



**Study of cytological findings of lymphocytic thyroiditis and its correlation with anti-thyroid peroxidase (anti-TPO) antibody levels and thyroid-stimulating hormone (TSH) levels:
A retrospective observational study.**

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Abstract

Introduction: Lymphocytic thyroiditis is an autoimmune thyroid disorder marked by diffuse lymphocytic infiltration of the thyroid gland. It is the second most common thyroid pathology encountered on fine-needle aspiration cytology (FNAC), predominantly affecting women. The disorder presents with variable thyroid functional states, including hypothyroidism, euthyroidism, and hyperthyroidism.

Objective: To evaluate the cytological spectrum of lymphocytic thyroiditis and to correlate cytological grades with serum Anti-thyroid peroxidase (anti-TPO) antibody titers and thyroid-stimulating hormone (TSH) levels.

Materials and methods: A retrospective study was carried out over 30 months (2021–2023), including 44 FNAC-confirmed cases of lymphocytic thyroiditis. Cytological grading was performed using the system proposed by Bhatia et al., and correlation with Anti-TPO antibody levels and TSH values was assessed. Both parameters were measured using ADVIA Centaur XP immunoassay analyser employing chemiluminescent technology. Data were analysed with SPSS software, and statistical significance was set at $p < 0.05$.

Results: Of the 44 cases, 39 were females (88.63%), with the 21–30 years age group being most commonly affected (29.5%). Cytological grading revealed Grade I in 18 cases (40.9%), Grade II in 17 cases (38.63%), and Grade III in 9 cases (20.45%). Elevated Anti-TPO antibody levels were observed in 11 cases overall, with the highest frequency in Grade III (88.88%). Raised TSH levels were detected in 13 patients, more frequently in Grade II (58.82%). Correlation between cytological grades and biochemical markers was statistically significant ($p < 0.05$).

Conclusion: Cytological grading in conjunction with biochemical evaluation provides a comprehensive assessment of lymphocytic thyroiditis, facilitating early diagnosis and appropriate management.

Recommendations: Routine integration of FNAC grading with Anti-TPO and TSH estimation is recommended for timely diagnosis, monitoring, and individualized patient management.

Keywords: Lymphocytic thyroiditis, Fine-Needle Aspiration Cytology (FNAC), Cytological grading, Thyroid-Stimulating Hormone (TSH) levels, Anti-Thyroid Peroxidase (Anti-TPO) antibodies.

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Introduction

Hakaru Hashimoto described lymphocytic thyroiditis in 1912 [3]. Lymphocytic thyroiditis is an autoimmune disorder characterized by lymphocytic infiltration of the thyroid gland, destroying the thyroid follicles, which are eventually replaced by fibrosis. It is the second most common thyroid disorder diagnosed on Fine needle aspiration cytology (FNAC) [3]. It is frequently seen in women [1]. Globally, the commonest cause of hypothyroidism is iodine deficiency; lymphocytic thyroiditis remains the commonest cause of spontaneous hypothyroidism in regions with adequate iodine intake.

It can be associated with hypothyroidism, euthyroidism, and even hyperthyroidism. The clinical presentation of autoimmune thyroiditis can vary from diffuse to nodular swelling without symptoms. Fine needle aspiration cytology (FNAC) is a sensitive tool in diagnosing lymphocytic thyroiditis with a diagnostic accuracy rate of 92 % [2].

A predefined set of criteria was used for grading cytological features on FNAC smears, similar to the criteria used by Bhatia et al [3]. The goal was to determine the incidence of chronic lymphocytic thyroiditis by grading the cytological features of thyroid FNAC according to lymphocytic infiltration and comparing them with thyroid-stimulating hormone (TSH) levels and anti-thyroid Peroxidase Antibody (TPO) antibody levels.

Aims and objectives

1. To evaluate the cytological spectrum of lymphocytic thyroiditis.
2. To correlate the cytological grades with levels of Anti-TPO antibodies and TSH in serum to improve the diagnosis of autoimmune thyroiditis.

Materials and methods

Study design and setting

This was a retrospective observational cross-sectional study conducted over a period of 30 months (January 2021 – June 2023) in the Department of Pathology at D. Y. Patil School of Medicine and Hospital, Navi Mumbai, Maharashtra, India. The institution is a tertiary care postgraduate teaching hospital catering to patients from urban, semi-urban, and rural regions of Navi Mumbai and neighboring districts. As the hospital receives a high volume of thyroid cases, it provides a diverse patient population, making it an appropriate setting for evaluating cytological and biochemical correlations in lymphocytic thyroiditis.

