Role of Soluble CD^{23} in Patients with Hyperthyroidism: Case–Control Study

Salim Hussein Hassan, Aqeel S. Abd Al-Salam, Nawras A. Esmaeel[1]

Department of Community Health Technique, Karbala Technical Institute, Al-Furat Al-Awsat Technical University, [1]Department of Medical Laboratory Technique, Babylon Technical Institute, Al-Furat Al-Awsat Technical University, Kufa, Iraq

Abstract

Background: Hyperthyroidism, or Graves' disease (GD), is the consequence of an overproduction of thyroid hormones. **Objective:** This study aimed to determine the concentration of soluble CD^{23} in GD patients and the correlation of its level with biomarkers (T.3, T.4, thyroid stimulating hormone [TSH], FT.3, FT.4, and vitamin D, among those. **Materials and Methods:** There were eighty patients (50 patients with hyperthyroidism and 30 controls), during the time frame beginning in February 2021 and ending in April 2022 at Karbala city. In this research, participants were required to have a positive result on both an ultrasound of the thyroid and a test for thyrotropin receptor autoantibody (TRAB). FT.3, FT.4, and TRAB. Levels were determined by the VIDAS technique. Serum sCD^{23} and vitamin D3 levels were determined by ELISA using commercial test kits. **Results:** The mean age of the patients included in this study was 39 ± 12 years, while that of the control group was 30 ± 10 years. GD was noticed among female more than male patients. Regarding the age groups of GD, more patients were in the 25–44 years age group than in the other age groups. The immunological marker sCD^{23} is higher in the patients' group when compared with the control group (486.16 ± 185.39, 166.64 ± 61.15, respectively) and no correlation between levels of it and T3, T4, TSH, and vitamin D. **Conclusion:** There was a statistically significant difference between the patient and control groups in the levels of sCD^{23} and thyroid panel test.

Keywords: Graves' disease, sCD^{23}, thyroid panel test, thyroid-stimulating hormone

Introduction

Graves' disease, also known as GD, is a systemic autoimmune disorder that causes follicular cell hypertrophy, thyroid enlargement, increased synthesis of thyroid hormone, and hyperthyroidism. These symptoms arise as a result of thyroid-stimulating autoantibodies that are directed against the thyrotropin (thyroid stimulating hormone [TSH]) receptor on thyroid follicular cells. GD is also known as autoimmune thyroiditis. Even though it only affects a very small percentage of the population (approximately 0.5% of the population), GD has been linked to between 50% and 80% of all cases of hyperthyroidism.[1] This is the case even though GD is very rare. Clinically, GD is characterized by thyrotoxicosis, the presence of antithyroid antibodies in the blood, and the presence of auto reactive lymphocytes in the gland.[2] Thyroid peroxidase, thyroglobulin (Tg), and the TSH receptor (TSH-R) each have distinctive characteristics (also known as "immunogenicity") that contribute to the destruction of tolerance. Because thyroid hormones have such a wide-ranging influence on the body, the symptoms of GD may be highly diverse and have a significant impact on the quality of life of the individual who suffers from them.[3] GD is a well-known medical disorder that has been associated with a rapid progression of many diseases.[4] Symptoms such as tremor, heat intolerance and warmth, weight loss (even with a regular diet), anxiety and irritability, a swollen thyroid gland (goiter), changes in the menstrual cycle, erectile dysfunction or reduced libido, weariness, frequent bowel movements, palpitations,

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_924_23

Address for correspondence: Dr. Salim Hussein Hassan, Department of Community Health Technique, Karbala Technical Institute, Al-Furat Al-Awsat Technical University, Kufa, Iraq.
E-mail: inkr.salm@atu.edu.iq

Submission: 06-Jul-2023 **Accepted:** 10-Aug-2023 **Published:** 23-Dec-2024

How to cite this article: Hassan SH, Abd Al-Salam AS, Esmaeel NA. Role of soluble CD^{23} in patients with hyperthyroidism: Case–control study. Med J Babylon 2024;21:827-31.

