

A Cross-sectional Study of Cytological Grading of Lymphocytic Thyroiditis and its Association with Thyroid Hormone

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ABSTRACT

Following Goiter, Lymphocytic thyroiditis (LT) is one of the common thyroid lesions found on Fine Needle Aspiration Cytology (FNAC). In addition to FNAC, clinical signs, thyroid profile, anti-thyroid antibody and ultrasonography (USG) can help in diagnosing the LT. This study analyzed thyroid Fine Needle aspirates for cytological features of lymphocytic thyroiditis, rated cases based on established criteria, and associated cytological categories to thyroid hormone levels.

Materials and Methods: A three-year retrospective study was undertaken at a Mumbai-based tertiary health care center's pathology department. Bhatia and colleagues used precise cytological criteria to assess 155 cases of lymphocytic thyroiditis described using the Bethesda method. Thyroid hormone status was associated with cytological grades where available.

Our research comprised 155 cases of lymphocytic thyroiditis reported through the Bethesda system. Further microscopic grading found that Grade II Lymphocytic thyroiditis affected most of the cases (114, 73.54%), followed by Grade I (31, 20%) and Grade III (10, 6.35%). The majority of patients in the 132 cases with available thyroid profiles were hypothyroid (68; 51.51%), followed by hyperthyroid (39; 29.54%) and euthyroid (25; 18.93%). There was no significant relationship between cytomorphological grading and hormonal state (p -value > 0.05). Additionally, no statistical significance was found between cytological grading and clinical characteristics.

Conclusion: FNAC is still the "gold standard" for diagnosing lymphocytic thyroiditis. However, in our study, there was neither a statistically significant relationship between cytological grades and ultrasonographic findings nor between cytological grading and hormonal status.

Keywords: Hashimoto's thyroiditis, Lymphocytic thyroiditis, Thyroid Hormone

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INTRODUCTION

Thyroid problems are among the most prevalent endocrine illnesses in the world, impacting around 42 million people in India alone.¹ FNAC is a standard diagnostic method for judging thyroid abnormalities. It may differentiate amongst non-neoplastic and neoplastic lesions.² Most of the thyroid nodules are benign, and the most common FNA interpretation is a benign finding (about 60-70%).

Chronic lymphocytic thyroiditis (CLT) is another common benign lesion of thyroid on FNAC diagnosis, behind only benign follicular nodule,^{2,4} and the second most common thyroid abnormality detected after goiter.⁵ Hashimoto's thyroiditis (HT) which is also known as CLT, is an autoimmune condition that affects more women, with a 1-4% prevalence rate and an annual incidence of 30-60/100000 people.

FNAC is particularly successful in detecting HT, with a 92% diagnostic success rate.⁶ The majority of patients experience asymptomatic growth of the thyroid that is homogeneous and wide. It is one of the most prevalent manifestations of hypothyroidism in iodine-rich regions of the world.⁷ Aside from FNAC, ultrasonography, clinical signs and thyroid hormone levels can also aid in diagnosis.⁶⁻⁸ The present research analyzed fine needle aspirates of thyroid for cytological features of LT, graded cases based on preset cytological criteria, and associated cytological grades with thyroid hormonal condition.

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MATERIAL AND METHOD

The three-year retrospective study was conducted in the Laboratory of Pathology of a corporation hospital linked with a tertiary health care institute in Mumbai. Prior to commencing the study, institutional scientific research and ethics committee approval was requested. Cytology identified 155 cases of chronic lymphocytic thyroiditis from 1573 thyroid needle aspirations performed during the research period. All Chronic lymphocytic thyroiditis cases were assessed based on age, gender, clinical presentation, and thyroid function tests. The Bethesda System for Reporting Thyroid Cytopathology has been utilized to evaluate cytomorphological features,

and cases with several polymorphic lymphoid cells associated with Hurthle cells and/or benign thyroid follicular cells were classified as LT.

Diagnosing lymphocytic thyroiditis (LT) did not require a minimum number of Hurthle or follicular cells.³

In Bhatia *et al.*, these cases were evaluated further based on the following cytological criteria:

Mild (Grade I)- Few lymphoid cells breaching the follicles/ increased number of lymphocytes in the background;

Moderate (Grade II)- Moderate lymphocytic infiltration or mild lymphocytic infiltration alongside Hurthle cell change/giant cells/anti-nucleosis;

Severe (Grade III)- Florid lymphocytic inflammation with germinal centre formation along with very few follicular cells left.⁸

All patients underwent clinical examinations, and thyroid hormonal profiles were performed where available. Patients' serum TSH, T4, and T3 levels determined whether they were euthyroid, hypothyroid, or hyperthyroid. Cytological grades were linked to thyroid hormone levels. The Fischer Exact test was used to determine the association between grades and hormone status with *p-value* < 0.05 showing statistical significance.

