



## CYTOMORPHOLOGICAL SPECTRUM OF HASHIMOTO'S THYROIDITIS AND ITS CORRELATION WITH CLINICAL PRESENTATION, THYROID FUNCTION TEST AND ANTIBODY LEVELS

### Pathology

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### ABSTRACT

Hashimoto's thyroiditis is most common form of autoimmune thyroiditis and the second most common thyroid lesion next to goiter. Middle aged women are most commonly affected and the commonest presentation is hypothyroidism with diffuse enlargement of thyroid gland. The purpose of this study is to review the cytomorphologic spectrum of HT and to correlate with clinical presentation, thyroid function tests and antibody profile. This is a prospective study conducted in the Department of Pathology, KIMS, Bhubaneswar, from January 2016 to December 2017. 115 cases of Hashimoto's thyroiditis were included in this study. Cytomorphologic features were reviewed, graded & were correlated with clinical presentation, anti-thyroid peroxidase (anti-TPO) antibodies and TFT. Out of total 115 cases, 3.5% were males and 96.5% were females. Most common age group was 31- 40yrs. 80 cases (69.6%), 22 cases (19.1%) and 13 cases (11.3%) had diffuse, nodular & solitary thyroid swellings respectively. Hypothyroidism was the commonest finding (68 cases, 59.1%). 32 cases (27.4%), 65 cases (56.5%) and 18 cases (16.1%) were of grade I, grade II & grade III HT respectively. Anti-TPO was raised in 85.4%, 95.3% and 98.5% cases of Grade I, Grade II & Grade III cases respectively. A multidisciplinary approach including clinical, radiological, biochemical and cytological parameters should be utilized for detecting subclinical hypothyroid state and provide a guide to therapy.

### KEYWORDS

Hashimoto's thyroiditis (HT), Anti-TPO Antibody, TFT.

### INTRODUCTION

Hashimoto's thyroiditis (HT), was first described by Hakaru Hashimoto in 1912. It is synonymous with chronic lymphocytic thyroiditis & autoimmune thyroiditis<sup>1</sup>. Its incidence is 30–60/1,00,000 population per year with a prevalence rate of 1–4%<sup>2</sup>. It is the most common form of thyroiditis and the second most common thyroid lesion next to goiter, diagnosed on fine-needle aspiration cytology (FNAC)<sup>3,4</sup>. It is more prevalent among Asians<sup>5</sup>. Women are more frequently affected than men. Patients may be hypothyroid, euthyroid or hyperthyroid. However, most cases present with hypothyroidism. It is important to diagnose Hashimoto's thyroiditis as it is the leading cause of hypothyroidism requiring lifelong supplementation with thyroxine<sup>6</sup>. As it is an autoimmune disease, the most important antibody directed against the thyroid tissue is thyroid peroxidase (Anti TPO Ab)<sup>7</sup>. It is usually associated with raised Anti TPO Ab, but 10–15% patients may be antibody negative.<sup>8</sup> Hurtle cell change of follicular cells along with increased number of mature and transformed lymphocytes impinging on follicular cells are characteristic cytological features<sup>9</sup>. Clinically it can present as diffuse or nodular asymptomatic swelling<sup>1</sup>. Despite availability of several tests for its diagnosis, FNAC remains the gold standard with a diagnostic accuracy of 92%<sup>2,10</sup>. FNAC is a simple, cost effective, safe and sensitive diagnostic tool<sup>11</sup>.

### AIMS & OBJECTIVES

The purpose of this study is to review the cytomorphologic spectrum of Hashimoto's Thyroiditis (HT) and to correlate with clinical findings, thyroid function tests (TFT) and antibody profile.

### MATERIALS AND METHODS

This is a prospective study conducted in the Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha from January 2016 to December 2017. 115 cases of newly diagnosed Hashimoto's thyroiditis on FNAC were included in this study. Cases of colloid goiter were excluded from the study. FNAC was performed using nonaspiration or aspiration techniques by 23 G needle with 10 mL syringe. Air-dried smears were stained with Leishman's stain and wet ethanol fixed smears were stained with Hematoxylin and Eosin. TFT and Anti TPO Ab were performed in Cobas e 441. Cytological grading on FNAC smears was done according to density of lymphocytic infiltration, presence of granuloma, Hurthle cells, degree of anisonucleosis and giant cells as per the criteria mentioned in Table-3 and it was correlated with clinical presentation, TFT anti-TPO antibody levels.

### INCLUSION CRITERIA

Newly diagnosed cases of Hashimoto's thyroiditis on FNAC.

### EXCLUSION CRITERIA

- Subjects receiving either thyroxine or any other drugs known to interfere with TFT.
- Old cases of Hashimoto's thyroiditis.
- Any other additional lesions observed with Hashimoto's thyroiditis diagnosed on cytology.
- Cases diagnosed as colloid goiter on cytology.

