

Assessment of the Correlation Between Vitamin D and T3, T4, FT3, FT4 and TSH Among Patients with Graves' Disease

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ABSTRACT

Background: Graves' disease is characterized by a diffuse hyperfunctional goiter that develops suddenly and is linked to an immune thyroid stimulating factor. Graves' disease hyperthyroidism is caused by circulating IgG antibodies binding to and activating the G-protein-coupled thyrotropin receptor. This activation causes thyroid enlargement by stimulating follicular hypertrophy and hyperplasia, as well as increases in thyroid hormone synthesis.

Objectives: This study aims to assess the Determination the concentration of vitamin D in patients with graves diseases, Measurement T3, T4, FT3, FT4 and TSH hormones and Determination the correlation between immunological markers by the (SPSS).

Materials and Methods: This research included a total of (90) people of various sexes and ages (30 men and 60 females), including (60) Graves' disease patients and (30) healthy people. Patients with Graves' disease were seen at Alsader Medical City (Najaf Center for Diabetes and Endocrinology). Between November 2021 and January 2022.

Results: In this research, the levels of (T3, T4, TSH, FT3 and FT4) hormones and Vitamin D revealed a very significant association ($P.value > 0.005$) across the groups tested. A non-significant association was also found between vitamin D and other variables. According to the patients' group, the FT3 revealed a strong negative connection with vitamin D in comparison to the other parameters.

Conclusion: The Thyrotropin receptor antibody (TRAb) test and ultrasonography of the thyroid gland are useful diagnostic tools for autoimmune Graves' disease. Grave's disease is connected with decreased vitamin D levels in the blood and could be made worse by high serum levels of T3, T4, FT3, FT4, and TRAb-positive and a low serum level of TSH.

INTRODUCTION

Graves' disease is one of the most common autoimmune disorders (AID) affecting 60-80% of hyperthyroid cases and affecting 13 million people, with women being seven times more afflicted than men⁽¹⁾. GD is defined by a lack of immune tolerance to autoantigens such as the thyroid stimulating hormone receptor (TSH-R), thyroid peroxidase (TPO), and thyroglobulin (Tg)⁽²⁾. Thyrotoxicosis and autoreactive lymphocytes in the thyroid gland are clinical features of Graves' disease. Graves' illness is characterized by hyperthyroidism in 60-90% of patients; it was often accompanied by anxiety, weight loss, bulging eyes, enlarged thyroid gland, heat sensitivity, nervousness, and hand and finger tremors⁽³⁾⁽⁴⁾.

Vitamin D deficiency is thought to have a major impact on the immune system (regulating T helper cell type 2 (Th2)/T regulatory cell (Treg) and, to a lesser degree, Th1 and Th17 cells). Low vitamin D levels have been associated with a higher risk of autoimmune disorders such as diabetes, multiple sclerosis, and rheumatoid arthritis. The effect of vitamin D on autoimmune illnesses is yet unknown and further study is needed. ⁽⁵⁾. Vitamin D has been linked to autoimmune disorders such as type 1 diabetes mellitus (T1DM), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and multiple sclerosis. Low levels of 25-hydroxyvitamin D are seen in Graves' disease, and the deficiency should be treated before starting antithyroid medication. Treatment may be fine-tuned based on basal TSH alone after early down regulation and stabilization of free hormone levels⁽⁶⁾⁽⁷⁾. Thyroid storm (TS) is a life-threatening condition that requires immediate medical attention. Thyrotoxic people develop the illness, which is commonly brought on by extreme physical or mental stress. As a consequence of the failure of compensatory mechanisms, these individuals develop multiple organ failure. In the development of TS, an abrupt increase in thyroxine (T4) or triiodothyronine (T3) release from the thyroid plays a role ⁽⁸⁾. The thyroid gland produces the hormones thyroxine (T4) and triiodothyronine (T3), which control the body's metabolism⁽⁷⁾. Thyroid stimulating immunoglobulin (TSI), also known as TSH receptor antibody, is an antibody, produced by the immune system that attaches to thyroid cells in deadly hyperthyroidism⁽⁹⁾.

METHODOLOGY

The research was a case-control study with a total of (60) individuals with graves' disease who attended from Alsader Medical City (Najaf Center for Diabetes and Endocrinology). This research covered the period from November 2021 to January 2022. A thyroid ultrasound and a TRAb test were used to identify all individuals with Graves' disease. Individuals in the healthy group were 30 years old and had no history or clinical symptoms of hyperthyroidism or any other chronic condition.

Inclusion criteria: All patients with Graves' disease.

Exclusion criteria: Patients with active hyperthyroidism, diabetes mellitus and pregnant women were excluded from the research.

Ethical issue: The ethics committee at the College of Health and Medical Techniques/Kufa, as well as the corresponding ethical committee of the Najaf health directorate, gave their permission for the research. Before taking the sample, the patients will also provide their verbal consent. We notified patients that their blood will be used for research reasons before collecting information from them, and most of them were cooperative and helpful. Alsader medical city had given approval (Najaf Center for Diabetes and Endocrinology).

