

# Comparative Study of Cytomorphological Grading of Hashimoto's Thyroiditis with Thyroid Hormone Levels

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## ABSTRACT

**Introduction:** Hashimoto thyroiditis (HT) is one of the common causes of hypothyroidism in patients with adequate iodine levels and is diagnosed by performing thyroid hormone assay, thyroid imaging, Fine needle aspiration cytology (FNAC) and thyroid antibody levels. Thyroid FNAC is a very simple, cost effective and accurate test. Study objectives were to know the severity of Hashimoto thyroiditis by cytological grading and thyroid stimulating hormone levels (TSH) and to know the degree of correlation between the cytological grading and TSH grading in Hashimoto thyroiditis

**Material and methods:** A prospective study was conducted on 50 cases of thyroid swelling attending FNAC clinic at our institute and diagnosed as HT. Results of thyroid hormone assay were obtained from the patient. Cytological grading was done based on predefined set of criteria and thyroid hormone levels were categorized arbitrarily. The FNAC grading and hormonal level grading were compared and statistically analysed.

**Results:** Maximum number of cases were in the age range of 21-30 years (38%) and 98% of the cases were female. The most common presentation was painless enlargement of thyroid. 18% of cases were grade I, 50% of cases were grade II and 32% of cases were grade III on cytological grading. Cytological grades matched with TSH. Correlation analysis showed a positive correlation between FNAC grading and TSH grading (Pearson coefficient-0.41)

**Conclusion:** There is statistically significant correlation of cytological grading and TSH grading in HT. FNAC is a very useful diagnostic modality to know the severity by cytological grading and can be used for follow-up management.

**Keywords:** FNAC, Hashimoto Thyroiditis, TSH Grading

## INTRODUCTION

Hashimoto thyroiditis was first described by Dr. Hakuru Hashimoto in 1912.<sup>1</sup> He originally used the term "Struma Lymphomatosa" based on the histological findings. HT is an autoimmune thyroid disorder.<sup>2</sup> It is the most common cause of hypothyroidism<sup>3-6</sup> and more common in women than men.<sup>7</sup> It is associated with wide variety of symptoms and it affects the quality of life of people suffering from it.<sup>8</sup> There are various diagnostic modalities available. Among them; thyroid hormone assay, thyroid imaging, FNAC and thyroid antibody levels are routinely done. It has been observed that thyroid FNAC has reduced the rate of surgeries for benign thyroid lesions which can be managed with medications alone.<sup>9</sup> This study is an effort to grade the severity of HT on FNAC and compare with an arbitrary grading of thyroid hormone levels and also to estimate the degree of correlation.

In set up where there is no ease to access for other diagnostic modalities like hormone assay and imaging, FNAC serves as a very useful diagnostic modality for diagnosis and follow up of patients suffering from HT.

## MATERIAL AND METHODS

A prospective study was done over a period of one year on patients presenting with thyroid swelling and diagnosed as HT on FNA. 50 cases were diagnosed as HT on FNAC and their respective thyroid hormone assay reports were obtained. We included both new and follow up cases in our study. For follow-up patients, the previous FNAC reports and slides were retrieved.

The standard approach for thyroid lesion was followed using 22-23 gauge needle and 10 ml disposable syringe. Aspirates were obtained from 2 to 3 sites and smears were made, few of them were air dried and the rest were fixed in alcohol and stained with May-Grunwald-Giemsa (MGG) and Hematoxylin & Eosin (H&E) respectively. The smears were examined and opined. Cases diagnosed as HT were chosen for the study. Corresponding thyroid hormone assay reports were obtained from the patient. (Thyroid hormone assay was done by chemiluminescence method in our laboratory).

Cytological grading to assess the severity of HT was done (Table 1) based on the criteria mentioned by Alka Bhatia et al.<sup>10</sup> The criterion was based on amount of lymphocytic infiltration of the gland and in the background, presence of germinal centres, Hurthle cells, giant cells and anisonucleosis. We categorized the thyroid stimulating hormone (TSH) levels arbitrarily (Table 2) to assess severity of disease based on TSH levels.

The FNAC grading and TSH level grading of Hashimoto's thyroiditis were compared and statistically analysed for the level of significance.

Statistical analysis: Chi-Square Test was done and a p value of 0.003 was obtained, which is statistically significant.

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Correlation analysis by using Pearson coefficient showed a positive correlation between FNAC grading and TSH grading (Pearson coefficient-0.41).

