The Egyptian Journal of Hospital Medicine (July 2022) Vol. 88, Page 3602-3608

Are Doppler Ultrasound Parameters Correlated with Thyroid Antibody Levels in Hypothyroid Patients with Hashimoto's Thyroiditis?

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ABSTRACT

Background: Hashimoto's thyroiditis is the most frequent etiology of hypothyroidism. The most popular imaging technique for assessing thyroid nodules and the thyroid gland's echogenicity and vascularity is thyroid ultrasonography.
Objective: To compare Doppler ultrasound parameters and thyroid-stimulating antibodies in Hashimoto's thyroiditis.
Patients and methods: Seventy-eight patients diagnosed with Hashimoto's thyroiditis were prospectively evaluated by grayscale and Doppler ultrasound examination. This study was done between October 2019 and October 2021 at South Egypt Cancer Institute. We evaluated the overall vascularity of the thyroid gland. Peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) of the inferior thyroid arteries (ITAs) were measured. The serum levels of T3, T4, T3, T4, TSH, anti-thyroid peroxidase antibody (anti-TPO), and anti-thyroglobulin antibody (anti-TG) were assessed for all patients. We tested the correlations between the following variables: serum levels of TSH, T3, T4, anti-TPO, anti-Tg, and ITA-PSV, EDV, and RI of the ITAs.
Results: We found a strong correlation between thyroid antibodies and the Doppler ultrasound parameters. Anti-Tg and Anti-TPO are strongly correlated with PSV, EDV, and RI of the ITAs.
Conclusion: In Hashimoto's thyroiditis patients, PSV, EDV, and RI of both ITAs are significantly correlated with the thyroid antibodies. These findings may help in the assessment of the efficacy of treatment and follow-up of these patients.
Keywords: Thyroiditis, Hashimoto's, Ultrasonography, Doppler.

INTRODUCTION

Hashimoto's thyroiditis, which is additionally called chronic autoimmune thyroiditis, or lymphocytic thyroiditis is a common reason for hypothyroidism [1,2].

It tends to manifest after the age of fifty. Women are more frequently affected than men. Five to fifteen percent of women and five percent of men are usually affected by Hashimoto's thyroiditis [3].

B-mode and Color Doppler Ultrasonography are the imaging modalities most frequently used to evaluate the echogenicity and vascularity of the thyroid gland without harmful exposure to radiation [4,5].

Autoimmune thyroid diseases like Graves' disease and Hashimoto's thyroiditis show increased vascularity of the thyroid gland. This finding is helpful in the evaluation of the progression of these diseases [6]. Some authors used Color Flow Doppler Ultrasound to differentiate between Graves' disease and chronic autoimmune thyroiditis. They found that the mean peak systolic velocity (PSV) is significantly higher, and the resistive index (RI) is significantly lower in Graves' disease [7-9].

The vascularity of the thyroid gland is usually controlled by TSH receptor stimulation. Thyroid hypervascularity in Hashimoto's thyroiditis is not entirely understood [10].

To explain this finding, some authors proposed an autoimmune theory, angiogenesis, or an elevation in the TSH level. They found that thyroid blood flow increases in patients with elevated thyroid-stimulating antibodies [11-13].

This elevation in the thyroid-stimulating antibodies is used in the early diagnosis of Hashimoto's thyroiditis [14].

In this study, we tried to find the relation between the laboratory results and Doppler ultrasound findings in Hashimoto's thyroiditis patients who are suffering from hypothyroidism. This relationship may be helpful in the follow-up of these patients and assessment of the efficacy of the received treatment.

PATIENTS AND METHODS

This study was done prospectively between October 2019 and October 2021 at South Egypt Cancer Institute. Untreated patients diagnosed with Hashimoto's thyroiditis were incorporated in this study. These patients were diagnosed by clinical examination, laboratory tests, and Tru-cut needle biopsy from the thyroid. The study population consisted of 78 patients. Nineteen of them were males, and fifty-nine were females. The mean age was 38.3 ± 11.9 (range 10-70 years).

