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Evaluation of the Dysregulation of Cholesterol and Glucose Levels in Graves' Disease Using Clinical Data Analysis

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Abstract

Background: Graves' disease (GD) is the most frequent reason for hyperthyroidism, which is brought on by an excess of thyroid hormone and a form of autoimmune thyroid disease (AITD). Patients with GD have higher levels of thyroid receptor antibody (TRAb). The current study, investigates the impact of excessive thyroid hormone production on glucose and cholesterol metabolism in thyroid disorders, particularly focusing on GD.

Methods: This study included 96 subjects (32 GD patients, 32 from non-autoimmune hyperthyroidism and 32 from healthy controls). All samples were obtained from Al-Kadhimiya Teaching Hospital (Baghdad) for the period between September 2023 and January 2024.

Results: The results revealed that mean± SD values of FT3 and FT4 for GD patients were significantly higher ($P<0.001$) accompanied by a significant decrease in mean±SD values of TSH ($P<0.001$) when compared to non-autoimmune hyperthyroidism and control groups. Conversely, TC and glucose levels did not show significant variations among GD patients, the non-immune hyperthyroidism and control groups ($P > 0.05$).

Conclusion: Our findings indicated thyroid function analysis is crucial for the diagnosis and differentiation of GD, TC and glucose levels do not contribute additional discriminatory power.

Keywords: Autoimmune Thyroid disease, Glucose, Graves' disease, Hyperthyroidism, Cholesterol.

Introduction

The Thyroid gland is the biggest endocrine organ in the human body and is responsible for secreting thyroid hormone, which plays a vital role in controlling growth and development and various metabolic processes (1-4). Cellular energy regulation and homeostasis are highly dependent on thyroid hormones, as they influence numerous genes involved in physiological functions, basal metabolic rate, and the production of heat by the adrenergic nervous system in response to cold. Additionally, thyroid hormones play a key role in promoting gluconeogenesis, lipolysis, and lipogenesis, contributing to essential metabolic processes (5). Thyroid dysfunction encompasses a range of thyroid gland abnormalities, presenting as either hyperthyroidism or hypothyroidism and is typically defined by the levels of thyroid-stimulating hormone (TSH) in the blood (6,7). There is substantial evidence suggesting that thyroid dysfunction has a significant impact on blood pressure, body weight, as well as the metabolism of lipids and glucose. These factors are closely linked to several metabolic parameters and may contribute to the onset or worsening of components of the metabolic syndrome (8). Graves' disease (GD) is the most frequent cause for hyperthyroidism, which is brought on by an excess of thyroid

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hormone and a form of autoimmune thyroid disease (AITD). Patients with GD have higher levels of thyroid receptor antibody (TRAb), which binds to the thyroid follicular cells' TSH receptor (TSHR) increasing the synthesis and release of thyroid hormones. Even though the precise cause of GD is still unknown, the findings emphasize the vital roles that genetic and environmental factors play (9). Notably, females ranging in age from 30 to 60 are five to ten times more likely to experience GD. The prevalence of GD in the general population is approximately 0.5%, with a lifetime risk of 3% for women and 0.5% for men (10). In patients with GD, excessive thyroid hormones can influence insulin-dependent glucose absorption, gluconeogenesis, and glycogenolysis. The overproduction of thyroid hormones can significantly impact insulin secretion, elevate gluconeogenesis, and affect carbohydrate metabolism, leading to hyperglycemia (11). Moreover, increased LDL turnover and enhanced cholesterol excretion can result in reduced total and LDL cholesterol levels without affecting HDL levels (12). Our current study aims to investigate the metabolic effects of excessive thyroid hormone production on glucose and cholesterol in thyroid disorders, with a specific focus on GD.