Study population

Patients aged 11–80 years presenting to the outpatient department with painful or painless midline neck swelling, along with a relevant clinical history suggestive of hypothyroidism or hyperthyroidism, were referred for cytological evaluation.

Inclusion criteria

All cases diagnosed as lymphocytic thyroiditis on FNAC during the study period.

Availability of corresponding biochemical parameters (TSH and Anti-TPO antibody levels).

Exclusion criteria

Patients with a history of thyroid-related drug intake.

Patients with prior thyroid surgery.

Cytological procedure

Fine-needle aspiration cytology (FNAC) was performed using a 24-gauge needle attached to a 5 ml syringe employing the non-aspiration technique. Multiple smears were prepared and stained with:

Papanicolaou stain

Hematoxylin and Eosin (H&E) stain

Giemsa stain

Smear adequacy was assessed by two independent pathologists using Hamburger's criteria, wherein smears were considered satisfactory if six clusters of benign follicular cells were identified in at least two slides from two separate needle passes.

Cytological evaluation

Qualitative features analyzed included:

Lymphocytes and plasma cells infiltrating thyroid follicles

Increased lymphocytes in the background

Presence of multinucleated giant cells

Cytological grading was performed according to Bhatia et al. into three categories:

Grade I (Mild): Scant lymphoid infiltration of follicles with increased background lymphocytes.

Grade II (Moderate): Moderate infiltration with the presence of giant cells or anisonucleosis.

Grade III (Severe): Dense infiltration with germinal center formation and scant residual follicular cells.



Biochemical analysis

Serum TSH and Anti-TPO antibody levels were estimated using the ADVIA Centaur XP immunoassay analyzer based on chemiluminescent immunoassay (CLIA) technology. Reference ranges were:

TSH: 0.35 – 4.94 μ IU/ml

Anti-TPO antibodies: <30 IU/ml (Equivocal: 30–40 IU/ml)

Sample size

A total of 44 cases diagnosed as lymphocytic thyroiditis on fine-needle aspiration cytology (FNAC) with corresponding biochemical data (thyroid-stimulating hormone [TSH] and anti-thyroid peroxidase [Anti-TPO] antibody levels) were included. The sample size thus comprised all consecutive eligible patients during the 30-month study period. As this was a retrospective analysis, no prior formal sample size calculation was performed; instead, a census sampling approach was adopted to minimize selection bias. For methodological justification, the minimum required sample size for correlation studies was estimated using the formula: $n = Z^2 \times p(1-p) / d^2$

Where:

$Z = 1.96$ at 95% confidence level

$p = 0.30$ (anticipated proportion of hypothyroidism among lymphocytic thyroiditis cases from previous studies [4])

$d = 0.15$ (allowable error)

This yielded a minimum sample size of 40. Our study included 44 cases, thus meeting the required sample size threshold.

Statistical analysis

Cytological grades were correlated with TSH and Anti-TPO antibody levels using IBM SPSS Statistics Version 27. A p -value < 0.05 was considered statistically significant.

Bias and limitations subsection

Potential sources of bias included selection bias, as only patients with complete cytological and biochemical data

were included. To minimize this, consecutive sampling of all eligible cases was employed. Information bias was addressed by having two independent pathologists review the FNAC smears, and any discrepancies were resolved by consensus. Recall bias was not applicable due to the retrospective design, and observer bias was reduced through blinded assessment of cytology slides without prior knowledge of biochemical results.

Ethical considerations

The study was approved by the Institutional Ethics Committee of D. Y. Patil School of Medicine and Hospital, Navi Mumbai, Maharashtra, India, before commencement. As this was a retrospective analysis, patient confidentiality was strictly maintained by anonymizing records. No additional interventions or financial burden were imposed on participants. All procedures adhered to the ethical principles outlined in the Declaration of Helsinki.

Results

A total of 61 thyroid FNAC cases were screened during the study period (January 2021 – June 2023). Of these, 8 were excluded due to inadequate cytological material, 5 were excluded as they represented other thyroid pathologies (colloid goiter, papillary carcinoma, and follicular neoplasm), and 4 were excluded due to incomplete biochemical records. Thus, 44 cases were confirmed as lymphocytic thyroiditis on FNAC with corresponding thyroid-stimulating hormone (TSH) and anti-thyroid peroxidase (Anti-TPO) antibody data available, and were included in the final analysis.

