

# Cytomorphological, Biochemical & Radiological Correlation in Hashimoto's Thyroiditis

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## Abstract:

**Background:** Hashimoto's thyroiditis is synonymous with chronic lymphocytic thyroiditis and autoimmune thyroiditis. It is an autoimmune disease that affects women more frequently than men and is associated with hypothyroidism, euthyroidism or occasionally hyperthyroidism. The prevalence rate of Hashimoto's thyroiditis is 1–4% with incidence of 30–60/100000 population per year. Hashimoto's thyroiditis can be graded on cytomorphological features of FNAC. In this study an attempt has been made to correlate the grades of Hashimoto's thyroiditis with biochemical and ultrasonography findings.

**Methods:** A total of 80 patients diagnosed on FNAC as Hashimoto's thyroiditis were included in the study. Quantitatively FNAC smears were evaluated and graded based on the criteria given by Bhatia et al. Thyroid function test (TFT) was used to determine the blood concentrations of thyroid hormones. USG of thyroid gland was performed by using high resolution ultrasound machine with 5 – 10 MHz Broad band linear transducer.

**Results:** Females (95%) were affected more than males (5%). Maximum number of cases were seen between 2nd to 4th decade of life. 32.5% patients had grade I thyroiditis. 41.25% had grade II disease. Grade III thyroiditis was noted in 26.24% patients. 50% cases were biochemically hypothyroid, 42.64% cases were euthyroid and 7.35 % cases were hyperthyroid. Diffuse thyroiditis was observed in 50.81% cases, goitre was observed in 34.42% cases, thyroid nodules were observed in 8.19% cases and normal study was seen in 6.55% cases by ultrasonography.

**Conclusions:** Higher grades of Hashimoto's thyroiditis in FNAC are more associated with abnormal biochemical findings. Diffuse thyroiditis can occur in the early stage of the disease (grade I) even before overt thyroid failure and is the strong predictor of the autoimmune process even when the disorder has not been suspected clinically. A combined approach of cytological grading of Hashimoto's thyroiditis along with ultrasonography and biochemical levels can detect subclinical hypothyroid state and provide a guide to therapy.

**Keywords:** Fine needle aspiration cytology, Hashimoto's thyroiditis, Autoimmune thyroiditis, Hypothyroid, Ultrasonography.

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## Introduction

Hashimoto's thyroiditis, was first described by Hakaru Hashimoto in 1912. It is synonymous with chronic lymphocytic thyroiditis and autoimmune thyroiditis.<sup>1</sup> It is an autoimmune disease that affects women more frequently than men and is associated with hypothyroidism, euthyroidism or occasionally hyperthyroidism. However, most cases present with hypothyroidism. The most important antibody directed against the thyroid tissue is thyroid peroxidase.<sup>2</sup> The prevalence rate of Hashimoto's thyroiditis is 1–4% with incidence of 30–60/100000 population per year.<sup>3</sup> It has been seen that iodine supplementation in iodine deficient areas increases the prevalence of lymphocytic infiltration of thyroid by three-fold, with 40 % increase

in prevalence of antithyroid antibodies in serum over 0.5 to 5 years.<sup>4</sup>

Clinically Hashimoto's thyroiditis can present as a diffuse or nodular swelling being totally asymptomatic.<sup>1</sup> Despite the availability of several tests for diagnosis of Hashimoto's thyroiditis, Fine Needle Aspiration Cytology (FNAC) remains the gold standard.<sup>5</sup> FNAC is simple, cost effective, safe and a sensitive & specific diagnostic tool in diagnosing Hashimoto's thyroiditis.<sup>1</sup> Hashimoto's thyroiditis, is the second most common thyroid lesion diagnosed on FNAC after goiter.<sup>3</sup> In the present study an effort was made to grade Hashimoto's thyroiditis on FNAC smears and to know their significance in predicting thyroid injury by comparing with biochemical and ultrasonography findings.<sup>5</sup>

## Materials and Methods

This was a retrospective study conducted in the department of pathology, S.Nijallingapa Medical College, Bagalkot, Karnataka from January 2013 to December 2014. A total of 80 cases of Hashimoto's thyroiditis were included in this study. The study was approved by institutional ethical committee.