Materials and Methods

Study subjects

The current case-control study includes 64 patients (32 GD patients and 32 non-autoimmune hyperthyroidism patients) and 32 controls matched by gender and age. Laboratory profiles and clinical signs were utilized to diagnose GD and non-autoimmune hyperthyroidism patients. All samples were obtained from Al-Kadhimiya Teaching Hospital (Baghdad) for the period between September 2023 and January 2024. Exclusion criteria for patients included those with autoimmune hypothyroidism, Hashimoto's thyroiditis (HT), other autoimmune diseases (e.g., AIDS) and pregnant women due to physiological changes affecting thyroid, glucose and cholesterol metabolism. Individuals with no personal or family history of any thyroid disorder or autoimmune disease, including only non-pregnant females, were selected as a healthy control group.

Sample collection

Five ml peripheral blood samples were collected from each participant. The serum was separated by centrifuging at 1500 x g for 3 min at room temperature then the separated serum was stored at -20 °C until use for analysis.

Study protocol

All information regarding age, height, weight, hip, and waist circumferences was taken from participating patients and healthy control groups. The following formula was used to determine body mass index (BMI): kg/m2, or bodily weight in kilograms divided by height in meters squared. Waist circumference was measured while standing, and the waist-to-hip ratio (measured in cm) was calculated using the waist-to-hip ratio (WHR) (13).

Biochemical tests

Hormonal tests of serum included thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4). Metabolic tests included glucose and total cholesterol (TC). All tests were done using the Abbott Architect c-4000 auto analyzer.

Statistical analysis

IBM SPSS (version 26) was used to analyze the data, which were then displayed as mean ± standard deviation (SD). A one-way ANOVA test was used to compare the data between the three studied groups (control, non-autoimmune hyperthyroidism, and GD). Graph plotting was performed using GraphPad Prism 8.0. P-values less than 0.05 were indicated as significant.

Results

Demographic characteristics of patients and control groups

This study included 96 subjects. The mean ±SD age for control, non-autoimmune

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hyperthyroidism and GD groups were 43.16 ± 9.44, 44.84 ± 10.89, and 45.19± 9.23, respectively, reviling a non-significant difference (P> 0.05) in the mean of age between patients and control. The percentage of females and males in control was 20 (62.50%), 12 (37.50%), non-autoimmune hyperthyroidism 27 (84.38%), 5 (15.63%) and GD was 25 (78.13%), 7 (21.88%). Females' frequency was higher in the three studied groups.

Table 1 demonstrates the demography characteristics of patients and controls revealing no significant differences (P>0.05) in mean±SD height, weight, BMI and HC among GD patients, non-autoimmune hyperthyroidism and control groups. In contrast, WC and WHR demonstrated highly significant differences (P<0.001) when comparing the mean±SD for GD with non-autoimmune hyperthyroidism and control groups.

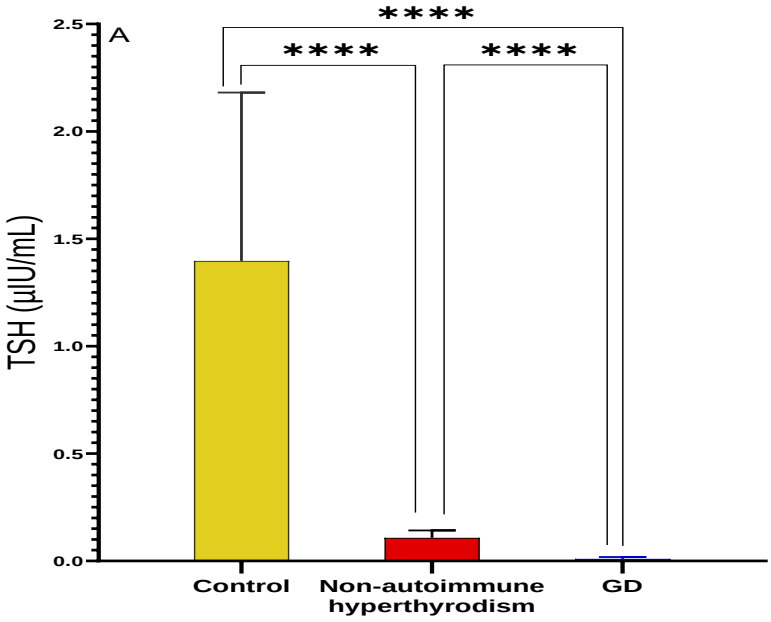
Table 1. Mean ±SD and P values of demographic characteristics of studied subjects.

