyroid parenchymal structure (17,18). HT is characterized by hypothyroidism brought on by an inflammatory response driven by T lymphocytes that are specific to thyroglobulin (19).

According to the demographics of the Hashimoto patients in the current study, women made up the majority of patients (68.3%) as opposed to males (31.6%). The American Thyroid Association states shown the high percentage of women

compare to male patients, which is caused by a connection between thyroid hormones and hormone fluctuations during the menstrual cycle (20). The previous study in Iraq showed that most patients were women (92.59%) compared to men (7.4%) (21). Previous study found that the loss of self-tolerance in women infected with Hashimoto's disease may occur in high percentage to the X-linked antigens which lead to autoimmune thyroid disease (22). According to a previous study, females may be more susceptible to developing AITD if chromosomal X is deactivated in about 80% of cells (23). According to previous studies, the estrogen hormone causes a pro-inflammatory response that makes women more vulnerable to autoimmune illnesses (24).

The current study compared the levels of thyroid hormones (T3, T4 and TSH) in group of Hashimoto's thyroiditis patients and control group. The study shown high levels of T3, TSH and shown low levels of T4 in patients compare to control group with significantly ($p<0.05$). Other study found that TSH levels were greater in Hashimoto's patients than in controls that agreed with this study (25).

This study shown high levels of cytokines (IL- 5, IL-18, IL-23 and TGEB1) in patients with HT, the reason for the increase in interleukins may be due to the important role that interleukins play in the immune response or causing immune diseases, including those affecting the thyroid gland (26). In addition to stimulating B cells and plasma cells that create antithyroid antibodies, Th2 lymphocytes also produce IL-4, IL-5, IL-6, and IL-13, all of which contribute to inflammation. The pathophysiology of HT must take into account Th2 cells, which stimulate a humoral immune response, even if a Th1 lymphocyte-associated response is more common in this condition (8).

Dendritic cells and macrophages release IL-23, which binds to IL-23 receptors to stimulate the release of inflammatory agents, cytokines, and chemokines (27). In combination, IL-23 and its receptor may trigger the STAT3 signal, cause memory T cells to develop into Th17 cells, influence IL-17 production by upregulating RORγt, and eventually support inflammation and autoimmune disorders (28). The pathophysiology of the illness may also involve IL-23, which is generated by nonspecific immune cells and affects the strength of the Th1 response, this cytokine was detected in 56% of Hashimoto's thyroiditis patients (29).

Regarding studies from Iraq, research on autoimmune thyroid diseases, including Hashimoto's thyroiditis, has been conducted to assess the cytokine profiles and immune responses in affected patients. One study from Iraq explored the serum levels of pro-inflammatory cytokines in patients with HT and their correlation with disease activity and thyroid function. This study found elevated levels of specific cytokines, such as TNF-α and IL-6, which are associated with increased inflammation and immune dysfunction in HT patients (30). Previous study indicated significant elevation in the serum levels of IL-17, which suggests their potential role in the inflammation and immune dysregulation that characterize the disease in these patients (31). Other previous study in Iraq investigated the levels of interleukins in the serum of Iraqi patients diagnosed with Hashimoto's thyroiditis. The research specifically focused on IL-6 and IL-17, which are known to be key cytokines in the inflammatory pathways involved in autoimmune thyroid diseases. Elevated levels of IL-6 were found in patients with active disease, suggesting that IL-6 contributes to the inflammatory process and possibly to the destruction of thyroid tissue. Additionally, higher IL-17 levels were observed in those with more severe disease manifestations, pointing to its role in promoting tissue damage and exacerbating autoimmune responses (32).

The previous study in Iraq found increased levels of IL-17, TNF-α, and IFN-γ in Iraqi patients with autoimmune thyroid disease, suggesting a strong pro-inflammatory immune response in HT. Additionally, they observed reduced IL-10 levels, indicating a loss of immune regulation, which might promote autoimmunity (33).Other previous study in Iraq observed elevated levels of TNF-α, IL-6, and IL-1β in the serum of patients with autoimmune thyroid disease, Elevated cytokine levels were linked to increased thyroid antibodies such as anti-TPO and anti-Tg, which are key markers of HT(34).Other study revealed that elevated TNF-α, IL-6, and IL-1β were observed in HT patients, along with an imbalance in regulatory cytokines like IL-10 and TGF-β, which were found to be lower in these patients. These cytokine imbalances were linked to increased thyroid autoimmunity and chronic inflammation (35). Other study the study demonstrated a significant increase in Th1 cytokines (IFN-γ, TNF-α) and Th17 cytokines (IL-17) in HT patients. The cytokine profile also indicated a reduced regulatory response as evidenced by low levels of IL-10 and TGF-β. These findings pointed to an inflammatory environment conducive to thyroid autoimmunity in Iraqi HT patients (36).Other previous study in Iraq found increased cytokines levels with autoimmune disease(37).

Previous study examined the correlation between cytokine levels and thyroid function tests, finding that higher levels of these interleukins were associated with reduced thyroid function (hypothyroidism), which is the hallmark of Hashimoto's thyroiditis. These findings emphasize the importance of interleukins in both the pathogenesis and progression of HT, and their potential as biomarkers for disease activity (32).

5. Conclusion

In conclusion, increased levels of study cytokines (IL-5, IL-18, IL-23 and TGEB1) in Hashimoto's Thyroiditis diseases, this may indicate that these cytokines are closely related to the pathogenesis of the disease and its severity, they may be having a protective effect against auto destruction of thyroid gland. Further, targeted studies in Iraq are needed to confirm these findings and explore the roles of genetic and environmental factors on cytokine expression in HT.

Compliance with ethical standards

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Statement of ethical approval

It is stated that all ethical considerations were taken into account when collecting samples.

Authors' Contribution

The author designed this study, acquired and analyzed the data, write the manuscript.

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