

Diagnostic Accuracy of Ultrasound in Diffuse Form of Hashimoto's Thyroiditis

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ABSTRACT

BACKGROUND

Hashimoto's thyroiditis is a common thyroid disorder of autoimmune aetiology with circulating antithyroid antibodies. It has a high prevalence of 12 % among the female population and has varied clinical and serological presentation. We wanted to describe the sonological findings in diffuse form of Hashimoto's thyroiditis and assess the diagnostic accuracy of different sonological parameters in the detection of Hashimoto's thyroiditis.

METHODS

Ultrasound features associated with Hashimoto's thyroiditis namely gland enlargement, echogenicity, presence of micronodules, echogenic septations, ill-defined macroscopic areas, surface micro-lobulations, vascularity, and level VI cervical lymph nodes were evaluated in 60 patients with diagnosed Hashimoto's thyroiditis and were compared with 60 control subjects. Sensitivity, specificity, positive predictive value and negative predictive values were calculated for separate sonological features.

RESULTS

Altered echotexture of the gland was seen in all patients with Hashimoto's thyroiditis. Echogenic septations showed most sensitivity (83.3 %) in detecting Hashimoto's thyroiditis. Presence of micro nodules was found to have high specificity (98.3 %), but decreased sensitivity. Surface microlobulations had a positive predictive value and specificity of 100 % in the diagnosis of Hashimoto's thyroiditis. Macroscopic ill-defined areas were found to have intermediate accuracy values. Increase in the gland vascularity on Doppler and presence of benign cervical lymph nodes in level VI region were found to have high sensitivity and specificity values.

CONCLUSIONS

Echogenic septation was the most sensitive parameter in diagnosing Hashimoto's thyroiditis, a finding which represented the ongoing fibrosis within the gland. Sonological findings of micronodules and surface micro-lobulations were found to be specific to Hashimoto's thyroiditis. Along with the assessment of gland vascularity and level VI cervical lymph nodes, ultrasound has high specificity and sensitivity in the diagnosis of Hashimoto's thyroiditis.

KEYWORDS

Autoimmune, Thyroiditis, Hashimoto's, Micronodules, Ultrasound, Accuracy, Sensitivity, Specificity, Septations

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BACKGROUND

Hashimoto's thyroiditis, which is also referred to as chronic lymphocytic thyroiditis is a common thyroid disorder of autoimmune aetiology where there is infiltration of the thyroid by T and B cells, reactive to thyroid antigens. The activated B cells generate auto antibodies to thyroglobulin, thyroid peroxidase, and thyroid-stimulating hormone receptor. The activated cytotoxic T cells elicits destruction of the thyroid parenchyma.¹

The histopathologic appearance of Hashimoto's thyroiditis is a result of the inflammatory process in response to the activated B and T cells which results in lymphocyte aggregates with germinal centres, oxyphilic changes of epithelial cells and small thyroid follicles with sparse colloid initially, followed by varying degrees of fibrosis.² The aetiology of Hashimoto's thyroiditis is unknown. However, it is thought to be multifactorial with genetic predispositions and environmental factors both playing a role. Commonly associated environmental factors are infection and high iodine intake.³

Hashimoto's thyroiditis has a strong female predilection and affects about 2 % of all women in the between the ages of 30 to 50 years,⁴ Hashimoto's thyroiditis has extremely variable clinical and serological presentation. Hashimoto's thyroiditis most commonly presents with hypothyroidism and is in fact one among the common causes of hypothyroidism in woman. But it has variable presentation and in the early phase of the disease can present as hyperthyroidism. A substantial subset of population with Hashimoto's thyroiditis can be euthyroid to begin with. Some patients remaining symptomatic without physical signs or symptoms.⁵ Mild hypothyroidism symptoms is seen in 20 % of patients initially and rest develops hypothyroidism over several years.¹ The clinical diagnosis is established by the presence of high levels of circulating autoantibodies to thyroglobulin and thyroid peroxidase. Antithyroglobulin antibodies are present in 55 % – 90 % of patients and TPO (Thyroid Peroxidase) antibodies are present in 90 % – 95 %.⁶

High resolution ultrasound is the primary and most commonly used imaging modality for the assessment of thyroid gland.