### OBSERVATIONS

#### TABLE NO-1 INCIDENCE ACCORDING TO DIFFERENT AGE GROUPS (N=115)

AGE GROUP	NO OF CASES	%
10-20	08	6.9
21-30	34	29.6
31-40	37	32.2
42-50	16	13.9
51-60	14	12.2
61-70	06	05.2
TOTAL	115	100%

#### TABLE NO-2

#### INCIDENCE ACCORDING TO CLINICAL PRESENTATION (N=115)

CLINICAL PRESENTATION	NO OF CASES	%
Diffuse swelling	80	69.6
Nodular swelling	22	19.1
Solitary nodule	13	11.3
TOTAL	115	100%

#### TABLE NO-3

#### INCIDENCE ACCORDING TO CYTO-MORPHOLOGICAL GRADING (N=115)

GRADES	CYTOMORPHOLOGY	NUMBER (%)
Grade-1	Mild lymphocytic infiltration in the follicles	32 (27.4 %)
Grade-2	Moderate lymphocytic infiltration with presence of Hurthle cell, giant cells/anisonucleosis	65 (56.5 %)
Grade-3	Florid lymphocytic infiltration with germinal center formation & follicular destruction	18 (16.1 %)

**TABLE NO-4  
INCIDENCE ACCORDING TO HORMONE STATUS (N=115)**

HORMONE STATUS	NO OF CASES	PERCENTAGE
Euthyroid	20	17.5
Hypothyroid	68	59.1
Hyperthyroid	27	23.4
<b>TOTAL</b>	<b>115</b>	<b>100%</b>

**TABLE NO-5  
CORRELATION BETWEEN CYTOMORPHOLOGICAL GRADING WITH HORMONE PROFILE (N=115)**

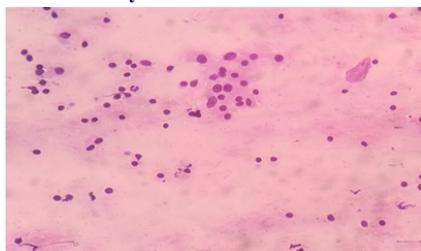
GRADES	HYPOTHYROID (No, %)	EUTHYROID (No, %)	HYPERTHYROID (No, %)
Grade-I	6 (18.8%)	12 (37.5%)	14 (43.8%)
Grade-2	46 (70.8%)	6 (9.2%)	13 (20%)
Grade-3	16 (88.9%)	2 (11.1%)	0%

**TABLE NO-6  
CORRELATION BETWEEN CYTOMORPHOLOGICAL GRADING WITH INCREASED ANTI-TPO ANTIBODY LEVEL (N=115)**

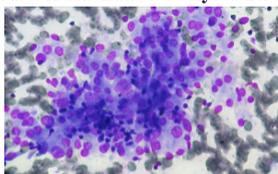
GRADES	INCREASED ANTI-TPO Ab (No, % cases)
I (32)	27(85.4%)
II (65)	61(95.3%)
III (18)	17(98.5%)

Out of Total 115 cases, 4 cases (3.5%) were males and 111 cases (96.5%) were females. Most common age group was between 31- 40 yrs. with a mean age of 35yrs [Table no- 1]. Diffuse thyroid swelling was the commonest clinical presentation in 80 cases (69.6%). Nodular & solitary thyroid swellings were in 22 cases (19.1%) and 13 cases (11.3%) respectively [Table no- 2]. Hypothyroidism was the commonest finding 68 cases (59.1%). Euthyroid and hyperthyroid were observed in 20 cases (17.5%) & 27 cases (23.4%) respectively [Table no- 4]. Out of 115 cases, 32 cases (27.4%) were in Grade I, 65 cases (56.5%) were in Grade II & 18 cases (16.1%) were in Grade III [Table no- 3]. Correlating cytological grading with hormone status, 46 cases (70.8%) of Grade II were hypothyroid and 14 (43.8%) of Grade I were hyperthyroid [Table no- 5]. Anti-TPO antibody was raised in 27 cases (85.4%), 61 cases (95.3%) and 17 cases (98.5%) of Grade I, Grade II & Grade III HT respectively [Table no- 6].

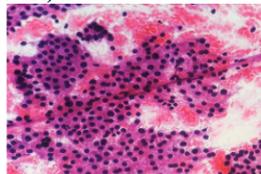
**Grade I Hashimoto's thyroiditis**



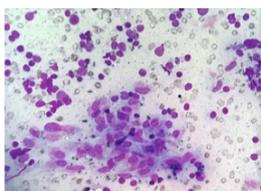
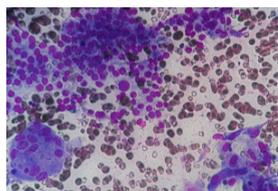
**400X H & E (Mild lymphocytic infiltration with follicular cells)  
Grade II Hashimoto's thyroiditis (400X)**



**400X Leishman stain (hurthle cell change with moderate lymphocytes)**



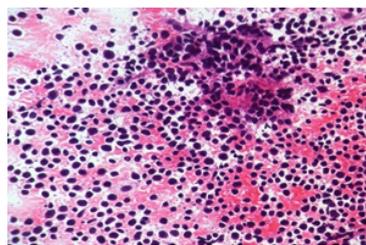
**400X H&E (hurthle cell change with moderate lymphocytes)**