and other symptoms are common.[5] A breakdown in immunological tolerance toward the thyroid may be involved in the development of GD.[6] This breakdown occurs as a result of an autoimmune multifactorial process that includes environmental and endogenous variables in patients who are genetically susceptible to the disease. B-cell clones penetrate the gland and induce an autoimmune reaction, which ultimately leads to the production of anti-TSH-R autoantibodies in patients with GD (thyrotropin receptor autoantibody [TRAB]).[7] There are extra thyroidal symptoms of GD that have been associated with TRAB antibodies.[8] TSH binding to the TSH-R may be imitated by TSAb, which results in enhanced thyrocyte proliferation, thyroid growth, and synthesis of T4 and T3.[7] On the other hand, TBAB is able to bind to the A subunit, which inhibits TSH activity and the consequences it has on follicular cells.[9] Vitamin D3 deficiency in people is usually resulted from decreased nutritional vitamin D intake, decreased skin synthesis of vitamin D, and the decreased in the time spent in the outdoors' activities and this play important role in many diseases including the disorders of thyroid gland.[10] Orbital fibroblasts have been shown to express the estrogen receptor, and the expression of this receptor may be changed by glucocorticoids.[11] Both estrogens and X-inactivation have an effect on the immune system, which may help explain why GD occurs more often in females. In females, the X chromosome is activated in a mixture of cells that have been inherited from both of the individual's parents.[12] Regard to IgE, sCD^{23} is the low-affinity receptor. Extremely low levels of expression are seen in marginal zone B cells and T1 transitional B cells in the spleen, although it is expressed throughout the entire B-cell life cycle, and sCD^{23} is found in two different versions (or "isoforms"): sCD^{23}a and sCD^{23}b. Among these isoforms, only the first is produced naturally. The results of an antibody's interaction with sCD^{23} might be positive or negative.[13] Current study was designed to find the correlation of level sCD^{23} with biomarkers (T.3, T.4, TSH, FT.3, FT.4, and vitamin D) among GD patients.

Materials and Methods

Study design

The current study was case-control and included eighty patients (50 patients with hyperthyroidism and 30 controls) at Karbala City during the period from February 2021 to April 2022. The clinical and biochemical manifestations of hyperthyroidism, as well as clinical and laboratory features, were used to diagnose the disease. All patients with a positive thyroid ultrasound and TRAB test were enrolled in this study. Demographic, clinical, and laboratory data were extracted from medical records using a standardized data collection form that included age and sex. Blood samples were collected by venipuncture from all (patients and control) for the purpose of obtaining a serum to evaluate all hormonal and immunological parameters to be studied.

Biochemical parameters (hormones)

Thyroid panel test, FT3, FT4, and TRAB levels were determined by the VIDAS technique using commercial test kits, while human sCD23 ELISA kits (BioSource, Inc., Atlanta, Georgia, USA) were used exactly as directed by the manufacturer. Supernatants were applied for 2 h at room temperature to microliter plates precoated with a mixture of monoclonal anti-CD^{23} antibodies and anti-CD23-HRP. Tetramethyl benzidine was used to create the color reaction, which was then measured at 450 nm. Results were obtained through a standard curve; the sensitivity of the assay is 6 ng/mL. Also, vitamin D3 levels were determined by the ELISA technique using commercial test kits (Bioassay Technology Laboratory, Shanghai, China). Testing procedures were performed according to the manufacturer's instructions of company mentioned above.

Statistical analyses

To investigate the connection between sCD^{23} and the other characteristics, a correlation analysis was carried out. The *T*-test was used to test differences among groups. A *P* value of ≤0.05 was considered statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before a sample was taken. The study protocol and subject information, and consent form were reviewed and approved by a local ethics committee according to document number 451 on January 23, 2021, to get this approval.

Results

Demographic data of the studied groups

This study was conducted on a total of 80 individuals, 50 of whom were patients with GD and 30 of whom were controls. The mean age in the patient group was (39.59 ± 12.411 years) while in the control group, it was (30.80 ± 10.24 years). GD was noticed among the female patients more than among the male patients. Regarding the age groups of GD (25–44 years) were more common than other age groups; as shown in Table 1.