Exclusion criteria:

We excluded patients who underwent surgical or medical management for any thyroid disease. Hyperthyroid patients with high T4 and low TSH levels were also excluded from this research.

Two radiologists, by consensus, performed grayscale and Doppler ultrasound for all patients.

Received: 16/3/2022
Accepted: 15/5/2022

Equipment:

High-resolution equipment (Aloka ProSound Alpha 6) with a linear transducer (5-12 MHz) was used for both grey-scale and Doppler ultrasound examinations.

Grayscale ultrasound:

We examined thyroid gland echogenicity, echotexture, and the neck lymph nodes. The existence of the thyroid nodule was also evaluated.

Color Doppler and pulsed Doppler ultrasound:

We evaluated the overall vascularity of the thyroid gland. We also measured peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) of both inferior thyroid arteries (ITAs).

Biochemical measurements:

The serum levels of total T3, total T4, free T3, free T4, TSH, anti-thyroid peroxidase antibody (anti-TPO), and anti-thyroglobulin antibody (anti-Tg) were measured for all patients. These laboratory tests were done by using the immunoassay method in fully automated equipment (Beckman Coulter Access 2, USA).

The reference values for the biochemical measurements are shown in table 1. When the thyroid antibodies exceeded the detection limits, we used their highest values.

Table.1: Normal values for the biochemical measurements.

Biochemical test	Normal values
Free T3	1.8–4.1 pg/mL
Total T3	70–220 ng/mL
Free T4	0.7–1.8 ng/dL
Total T4	5.1–13.5 μg/dL
TSH	0.4–4.3 μUI/mL
Anti-Tg	< 60 UI/mL
Anti-TPO	< 60 UI/mL

Ethical approval:

Approval of this research was done by the Ethics Committee of South Egypt Cancer Institute and we took informed written consent from each patient. This research was done in the agreement with Helsinki Declaration, the ethical code of the World Medical Association for studies including humans.

Statistical interpretation:

The researchers used SPSS software version 20.0. We used the Pearson coefficient to evaluate the correlation between the normally distributed variables and the Spearman coefficient for abnormally distributed variables. We tested the correlations between the following parameters: serum levels of free T3, total T3, free T4, total T4, TSH, anti-Tg, anti-TPO, PSV of the inferior thyroid artery on each side, EDV of the inferior thyroid artery on each side, and RI of the inferior thyroid artery on each side. We consider Doppler ultrasound parameters as dependent variables, whereas biochemical variables were deemed to be independent ones. *P*-values < 0.05 were considered statistically significant. P-values <0.001 were judged as markedly significant.

RESULTS

This research was done on 78 patients. The diagnosis was established by clinical examination, laboratory tests, and ultrasound-guided fine-needle aspiration cytology from the thyroid gland. Demographic data of all patients are shown in **Table 2**.

Table2: Demographic data of Hashimoto's thyroiditis.

Demographic data		No.	Percent
Age in years	<20 years	21	27%
	20-	28	36%
	40-	23	29%
	60+	6	8%
Gender	Male	19	24%
	Female	59	76%
Duration of symptoms (in years)	1-2	46	59%
	3-4	20	26%
	>4	12	15%
Family history of thyroid disease	No	63	81%
	Yes	15	19%
Body mass index	Normal	14	18%
	Overweight	21	27%
	Obese	43	55%
Comorbidity	None	37	47%
	Diabetes Mellitus	18	23%
	Hypertension	13	17%
	Bronchial Asthma	26	33%
	Renal insufficiency	2	3%

Biochemical measurements:

All patients have low T4 levels. Seventy-five patients have a low T3 level. Only three patients have a normal T3 level. Seventy patients have a high TSH level and eight patients have a normal TSH level. All patients have high anti-Tg and anti-TPO levels.

