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The Utility of Serum CD152 Concentration as a Differential Biomarker in Hashimoto's Thyroiditis

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Abstract

Background: Hashimoto's disease is an autoimmune disorder that affects the thyroid gland. The thyroid gland, shaped like a butterfly, is located at the base of the neck, directly beneath the Adam's apple. The thyroid produces hormones that help to regulate a variety of body processes. An autoimmune illness occurs when the immune system attacks healthy tissues. In Hashimoto's disease, immune system cells cause the death of thyroid hormone-producing cells. Hypothyroidism is a common consequence of the condition.

Objectives: Aim of study is to investigating the levels of CD152 and its correlation TSH, T3 and T4 to provide the reference for the diagnosis of Hashimoto's.

Materials and Methods: This study included (80 patients "40 males and 40 females" with Hashimoto's and 40 healthy persons as control group). Five ml of blood were taken from all to assess T3, T4, TSH, Vitamin D and CD152 according to procedures that

provide with kits. By SPSS v.29, all data were analyzed at *P* value equal or less than 0.5.

Results: The level of CD152 is higher in female group when compare with male group P- value 0.05, the ROC carve show the CD152 is greater than vitamin D and TSH and more specific to distinguish between the groups, In Hashimoto's thyroiditis patients, there was a link between CD152 and thyroid function tests.

Conclusion: It was concluding CD152 is depend alone is a novel biomarker to HT diagnosis, in addition there is correlation between CD152 and TSH, T3, T4.

Keywords: Hashimoto's, CD152, autoimmune disease, TSH, T3.

Introduction

Autoimmune diseases (AID) are complicated genetic disorders that are inherited. It has been shown that certain autoimmune illnesses tend to cluster in families and are thought to have some similar etiological causes. It has been challenging to discover the genes that contribute to vulnerability to various disorders, except from the major histocompatibility complex (MHC) **[1].**

The majority of cases of organ-specific autoimmune thyroiditis (AIT) driven by T lymphocytes occur in Hashimoto's thyroiditis (HT). Whether or not hypothyroidism is present, it is characterized by elevated blood quantities of thyroid antibodies, namely thyroglobulin and thyroid peroxidase antibodies (TPOAb)[12] . The etiopathogenesis of Hashimoto thyroiditis (HT), a chronic inflammation of the thyroid gland that was first identified more than a century ago, is still not fully understood. It is now regarded as the most prevalent endocrine illness, the leading autoimmune disorder and main culprit in hypothyroidism [2]**.**

The complex and well understood pathophysiology of this autoimmune disorder involves both genetic and environmental varibles [3]. An example of organ-specific autoimmunization is chronic lymphocytic thyroiditis. Thyrocytes and thyroid epithelial tissue are destroyed when the thyroid gland is attacked by CD4+ and CD8+ T cells, CD19+ B cells, macrophages, and plasma cells. The development of the illness is also significantly influenced by T helper cells (Th), particularly Th1 and Th17 [4]. Additionally, thyroid hormone production is hindered simultaneously. The development of the illness may be dependent on autoreactive T cells and B lymphocytes. These cells are the primary source of autoantibodies against thyroglobulin and thyroid peroxidase. The development of antibodies against thyroid peroxidase, or anti-TPO, is one clinical sign that confirms the existence of the illness. When no autoantibodies are found in the blood, potential diagnostic use of thyroid ultrasonography (USG).

Abnormalities in thyroid imaging such as decreased echogenicity, heterogeneity, increased vascularity, and the formation of small cysts may suggest Hashimoto's thyroiditis [5]. The thyroid parenchyma's atrophy and fibrosis are two hallmark signs of HT. This article aims to review recent scientific research on Hashimoto's thyroiditis and how the immune system plays a role in the disease's pathophysiology. It stresses the importance of monitoring the levels of different subpopulations of lymphocytes for diagnosis, treatment, and disease progression evaluation [5]. One such possibility that may be able to unite a number of autoimmune illnesses is CD152.

Here, we examine the data supporting CD152's role as a general susceptibility factor for a number of autoimmune disorders and talk about the potential roles that CD152 and other co-stimulatory pathways may play in the etiology of autoimmune illnesses [1].