Statistical Analysis: SPSS, statistical software for the social sciences, was used to conduct statistical analyses (version 20.0 for windows, SPSS, Chicago, IL, USA). The mean and standard deviation are used to depict quantitative data. Count and percentage are used to convey qualitative data. It was necessary to do a correlation test in order to determine whether or not two variables are related. ANOVA test was used to test differences among groups. P value of < 0.05 was considered statistically significant.

Blood Sample Processing: The research comprised sixty individuals with Graves' disease, as determined by thyroid ultrasound and TRAb test. A syringe was used to take five millimeters of venous blood under sterilization and placed into a gel tube. The serum was collected in an Apandtroft tube and held at -20°C for an ELISA test to assess vitamin D.

RESULTS AND DISCUSSION

This research included a total of (90) people of various sexes and ages (30 men and 60 females), including (60) Graves' disease patients and (30) healthy people. Patients with Graves' disease

were seen at Alsader Medical City (Najaf Center for Diabetes and Endocrinology). Between November 2021 and January 2022.

All patients were diagnosed using a thyroid ultrasound and a TRAB test with a thyroid panel (T3, T4, TSH, FT3 and FT4). The patients group consisted of 20 men (33.3%) and 40 females (66.7%). The age of the participants in the study ranged from 14 to 73 years, with a mean age of ten years in the sick group and five years in the control group. Female patients with Graves' illness were noticed more than male patients. There are 38 patients who live in cities and 22 who live in rural areas. When clinical symptoms are inconclusive, the (TRAB) test may aid in the diagnosis of Graves' disease. This is an autoimmune disorder in which antibodies to the thyroid stimulating hormone receptor (TSHR) cause the thyroid gland to release excessive amounts of hormone⁽¹⁰⁾⁽¹¹⁾. According to (Amballi, 2007), in untreated Grave's disease, 95% of patients were TRAB positive, compared to 15% who were diagnosed with nodular toxic goiter⁽¹²⁾. Although GD is usually diagnosed clinically, scintigraphy is virtually always done and is still regarded a critical step in the treatment of hyperthyroidism patients. Furthermore, several recommendations recommend scintigraphy as the initial instrumental modality for evaluating hyperthyroid patients⁽¹³⁾. Echography has been a crucial method for the research of numerous organs since the introduction of ultrasound into clinical practice⁽¹⁴⁾.

Comparisons mean of T3, T4, TSH, FT3, FT4 and vitamin D between the studied groups: T3, T4, TSH, FT3, FT4, and vitamin D levels were compared in Graves' disease and control groups in Table (1). As seen in table (1), the mean value of the T3 parameter in Graves' disease patients was substantially greater than in controls . P. value < 0.005 for (4.91±1.65 nmol/L) and (1.49 ± 0.44 nmol/L), respectively. The mean of T4 and TSH in the GD patient group was (174.49±33.15; 0.0615±0.190), whereas the mean of the control group was (92±12.63, 2.73±1.19). There was a significant difference between the analyzed groups P. value < 0.005.

In individuals with Graves' disease, T3 and T4 levels in the pituitary and hypothalamic axis are increased by antibodies produced by immune competent plasma cells. These antibodies bind with TSHR to initiate and increase T3 and T4 synthesis and production regardless of a decrease in TSH⁽¹⁵⁾. A total T3/T4 ratio and TSH value may be used to quickly distinguish Graves' illness from hyperthyroidism. According to (Hüser et al., 2018), variations in T3 and T4 levels, as well as TSH, are indicators of goiter⁽¹⁶⁾. There is no need for further testing beyond thyroid hormones and TSH if there are evident extrathyroidal indications of Graves' disease (e.g., proptosis, dermopathy) In the absence of these characteristics, an etiological diagnosis should be attempted⁽¹⁷⁾.

Table 1: Comparison mean of T3, T4, TSH, FT3, FT4 and vitamin D between the studied groups.

Parameters	Patients	Controls	P value
	Mean ±SD	Mean ±SD	
T3	4.91±1.65	1.49±0.44	0.000
T4	174.49±33.15	92±12.63	0.000
TSH	0.0615± 0.190	2.73±1.19	0.000
FT3	9.11±3.90	4.27±1.54	0.000
FT4	8.37±5.53	1.23±0.25	0.000
Vitamin D	17.45±6.77	40.21±5.93	0.000

*. The mean difference is significant at the 0.05 level.
 *. The mean difference is significant at the 0.01 level.

Furthermore, as compared to the control group (4.27±1.54; 1.23±0.25), the mean of FT3 and FT4 in the patient group was high (9.11±3.90; 8.37±5.53). In terms of vitamin D, the mean of the patients was (17.45±6.77), whereas the mean of the controls was (40.21±5.73). The findings were extremely significant when compared to the study groups (P < 0.005), as shown in table (1). Small variations in T4 concentration cause substantial changes in serum TSH. The TSH reference range must be established correctly in order to identify moderate (subclinical) hypothyroidism

or hyperthyroidism. As a result, TSH testing seems to be the preferred option for determining hormone levels⁽¹⁸⁾.

