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ORIGINAL ARTICLE

Estimation the Relationship Between Vitamin D and Some Immune Parameters Among Patients with Graves' Disease

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ABSTRACT

Background: Graves' disease is an autoimmune condition caused by thyroid-stimulating immunoglobulins binding to the thyrotropin receptor on the thyroid gland. This leads to increased thyroid hormone production, hyperthyroidism symptoms, and the development of diffuse goiter.
Objectives: This research seeks to measure the concentrations of CD40, CD80, and CD86 in Graves'disease patients, as well as their vitamin D levels, 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: The mean blood levels of Vitamin D revealed a very significant association (P.value> 0.005) across the groups tested for Graves ' disease. The patients group comprised 20 men (33.3%) and 40 females (66.7%) and their mean CD40 serum levels were (36.89± 30.50 ng / ml) in the patients and 46.61± 16.14 ng / L in the controls.
Conclusion: The Thyrotropin receptor antibody (TRAb) test and ultrasonography of the thyroid gland are useful diagnostic tools for autoimmune Graves' disease (GD) since they may diagnose AITD early. Graves' illness is connected with decreased vitamin D levels in the blood.

INTRODUCTION

Graves' disease (GD) is an autoimmune disorder characterized by high levels of autoantibodies against thyroid-specific autoantigens such as the thyroid stimulating hormone receptor (TSH-R), thyroid peroxidase (TPO), and thyroglobulin (Tg) (Cho et al., 2020).GD is one of the most common autoimmune thyroid diseases (AITD), which are characterized by a loss of immunological tolerance to thyroid antigens (McLachlan et al., 2014). Thyrotoxicosis is a clinical feature of GD, as is the development of serum anti-thyroid antibodies (ATA) and autoreactive lymphocytes in the gland (Ferrari et al., 2019). GD is characterized by lymphocyte infiltration of the thyroid and generation of thyroid specific antibodies in response to thyroid self-antigen. Anti-TSH-R autoantibodies (TRAb) are produced by B-cell clones that infiltrate the gland as a result of an autoimmune response in GD (Kotwal et al., 2018). CD40 is a tumor necrosis factor (TNF) receptor located on APCs and thyrocytes that is necessary for an adaptive immune response to work properly. CD154 (expressed on T cells) interacts with it to give costimulatory signals that increase B cell proliferation, immunoglobulin class switching, and germinal center development (Jacobson et al., 2007).Thyroid cells are important players in the autoimmune process. Thyroid cells offer antigens like the thyrotropin receptor to activated T cells. They do not excite naive T cells, which need a costimulatory signal from antigen-presenting cells (Smith et al., 2016).

METHODIOLOGY

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: Ethics committee of College of Health and Medical Techniques/Kufa and corresponding ethical committee of Najaf health directorate gave their permission for the research. Alsader medical city had given approval (Najaf Center for Diabetes and Endocrinology) for the study.
Statistical Analysis: Data analysis was carried out using SPSS software (version 20.0 for windows, Chicago, IL, USA). P value of > 0.05 was considered statistically significant. ANOVA test was used to test differences among groups. Count and percentage are used to convey qualitative data.
Blood Sample Processing: Blood samples taken from 90 patients with Graves' disease were tested for levels of vitamin D, CD40, CD80, and CD86. The serum was collected in an Apandtroft tube and held at -20°C for an ELISA test.

RESULTS AND DISCUSSION

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. Vitamin D, CD40, CD80, and CD86 levels were compared in Graves' disease and control groups. The mean value 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).The Mean ± SD of CD86 and CD80 levels were (2.58 ± 6.40; 1306.92 ± 1312.78) in the patients group and (0.52 ± 0.96; 1247.86 ± 548.40) in the control group, respectively. While the mean±SD of CD40 levels was (46.61±16.14) in both groups, there was no significant correlation between them and the tested groups (P. value > 0.05).

Table 1: Comparisons mean of Vitamin D, CD40, CD80 and CD86 between the studied groups:

Parameters	Patients	Controls	P. value
	Mean ±SD	Mean ±SD	
Vitamin D	17.45±6.77	40.21±5.93	0.000
CD86	2.58±6.40	0.52±0.96	0.000
CD40	36.89±30.50	46.61± 16.14	0.323
CD80	1306.92±1312.78	1247.86±548.40	0.000

Serum CD80 and CD86 level: In the current research, patients with Graves' disease had significantly higher levels of CD80 and CD86 than healthy controls. Scientists at the University of Bristol in the UK have shown that a high proportion of CD80+ cells in B lymphocytes is more common in patients with Hashimoto' disease HD, intractable GD, and severe HD than in control subjects who had normal levels of the hormone testosterone. Furthermore, they discovered for the first time that a high proportion (>8%) of CD80+ cells in B lymphocytes was more common in patients with GD, Hashimoto' disease HD, intractable GD, and severe HD than in control subjects, and that it was also more common in patients with intractable GD than in those with GD in remission (Menezes et al.,

2014).Mast cell (MC) local intrafollicular infiltration, active degranulation of MC in the thyroid, and elevated expression of the costimulatory marker CD86 in GD are all compatible with these findings (Zdor et al., 2020).

Serum CD40 level: Thyroid follicular cells express CD40, a key receptor in B cell growth, T cell priming, antigen presentation, and overall adaptive immunity.CD40, which is expressed on antigen-presenting cells including dendritic cells and B-cells, has been identified as a significant susceptibility gene for GD and other autoimmune disorders. Thyroidal CD40 overexpression increased the synthesis of TRAb by activating downstream cytokines and chemokines, resulting in more severe experimental autoimmune Graves' illness (Chen et al., 2015).

Person's correlation coefficient among the immunological markers in samples studied: In the patient group, there was a strong positive correlation between CD40 and CD80 (R=0.796, P=0.000). Furthermore, there was a strong positive correlation between CD40 and CD86 (R=0.909, P=0.00). As in the table (2).

Table 2: Person's correlation coefficient among the immunological markers in samples studied.

	person's Correlations		
		CD80	CD86
CD40	R	0.796**	0.909**
	P	0.000	0.000

CTLA-4 is a regulatory molecule linked to the down regulation of T-cell responses by competing with CD28 for binding to CD80/CD86 in numerous autoimmune disorders (Ye et al., 2012).

Person's correlation coefficient between CD80 and CD86 in samples studied: In the patient group, there was a strong positive correlation between CD80 and CD86 (R=0.885, P=0.000). As in the table (3).

Table 3: Person's correlation coefficient between CD80 and CD86 in samples studied.

Person's Correlations		
	CD86	
CD80	R	0.885**
	P	0.000

CONCLUSIONS

The study showed that the serum levels concentration of CD80 and CD86 are higher in people with Graves' disease and have a strong link to the hyperthyroid phase of the disease. The results of this study show that people with Graves' disease tend to have low amounts of vitamin D in their blood.

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