**RESULTS**

The present study highlights the severity of HT based on cytological grading of FNAC smears and correlation with TSH grading in fifty cases of thyroid lesions. The incidence of HT was highest in the age group of 21-40yrs with a female preponderance (Figure 1& 2 respectively). There were seven follow up cases and the remaining were fresh cases. Of seven, we could review and grade slides of six patients, the other slide was faded and hence was difficult to grade. The most common presentation was diffuse painless thyroid enlargement, followed by fatigue, weight gain, menstrual irregularities and palpitations. Of fifty patients, nine required ultrasound guidance for performing FNAC as the enlargement was not clinically significant but had symptoms suggestive of hypothyroidism with elevated TSH levels. Cases with predominantly haemorrhagic aspirate posed a diagnostic challenge as the lymphocytes from blood were admixed with the lymphocytes infiltrating the gland. In these cases repeat aspirate was done and subsequently graded. One of the interesting cases we came across was HT in a background of papillary carcinoma. On cytological grading, it was grade II.

Based on cytological grading, grade II was most common in our study and accounted for 50% (25 cases), followed by grade III -32 % ( 16 cases) and grade I-18 % ( 9 cases).

Of the six cases of follow up with available previous slides, three were graded as grade II on

initial slides and on follow up two remained grade II and one was grade I. Two cases were graded as grade I and on follow-up smear, one remained grade I and other was grade II. 1/6 of follow up case was grade III on initial aspirates and follow up smear revealed the same grade.

Based on TSH grading, incidence of grade III was highest which accounted for 52 % ( 26 cases) followed by grade II

-28 % ( 14 cases) and grade I-20 % ( 10 cases). There is a statistically significant correlation (p value-0.003) between TSH grading and cytological grading of HT. Thus, implying that the severity of the disease can be assessed by grading the cytological findings like the relative number of lymphocytes infiltrating the gland, presence of lymphocytes in the background, presence of germinal centres, Hurthle cells, giant cells and anisonucleosis.

**DISCUSSION**

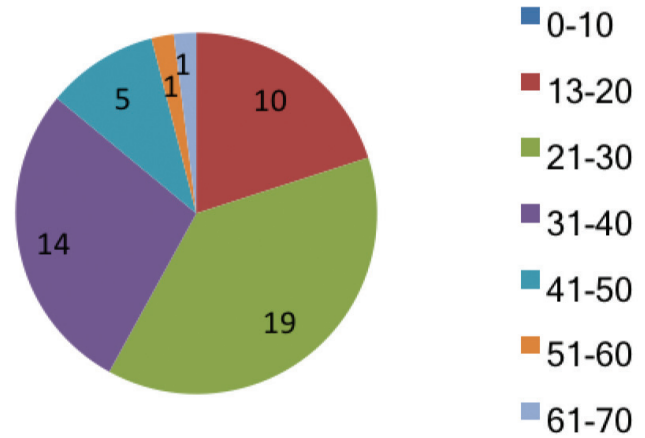


Figure-1: Pie chart showing age distribution of cases

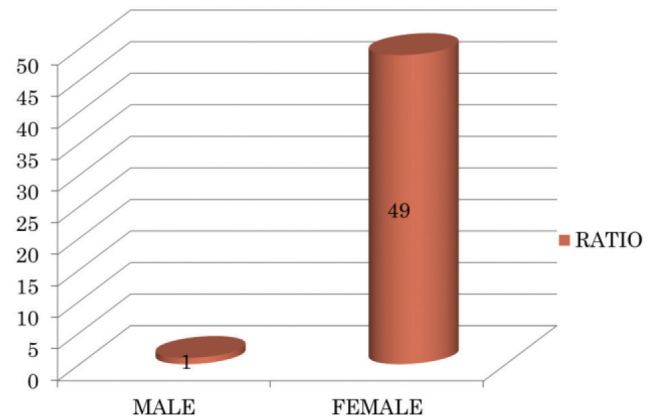


Figure-2: Bar chart showing sex distribution of cases

Grade I (Mild)	Few lymphoid cells infiltrating the follicles/ increased number of lymphocytes in the background
Grade II (Moderate)	Moderate lymphocytic infiltration with Hurthle cell change/ giant cell/ anisonucleosis
Grade III (Severe)	Florid lymphocytic infiltration with germinal center formation, very few follicular cells left
* Courtesy Dr Alka Bhatia and colleagues	
<b>Table-1:</b> Cytological grading of Hashimoto's thyroiditis <sup>10*</sup>	