Materials and Methods

Group I consisted of eighty individuals with HT. They were chosen from Alsader Medical City (Najaf Center for Diabetes and Endocrinology) Department's outpatient clinic from April and October of 2024. As the control group (group II), they included forty individuals who were matched in both age and sex and appeared to be in good health. Every individual underwent a thorough clinical examination, a detailed medical history, the five milliliters of blood were drawn from all of them (including controls) to enable to evaluate the laboratory tests that were used in the current study.

Inclusion criteria: Every patient who has Hashimoto's disease.

Exclusion criteria: The study excluded pregnant women, patients with diabetes mellitus, and patients with active hypertension.

Ethical Issue: The study was approved by the ethics committees of the Ministry of Higher Education and Scientific Research, the University of Alkafeel College of Health and Medical Technology, AL-Furat al-Awsat Technical University Karbala Technical Institute, and the Karbala Health Directorate. The research has been approved by Alsader Medical City (Najaf Center for Diabetes and Endocrinology).

Statistical Analysis: SPSS software (SPSS v.29) was used to evaluate the data, and all data were examined at a P value of 0.5

or less. Group differences were tested using the ANOVA test. Qualitative data is communicated using counts and percentages.

Blood Sample Processing: Blood samples from 80 Hashimoto's patients were examined for CD152, T3, T4, TSH, and vitamin D levels. For an ELISA test, the serum was obtained in an Apandtroft tube and stored at -20°C.

Laboratory investigations: A number of tests in the lab. Were performed: T3, T4 and TSH vitamin D as well as complete blood count. Serum CD152 levels were evaluated by an ELISA method according to with the manual supplied by the test kit company, BioSource com. USA.

Result

The current study, which was conducted on patients with HT, who numbered 80 patients (40 males and 40 females), and the study also included 40 persons (21 males and 19 female) who appear to be healthy as a control group. The distribution of patients was according to the age group that the age group (34-43) years is the highest (36.25%). that included in the study as illustrated in table (1).

Table (1) Factors influencing patient and control group demographics

Variable	Patient group			Control group			P – value
		No.	%		No.	%	
Age group in years	(14-23) years	8	10	(14-23) years	7	17.5	.000
	(24-33) years	19	23.75	(24-33) years	10	25	
	(34-43) years	29	36.25	(34-43) years	14	35	
	(44-53) years	10	12.5	(44-53) years	4	10	
	(54-63) years	8	10	(54-63) years	7	17.5	
Sex	Male	40	50	Male	21	52.5	.003
	Female	40	50	Female	19	47.5	
Family history	Present	14	17.5	Present	0	0	.000
	Absence	66	82.5	Absence	40	100%	

Table (2) show the comparison mean between patients and control groups

Variable	Male group Mean ± SD	Female group Mean ±SD	Control group Mean ±SD	*P* - value
T3	2.6230± 1.23	5.40 ± 2.62	7.55±2.31	.000
T4	129.85±50.72	173.98±31.25	145.17±49.86	.000
TSH	1.38830±1.44	.10687±.184	1.90± 0.19	.000
Vitamin D	31.78±15.74	15.13±5.59	44.58±6.78	.000
CD152	350.588±876.50	896.62±1155.75	846.62±1101.39	.040

When comparing these patients' blood variables to those of the control group, researchers found that T3 levels were much lower in the former. Additionally, the findings showed that compared to the control group, the male group's CD152 level was significantly lower ($p = 0.04$). Likewise, CD152 in female increased significantly compared to control group. As show in table (2).

Table (3) correlation between CD152 with the other parameters

Variable		Correlation of CD152
T3	R	.413**
	P	.000
T4	R	.316**
	P	.000
TSH	R	-.271**
	P	.003
Vitamin D	R	-.393**
	P	.000
**. Correlation is significant at the 0.01 level (2-tailed).		

As for the study of the strength of the correlation between CD152 levels and other factors (T3, T4), it was found that there is positive significant correlation. Also, there is negative significant correlation of CD152 with other factors (TSH, vitamin D) as in table (4).