Table 1: Lymphocytic thyroiditis: Distribution by age and gender.

| Age Groups | Sex wise | | | |
|------------|----------|-------------|--------|-------------|
| | Male | Percentages | Female | Percentages |
| 0-10 | 0 | 0.00 | 2 | 1.40 |
| 30-Nov | 1 | 8.33 | 16 | 11.19 |
| 21-30 | 1 | 8.33 | 41 | 28.67 |
| 31-40 | 2 | 16.67 | 42 | 29.37 |
| 41-50 | 5 | 41.67 | 19 | 13.29 |
| 51-60 | 3 | 25.00 | 23 | 16.08 |
| Total | 12 | 100.00 | 143 | 100.00 |

Table 2: Distribution of lymphocytic thyroiditis according to cytomorphology.

| | Severity | Frequency | Percentages |
|-----------|----------|-----------|-------------|
| Grade I | Mild | 31 | 20% |
| Grade II | Moderate | 114 | 73.54% |
| Grade III | Severe | 10 | 6.45 |
| Total | | 155 | 100% |

RESULTS

According to Table 1, there were 155 instances of lymphocytic thyroiditis reported in our study by utilizing the Bethesda system. The majority of patients were among the age range of 31 and 40 (44, 28.39%), followed by 21 and 30 (42, 27.09%), 51 and 60 (26, 16.77%), and 41 and 50 (24, 15.48%). The average age was 38.43 years, with a range of 6 to 65 years. The study included 143 (92.25%) females and 12 (7.43%) males, for a female-to-male proportion of 11.91. These instances were afterward assessed utilizing the cytomorphological analytical standards. The highest number of cases were of Grade II thyroiditis, followed by Grade I and Grade III (Table 2) (Figures 1 to 3).

Thyroid hormone profiles were carried out on 132 of the 155 instances of lymphocytic thyroiditis. The majority of patients were hypothyroid (68.51.5%), followed by hypetthyroid (39.29.54%) and euthyroid (23.18.93%). On clinical examination, the majority of patients had diffuse goiter (101, 54.19%), followed by nodular goiter (47, 32.25%) and a single thyroid nodule (7, 3.87%). The correlation

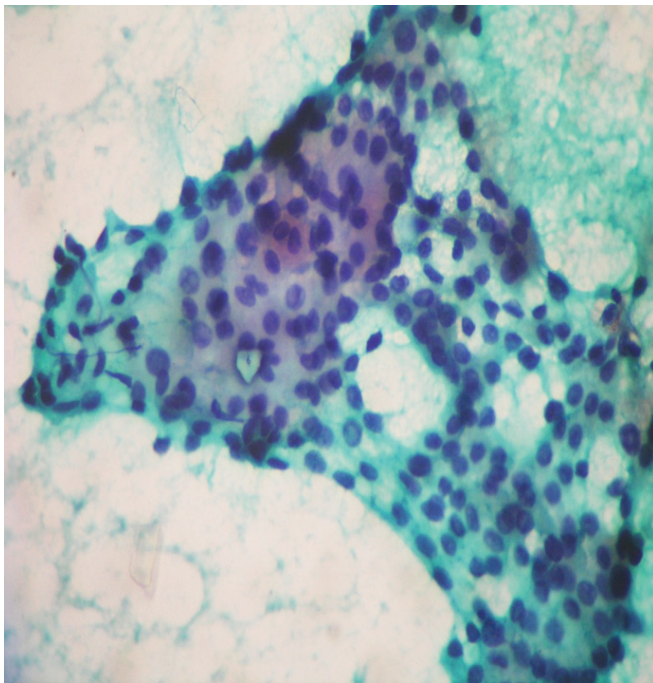


Figure 1: Grade 1: (31 cases) Few lymphoid cells infiltrating the follicles/increase number of lymphocytes in background.