**Inclusion criteria:** Newly diagnosed cases of Hashimoto's thyroiditis.

**Exclusion criteria:**

1. Subjects receiving either thyroxine or any other drug known to interfere with thyroid function at the time of evaluation.
2. Old cases of Hashimoto's thyroiditis.
3. Any other additional lesions observed in association with Hashimoto's thyroiditis diagnosed on cytology.

FNAC of thyroid was carried out by using non aspiration/aspiration technique with 23 gauge needle attached 10 ml syringe. In case of large swelling multiple point aspiration was carried out. Smears were air dried and stained with leishman and Giemsa. Alcohol fixed slides were stained with hematoxylin and eosin. The smears were evaluated by a single pathologist. Hamberger's criteria<sup>6</sup> was applied while judging the adequacy of the smears. In case unsatisfactory material, was obtained a repeat aspiration was done but no more than 2 aspirations were tried on each patient. Qualitative criteria used for cytologic diagnosis were lymphocytes and plasma cells infiltrating the thyroid follicles and increased number of lymphocytes in the background with or without Hurthle cell change, presence of multinucleated giant cells, epithelioid cell clusters, anisonucleosis in the aspirate. Quantitatively the smears were evaluated and graded based on the criteria given by Bhatia et al.<sup>7</sup>

**Bhatia et al grading system.<sup>7</sup>**

**Grade I [Mild]:** Few lymphoid cells infiltrating the follicles /increased number of lymphocytes in the background.

**Grade II [Moderate]:** Moderate lymphocytic infiltration or mild lymphocytic infiltration with Hurthle cell change/ giant cells / anisonucleosis.

**Grade III [Severe]:** Florid lymphocytic inflammation with germinal centre formation, very few follicular cells left.

Thyroid function test (TFT) was used to determine the blood concentrations of thyroid hormones. The patients had estimation of T3, T4 & TSH by enzyme linked immunosorbent assay. The reference normal range used were, T4 = 5 – 12 µg/dl, T3 = 80 – 180 ng/dl and TSH = 0.5 – 5 mU/L. Depending on these results patients were graded as euthyroid, hypothyroid or hyperthyroid.

USG of thyroid gland was performed by a single sonologist using high resolution ultrasound machine with 5 – 10 MHz Broad band linear transducer who was blinded to the clinical and biochemical status of the subjects .

## Results

Table-1 shows age and sex wise distribution of Hashimoto's thyroiditis cases. Females (95%) were affected more than males (5%). Maximum number of cases were seen between 2<sup>nd</sup> to 4<sup>th</sup> decade of life.

Table-2 shows cytological grading of Hashimoto's thyroiditis cases. Twenty six (32.5%) patients had mild lymphocytic infiltration of the gland and were graded as grade I thyroiditis (Figure-1 ). Thirty three (41.25%) had grade II disease characterized by moderate degree of lymphocytic infiltrate with evidence of follicular destruction, Hurthle cell change, giant cells (Figure-2 ). Grade III thyroiditis was noted in 21 (26.24%) patients characterized by dense lymphocytic infiltrates with germinal centers and with very few follicular cells left (Figure-3).

In our study, out of the total 80 cases, only 68 cases had biochemical parameters available. Table-3 shows, comparison of grades of Hashimoto's thyroiditis with biochemical parameters. In the present study, 34 (50%) cases were biochemically hypothyroid, 29 (42.64%) cases were euthyroid and 5 (7.35 %) cases were hyperthyroid. Hypothyroid state was the most common presentation.

Again among total 80 cases, only 61 cases had ultrasonography reports. Table-4 shows, comparison of grades of Hashimoto's thyroiditis with ultrasonography findings. In the present study, diffuse thyroiditis was observed in 15 (24.59%) cases, 10 (16.39 %) cases and 6 (9.83%) cases in grade I, II and III respectively, whereas goitre was observed in 5 (8.19%) cases, 9 (14.75%) cases and 7 (11.47%) cases in grade I, II and III respectively. Thyroid nodules were observed in 1 (1.63%) case, 3 (4.91%) cases and 1 case ( 1.63%) of grade I, II and III respectively. Normal study was seen in 4(6.55%) cases in grade I Hashimoto's thyroiditis cases.