Patients included in this study were in the age group 11 to 80 years with a male-to-female ratio of 1:8. The maximum number of patients were seen in the age group of 21-30 years (29.5%), with the majority of patients being females (89%). Table 1 and 2 shows the age and sex distribution of lymphocytic thyroiditis.



Table 1- age group distribution.

AGE (Years)	FREQUENCY	PERCENT(%)
11-20	7	15.9
21-30	13	29.5
31-40	10	22.7
41-50	11	25.0
51-60	02	4.5
61-70	00	0
71-80	01	2.3
TOTAL	44	100

Table 2 – age & sex distribution

AGE GROUP(Years)	Male	Female
11-20	00	07
21-30	01	12
31-40	01	09
41-50	02	09
51-60	00	02
61-70	00	00
71-80	01	00
TOTAL	05	39

Table 3 displays the cytological grading of lymphocytic thyroiditis, with 18 patients (40.9%) being classified as Grade-1 1, 17 patients (38.63%) being classified as Grade-2 2 and 9 patients (20.45%) being classified as Grade-3 3.

Table 3 – cytomorphological grading of lymphocytic thyroiditis cases

GRADE	NUMBER OF CASES	PERCENTAGE %
I	18	40.9
II	17	38.63
III	9	20.45

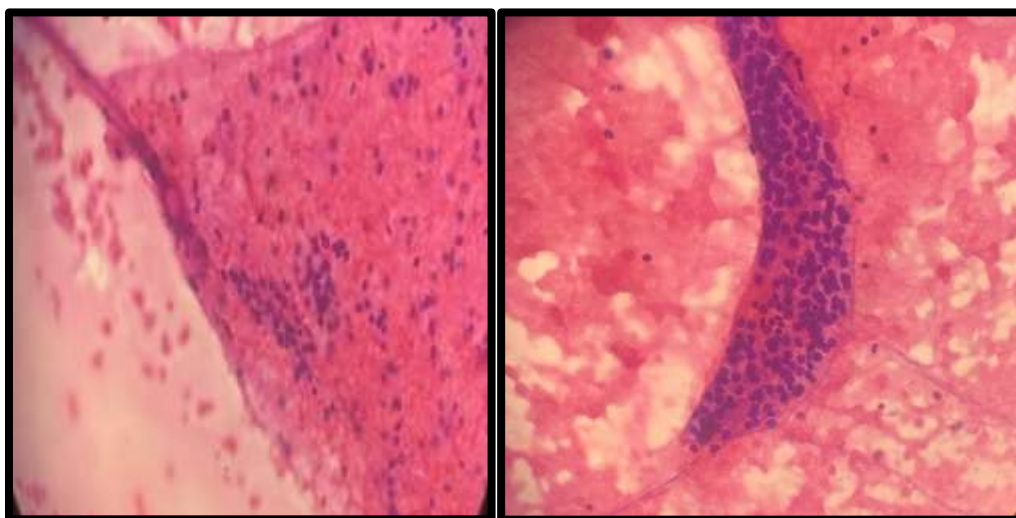


Figure 1 – grade-1, 1 lymphocytic thyroiditis.

Figure 1 shows Cytomorphological Grade 1 displaying a small number of lymphoid cells infiltrating the thyroid follicles and an increased number of lymphocytes in the background. (H & E stain 400x).

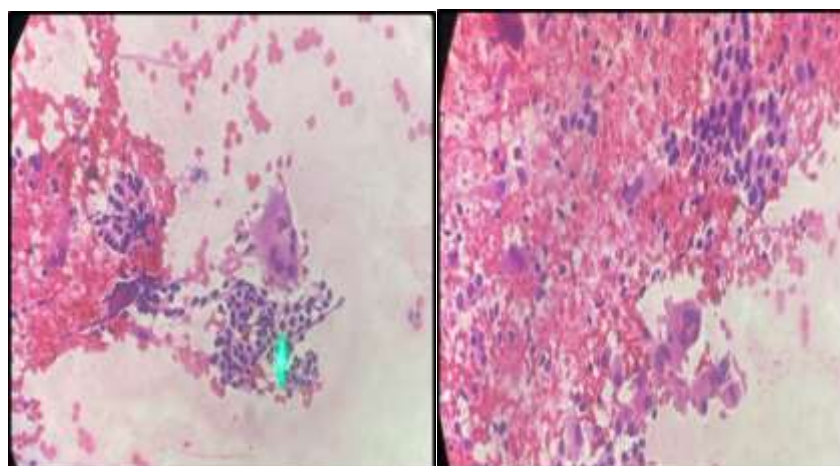


Figure 2 - grade 2 lymphocytic thyroiditis

Figure 2 shows Cytomorphological grade 2 displaying a moderate degree of lymphocytic infiltration or a few lymphocytic infiltrations with the presence of giant cells or anisonucleosis. (H & E Stain 400x).