**400X Leishman stain (hurthle cell change with giant cell)**

**400X Leishman stain (moderate lymphocytes with epithelioid cells)**

**Grade III HT**



**400X H& E (florid reactive lymphoid cells with follicular destruction)**

**Discussion**

HT is an autoimmune chronic inflammatory disease of the thyroid gland. It involves infiltration of thyroid gland by T and B lymphocytes which are reactive to thyroid antigens. Activated B cells secrete thyroid autoantibodies. Cytotoxic T lymphocytes are largely responsible for destruction of thyroid parenchyma. In the long run, follicular architecture is totally destroyed and replaced by fibrosis. The active phase of the disease is transient with clinical manifestation of thyrotoxicosis. Evolution and destructive phases manifest with subclinical and overt hypothyroidism. Exact etiology of Hashimoto's thyroiditis is unknown; however, predisposing factors include iodine deficiency, medication, infection, smoking, stress etc.<sup>11</sup> It has a risk of transforming into malignancy, most commonly extra nodal marginal B cell lymphoma and papillary carcinoma<sup>12,13</sup>. Hence patients diagnosed as HT need follow up.

In our study, majority of the patients were females (96.5%). Aswin et al<sup>11</sup> reported 95% female patients. Neelam Sood et al<sup>14</sup> observed male: female ratio to be 1:10 and Anila KR et al<sup>15</sup> also found female preponderance (91.7%).

The most common age-group in our study was 31- 40yrs with mean age of 35yrs which is similar to study conducted by S Bhatia et al<sup>9</sup> and Bajaj et al<sup>8</sup>. Ashwin et al<sup>11</sup> found common age group to be 20-40yrs.

The common presentation in our study was diffuse thyroid swelling (69.6%) which bears resemblance with studies by Ashwin et al<sup>11</sup> (50.81%) and Kartha S et al<sup>10</sup> (66%).

Grading of autoimmune thyroiditis was done as per the criteria described in Table-3. Majority of our cases belonged to Grade II (56.5%). Ashwin et al (41.3%)<sup>11</sup> and P Agrawal et al (50%)<sup>17</sup> also got similar results.

On analyzing the TSH levels, we found 59.1% patients to be Hypothyroid which was in concordance with study by Rathi et al (56.09%)<sup>7</sup>, Ashwin.P et al (50%)<sup>11</sup>, Bhatia et al<sup>9</sup> (73.6%) and P Agrawal et al (50%)<sup>17</sup>.

On correlating between grading and thyroid profile, our study showed 18.8%, 70.8%, 88.9% cases of grade I, II and III were hypothyroid respectively. 37.7%, 9.2% and 11.1% cases of grade I, II and III were euthyroid respectively. 43.8%, 20% and 0% cases of grade I, II and III were hyperthyroid respectively.

In our study Anti-TPO was raised in 85.4%, 95.3% and 98.5% cases of Grade I, Grade II & Grade III respectively. Neelam Sood et al<sup>14</sup> also observed Anti-TPO and TSH were elevated in 91.67%, 94.12% and 96.16% cases of grade I, grade II & grade III HT respectively. Correlating cytological grading with hormone status, our study showed 46 cases (70.8%) of Grade II were hypothyroid and 14 cases (43.8%) of Grade I were hyperthyroid.

**COMPARISON OF PRESENT STUDY WITH OTHERS**

STUDY	AGE GROUP (Yrs)	CLINICAL PRESENTATION	HORMONAL STATUS NO & %	GRADING & %
<b>Present study</b>	31-40	Diffuse swelling	Hypothyroid (59.1%)	II 56.5%

<b>Ashwin et al</b>	20-40	Diffuse swelling	Hypothyroid (50%)	II	41.3%
<b>P Agrawal et al</b>	20-35	Diffuse swelling	Hypothyroid (50%)	II	50%
<b>Bhatia et al</b>	30-40	Diffuse swelling	Hypothyroid (73.6%)	II	44%
<b>Anila KR et al</b>	31-40	Diffuse swelling	Hypothyroid (38%)	II	38%

#### LIMITATION OF OUR STUDY

We were unable to correlate with radiological findings as in majority of cases USG reports were not available.

#### CONCLUSION

Hashimoto's thyroiditis is an autoimmune disorder affecting predominantly females in third to fourth decades. There is a strong association of antithyroid antibodies, especially anti-TPO antibody. Anti-TPO and TSH together are significant even if no lymphocytic infiltration is present. This could be due to very early stage of lymphocytic thyroiditis. In spite of various diagnostic modalities available, cytomorphological features seen in FNAC smears still remain the gold standard. A correct cytological diagnosis can prevent the need for a surgical intervention. However, a multidisciplinary approach including clinical, radiological, biochemical and cytological parameters should be utilized for detecting subclinical hypothyroid state and providing a guide to therapy.

**CONFLICT OF INTEREST** The authors declare that there is no conflict of interest regarding the publication of this paper.

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