**Table 1: Age & sex wise distribution of Hashimoto's thyroiditis cases.**

Age Interval (Years)	Male N (%)	Female N (%)	Total cases N (%)
0-10	0 (0)	0(0)	0(0)
11-20	3(3.75)	13(16.25)	16(20)
21-30	1(1.25)	21(26.25)	22(27.50)
31-40	0(0)	15(18.75)	15(18.75)
41-50	0(0)	12(15)	12(15)
51-60	0(0)	10(12.50)	10(12.50)
61-70	0(0)	5(6.25)	5(6.25)
Total	4(5)	76(95)	80(100)

**Table 2: Cytological grading of Hashimoto's thyroiditis cases.**

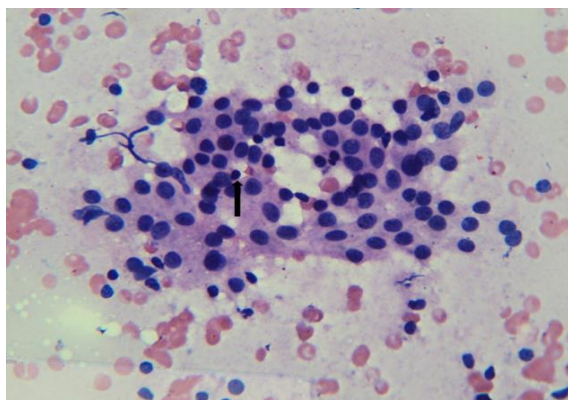
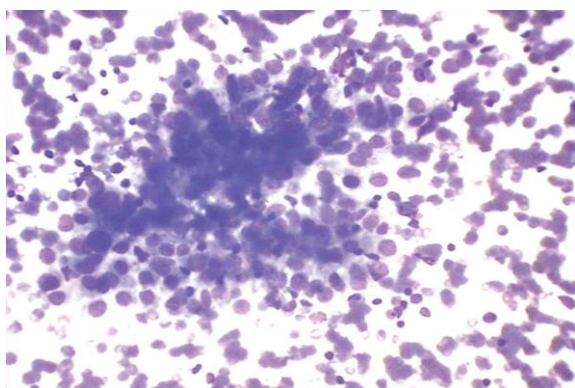
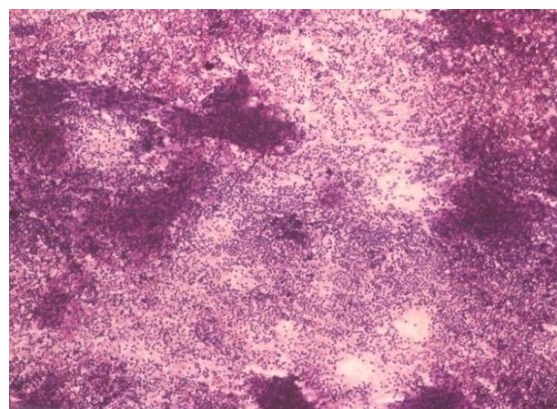
Grades of Hashimoto's Thyroiditis	No of cases. N(%)
I	26 (32.5%)
II	33 (41.25%)
III	21 (26.25%)
Total	80(100)

**Table 3: Comparison of Hashimoto's thyroiditis grades with biochemical values**

Grades	Euthyroid N(%)	Hypothyroid N(%)	Hyperthyroid N(%)
I	19(27.94)	04(5.88)	02(2.94)
II	8(11.76)	20(29.41)	03(4.41)
III	02(2.94)	10(14.70)	0(0)
Total	29(42.64)	34(50)	5(7.35)

**Table 4: Comparison of Hashimoto's thyroiditis grades with ultrasonography findings**

Grade	Diffuse Thyroiditis N(%)	Goitre N(%)	Thyroid nodule N(%)	Normal study N(%)
I	15(24.59)	5(8.19)	1(1.63)	4(6.55)
II	10(16.39)	9(14.75)	3(4.91)	0(0)
III	6(9.83)	7(11.47)	1(1.63)	0(0)
TOTAL	31(50.81)	21(34.42)	5(8.19)	4(6.55)