Ultrasound is a relatively cheap and widely available investigation and has the added advantage of being safe as it does not use radiation or cause tissue damage. Being a non-invasive procedure, it is more affordable and offers higher patient comfort than blood investigations or other imaging modalities. There is no need for discontinuation of medications or prior preparations needed for ultrasound examination. Though conventionally used for the assessment of thyroid nodules, ultrasound is widely used now for the evaluation of diffuse thyroid diseases as well. It is also used for guiding fine needle aspiration biopsy. The gland size and echogenicity, nodule size and characterisation, calcifications and specific patterns are easily identified on ultrasound.⁷

The thyroid tissue has a uniform echotexture and a homogeneous echogenicity which is higher than that of the overlying strap muscles. The thyroid lobes normally measure

1.3 - 1.8 cm in anteroposterior diameter and when it is more than 2 cm, is considered to be enlarged. Lymphatic drainage of thyroid gland is predominantly to level VI cervical lymph nodes.⁸

On ultrasound, two different forms are described. The diffuse form of Hashimoto's thyroiditis manifests as altered parenchymal echotexture, commonly with decreased echogenicity and associated echogenic septations. The decreased echogenicity is contributed by the lymphocyte infiltration in the gland. Presence of multiple scattered micronodules of size varying from 1 to 7 mm is also a strong predictor.¹ As the disease progresses, the thyroid gland presents an aspect of chronic hypertrophic thyroiditis, which is characterized by poorly defined hypoechoic areas with interspersed fibrous layers, which appear as echogenic septations and gives the gland a pseudo lobular appearance.⁹ In few cases, further disease progression occurs, with the gland becoming atrophic, when the gland shrinks in size, shows diffusely heterogeneous parenchymal echotexture and ill-defined contours.¹⁰

The nodular focal variant of Hashimoto's thyroiditis, usually presents as a small hypoechoic thyroid nodule with ill-defined borders and is often difficult to differentiate from a malignant thyroid nodule. The diagnosis can be made with certainty only with fine needle aspiration biopsy. These focal thyroiditis nodules can have varied patterns of flow which contribute to non-specificity of Doppler ultrasound in their evaluation.¹⁰

In this study, the sonological findings in diffuse form of Hashimoto's thyroiditis were studied and the diagnostic accuracy of different sonological parameters in diagnosing Hashimoto's thyroiditis were calculated.

METHODS

The study was designed as a diagnostic test evaluation conducted among all patients with Hashimoto's thyroiditis visiting Believers Church Medical College, Thiruvalla. The duration of the study was 1 year from December 2016 to December 2017.

Sample size was calculated as 40 with pre-determined values of sensitivity, marginal error and prevalence of disease at 90 %, 0.10 and 12 % respectively and according to the sample size calculation formula by Hajian-Tilaki et al.¹¹

The patients diagnosed to have diffuse thyroid disease on high resolution ultrasound and with diagnosed to have Hashimoto's thyroiditis either by a positive biopsy / FNAC report or antithyroglobulin or anti TPO antibody positivity were included in the study. Patients with diffuse thyroid disease on high resolution ultrasound but without an antibody assay or biopsy were excluded from the study. Another 60 patients who had come for ultrasound evaluation of thyroid for varied reasons and without evidence of Hashimoto's thyroiditis either on FNAC / biopsy were included as controls.

Data was collected using a sonological parameter. Data collection chart and finding were entered in Microsoft Excel software. SPSS version 2.0 was used for statistical analysis.

The sensitivity, specificity, positive and negative predictive values were calculated for the separate sonological features. The sonological features included in the study were gland enlargement, gland echogenicity, presence of micronodules, echogenic septations, ill-defined macroscopic areas, surface micro-lobulations, vascularity and level VI cervical lymph nodes.

The thyroid was assigned hypoechoic when it showed echogenicity equal to or less than that of the overlying strap muscles. Nodules of size varying from 2 – 6 mm, irrespective of echogenicity and borders were called micronodules. Large areas more than 6 mm were classified as macronodules. Vascularity was assessed subjectively by colour Doppler and was categorised as increased, decreased or normal. The surface micro lobulations were identified by gentle and abrupt undulations in the gland surface. The presence of level VI cervical lymph nodes was noted irrespective of their size and fat hilum.

RESULTS

A total of 128 patients were diagnosed to have diffuse thyroid disease during the course of the study. Of these patients with coexisting nodules, and those without thyroid antibody assay or biopsy to establish a final diagnosis were excluded. 60 patients were diagnosed to have Hashimoto’s thyroiditis by the case definition. Of the 60 patients diagnosed to have Hashimoto’s thyroiditis, 56 were female.

Majority of the patients were in the age group of 19 - 40 years (45 %), followed by 41 - 60 years (30 %). The youngest patient was 9 years old and the oldest 65 years. The female to male ratio in our study was 7.6 : 1.

Majority of the patients presented with the complaints of neck swelling or dysphagia (64 %). Rest were referred for sonological examination after an altered thyroid function test (41 %) and a minority (10 %) was evaluated for neck pain.

Of the 60 patients with Hashimoto’s thyroiditis, TSH was normal in 27, raised in 28 and low in 5 patients. 44 patients with Hashimoto’s thyroiditis had thyroid gland enlargement whereas 16 had normal sized glands. Hypoechoic gland was found in 41.6 % of the Hashimoto’s patients while rest had iso or hyperechoic thyroid gland. The most common sonographic feature associated with Hashimoto’s was echogenic septations which were found in 50 patients, followed by multiple micro nodules which were seen in 40 patients.

