

Hashimoto's Thyroiditis - Diagnostic Accuracy of Antimicrosomal Antibodies

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Abstract

Introduction: Hashimoto's thyroiditis (HT) is an autoimmune disease in which the thyroid gland is gradually destroyed by a variety of cell- and antibody-mediated immune processes.

Objectives: To compare the sensitivity, specificity, and diagnostic accuracy of antimicrosomal antibody and fine needle aspiration cytology (FNAC), and ultrasonography in diagnosis in HT.

Materials and Methods: Descriptive study with diagnostic test evaluation of 200 patients was carried out in the Department of Surgery in Thiruvananthapuram Medical College, and in whom thyroidectomy being done during the period 2013-2014 for the duration of 18 months. 100 patients were with HT and 100 patients were taken as control.

Results: The result indicates that in people with nodular goiter, sensitivity and specificity of antithyroid peroxidase antibody (TPO-Ab) test to detect HT were estimated to be 88% and 89%, respectively, with an overall accuracy of 88.5%. The positive predictive values (PPVs) and negative predictive values (NPVs) were 88.9% and 88.1%, respectively, and in patients with nodular goiter, the sensitivity and specificity of FNAC to detect HT were estimated to be 88% and 91%, respectively, with an overall accuracy of 89.5%. The PPV and NPVs were 90.7% and 88.3%, respectively.

Conclusion: There is a high degree of concordance between serological and cytological findings of HT in people with nodular goiter. Assays of anti-TPO-Abs in this study have a high sensitivity, specificity, and accuracy to detect HT which justifies the use of anti-TPO-Abs as a screening test in the evaluation of patients with nodular goiter.

Key words: Accuracy, Antibodies, Antithyroid peroxidase, Fine needle aspiration cytology, Hashimoto's thyroiditis, Positive and negative predictive value

INTRODUCTION

The first report of chronic thyroiditis, struma lymphomatosa was described by Hakaru Hashimoto in 1912.¹⁻³ Hashimoto's thyroiditis (HT) is an autoimmune disease in which the thyroid gland is gradually destroyed by a variety of cell- and antibody-mediated immune processes.² The first report of chronic thyroiditis, struma lymphomatosa was described by Hakaru Hashimoto in 1912.¹⁻³ It was the first disease to be recognized as an autoimmune disease. The mean annual

incidence rate of autoimmune hypothyroidism is up to 4 per 1000 women and 1 per 1000 men.²

A family history of thyroid disorders is common; HLA-DR3, HLA-DR4, and HLA-DR5 are the best documented genetic risk factors.² Hashimoto's may be associated with CTLA-4 gene. Gross examination, the thyroid gland is usually mildly enlarged throughout and has a pale gray tan cut surface that is granular nodular and firm.⁴ On microscopy, the gland is diffusely infiltrated by small lymphocytes and plasma cell and occasionally show well developed germinal centers. Thyroid follicles are smaller than normal with reduced amount of colloid and increased interstitial connective tissue (Figure 1). The follicles are lined by Hurthle or Askanazy cells (Figure 2) which are characterized by abundant eosinophilic granular cytoplasm.⁴ Follicular cell destruction often with mononuclear cell invasion of the follicular spaces is a diagnostic pathological finding.³

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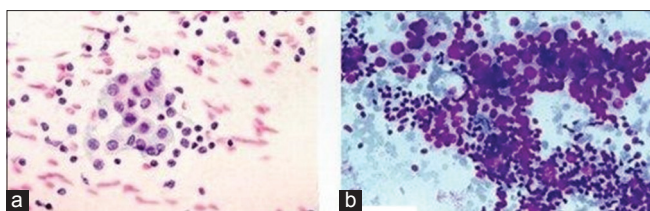


Figure 1: (a and b) Hashimoto's thyroiditis cytology images

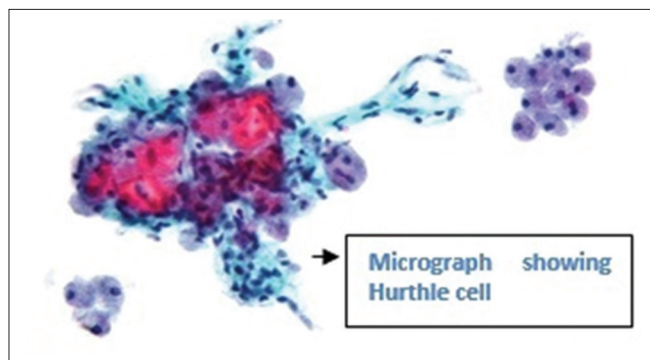


Figure 2: Hurthle cell

The diagnosis of HT can be made only by histopathology.^{5,6} Antimicrosomal antibody represents an important tool in the diagnosis of autoimmune thyroiditis.³ Antimicrosomal antibody test is less invasive and can be used to assess disease activity in patients that have developed such antibodies. Value >34.0 IU/ml generally are associated with autoimmune thyroiditis.⁵ The median disappearance time is 6.3 years for thyroid peroxidase antibodies (TPO-Abs).⁷ High TPO-Abs is associated with poor physical and psychological well-being and appears to predict future health perception in hypothyroidism patients.⁶ HT patients benefit from surgery at least for palliation and to relieve the persistence of symptoms.⁸ Hashimoto's thyroiditis has a predisposition to turn into malignant thyroid tumors especially differentiated thyroid cancer.