Grayscale and Doppler ultrasound examination:

All examined patients showed diffusely hypoechoic patterns with diffusely heterogeneous textures. Ill-defined areas of low echogenicity were found in seventy-one patients (91.02 %), which may suggest lymphocytic infiltrate. All patients had reactive (inflammatory) cervical lymph nodes. Seventy-five patients (96.15%) had an average thyroid volume, and three patients (3.85%) had a reduced thyroid volume. No calcification was detected in all patients. Increased vascularity was found in seventy-six patients (97.44%), while only two patients (2.56%) had decreased vascularity. The biochemical and Doppler ultrasound findings are summarized in **Table 3.**

Table 3. Biochemical and Doppler ultrasound parameters

Variable	Mean	SD	P-value
TSH (mIU/L)	12.28	2.34	0.0573
Total T3 (ng/mL)	55.21	2.02	0.0642
Free T3 (pg/mL)	1.26	0.3	0.0917
Total T4 (mcg/dL)	1.23	0.20	0.0753
Free T4 (ng/dL)	0.63	0.17	0.0822
Anti-TPO (U/mL)	335.09	86.21	<0.001
Anti-Tg (U/mL)	372.51	45.45	<0.001
Right ITA PSV (cm/s)	20.7	4.2	<0.001
Right ITA EDV (cm/s)	10.3	2.4	<0.001
Right ITA RI	0.58	0.12	0.0354
Left ITA PSV (cm/s)	17.4	3.3	<0.001
Left ITA EDV (cm/s)	10	4.5	<0.001
Left ITA RI (cm/s)	0.56	0.78	0.0363

TSH= Thyroid-stimulating hormone. ITA= Inferior thyroid artery, PSV=Peak systolic velocity. Anti-TPO=Anti-thyroid peroxidase antibody, Anti-Tg=Anti-thyroglobulin antibody, EDV=End-diastolic volume, RI=Resistive index.

Correlation between variables:

We found a strong correlation between thyroid antibodies and the Doppler ultrasound parameters. Anti-Tg is strongly correlated with PSV of the inferior thyroid arteries on both sides (r=0.750, P<0.001on the right side; r=0.733, P<0.001 on the left side).

Anti-Tg is also strongly correlated with the EDV of the inferior thyroid arteries (r=0.652, P<0.001 on the right side; r=0.593, P<0.001 on the left side).

Also, there was a strong correlation between Anti-Tg and RI of both inferior thyroid arteries (r=-0.561, P=0.0354 on the right side and r=-0.582, P=0.0363 on the left side).

Anti-TPO is strongly correlated with PSV of both inferior thyroid arteries (r=0.856, P<0.001 on the right side; r=0.873, P<0.001 on the left side).

Anti-TPO is strongly correlated with EDV of both inferior thyroid arteries (r=0.901, P<0.001 on the right side; r=0.894, P<0.001 on the left side). Also, there was a strong correlation between Anti-TPO and RI of both inferior thyroid arteries (r=-595, P=0.0384 on the right side and r=-502, P=0.0392 on the left side) (Figures 1 and 2).

We did not find a significant correlation between the other biochemical values (T3, T4, and TSH) and the Doppler ultrasound parameters. The Doppler ultrasound parameters of the right ITA were strongly correlated with those of the left one (r=0.956, P<0.001).