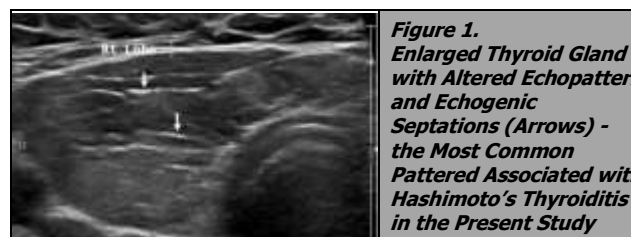
Increased gland vascularity was found in 47 Hashimoto’s patients and 16 of the control patients. Prominent or enlarged level VI cervical lymph nodes were noted in 49 of Hashimoto’s patients and a total of 58 study subjects. The distribution of different sonological parameters in patients with and without Hashimoto’s thyroiditis is provided in Table 1. The sensitivity and specificity of individual sonological features are provided in Table 2.

Sonological Parameters		Hashimoto’s Thyroiditis	
		Positive	Negative
1. USG Enlargement	Present	44	24
	Absent	16	36
2. Echogenicity	Hypoechoic	25	7
	Isoechoic	35	53
3. Echo Texture	Altered	60	7
	Normal	0	53
4. Micro Nodules	Present	15	1
	Absent	45	59
5. Echogenic Septations	Present	50	3
	Absent	10	57
6. Macroscopic Ill-Defined Areas	Present	16	10
	Absent	44	50
7. Surface Micro Lobulations	Present	23	0
	Absent	37	60
8. Increased Vascularity	Present	47	16
	Absent	13	44
9. Level VI Cervical Lymph Node	Present	49	9
	Absent	11	51

Table 1. Distribution of Different Sonological Parameter within the Study Population

Sl. No	Ultrasound Characteristic	Sensitivity (95 % CI)	Specificity (95 % CI)	Positive Predictive Value (95 % CI)	Negative Predictive Value (95 % CI)
1.	USG Enlargement	73.33 % (60.34 % to 83.93 %)	60.00 % (46.54 % to 72.44 %)	64.71 % (56.48 % to 72.14 %)	69.23 % (58.50 % to 78.22 %)
		41.67 % (29.07 % to 55.12 %)	88.33 % (77.43 % to 95.18 %)	78.12 % (62.60 % to 88.40 %)	60.23 % (54.54 % to 65.65 %)
2.	Echogenicity	100.00 % (94.04 % to 100.00 %)	88.33 % (77.43 % to 95.18 %)	89.55 % (81.03 % to 94.50 %)	100.00 %
		25.00 % (14.72 % to 37.86 %)	98.33 % (91.06 % to 99.96 %)	93.75 % (67.16 % to 99.10 %)	56.73 % (53.02 % to 60.36 %)
3.	Echo Texture	83.33 % (71.48 % to 91.71 %)	95.00 % (86.08 % to 98.96 %)	94.34 % (84.61 % to 98.06 %)	85.07 % (76.35 % to 90.96 %)
		26.67 % (16.07 % to 39.66 %)	83.33 % (71.48 % to 91.71 %)	61.54 % (44.17 % to 76.39 %)	61.54 % (44.17 % to 76.39 %)
4.	Micro Nodules	38.33 % (26.07 % to 51.79 %)	100.00 % (94.04 % to 100.00 %)	100.00 % (100.00 % to 100.00 %)	61.86 % (57.05 % to 66.44 %)
		78.33 % (65.80 % to 87.93 %)	73.33 % (60.34 % to 83.93 %)	74.60 % (65.42 % to 82.02 %)	77.19 % (67.14 % to 84.86 %)
5.	Echogenic Septations	81.67 % (69.56 % to 90.48 %)	85.00 % (73.43 % to 92.90 %)	84.48 % (74.66 % to 90.96 %)	82.26 % (72.90 % to 88.88 %)
		81.67 % (69.56 % to 90.48 %)	85.00 % (73.43 % to 92.90 %)	84.48 % (74.66 % to 90.96 %)	82.26 % (72.90 % to 88.88 %)

Table 2. Summary of Diagnostic Accuracy of Ultrasound Characteristics in the Identification of Hashimoto’s Thyroiditis