Aim and Objectives

To compare the sensitivity, specificity, and diagnostic accuracy of antimicrosomal antibody and fine needle aspiration cytology (FNAC) and ultrasonography (USG) in diagnosis in HT.

MATERIALS AND METHODS

A prospective observational study was conducted at Medical College Thiruvananthapuram.

Inclusion Criteria

All patients above 12 years of age admitted in the Department of Surgery in Trivandrum medical college and in whom thyroidectomy being done. Thyroidectomy patients with clinical or cytological or serological

pre-operative diagnosis of HT will be the subject of study. Incidentally detected HT from thyroidectomy specimens will also be included.

Exclusion Criteria

Those not willing to participate in the study and patients with history of thyroid surgery or radioiodine therapy patients with radiation exposure to neck are excluded from the study.

- Study period is from March 21, 2012 to September 20, 2013.
- Study tool is antimicrosomal antibody titer.

Based on sensitivity and specificity and concerting PSM Department, sample size. I have taken 100 cases of histologically proven HT and 100 cases of histologically negative HT. Thyroid stimulating hormone (TSH) was measured by immunochemiluminometric assay with analytical sensitivity 0.01 mIU/ml. The serum anti-TPO-Abs were measured by immunochemiluminescent assay with a reference range value <34 IU/ml as negative.⁵

Following steps were followed during analysis of anti-TPO-Abs:

1. 1st incubation: 20 μ l of sample are incubated with anti-TPO-Abs labeled with a ruthenium complex
2. 2nd incubation: After addition of biotinylated TPO and streptavidin-coated microparticles, the anti-TPO-Abs in the sample compete with the ruthenium-labeled anti-TPO-Abs for the biotinylated TPO antigen. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin.
3. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with Procell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
4. Results are determined via a calibration curve which is instrument-specific generated by 2-point calibration and a master curve is provided via the reagent barcode.

Thyroid FNAC was performed on one or both lobes of the gland. Each aspiration was expelled and smeared on glass slides. The slides were immediately wet-fixed in 95% ethyl alcohol for Papanicolaou staining. Satisfactory smear was defined as one that contained five to six groups of well-preserved cells with at least 10-15 cells in each group. The diagnosis of HT for FNAC was made based on the presence of lymphocytes, plasma cells, and Hurthle cells.

Statistical Method Analysis

The normally distributed data were expressed as means, while the variables with a skewed distribution were reported

as median (interquartile range). The sensitivity, specificity, and receiver operating characteristic (ROC) curves were calculated by a two-by-two contingency table, and the optimal cut-off point was yielded from the closest point to the left upper corner of the ROC curve. All statistical analyses were performed with the SPSS Statistical Package (version 13.0). Values of $P < 0.05$ were considered statistically significant.

Ethics

This study was approved from the Human Ethics Committee, Medical College, Thiruvananthapuram on date March 21, 2012. Informed written consent was obtained from all participants.

RESULTS

The total of 200 patients participated in the study. 100 patients with histologically proven HT and age and sex matched 100 patients with histologically negative HT after informed consent were enrolled in the study.

When results of antimicrobial antibodies were plotted in ROC curve, the area under curve was 0.944, which is suggestive of assays of anti-TPO-Abs in this study have a high sensitivity, specificity, and accuracy to detect HT (Figure 3).

The results indicate that in people with goiter, the sensitivity, specificity of positive antimicrobial antibody in diagnosis of HT were 88% and 89%, respectively, with an overall accuracy of 88.5% and positive predictive values (PPVs) and negative predictive value (NPV) were 88.9% and 88.1%, respectively, (Table 1).

Sensitivity, specificity, overall accuracy, PPV of FNAC in diagnosis of HT is 88%, 91%, 90.7%, 88.3% and 89.5% respectively (Table 2).

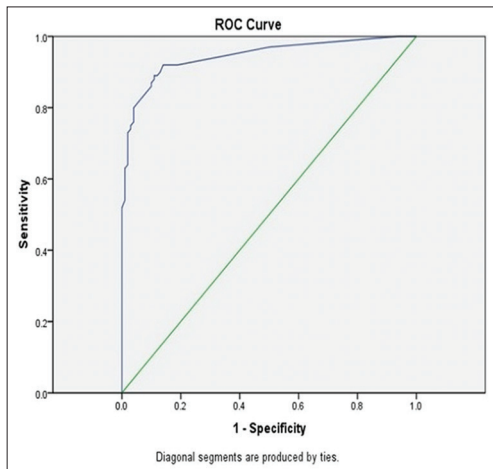


Figure 3: Receiver operating characteristic curve of results of antimicrobial antibodies

Sensitivity, specificity, PPV, NPV, and accuracy of USG neck in diagnosis of HT is 75%, 82%, 80.6%, 76.6%, and 78.5%, respectively, (Table 3).