	Control (n=32)	Non-autoimmune Hyperthyroidism (n=32)	GD (n=32)	P-value
Height (m)	1.65 ± 0.07	1.64 ± 0.061	1.66 ± 0.063	0.46
Weight (Kg)	64.72 ± 8.79	66.09 ± 10.27	67.06 ± 9.12	0.60
BMI (kg\m^2)	23.79 ± 2.23	24.56 ± 2.68	24.54 ± 2.86	0.41
HC (cm)	97.44 ± 8.59	97.38 ± 8.74	98.09 ± 6.67	0.92
WC (cm)	82.94 ± 8.23	87 ± 4.71	98.19 ± 9.88	<0.001
WHR	0.85 ± 0.05	0.89 ± 0.05	1.00 ± 0.05	<0.001

BMI: Body mass index, HC: Hip circumference, WC: Waist circumference, WHR: Waist to hip ratio.

Thyroid hormonal parameters analysis

Alterations in thyroid hormone levels among patients (i.e., non-autoimmune hyperthyroidism and GD) compared to control. The data showed a highly significant decrease in mean levels of serum TSH (0.01 ± 0.01 U/mL) in GD patients compared with non-autoimmune hyperthyroidism (1.08 ± 0.34 U/mL) and control group (1.40 ± 0.78 U/mL). Additionally, there was a highly significant increase in mean levels of serum FT3 and FT4 in GD patients (7.24 ± 1.15 pg/mL and 5.34 ± 1.18 ng/dL, respectively), respectively, compared with non-autoimmune hyperthyroidism (4.71± 0.70 pg/mL and 1.08 ±0.34 ng/dL) and control group (2.03± 0.20 pg/mL and 2.03±0.20) (Fig. 1).



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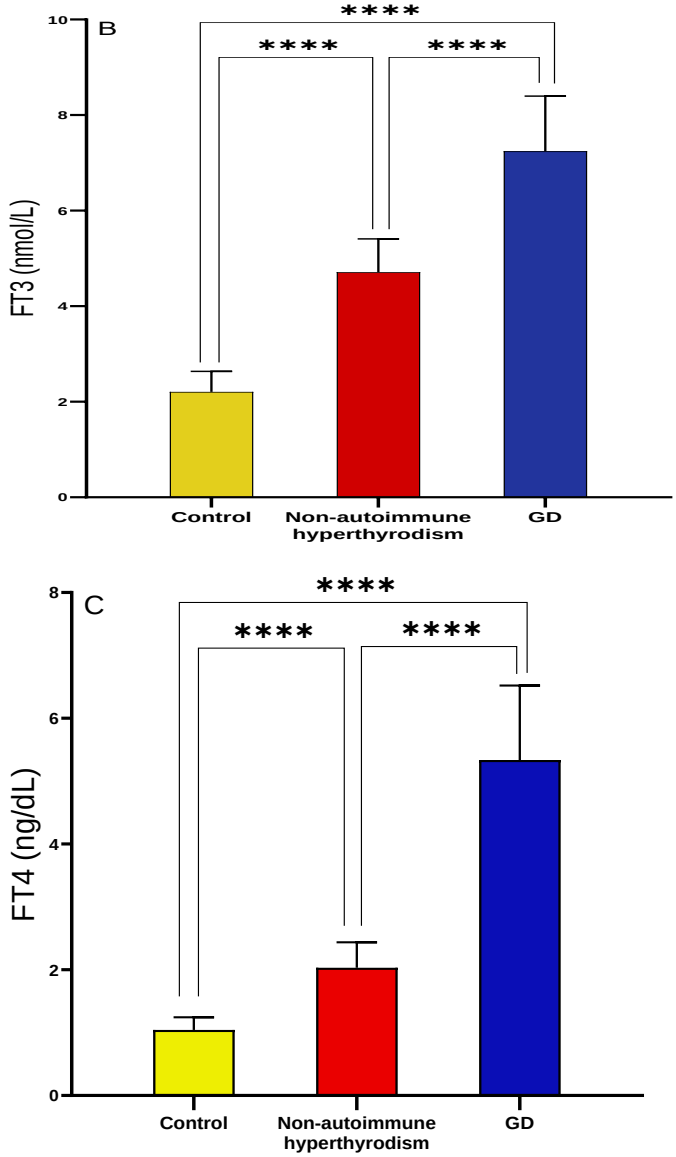