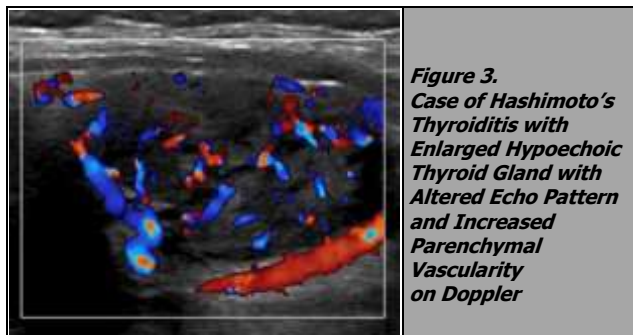


Figure 3.
Case of Hashimoto's
Thyroiditis with
Enlarged Hypoechoic
Thyroid Gland with
Altered Echo Pattern
and Increased
Parenchymal
Vascularity
on Doppler

DISCUSSION

Thyroid enlargement was seen in 44 patients with Hashimoto's thyroiditis and 24 of the control subjects. All the patients with Hashimoto's thyroiditis in our study had an altered echotexture on sonography. This is thought to be due to the diffuse inflammation of the gland and hence can be seen in other forms of thyroiditis including Riedel's thyroiditis, acute bacterial thyroiditis and De Quervain thyroiditis. These conditions usually differ in their clinical manifestations¹² and can be differentiated clinically.

Among the different sonological parameters studied, echogenic septations showed most sensitivity (83.3 %) in detecting Hashimoto's thyroiditis. These septations correlate with the varying degrees of fibrosis within the gland. Echogenic septations has a positive and negative predictive value of 94.3 % and 85 % in the present study. These findings compare well with the previous study by Kapali, et al¹² which studied echogenic septations among others sonological features in Hashimoto's thyroiditis.

Micronodules were found to have a high positive predictive value (93.75 %) and high specificity (98.3 %), in the present study. Similar findings were seen in the studies by Kapali, et al¹² and Islin et al.¹³ However micronodules has decreased sensitivity of 25 %, seen only in 15 out of 60 Hashimoto's patients in our study.

Diffuse hypoechoogenicity of the gland, which is attributed to diffuse lymphocytic infiltration of the gland was seen in 25 of patients with the Hashimoto's and has a specificity of 88 % and sensitivity of only 41 %. Our findings are comparable with the previous study by Pishdad P. et al.⁷ However the study by Kapali, et al¹² showed increased specificity and sensitivity values for hypo echogenicity of the gland.

Surface micro lobulations had a positive predictive value and specificity of 100 % in our study. These develop as a result of sub capsular nodules which contribute to undulation of the thyroid gland margins. This finding was observed in 23 patients. Previous study by Islin et al¹³ also demonstrates similar diagnostic values.

Macroscopic ill-defined areas were observed in 16 Hashimoto's patients and had a high specificity of 83.3 %. This finding is thought to be seen as the gland progresses into that of a chronic hypertrophic phase. Not many studies could be found in the literature which evaluated the role of ill-

defined macroscopic areas within the gland, probably due to its very low sensitivity in diagnosing Hashimoto's thyroiditis.

Slight to marked increase in the gland vascularity on Doppler was found have a sensitivity and specificity of 78.33 % and 73.33 % for Hashimoto's thyroiditis. Increased gland vascularity is associated with the development of hypothyroidism. Similar findings were seen in a study by Islin et al.¹³ Diffuse hypervascularization on Doppler examination, similar to the pattern seen in Graves' disease could also be demonstrated in initial stages of Hashimoto's thyroiditis. In the later phases of the disease when the gland atrophies due to profound fibrosis, reduced vascularity is seen on colour Doppler with associated diffuse gland heterogeneity.

Infrathyroidal and pretracheal areas (level VI cervical lymph nodes) are the preferred sites of lymphatic drainage of thyroid and enlarged lymph nodes in these areas are seen in inflammatory conditions of the thyroid. Islin et al¹³ showed the presence of lymph nodes in infrathyroidal and pretracheal locations indicated Hashimoto's thyroiditis with specificity of 97.8 % and PPV (Positive Predictive Value) of 96.2 %. Enlarged level VI cervical lymph nodes were found to have a positive predictive value and specificity of 84.4 % and 85.00 % respectively in our study.

Limitations

The present study takes into account only the diffuse form of Hashimoto's thyroiditis. This could be feature attributed to the high sensitivity of altered echotexture. The nodular form of Hashimoto's thyroiditis presents either as solitary or multiple thyroid nodules and nodules in the background of thyroiditis. The association of different sonological parameters with thyroid status of patients with Hashimoto's thyroiditis could also be further studied upon.

CONCLUSIONS

Other than altered echotexture of the gland, echogenic septation is the most sensitive predictor of Hashimoto's thyroiditis, followed by increased gland vascularity. Presence of surface micro-lobulations and micronodules is found to be highly specific for Hashimoto's thyroiditis. Ill-defined macroscopic areas and surface micro lobulations were found to have high specificity and low sensitivity in the diagnosis of Hashimoto's disease and hence to be used as adjuvant findings. Additional findings of level VI cervical lymph nodes of benign morphology help in increasing the accuracy of ultrasound.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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