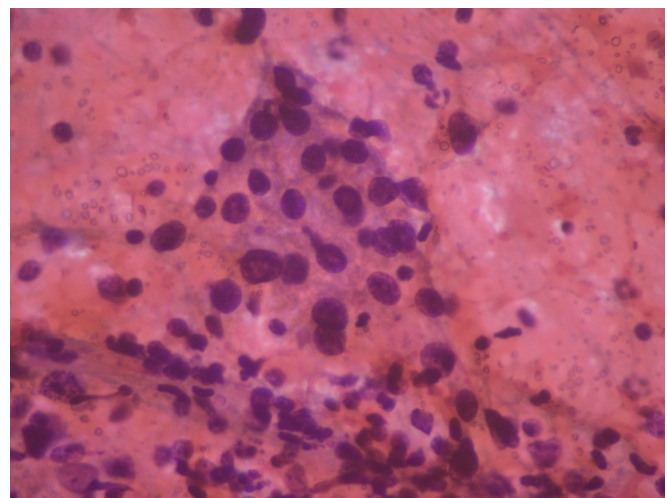


Figure 2: Grade 2 (114 cases) Moderate lymphocytic infiltration with hurthle cell change/giant cells/ anisonucleosis.

Table 3: Association of thyroid function with cytological grading of lymphocytic thyroiditis.

| Grades of Cytology | Thyroid Function | | | |
|--------------------|------------------|--------------|-----------|-------------|
| | Hypothyroid | Hyperthyroid | Euthyroid | Not done |
| I | 13 (19.12%) | 8 (20.52%) | 6 (24%) | 4 (17.39%) |
| II | 48 (70.59%) | 30 (76.92%) | 18 (72%) | 18 (78.26%) |
| III | 7 (10.29%) | 1 (2.56%) | 1 (4%) | 1 (4.35) |
| Total | 68 (100%) | 39 (100%) | 25 (100%) | 23 (100%) |

Fischer exact test applied. Chi-square Value- 2.88, p-value= 0.57, Not significant

Table 4: Association of thyroid functions with Clinical presentations in Lymphocytic thyroiditis.

| Ultrasonography findings | Thyroid Function | | | |
|--------------------------|------------------|-----------------------|----------------------|------------------|
| | Normal N (%) | Hyperthyroidism N (%) | Hypothyroidism N (%) | Not tested N (%) |
| Solitary Thyroid Nodule | 1 (45.0) | 1 (2.6) | 1 (1.5) | 3 (13.0) |
| Nodular | 9 (36.0) | 12 (30.8) | 24 (35.3) | 3 (13.0) |
| Diffuse | 15 (60.0) | 26 (66.6) | 43 (63.2) | 17 (74.0) |
| Total | 25 (100.0) | 39 (100.0) | 68 (100.0) | 23 (100.0) |

Fischer's exact test was applied. Chi-square Value- 9.61, p-value= 0.142, Not significant

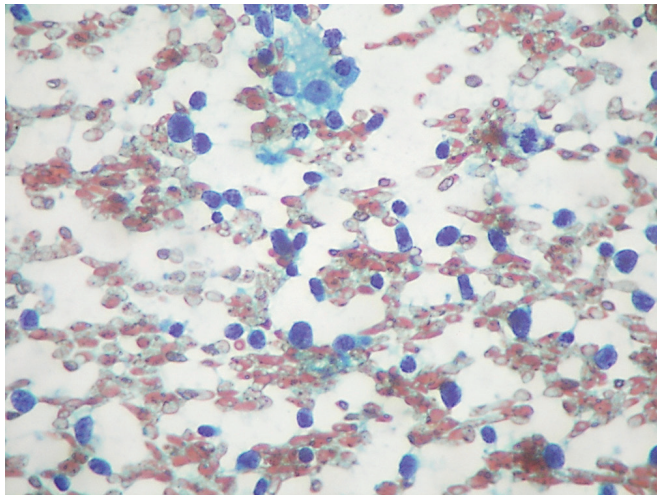


Figure 3: Grade 3 (10 cases) Grade 3 Florid lymphocytic inflammation with germinal center formation, very few follicular cells left.

between clinical presentation and thyroid hormone profile was likewise shown to be insignificant. (Table 3). The association between cytological grading with thyroid hormone profile wasn't determined to be significant (Table 4).