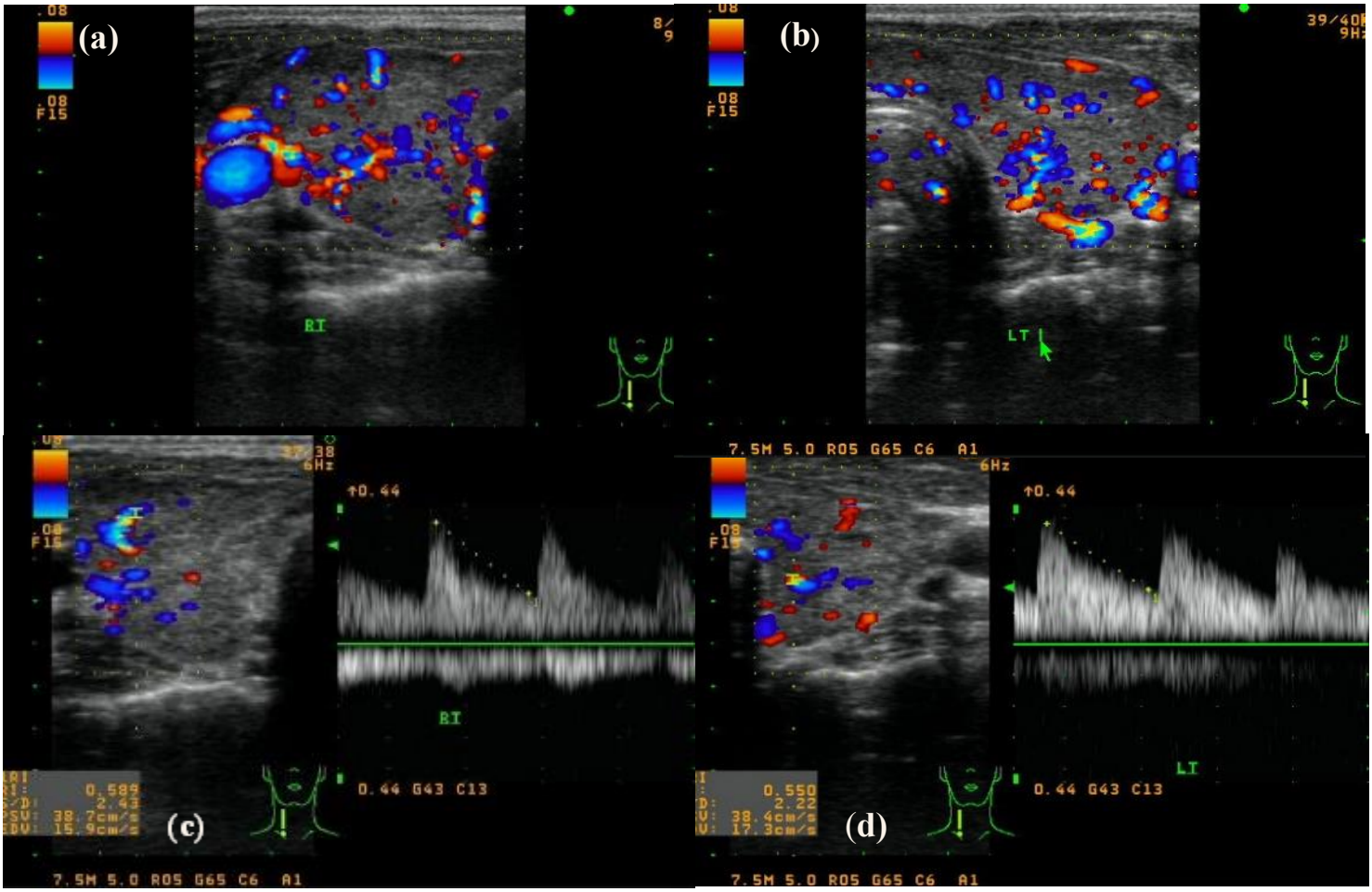

Figure 1: A 24-year-old female patient with chronic autoimmune thyroiditis. Both thyroid lobes show heterogeneous echogenicity and hypervascularity (a,b). PSV, EDV, and RI of the right inferior thyroid artery are 38.7 cm/sec., 15.9 cm/sec., and 0.59 respectively (c). PSV, EDV and RI of the left inferior thyroid artery are 38.4 cm/sec., 17.3 cm/sec., and 0.55 respectively(d). TSH level was 19.62 mIU/L, Total T3 was 18.23 ng/mL, free T3 was 0.89 pg/mL, Total T4 was 0.85 mcg/dL, free T4 was 0.58 ng/dL, Anti-TPO was 638.26 U/mL, and Anit-Tg was 748.39 U/mL.