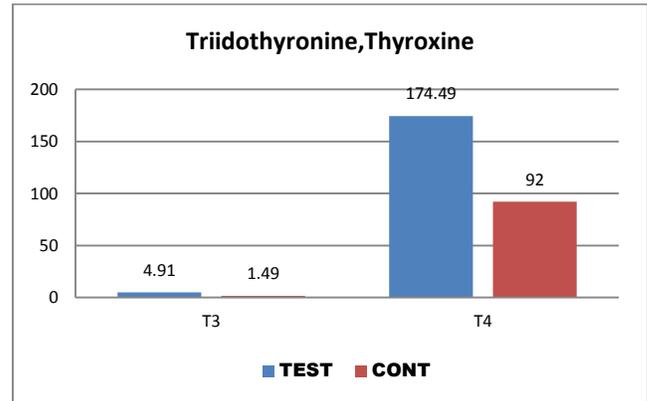


Figure 1: Comparisons mean of T3 and T4 between test and controls.

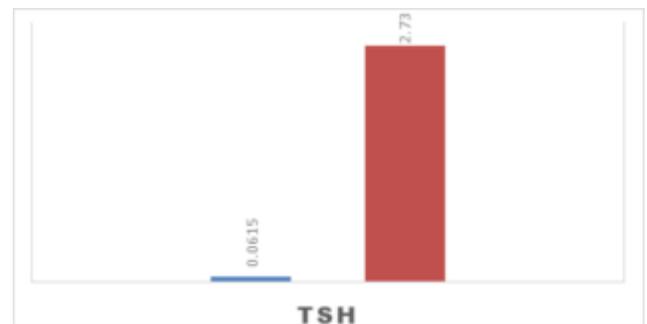


Figure 2: Comparisons mean of TSH between test and controls

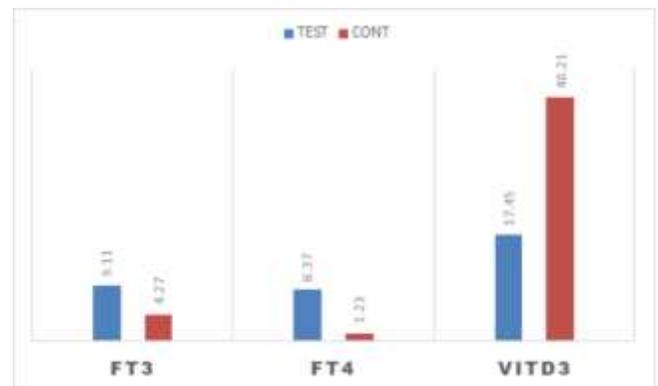


Figure 3: Comparisons mean of FT3, FT4 and vitamin D between test and controls.

Correlation between vitamin D with other parameters in samples studied: The study showed no statistically significant link between vitamin D and other variables. In the patient group, there was a significant negative correlation between free T3 and vitamin D (R=-.451, P=0.000), Furthermore, there was a negative correlation between vitamin D and T3, vitamin D and TSH (R= -.020, P=.878, R= -.095, P=.470), and vitamin D with free T4 (R=-.012, P= .929) in patient group. As shown in table (2).

As a result (Holick et al., 2011). The findings are intriguing because they demonstrate the necessity of vitamin D therapy in GD patient's⁽¹⁹⁾. Both vitamin D and thyroid hormone are known to bind to steroid hormone receptors. Low vitamin D levels in hyperthyroidism individuals may be explained by one of two mechanisms: first, low vitamin D levels might be caused by poor intestinal absorption of vitamin D, and the second explanation

could be incorrect vitamin D activation by the body ⁽²⁰⁾. Vitamin D insufficiency has been linked to larger thyroid volume in individuals with newly diagnosed GD ⁽²¹⁾. Vitamin D-receptor gene and vitamin D-binding protein gene variants have also been linked to GD ⁽²²⁾.

Table 2: Correlation between vitamin D with other parameters in samples studied.

Parameters	PC & P-value	Correlation Vitamin D3
T3	R	-0.020-
	P	0.878
T4	R	0.092
	P	0.487
TSH	R	-0.095-
	P	0.470
FT3	R	-0.451-*
	P	0.000
FT4	R	-0.012-
	P	0.929

** . Correlation is significant at the 0.01 level (2-tailed).
 * . Correlation is significant at the 0.05 level (2-tailed).

CONCLUSIONS

People with Graves' disease who are over 40 years old are more likely to get it than people in other age groups. Testing for TRAB can help figure out if someone has Graves' when the symptoms aren't clear. Graves' could be made worse by a high serum level of T3, T4, FT3, FT4, and TRAB-positive and a low serum levels of TSH.

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