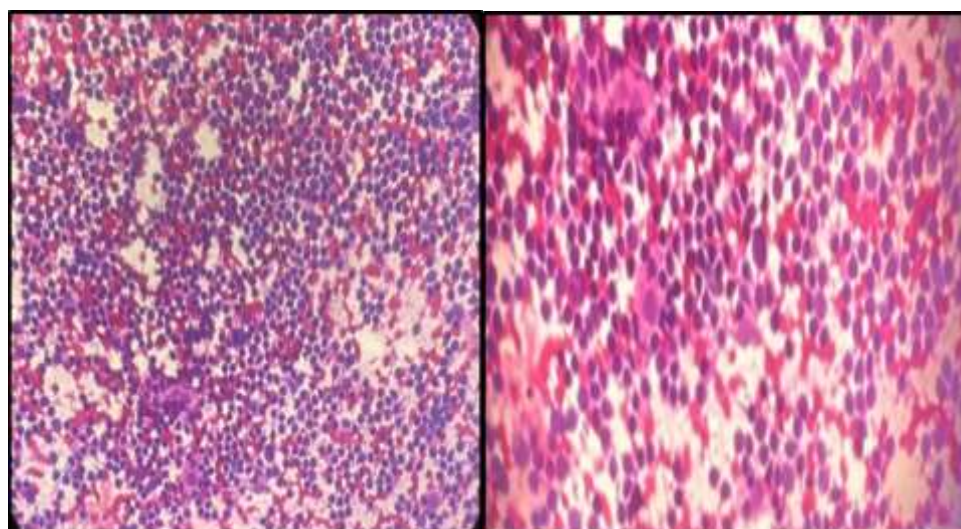


Figure 3 – grade 3 lymphocytic thyroiditis

Figure 3 shows Cytomorphological grade 3 displaying extensive lymphocytic inflammation with the formation of germinal centers and a limited presence of thyroid follicular cells. (H & E Stain 400x)

Through investigations, it was found that 26 patients (59.9%) were euthyroid, 13 patients (29.54%) were hypothyroid, and 4 patients (9.09%) were hyperthyroid. The thyroid panel was not done for 1 patient.

Table 4 – TSH and FNAC cross tabulation.

TSH	FNAC			TOTAL
	GRADE 1	GRADE 2	GRADE 3	
NORMAL	16	5	5	26
INCREASED	2	10	1	13
DECREASED	0	2	2	4
TOTAL	18	17	8	43

In Grade-1 1 lymphocytic thyroiditis cases, 16 were euthyroid and 2 were hypothyroid.

In Grade-2 2 lymphocytic thyroiditis cases, 5 were euthyroid, 10 were hypothyroid, and 2 were hyperthyroid.

In Grade-3 3 lymphocytic thyroiditis cases, 5 were euthyroid, 1 was hypothyroid, and 2 were hyperthyroid.

P-value for TSH-FNAC cross tabulation was 0.009, which is statistically significant (<0.05).

Table 5 - TPO and FNAC cross tabulation.

TPO	FNAC			TOTAL
	GRADE 1	GRADE 2	GRADE 3	
NORMAL	3	2	0	5
INCREASED	2	5	8	15
TOTAL	5	7	8	20

In Grade-1, 1 In lymphocytic thyroiditis cases, TPO levels were in the normal range in 3 cases and increased in 2 cases.

In 2 Grade-2 lymphocytic thyroiditis cases, TPO levels were in the normal range in 2 cases and increased in 5 cases.

In 3 Grade-3 lymphocytic thyroiditis cases, TPO levels were increased in 8 cases.

P-value for TSH-FNAC cross tabulation was 0.013, which is statistically significant (<0.05).