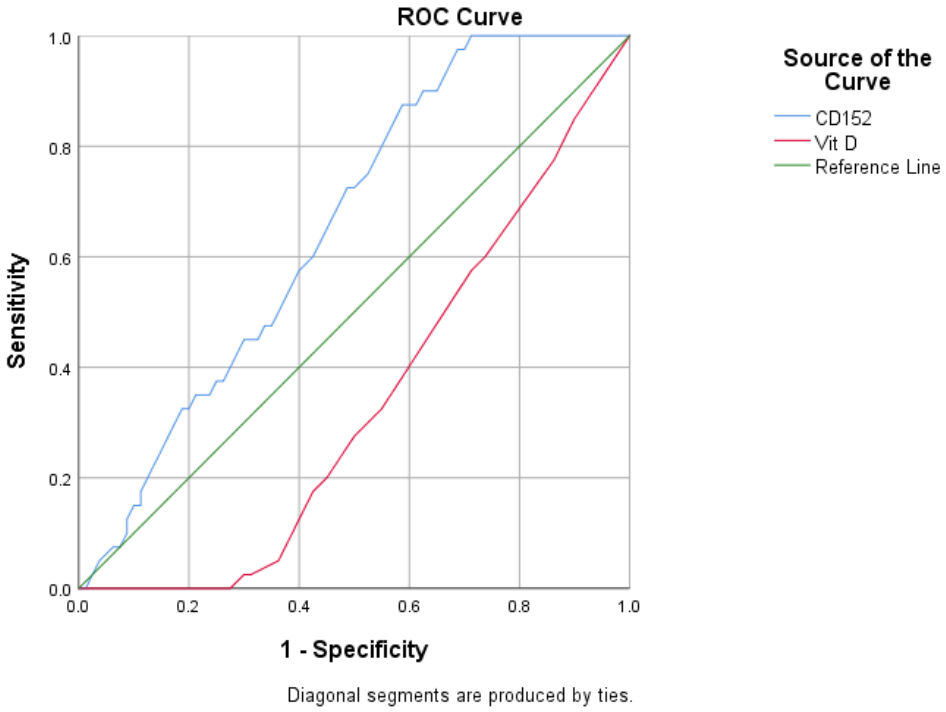

Figure (1) Show ROC curve between CD152 with Vitamin D levels

According to the ROC analysis findings, as shown in figure (1), CD152 has a higher area with a higher confidence level than vitamin D.