Thyroid hormones

Table 2 shows the comparison between GD and control groups in thyroid tests. According to T3 parameter the mean was (4.98 ± 1.76 nmol/L) in the patient group, while the mean in the control group was (3.67 ± 2.21 nmol/L). The T4 levels were elevated in the patient group more than in the control group, while the TSH test was less than the normal range when compared with the control group ($P = 0.01$).

Table 1: Demographic data of the studied groups

Variable	Groups					
	Patients			Controls		
Age	Mean ± SD (year)	39.59 ± 12.411		Mean ± SD (year)	30.80 ± 10.24	
	Patients	No.	%	Controls	No.	%
Age groups (year)	14–24	7	14.0	14–24	15	50.0
	25–35	10	20.0	25–34	10	33.3
	36–46	**17**	**34.0***	35–44	3	10.0
	47–58	8	16.0	45–54	2	6.7
	59–69	8	16.0	55–70	0	0
Total		**50**	**100%**		**30**	**100%**
Sex	Male	18	36.0	Male	9	30.0
	Female	32	64.0*	Female	21	70.0
Total		**50**	**100%**		**30**	**100%**

*significant differences at $P \leq 0.05$

Table 2: Comparison means of T3, T4, and TSH, between the studied groups

Parameters	Patients	Controls	*P*-value
	Mean ± SD	Mean ± SD	
T3 (nmol/L)	4.98 ± 1.76	3.67 ± 2.21	**0.04***
T4 (nmol/L)	176.97 ± 33.946	144.16 ± 50.869	**0.02***
TSH (mU/L)	0.064 ± 0.208	1.094 ± 1.510	**0.001****

Values expressed as mean±SD; *significant at $P \leq 0.05$; **highly significant at $P \leq 0.05$

Table 3: Comparison of means of sCD23, FT3, FT4, TRAB, and vitamin D3 between the studied groups

Parameters	Patients	Controls	*P* value
	Mean ± SD	Mean ± SD	
sCD 23 (ng/L)	486.16 ± 185.39	166.64 ± 61.15	**<0.05***
FT3 (pmol/L)	9.548 ± 4.061	4.14 ± 1.65	
FT4 (pmol/L)	8.73 ± 5.97	1.26 ± 0.27	
TRAB (mg/dL)	4.47 ± 4.44	0.57 ± 0.28	
Vitamin D3 (ng/mL)	16.96 ± 6.969	40.43 ± 5.60	**0.01****

Values expressed as mean±SD; *significant at $P \leq 0.05$; **highly significant at $P \leq 0.05$

Table 3 shows the mean sCD23, FT3, FT4, TRAB, and vitamin D3 levels between the studied groups (patients with GD and controls). The immunological marker sCD23 was higher in the patient group than in the control group. Regarding FT3, FT4, TRAB, and vitamin D3 were elevated significantly $P < 0.05$ in the patients group compared to control group, except vitamin D3 was higher in the control than in patients group ($P < 0.05$), as illustrated in Table 3.

Correlation analyses were performed between sCD23 levels and FT3, FT4, TRAB, and vitamin D3 in Graves' patients. There was no significant correlation between immunological markers and the thyroid panel test, FT3, FT4, TRAB, and vitamin D3. Also, it was observed that the factors T3, TSH, TRAB, and FT3 are inversely proportional to the immunological factor (sCD23) while the relationship of other factors T4, FT4, and vitamin D with the same immunological factor is directly at no significant value ($P > 0.05$) as illustrated in Table 4.