DISCUSSION

Hashimoto's thyroiditis (HT), commonly referred to as lymphocytic thyroiditis, is a condition characterized by inflammation triggered by the immune system and damaging certain parts of the body. The initial event is presumed to be the sensitization of (CD4)+ T-helper cell differentiation clusters to thyroid antigens. Thyrocytes are destroyed by CD8+ T-cells,

cytokines, and cell-mediated cytotoxicity by antithyroid antibodies, antithyroid peroxidase, antithyroglobulin, and anti-thyroid stimulating hormone (TSH) receptor antibodies attached to the thyrocyte. In recent years, overall incidence of HT is increasing and it is attributed to high iodine intake, particularly in areas near the coast.^{9,10}

Cytological observations of lymphoid cells (in the background), as well as lymphoid cell infiltration of follicular cells, reveal HT. Plasma cells, epithelioid cell granulomas, Hurthle cells and multinucleated giant cells are examples of less common yet varied characteristics.¹¹ In the majority of instances, hypothyroidism occurs gradually. Some people might encounter a short time of thyrotoxicosis, in which free T4 and T3 levels rise while TSH levels fall. As hypothyroidism progresses, T4 and T3 levels decrease, whereas TSH levels rise to compensate.⁷

The Bethesda method was applied to analyze thyroid fine needle aspirates for cytological indicators of lymphocytic thyroiditis, and 155 patients were found to have lymphocytic thyroiditis in this study. The age range with the highest prevalence among these patients in our research was 31-40 years old, which is analogous with findings from various Indian studies.^{8,12,13,14,15} The maximum cases discovered in this study were in younger age groups (mostly in third decade) than those reported in the literature, with one patient being a 6-year-old only. Many Indian research have detected lymphocytic thyroiditis at a young age in the Indian population, in contrast with Western studies, whereby the median age of the patient was 58 years.¹⁶

The current study found that females outweighed

males, which is consistent with the majority of previous research.^{5,6,8,17} The majority of the patients in the present investigation were hypothyroid, which is following other studies in the past.^{8,17,18} Our research showed no statistically significant association between cytological grading and the patient's thyroid hormone levels, which is consistent with earlier research.^{6,8,17} Grade 3 lymphocytic infiltration, on the other hand, suggests a statistically significant association with both TPO and TSH or only TSH.⁵ Similarly, Kumar et al discovered that the link between lymphocytic infiltration and hormonal state was statistically significant.¹³

In the present investigation, among cases with moderate to heavy infiltration, the hypothyroid state (50%) was more prevalent than the hyperthyroid state (31.25%), though no statistically significant correlation was found for hypo or euthyroid state ($p=2.88$). The proportion of hypothyroid patients with mild infiltration was the largest (48.14%), yet this wasn't statistically significant. Contrary Megalamane *et al.*¹⁹ present a statistically significant difference between TSH and cytological grades of LT. Hashimoto's thyroiditis and other thyroid lesions have similar clinical, radiological, and hormonal characteristics, rendering them ineffectual. Antibody testing is not successful in the early stages of HT because intrathyroidal lymphocytes produce local antibodies that do not flow over into the bloodstream.^{11,19} However, FNAC has certain drawbacks in detecting lymphocytic thyroiditis.⁹ Finding out about HT can be hard in the case of Graves disease, which is characterized by extensive colloid hyperplasia. Similarly, FNAC makes it difficult to diagnose thyroiditis in the toxic phase, often known as Hashitoxicosis. In such cases, only clinical and hormonal testing is necessary to distinguish between Hashitoxicosis and Graves' illness.¹¹ Smears with Hurthle cells, hyperplastic follicular cells, and a small population of lymphocytes (in the background) but no lymphocytes in epithelial groups pose a significant diagnostic challenge in iodine-deficient regions, with colloid/adenomatous/hyperplastic goitre being the primary differential diagnosis.

In the beginning stages of Hashimoto's thyroiditis, an exclusive sample collected from a hyperplastic nodule comprising exclusively Hurthle cells with no or minimal lymphocytic infiltration enhances the chance of Hurthle cell neoplasm.³ Hurthle cells in flat sheets contribute to thyroiditis, whereas poorly organized and cohesive cell clusters cause neoplasia.¹¹ The existence of lymphoid cells during grade III thyroiditis is possibly indicative of lymphoma.¹⁷ Hashimoto's thyroiditis is the underlying cause of around 75% of thyroid gland primary lymphomas.¹¹ The presence of polymorphic lymphoid cells assists in distinguishing these patients from non-Hodgkin lymphomas.^{3,8}

LIMITATION OF THE STUDY

Due to non-affordability of patients, thyroid antibody test,

ultrasonography of thyroid and thyroid scans were not done in most of patients.

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