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Evaluation of the serum levels of tumor necrosis factor-alpha in Iraqi patients with autoimmune thyroid disorders: a study from the Najaf Governorate

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ABSTRACT

Thyroid disorders frequently arise due to iodine deficiency or autoimmune conditions. Autoimmune thyroid disorders, such as Graves' disease (GD) and Hashimoto's thyroiditis (HT), result from dysregulation of the immune system. In this study, a total of 140 samples were analysed using immunodiagnostic methods. Participants were divided into two groups: 70 healthy controls and 70 patients (35 diagnosed with GD and 35 with HT), all recruited from medical facilities in the Najaf Governorate (Iraq) between July and October 2023. Participant ages ranged from 20 to over 50 years. Thyroid hormone levels – triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) – were measured in order to classify cases as hypothyroid or hyperthyroid. Results showed significantly reduced levels of T3, T4, and TSH in patients with hypothyroidism. On the other hand, the levels of anti-thyroglobulin (anti-TG) and anti-thyroid peroxidase (anti-TPO) antibodies were markedly elevated in patients with HT or with GD compared to the control group. HT was more prevalent among women aged 30 to 50 years. Smoking was found to be significantly associated with the presence of thyroid disorders. A notable difference in mean tumor

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necrosis factor-alpha (TNF-α) concentrations was observed between patients with GD and the control group, whereas no significant difference was found for patients with HT. The study concludes that TNF-α levels vary significantly between autoimmune thyroid conditions, underscoring its potential role in disease pathogenesis.

1. Introduction

Autoimmune diseases affect approximately 5% of the global population and remain challenging to treat, causing significant distress for patients and imposing a substantial economic burden[1]. These conditions arise when the immune system fails to recognize self-antigens, leading to chronic inflammation and tissue damage[2]. Autoimmune disorders may target specific organs or affect multiple systems. They are more prevalent in middle-aged women and represent a major cause of morbidity and mortality in this demographic. Moreover, the prevalence of autoimmune diseases increases with age and is consistently higher in women than in men[3].

The occurrence of multiple autoimmune disorders in a single individual ("polyautoimmunity") or within a family ("familial autoimmunity") supports the hypothesis that these diseases share common environmental, epigenetic, and genetic triggers[4]. Autoimmune thyroid diseases are the most common organ-specific autoimmune disorders, affecting 2%–5% of the population. Their prevalence is significantly higher in women (5%–15%) than in men (up to 5%)[5]. Autoimmune thyroid diseases include Graves' disease (GD; which causes hyperthyroidism) and Hashimoto's thyroiditis (HT; which leads to hypothyroidism). Thyroid hormones – triiodothyronine (T3) and thyroxine (T4) – regulate metabolism and are synthesized by the thyroid gland. T3, the more active form, is derived from T4 as needed. Disruptions in thyroid function can result in iodine deficiency, thyroid enlargement, or even thyroid cancer, and they are among the most common endocrine disorders globally[6]. Hyperthyroidism is characterized by suppressed thyroid-stimulating hormone (TSH) levels and elevated T3 and / or T4 concentrations. GD is marked by the presence of thyroid-stimulating autoantibodies that activate the TSH receptor[7]. In contrast, HT is a leading cause of hypothyroidism and is associated with chronic inflammation and the presence of anti-thyroid peroxidase (anti-TPO) antibodies that damage thyroid cells[8].

Cytokines such as tumor necrosis factor-alpha (TNF-α) play a critical role in regulating inflammation and immune responses. TNF-α has been implicated in the development and progression of autoimmune and inflammatory diseases[9]. This study's aim was to explore the relationship between serum TNF-α levels and autoimmune thyroid disorders in Iraqi patients.

2. Methodology

This study included 140 participants, divided into two groups: 70 healthy controls and 70 patients with autoimmune thyroid disorders (35 with GD and 35 with HT). Participants were recruited from the Al-Sadr Medical City (Diabetes and Endocrinology Center) and the Al-Zahraa Teaching Hospital in Najaf Governorate between July and October 2023. Ages ranged from 20 to over 50 years. Thyroid hormone levels (T3, T4, and TSH) were measured in order to classify the study's participants as hypothyroid or hyperthyroid. Anti-thyroglobulin (anti-TG) and anti-TPO antibody levels were also assessed. TNF-α concentrations were measured in order to evaluate their association with thyroid dysfunction. Statistical analysis was conducted using SPSS version 26. A *p*-value lower than 0.05 was considered statistically

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Table 1. Serum levels of biomarkers in patients with autoimmune thyroid diseases and healthy controls. Abbreviations used: anti-TG, anti-thyroglobulin (antibody); anti-TPO, anti-thyroid peroxidase (antibody); GD, Graves' disease; HT, Hashimoto's thyroiditis; SD, standard deviation; T3, triiodothyronine; T4, thyroxine; TNF-α, tumor necrosis factor-alpha; TSH, thyroid-stimulating hormone.