Table 4: Correlation analysis between sCD23 and thyroid panel test, FT3, FT4, TRAB, and vitamin D in patient samples

Parameters	Correlation	
	PC and *P*-value	CD 23
FT3 (pmol/L)	R	-0.114
	P	0.429
FT4 (pmol/L)	R	0.055
	P	0.706
TRAB (mg/dL)	R	-0.222
	P	0.122
Vitamin D3 (ng/mL)	R	0.067
	P	0.642
T3 (nmol/L)	R	-0.176
	P	0.221
T4 (nmol/L)	R	0.022
	P	0.879
TSH (mU/L)	R	-0.084
	P	0.563

Regarding the correlation between thyroid panel tests and FT3, FT4, TRAB, and vitamin D in Graves's patients. There was a nonsignificant correlation among these parameters, except between T4 and FT4, where there was a significant correlation ($r = 0.343^{**}$, $P = 0.007$), as shown in Table 5.

Discussion

According to the results of the present research, adults aged 25–44 years made up the largest demographic of patients diagnosed with GD. GD was more prevalent among women in/and before the age of 40, although GD

Table 5: Correlation between thyroid panel with FT3, FT4, TRAB, and vitamin D in the patient's samples

Thyroid panel test	Correlation				
	PC and P-value	FT3 (pmol/L)	FT4 (pmol/L)	TRAB (mg/dL)	Vitamin D3 (ng/mL)
T3 (nmol/L)	R	0.167	0.049	0.179	-0.020
	P	0.203	0.709	0.170	0.878
T4 (nmol/L)	R	0.201	0.343**	0.181	0.092
	P	0.124	0.007	0.166	0.487
TSH (mU/L)	R	-0.050	-0.059	-0.102	-0.095
	P	0.704	0.653	0.440	0.470

may afflict people of any age. This result was consistent with,[14] whose results were supported in multivariate models revealing age as a major predictor of referral in GD patients. Similarly, the current research concurred with several authors[15,16] who reported an increased incidence of "GD" in the (26–45) year old age bracket. Patients with GD were found to have a mean age of (39.59 ± 12.411) years. The results of this study were consistent with the findings of El-fadil *et al.*,[17] who found that the average age of patients with Graves' illness was 34.82 ± 11.13 years, our study found the same thing Al-Gazally *et al.*[15]

A similar trend was also noted, reporting that the mean age of patients with hyperthyroidism was 38.63 ± 10.03 years (range 15–61). Patients with Graves' illness had much lower TSH levels than the control group and significantly higher T3 and T4 levels than the control group, according to the findings of the present study. Since these antibodies originate in immunologically competent plasma cells, the elevated T3 and T4 synthesis and decreased TSH levels make sense. T3 and T4 exert a negative feedback mechanism on the pituitary and hypothalamus axis, and when the antibodies interact with TSHR, T3 and T4 synthesis and production are stimulated despite the lower levels of TSH.[15] Consistent with these findings, Al-Humaidi[18] found higher levels of sCD[23] in the sick group than in the control group and stated that the levels of sCD[23] (mean 164 ± 67.03 ng/mL) were significantly higher in GD patients than in the control group (mean 31.24 ± 11.53 ng/mL, $P < 0.001$). Serum vitamin D levels in TRAB-positive GD patients were considerably lower than those in the control group or TRAB-negative GD patients. However, in contrast to the placebo group. Patients with TRAB-positive GD had a substantially greater prevalence of vitamin D insufficiency (defined as serum 25[OH] D 50 nmol/L) than healthy controls or patients with TRAB-negative GD. In individuals with TRAB positivity and GD, serum 25(OH) D levels were negatively associated with TRAB titer.[19,20]

Conclusion

The sCD[23] concentration was significantly higher in the GD group than the control group. The levels of sCD[23] were not correlated with thyroid panel tests and vitamin D in individuals with GD. We recommend further study of sCD[23] to determine its function and impact in GDs.

Acknowledgments

We appreciate the efforts of every medical professional battling Graves' disease. We appreciate the participation of all patients whose information was used in this research. In addition, we appreciate the hard work of the hospital workers in assembling these data.

Authors' contributions

Salim H. H. Data curation and Formal analysis: Aqeel S. A. Investigation, Methodology: Supervision: Nawras A. Writing—original draft, Writing—review and editing.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Consent for publication

All Authors approve for publication.

Financial support and sponsorship

Nil.