Fig. 1. Mean ±SD of (A) TSH, (B) FT3 and (C) FT4 in GD compared with non-autoimmune hyperthyroidism and control. ****P < 0.001 was considered significant.

Metabolic parameters analysis

The mean values of TC showed a non-significant difference in GD patients were 158.09 ± 7.50 (mg/dl) compared with non-autoimmune hyperthyroidism 158.91 ± 12.33 (mg/dl) and control group 164.22 ± 25.62 with P>0.05. The TC mean values were non-significant (P=0.2) between GD and control, and (P=0.48) between control and non-autoimmune hyperthyroidism as well as (P=0.84) between the GD and non-autoimmune hyperthyroidism.

Similarly, glucose levels demonstrated a non-significant difference in GD patients were 97.06 ± 6.24 (mg/dl) compared with non-autoimmune hyperthyroidism 96.00 ± 7.30 (mg/dl) and control group 102.44 ± 17.15 (mg/dl) with P>0.05. The mean values of glucose were non-significant(P=0.15), between GD and control, non-significant between control and non-autoimmune hyperthyroidism (P=0.07), and (P=0.92) between the GD and non-autoimmune hyperthyroidism (Fig. 2).

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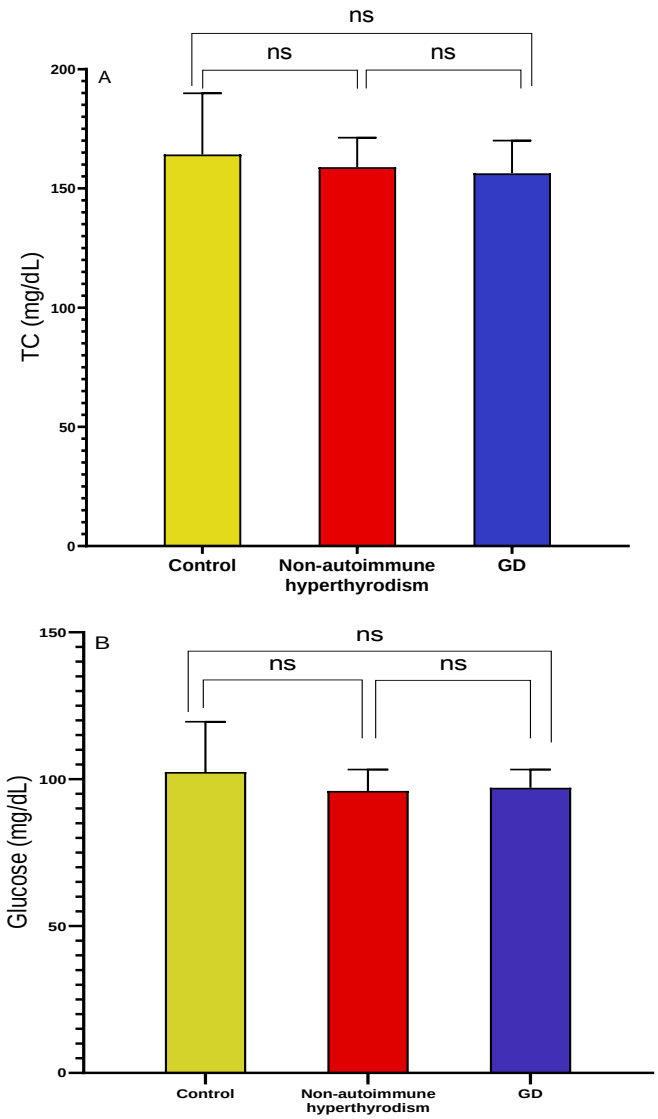