Discussion

The thyroid gland is essential for metabolic regulation, protein synthesis, growth, reproduction, and pregnancy. Autoimmune thyroiditis is a major cause of hypothyroidism, and when untreated, may result in menstrual irregularities, infertility, miscarriages, and congenital malformations. It is characterized by lymphocytic infiltration of thyroid tissue and is frequently accompanied by elevated thyroid autoantibodies, making cytological and serological assessments crucial for accurate diagnosis.

In the present study, the highest incidence was observed in the 21–30 years age group, which is consistent with earlier research [3]. A marked female predominance was also noted (88.63%), aligning with previous reports [1,3,4].

Cytological grading showed that the majority of cases belonged to Grade I (40.9%), comparable to earlier findings [4]. On biochemical correlation, hypothyroidism was detected in 29.54% of cases, similar to previous reports of 30% and 54.8% [4]. However, higher frequencies of hypothyroidism (73.6%) have also been reported [1], suggesting population-based variability.

In this study, anti-TPO antibody elevation was observed most frequently in Grade III cases (18.18%), followed by Grade II (11.36%) and Grade I (4.54%). This was lower than the elevated Anti-TPO levels reported in other studies, which ranged from 26.2% to 95% [3,4]. Nevertheless, more recent studies continue to demonstrate a strong correlation between Anti-TPO positivity and higher cytological grades [5–8].

Conclusion

In conclusion, lymphocytic thyroiditis should be diagnosed using a multidisciplinary approach. Many patients with lymphocytic thyroiditis may have neither symptoms nor signs of the disease. Therefore, relying solely on clinical features and serum findings may result in missed diagnoses. Clinical features, biochemical parameters, cytological findings, and radiological evaluation should be integrated to reach a definitive diagnosis. The study demonstrated a significant association between anti-thyroid peroxidase (Anti-TPO) antibody levels and cytological grades of lymphocytic thyroiditis. A significant correlation between thyroid-stimulating hormone (TSH) levels and cytological grades was also observed. Fine-needle aspiration cytology (FNAC) findings, together with the Anti-TPO antibody assay, represent essential components in the evaluation of thyroid nodules. The combined use of cytological grading, ultrasonography, and biochemical analysis can aid in detecting subclinical hypothyroidism and guide timely treatment.

Limitations

The present study is limited by its retrospective design, relatively small sample size, and single-center setting. Lack of long-term follow-up and exclusion of radiological findings have restricted the generalizability and comprehensive assessment of autoimmune thyroiditis.



Recommendations

Based on the study findings, it is recommended that cytological grading of lymphocytic thyroiditis be routinely correlated with biochemical and serological investigations, particularly TSH and Anti-TPO antibody levels, to improve diagnostic accuracy and guide timely clinical intervention. Incorporating both FNAC and serology enhances early detection of thyroid dysfunction, enabling individualized treatment and monitoring strategies. Multidisciplinary collaboration between pathologists, endocrinologists, and clinicians is essential for integrated patient care. Larger multicentric studies with longer follow-up are recommended to validate cytological grading as a prognostic tool and to explore its role in predicting long-term thyroid dysfunction and malignant transformation.

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Abbreviations

FNAC – Fine Needle Aspiration Cytology;
TSH – Thyroid Stimulating Hormone;
TPO – Thyroid Peroxidase;
Anti-TPO – Anti-Thyroid Peroxidase Antibody;
H&E – Hematoxylin and Eosin;
CLIA – Chemiluminescent Immunoassay;
SPSS – Statistical Package for the Social Sciences;

Source of funding

The study had no funding.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

SP-Concept and design of the study, results interpretation, review of literature, and preparation of the first draft of the manuscript. Statistical analysis and interpretation, revision of manuscript. **PD**-Concept and design of the study, results interpretation, review of literature, preparing the first draft of the manuscript, and revision of the manuscript. **SS**-Review of literature and preparing the first draft of the manuscript. Statistical analysis and interpretation.

Data availability

Data available on request

Author biography

Dr. Shreya Pandey completed her MBBS in 2017 from the Himalayan Institute of Medical Sciences, Dehradun, and obtained her MD degree in pathology in 2025 from D.Y. Patil Medical College, Navi Mumbai. She served as the principal investigator for the research project titled “Nitroblue Tetrazolium Test as an assay of Neutrophil function in Diabetes mellitus patients”. Currently, she is a senior resident in the department of pathology at D.Y. Patil School of Medicine, Navi Mumbai. <https://orcid.org/0009-0007-1333-157X>.

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