Conflicts of interest

There is no conflict of interest.

References

1. Bobanga ID, McHenry CR. Treatment of patients with Graves' disease and the appropriate extent of thyroidectomy. Best Pract Res Clin Endocrinol Metab 2019;33:101319.
2. Ferrari SM, Ruffilli I, Elia G, Ragusa F, Paparo SR, Patrizio A, *et al*. Chemokines in hyperthyroidism. J Clin Transl Endocrinol 2019;16:100196.
3. McLachlan SM, Rapoport B. Breaking tolerance to thyroid antigens: Changing concepts in thyroid autoimmunity. Endocr Rev 2014;35:59-105.
4. Rihab FA, Hussain A, Basma AI, Wasnaa HA. An endocrine perspective of juvenile moyamoya syndrome/disease: A literature review. Med J Babylon 2023;20:13-7.
5. Vaidya B, Pearce SH. Diagnosis and management of thyrotoxicosis. BMJ 2014;349:g5128.
6. Wemeau JL, Klein M, Sadoul JL, *et al*. Graves' disease: Introduction, epidemiology, endogenous and environmental pathogenic factors. Ann Endocrinol 2018;79:599e607.

7. Antonelli A, Ferrari SM, Ragusa F, Elia G, Paparo SR, Ruffilli I, *et al*. Graves' disease: Epidemiology, genetic and environmental risk factors and viruses. Best Pract Res Clin Endocrinol Metab 2020;34:101387.
8. Kahaly GJ, Diana T, Kanitz M, *et al*. Prospective trial of functional thyrotropin receptor antibodies in Graves' disease. J Clin Endocrinol Metabol 2020:105:e1006-e1014.
9. Kotwal A, Stan M. Thyrotropin receptor antibodies—an overview. Ophthalmic Plast Reconstr Surg 2018;34:S20-7.
10. Barrak FAO, Alya AAZ, Nazar M. T. J, Fang Z. Relationship between vitamin D3 level and body mass index in postmenopausal breast cancer patients. Med J Babylon 2022;19:671-5.
11. Cury SS, Oliveira M, Síbio MT, Clara S, Luvizotto RDAM, Conde S, *et al*. Gene expression of estrogen receptor-alpha in orbital fibroblasts in Graves' ophthalmopathy. Arch Endocrinol Metabol 2015;59:273-6.
12. Brooks WH. X chromosome inactivation and autoimmunity. Clin Rev Allergy Immunol 2010;39:20-9.
13. Kumpel BM. In vivo studies of monoclonal anti-D and the mechanism of immune suppression. Transfus Clin Biol 2002;9:9-14.
14. Carlé A, Pedersen IB, Perrild H, Ovesen L, Jørgensen T, Laurberg P. High age predicts low referral of hyperthyroid patients to specialized hospital departments: Evidence for referral bias. Thyroid 2013;23:1518-24.
15. Sinjari HY, Ibrahim JM. Thyroid function disorders in patients with chronic kidney disease. Med J Babylon 2022;19:76-80.
16. AL-Fatlawi R.B. The association between HLA-DQ alleles and the autoimmune thyroid diseases (AITDs) among Iraqi patients. MSc thesis, Iraq: Medical Microbiology/Clinical Immunology; University of Kufa 2014.
17. Elfadil GA, Eltahir IEM, Elmugadam AA. Anti-TRAAb, anti-TPO-Ab, and FT3 as a biochemical panel for differential diagnosis of Graves 'disease from hyperthyroidism. Ind J App Res 2014;4:408410.
18. Al-Humaidi MA. Serum cytokines levels in Graves' disease. Saudi Med J 2000;21:639-44.
19. Zhang H, Liang L, Xie Z. Low vitamin D status is associated with increased thyrotropin-receptor antibody titer in Graves' disease. Endocr Pract 2015;21:258-63.
20. Alabedi RF, Alsaffar H, Ibrahim BA, Abdullah WH. LAn endocrine perspective of Juvenile Moyamoya syndrome disease: A literature review. Med J Babylon 2023;20:13-17.