Fig. 2. Mean ±SD of (A) TC and (B) Glucose in GD compared with non-autoimmune hyperthyroidism and control. ns (P > 0.05) was indicates non-significant.

Discussion

Our study findings indicate a high difference between genders across the three groups studied control, non-autoimmune hyperthyroidism, and GD. higher percentage of females compared to males. This observation is consistent with prior research that suggests thyroid disorders are more common in females (14) which is attributed to the role of estrogen in regulating thyroid function.

Estrogen affects the synthesis of thyroid hormones and fluctuations in estrogen levels during various life stages such as pregnancy, puberty and menopause can lead to alterations in thyroid hormone levels which can increase the risk of thyroid disorders among women (15). Furthermore, AITDs, such as GD, exhibit a higher prevalence in females. that suggests a potential impact of sex hormones on immune responses (16).

Our findings demonstrate a highly significant decrease in serum TSH levels and a substantial increase in serum FT3 and FT4 levels in GD patients compared with non-autoimmune hyperthyroidism and control groups. These findings were supported by Al-Saadi MA et al.

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who confirmed that serum TSH levels were significantly lower with higher levels of FT3 and FT4 in Iraqi GD patients than for both non-autoimmune hyperthyroidism and control groups (17). Furthermore, the current results agreed with several studies that confirmed the clinical analysis of TSH was significantly decreased while FT3 and FT4 were significantly elevated in GD patients compared to the control group (18-22).

The results obtained from this study revealed no significant differences in TC and glucose levels among the three study groups. Sulu C et al. who also found no significant differences in TC levels between GD patients and controls (23). Although previous research points to a possible link between lipid metabolism and thyroid diseases, our analysis did not identify statistically significant variations in cholesterol levels across the groups. Hyperthyroidism is a main characteristic of GD which is known to influence lipid metabolism. An overabundance of thyroid hormones lowers cholesterol levels and promotes gluconeogenesis and lipolysis (24,25). Regarding glucose levels, several studies found increased glucose levels in hyperthyroidism patients. GD typically leads to various metabolic imbalance which affects glucose levels in the blood due to excessive production of thyroid hormones. Hyperthyroidism has a high rate of improper glucose metabolism potentially resulting in increased endogenous glucose synthesis, primarily through gluconeogenesis. The effects of thyroid hormones on various organs affect glucose homeostasis. These effects include elevated hepatic glucose output, increased glucose degradation product cycling between skeletal muscle and liver, decreased glycogen stores in both organs, modified oxidative and non-oxidative glucose metabolism, reduced pancreatic active insulin output, and elevated renal insulin clearance (26).

In conclusion, this lack of significant variation in TC and glucose levels can be attributed to the fact that these parameters are affected by many factors not related to thyroid function, such as the duration of the disease, treatment, diet, lifestyle and heredity. It could be concluded that thyroid function analysis is necessary for diagnosing and differentiating GD, TC and glucose levels do not contribute additional discriminatory power. Future research should focus on identifying alternative metabolic parameters that could contribute to enhancing diagnostic and therapeutic strategies for GD.

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Conflict of Interest Statement
The authors declare no competing interests.

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Ethics Approval
Not applicable.

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