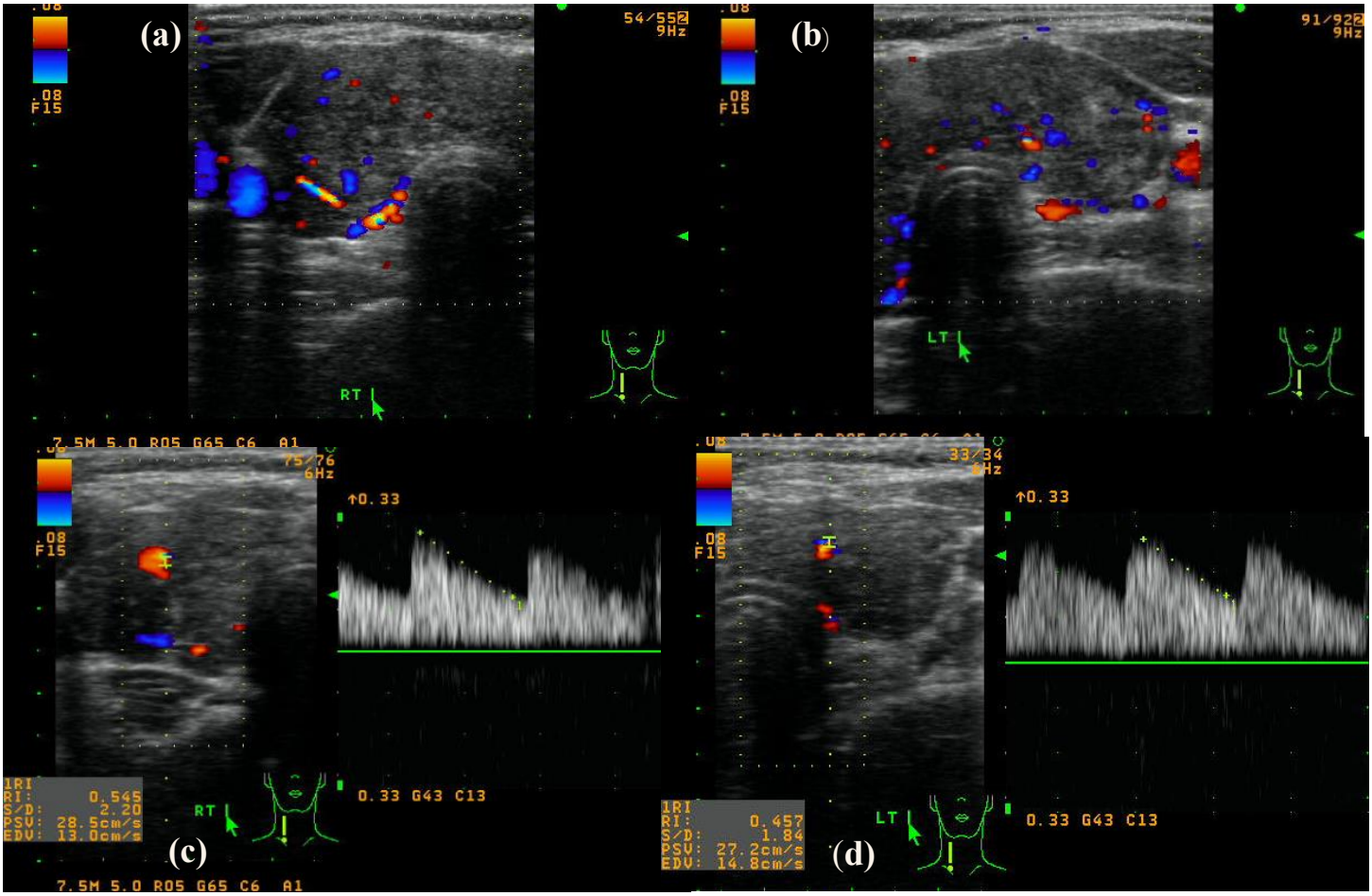

Figure 2: A 28-year-old female patient with Hashimoto's thyroiditis. Both thyroid lobes show heterogeneous echogenicity and hypervascularity (a, b). PSV, EDV and RI on the right side are 28.5 cm/sec., 13.0 cm/sec., and 0.55 respectively (c). PSV, EDV and RI on the left side are 27.2 cm/sec., 14.8 cm/sec., and 0.46 respectively (d). TSH level was 16.48 mIU/L, Total T3 was 23.78 ng/mL, free T3 was 2.33 pg/mL, Total T4 was 2.15 mcg/dL, free T4 was 0.62 ng/dL, Anti-TPO was 576.73 U/mL, and Anit-Tg was 594.62 U/mL.

DISCUSSION

Hashimoto's thyroiditis is considered the most frequent autoimmune thyroid disease and a common etiology of hypothyroidism. The patients suffering from this disease have antibodies against thyroglobulin (anti-Tg) and thyroid peroxidase enzymes (anti-TPO). These thyroid antibodies are used in the detection and evaluation of the severity of Hashimoto's thyroiditis patients [15-18].

Grayscale and color Doppler ultrasound is the imaging modality most frequently used to diagnose diffuse and nodular thyroid diseases. It is used to evaluate echogenicity, echotexture, margins, and vascularity. There is an overlap in the sonographic features among various causes of diffuse thyroid disease [19].

The diagnosis of Hashimoto's thyroiditis is typically done clinically, laboratory, and radiologically. Most of these patients present with symptoms of hypothyroidism and usually have a high TSH level and low T3 and T4 levels. Anti-Tg antibodies are found in approximately 70 % of cases, whereas Anti-TPO antibodies are found in 90 to 95% of cases [19].

By grayscale ultrasound, the features of Hashimoto's thyroiditis are widely variable and it is challenging to differentiate it from other thyroid pathology [20]. The thyroid gland is usually heterogeneous in echotexture with multiple hypoechoic micronodules [21]. On Doppler ultrasound examination, the thyroid gland is typically hypervascular, and this hypervascularity does not reflect thyrotoxicosis. In contrast, hypervascularity is more common in hypothyroid Hashimoto's patients [22].