Grade I (Mild)	0.4-5 µU/ ml
Grade II (Moderate)	5-10 µU/ ml
Grade III (Severe)	>10 µU/ ml
<b>Table-2:</b> Arbitrary TSH grading in assessing severity of Hashimoto's thyroiditis	

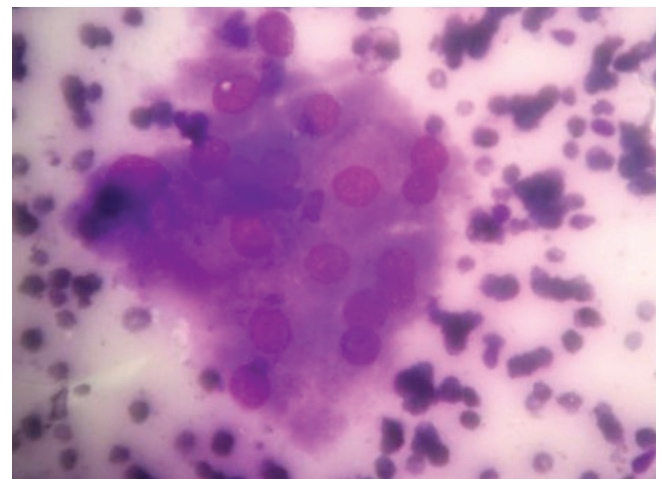
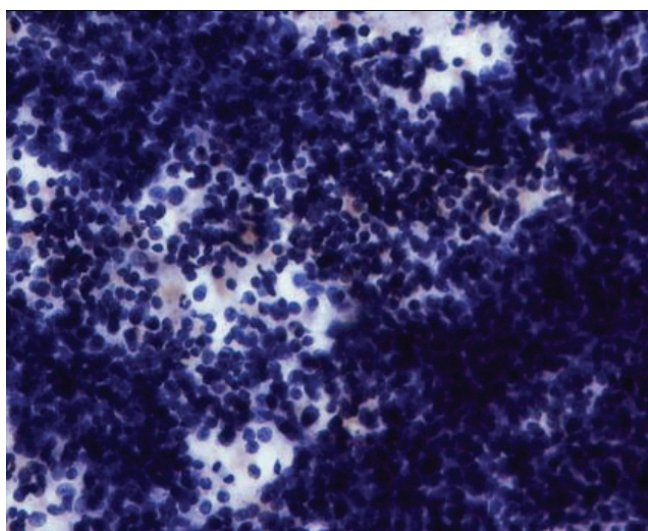


Figure-3: Giemsa;40X: Hurthle cell change



**Figure-4:** Giemsa;40X: Grade III: Florid lymphocytic thyroiditis

The incidence of HT is on rise in recent years.<sup>11</sup> This could probably be due to excess of iodine intake.<sup>12</sup> HT has to be diagnosed in its initial stages as patients will subsequently become hypothyroid and will require lifelong supplementation of thyroxine.<sup>13</sup>

Patients of HT are on increased risk of developing extranodal marginal B cell lymphoma.<sup>7</sup>

HT is associated with variable findings in the various diagnostic modalities available and is a diagnostic pitfall.<sup>14</sup> The significance of FNAC diagnosis of HT is that unnecessary surgeries can be avoided. FNAC is more superior and cost-effective than thyroid antibody screening in diagnosis of Hashimoto's thyroiditis.<sup>7</sup> The cytological features indicative of HT on FNAC include infiltration of thyroid follicles by lymphocytes/plasma cells, lymphocytes in background, formation of germinal centres, Hurthle cells, presence of moderate amount of colloid in the background and sometimes giant cells can be seen. In later stages, there is complete destruction of follicles and will be replaced by fibrosis. The cytological grading as first described by Alka Bhatia et al<sup>10</sup> depends on number of relative number of lymphocytes infiltrating the gland, presence of lymphocytes in the background, presence of germinal centres, Hurthle cells, giant cells and anisonucleosis. The present study was designed to correlate FNAC grading of HT with the arbitrary TSH grading in 50 cases of thyroid lesions. We included both new and follow up cases in our study. While grading the smears we faced a difference of opinion among us, hence we preferred to assign the grade which most of us had opted. There have been many studies in the past which have attempted to grade HT on cytology and correlated with other diagnostic modalities. To the best of our knowledge, this study is the first of its kind to arbitrarily grade the TSH levels and correlate it with the cytological grades to assess the severity.