Serum biomarkers	Groups	N	Mean	SD	*p*-value	95% confidence interval	
						Lower bound	Upper bound
TSH (μUI/mL)	HT group	35	23.27	2.68	<0.001	15.48	31.05
	GD group	35	0.34	0.13	<0.001	0.01	0.24
	Control group	70	2.43	1.67	<0.001	2.03	2.82
T3 (nmol/L)	HT group	35	0.67	0.80	0.330	0.40	0.95
	GD group	35	1.53	1.13	<0.001	1.14	1.92
	Control group	70	1.18	0.50	0.330	1.06	1.30
T4 (nmol/L)	HT group	35	5.01	2.27	<0.001	4.23	5.79
	GD group	35	12.72	9.53	0.002	9.45	15.99
	Control group	70	31.62	40.99	<0.001	21.85	41.39
anti-TPO (pg/mL)	HT group	35	928.76	685.75	0.031	693.20	1,164.32
	GD group	35	1,297.85	2,350.91	0.002	490.28	2,105.42
	Control group	70	159.37	240.77	0.031	101.96	216.78
anti-TG (pg/mL)	HT group	35	722.89	798.73	0.276	448.52	997.26
	GD group	35	608.76	361.69	<0.001	484.52	733.01
	Control group	70	123.92	87.72	0.276	103.01	144.84
TNF-α (pg/mL)	HT group	35	27.21	25.86	0.330	18.33	36.09
	GD group	35	22.37	18.20	<0.001	16.12	28.62
	Control group	70	25.28	13.94	0.330	21.96	28.60

significant. Ethical approval was granted by the Ethics Committee of the College of Medicine, University of Kufa (19-Sep-2023).

3. Results and Discussion

The distribution of age groups revealed a higher prevalence of thyroid disorders among participants aged 30 to 50 years. Among those with hyperthyroidism, 48.6% fell within this age range, while 68.5% of hypothyroid patients were also in the 30–50 age group. However, this difference in age distribution was not statistically significant (p=0.49). Gender analysis showed that thyroid disorders were more common in women, who comprised 75.7% of all participants. Within the patient groups, 82.8% of individuals with HT and 80% of those with GD were women, compared to 70% in the control group. This difference in gender distribution was also not statistically significant (p=0.277).

Body mass index (BMI) analysis categorized participants as normal weight (18–24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese (≥30 kg/m^2). Significant differences in BMI were observed between patients and healthy controls (p=0.0163), with obesity being more common among those with thyroid disorders: 40% of HT patients and 25.7% of GD patients were obese, compared to 14.3% of the control group. Smoking was also significantly associated with thyroid disorders (p=0.0133); 82.8% of hyperthyroid patients and 77.1% of hypothyroid patients were smokers, compared to only 21.6% of healthy controls. The analysis of the serum thyroid hormone levels revealed significant differences between the herein assessed groups. HT patients had markedly

elevated mean TSH levels of 23.27 μIU/mL, compared to 2.43 μIU/mL in controls (p<0.05), while GD patients had significantly lower mean TSH levels of 0.34 μIU/mL (Table 1). T3 and T4 levels were found to be significantly elevated in GD patients compared to both HT patients and controls (p<0.05) (Table 1). The levels of anti-TPO and anti-TG antibodies were also found to be significantly higher in patients with autoimmune thyroid disorders than in controls (Table 1). Finally, the mean serum concentration of TNF-α differed significantly across groups: GD patients had a mean level of 22.369 pg/mL, HT patients had a higher mean of 27.209 pg/mL, and the control group had a mean of 25.280 pg/mL (Table 1). A statistically significant difference (p=0.0001) was observed between the GD and the control group in terms of the TNF-α levels, although the difference between HT and controls was not statistically significant.

4. Conclusion

Our study has identified significant differences in serum TNF-α levels among patients with autoimmune thyroid disorders, underscoring the biomarker's potential role in the pathogenesis of these conditions. Notably, TNF-α concentrations were higher in patients with HT compared to those with GD, suggesting that pro-inflammatory cytokines may contribute differently to the development and progression of these disorders. These findings highlight the importance of further research into the role of inflammatory mediators such as TNF-α in autoimmune thyroid diseases.

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Conflicts of interest

None exist.

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