In this study, increased vascularity was found in 76 patients (97.44%), and this may be due to intra-thyroid

angiogenesis in Hashimoto thyroiditis patients. We found a strong correlation between thyroid antibodies and PSV, EDV, and RI of the inferior thyroid arteries on both sides. This finding may be helpful in the follow-up of these patients and monitoring the efficacy of their treatment by using Doppler ultrasound examination. Our Doppler ultrasound parameters in Hashimoto's thyroiditis are similar to the previous studies [10, 23]. Previous studies reported that Doppler ultrasound helps monitor the therapeutic response of Graves' disease patients [24]. This is the first study that tried to find a correlation between Doppler ultrasound parameters and thyroid antibodies in patients with Hashimoto's thyroiditis.

One limitation of this work is the relatively small number of cases. Another limitation is the absence of follow-up of these cases after the medical treatment.

Further studies should be done to test the role of Doppler ultrasound in the assessment of the medical treatment of Hashimoto's thyroiditis by comparing the Doppler ultrasound parameters of the inferior thyroid arteries before and after treatment.

CONCLUSION

Doppler ultrasound examination helps evaluate Hashimoto's thyroiditis patients. Peak systolic velocity, end-diastolic volume, and resistive index of the inferior thyroid arteries in these patients are strongly correlated with the thyroid antibodies. This result may help in the assessment of the response to treatment in Hashimoto's thyroiditis.

Conflict of interest: The researchers don't have any conflict of interest regarding the publications of this research.

Financial support: We did not receive any financial support for the work.

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