We graded the TSH levels arbitrarily as shown in table 2. The lower limit of TSH level was taken as 0.4 $\mu$ U/ml and upper limit of 10 $\mu$ U/ml. The incidence of HT was highest in age group of 21-40 years with a female preponderance, which is

similar to the findings of Alka Bhatia et al.<sup>10</sup> In comparison with the similar studies<sup>10,15</sup> the incidence of grade II on cytological grading was highest. There was 1 case of HT in a background of papillary carcinoma. On cytological grading, it was grade II. The current study is an attempt to assess the severity of HT based on FNAC. Most of the clinician's advice only thyroid hormone levels and TSH for follow up of the disease. TSH is subjected to fluctuations due to various factors like sample drawn in fasting state or not,<sup>16</sup> the method employed for estimation, factors like pregnancy, diabetes, liver disease, renal disease, sepsis, trauma, cardiac conditions<sup>17-19</sup> etc. Hence, assessing severity by TSH levels alone is not reliable. On the other hand, FNAC thyroid is a very reliable diagnostic modality as it is not subjected to fluctuations, it is conclusive and an OPD procedure. It is minimally invasive and can be adopted for follow up of Hashimoto's thyroiditis with cytological grading of FNAC smears. We graded the TSH levels and compared it with cytological grading to know the degree of correlation. We included the cytological grading in our reporting format and the clinicians found it useful to understand the severity of the disease and thus manage the patient accordingly.

Correlation analysis using Pearson coefficient showed a positive correlation between FNAC grading and TSH grading with a Pearson coefficient of 0.41.

Serum thyroid microsomal antibody titer though a useful diagnostic test is less sensitive in diagnosis and follow up of HT. Alka Bhatia et al<sup>10</sup> determined serum thyroid microsomal antibody (TMA) titers in 70 cases. Elevated values were seen in 46/70 (65.71%) and normal in 24(34.29%). The sensitivity of TMA was 62.6% and sensitivity of FNAC was 98.68%. Whereas Amino et al<sup>20</sup> reported elevated TMA levels in 95% of his cases. Such wide variations in sensitivity of TMA could be probably explained due to inclusion of patients in the early course of disease during which time the thyroid autoimmune process would have already started much before the serological evidence would appear.<sup>21</sup> Korah T<sup>22</sup> in a similar study describes the role of USG in HT. USG is required to detect the presence of thyroid nodule in a diffuse goitre and also the study highlights the significance of diffuse homogenous hypoechogenicity in determining coexisting hypothyroidism (13/16 patients who presented clinically and by thyroid hormonal assays with HT and hypothyroidism, had diffuse homogenous hypoechogenicity (DHOE) on ultrasound examination.) In our experience, FNAC with/without ultrasound guidance serves to be more accurate than other modalities in diagnosis and follow up of HT.

The other advantage of using FNAC for follow up of these cases is that emerging of malignancies like papillary carcinoma, lymphoma, etc. can be picked up as patients of HT are prone for these malignancies.

Though FNAC is superior in many aspects but does have certain pitfalls in diagnosing HT like overlap of certain cytological features with other lesions like multinodular goitre, degenerative changes, Hurthle cell neoplasm, follicular neoplasm, lymphoma etc.<sup>23</sup>

The other minor pitfalls which could be rectifiable include

inadequate material requiring repeat procedure, improper staining, drying artefacts etc. Though the current study highlights the significance of FNAC in diagnosis and follow up of HT, it has certain drawbacks, the major being the sample size. A study including larger sample size spread over wider geographical areas with both iodine sufficient and deficient regions is required. The cytological grading is subjected to inter-observer bias; hence a study which focuses on inter-observer variation in grading HT is required. The other drawback is we did not include other diagnostic modalities in our study like radio-iodine uptake, anti-thyroid antibodies, thyroid ultrasonography to compare the efficacy of each. One of the difficulties we came across in few cases was retrieving the previous FNAC slides. This can be overcome if the system of grading is incorporated in routine reporting formats. So that just the previous report grading can be compared on follow up and the management of patient decided accordingly.

## CONCLUSION

To conclude, FNAC of thyroid is a very useful, cost-effective, initial and follow up diagnostic modality in managing patients of Hashimoto's thyroiditis. Incorporation of cytological grading for HT in the reporting format should be followed to aid the clinicians for better management and follow-up.

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