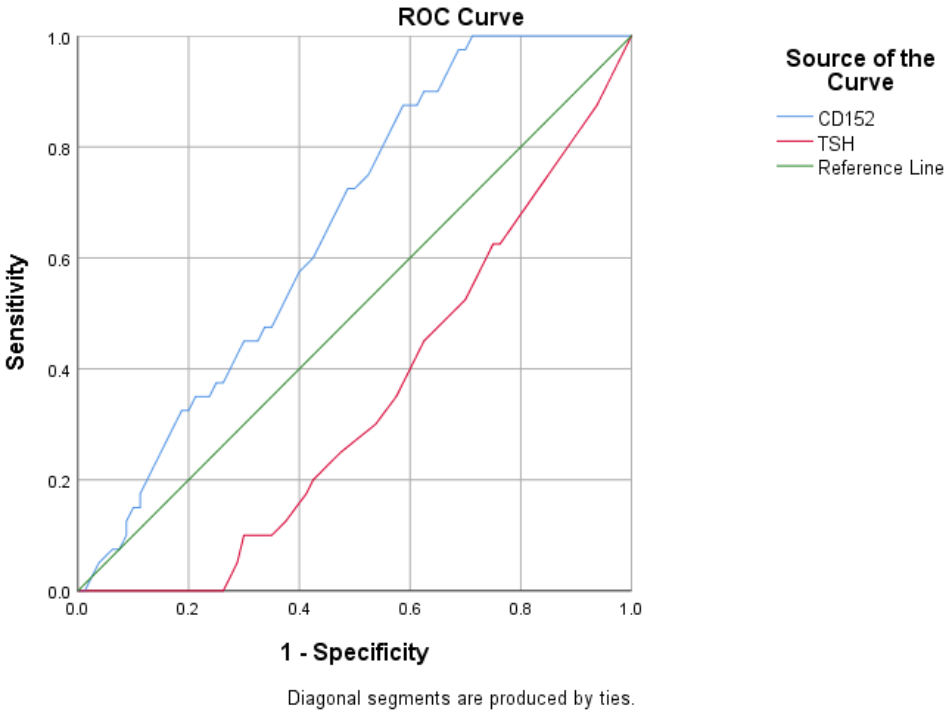

Figure (2) show ROC curve between CD152 with TSH levels

As shown in figure (2), the findings of the ROC analysis also indicated that CD152 has a higher area with a higher confidence level than TSH.

Discussion

These patients' T3 and T4 levels were considerably lower than those of the control group in this HT-focused investigation [6]. HT had a favorable connection with CD152 and a substantial drop in TSH when compared to control. Accordingly, the obtained results show that people with Hashimoto's thyroiditis have a significant increase in CD152.The results of our study are in line with a number of studies by other researchers that showed that serum CD152 levels in males are significantly lower than those in the control group [7,8]. As for CD152, the results showed that the level of this factor was higher than in the control group.

One important inhibitor of T cell activation is CD152 (CTLA-4). Prior research has shown that the CTLA-4 gene polymorphisms are implicated in the pathophysiology of autoimmune thyroid disorders, including Graves's disease and Hashimoto's thyroiditis. However, several polymorphisms have not yet had a functional impact [9]. The reduced surface expression of CD152 on T cells is thought to be the cause of the impairment of CTLA-4 function. It was explained by changes in the CTLA-4 signal peptide, which resulted in poor cell surface processing. In keeping with the data mentioned above, we previously found that children with Hashimoto's thyroiditis had a considerably decreased proportion of T lymphocytes expressing CD152 on their surface compared to healthy controls [10]. We discovered in this investigation that the level of anti-thyroglobulin antibodies was statistically higher in patients with less CD152+T cells. The role of CTLA-4 seems to be the logical explanation for this discovery. An essential component for the end of an immune response is the expression of CD152+ T cells. Thus, a persistent stimulation of auto-reactive T cells and the emergence of autoimmune processes may be caused by a reduction in CD152+T cells [11].

They noted a reduction in CTLA-4 on the surface of T cells, which may contribute to autoimmune illness by encouraging the proliferation of T lymphocytes. Anti-thyroid autoantibodies detect autoimmune thyroiditis in the lab. The only antibodies in our patients that correlated with lower CD152 expression were anti-thyroglobulin antibodies; anti-thyroperoxidase antibodies did not [11]. Vitamin D insufficiency is common in HT patients, although the role of vitamin D metabolism in the etiology of the disease is unclear.The binding of 1,25(OH)2 D3 to the intracellular vitamin D receptor (VDR) is the primary mechanism by which vitamin D exerts its effects. This interaction either

stimulates or inhibits the transcription of genes that are sensitive to vitamin D [13].

Treg cell, which are primarily characterized as CD4+CD25+FoxP3+ expressing T-lymphocytes, express CTLA4 constitutively and are critical in the HT pathogenesis. The current investigation found that T-cells from HT patients have lower transcript levels of CTLA4, a key regulator of thyroid autoimmunity [13]. Kucharska [14] also found decreased CTLA4 levels, although another study didn't find a noticeable drop in CD4+CTLA4+ cells [14]. The expression of both vitamin D receptor (VDR) and CTLA4 is tightly regulated and quickly co-induced by T-cell activation. Furthermore, CTLA4 is expressed constitutively on CD4+CD25+ Treg cells, is greater in Th2 and Th17 clones, and is significantly expressed in CD4+ than in CD8+ T-cells [13].

Last but not least, it has been recently reported that lymphoblastic cell lines exhibit vitamin D receptor (VDR) binding within the CTLA4 region in response to ligand stimulation.

Additionally, it has been reported that direct VDR binding to the FOXP3 gene increases the frequency of FoxP3+CTLA4+ T-cells and CTLA4 expression in a vitamin D-dependent manner [13].

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