**Fig. 1: Grade I Hashimoto's thyroiditis****Fig. 2: Grade II Hashimoto's thyroiditis****Fig. 3: Grade III Hashimoto's thyroiditis**

## Discussion

Hashimoto's thyroiditis is a common autoimmune disease which is characterized by marked lymphoid infiltrate destroying the thyroid follicles.<sup>8</sup> Follicular architecture is totally destroyed and replaced by fibrosis in the long duration of disease.<sup>9</sup> The active phase of disease is transient with clinical manifestations of thyrotoxicosis while the evolution phase and destructive phase manifest with subclinical or overt hypothyroidism.<sup>7</sup> As far as the pathogenesis of this disease is concerned, there is aggressive destruction of thyroid cells by various cell- and antibody mediated immune processes. Though exact cause why it occurs is not known, various environmental factors which trigger the autoimmune thyroid disease include iodine, medication, infection, smoking, stress, etc.<sup>1</sup>

In our study, maximum number of the patients diagnosed with Hashimoto's thyroiditis were in 2<sup>nd</sup>- 4<sup>th</sup> decade of life, which is similar to the study conducted by Sood N et al.<sup>8</sup> In our study female: male ratio of 19:1 was observed which is similar to the study conducted by Siriweera EH et al & Singh et al who reported a female : male ratio of 10.3:1 & 14:1 respectively in their study.<sup>10,11</sup> The incidence of the juvenile hashimoto's thyroiditis was 24.4% which is similar to the study conducted by Marwaha RK et al,<sup>12</sup> who reported 26.8% incidence of the juvenile hashimoto's thyroiditis in their study.

Grade II Hashimoto's thyroiditis was seen in 41.25% of cases in the present study, which is similar to the study conducted by Uma P et al<sup>13</sup> who reported incidence of 55.53% of grade II lesions.

In our study majority, 50% of the patients were hypothyroid and 42.64% were euthyroid. This is in concordance with the study conducted by Ekambaram M et al & Rathi M et al in whose study majority of the patients were hypothyroid(84% and 56.09% respectively).<sup>2,5</sup> Maximum number of euthyroid cases showed grade I Hashimoto's thyroiditis.

Maximum number of hypothyroid and hyperthyroid cases showed grade II Hashimoto's thyroiditis. In cases of grade III Hashimoto's thyroiditis, most cases were hypothyroid. Biochemical

thyroid abnormality was associated with higher grade of Hashimoto's thyroiditis in FNAC.

In the present study, 50.81% cases were documented with diffuse thyroiditis on USG which is similar the study conducted by Shreechitra K et al,<sup>5</sup> who reported 66% cases of diffuse thyroiditis in their study. Maximum cases of diffuse thyroiditis showed grade I Hashimoto's thyroiditis and maximum number of goiter and thyroid nodule showed grade II Hashimoto's thyroiditis. In cases of grade III Hashimoto's thyroiditis, most were goiter cases on USG. Four cases of normal thyroid study showed grade I Hashimoto's thyroiditis. USG abnormality was found to be associated with different grades of Hashimoto's thyroiditis than normal study. Though ultrasound is not diagnostic, it can be helpful in assessing size of the thyroid gland, echotexture and presence of the thyroid nodules.

Limitation of the study- Anti thyroid antibody testing was not done in the present study. Hence no correlation with anti thyroid antibodies was possible.

### Conclusions

Hashimoto's thyroiditis is an auto immune disorder affecting females more commonly than males with maximum of the cases in the 2<sup>nd</sup>- 4<sup>th</sup> decade of life. Hypothyroidism is the most common clinical feature and can be the presenting feature. Higher grades of Hashimoto's thyroiditis in FNAC are more associated with abnormal biochemical findings. Diffuse thyroiditis can occur in the early stage of the disease (grade I) even before overt thyroid failure and is the strong predictor of the autoimmune process even when the disorder has not been suspected clinically. A combined approach of cytological grading of Hashimoto's thyroiditis along with ultrasonography and biochemical levels can detect subclinical hypothyroid state and provide a guide to therapy.

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