DISCUSSION

HT is an autoimmune disease in which the thyroid gland is gradually destroyed by a variety of cell- and antibody-mediated immune processes over a period. The study on 100 patients of HT showed the following facts. HT is about 15-20 times more common in women than in men and frequently involves people between the ages of 30 and 50 years of age. In this study also, patients were mainly young females with mean age of 41.12 years (Tables 4 and 5). This is similar to most of the available literature although there are studies, which differ in the age of presentation of the diagnosis of HT. In a previous study⁹ from the United Kingdom, patients were mainly older women with mean age at diagnosis being 59 years.

Most of our patients had symptoms of hypothyroidism with a diffuse goiter although nodular presentation was also noted in few cases. Friedman *et al.*¹⁰ found nodular presentation in as many as 80% of their patients.

TSH was elevated in all with either decreased or normal T3, T4. Studies have suggested that impairments of physical, mental, and psychic well-being in patients with HT, but these impairments have been shown to be independent of

Table 1: Comparison of test result to reference standard (“gold standard”) for antimicrobial antibody

Antimicrobial antibody	HPR HT positive	HPR HT negative
Positive	88	11
Negative	12	89

Statistical analysis value of $P=0.000 (<0.05)$ for this study. HPR: Histopathological report, HT: Hashimoto’s thyroiditis

Table 2: Comparison of test result to reference standard (“gold standard”) for FNAC

FNAC	HPR HT positive	HPR HT negative
Positive	88	9
Negative	12	91

HPR: Histopathological report, FNAC: Fine needle aspiration cytology, HT: Hashimoto’s thyroiditis

Table 3: Comparison of test result to reference standard (“gold standard”) for USG neck

USG neck	HPR HT positive	HPR HT negative
Positive	75	18
Negative	25	82

USG: Ultrasonography, HPR: Histopathological report, HT: Hashimoto’s thyroiditis

Table 4: Age distribution of patients/age interval (in years)

Age (in years)	Hashimoto positive	Control
<21	5	4
21-30	19	15
31-40	38	31
41-50	19	30
51-60	9	11
61-70	7	5
>70	3	4

Table 5: Sex distribution of patients

Study patients	Female	Male
Hashimoto positive	88	12
Control	89	11

thyroid dysfunction. HT patients' positive for TPO-Abs showed poorer results when assessed for symptomatic distress as well as in the three domains: Somatization, obsessive compulsive symptoms, and depression (all $P \leq 0.02$). TPO-Abs positivity, defined as TPO-Abs >100 IU/L, significantly predicted poorer physical and psychosocial well-being.⁶

In a study by Ott *et al.*, symptoms such as chronic fatigue, dry hair, chronic irritability, chronic nervousness, a history of breast cancer and early miscarriage, and lower quality of life levels were significantly associated with anti-TPO levels exceeding the cut-off point ($P < 0.05$).¹¹

In the previous study, "The incidence of Hashimoto's disease in nodular goiter: The concordance in serological and cytological findings" by Chehade¹² the sensitivity and specificity of anti-TPO-Ab test to detect HT in nodular goiter were estimated to be 76.38% and 94.23%, respectively. The data in my study shows that the sensitivity, specificity of positive antimicrosomal antibody in diagnosis of HT were 88% and 89%, respectively.

In the previous study by Rho, TPO-Ab titer was significantly associated with the degree of inflammation and the specificity of TPO-Ab detection for HT diagnosis was found to be 96.9%.¹³ These results are almost comparable to my study.

The role of USG neck in evaluating HT is also not well-defined. A characteristic USG neck finding in HT is the diffuse hypoechoic pattern seen in up to 77% of individuals.¹⁴ The data in my study shows that the sensitivity of USG neck is 75%.

This study emphasizes routine pre-operative assessment of antimicrosomal antibodies in diagnostic evaluation of

patients suspected to have HT. This study also proved that in the south Indian population, antimicrosomal antibodies as almost as accurate as histopathology in diagnosing HT.

Antimicrosomal antibodies can be used as a screening tool also in diagnosing subclinical cases owing to its high specificity (89%) which is comparable to invasive histopathology (91%). Being a noninvasive and easily available test, application of this test on large scale is feasible on contrary to histopathology. Although TSH levels are usually elevated in HT, but can be normal in few cases. In these types of cases where diagnosis of Hashimoto is suspected clinically, but TSH is normal, antimicrosomal antibodies can be used preoperatively to diagnose HT because of its high sensitivity and specificity in diagnosing this disease.

CONCLUSION

Anti-microsomal antibodies can be used as a screening test because of its noninvasive nature and high specificity. Statistical analysis value of $P = 0.000$ (< 0.05) for this study. Histopathology is invasive, so cannot be used as screening test but its remains as "Gold standard" test because of its highest sensitivity and specificity.

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