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# Cytomorphological Features and Grading of Lymphocytic Thyroiditis: A Cross-Sectional Study among Patients in a Tertiary Care Hospital in Chengalpattu District

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## KEYWORDS

Thyroiditis,  
Autoimmune,  
FNAC,  
Hypothyroid,  
Hyperthyroid.

## ABSTRACT:

**Introduction:** Chronic lymphocytic thyroiditis is the second most common thyroid disorder diagnosed using Fine Needle Aspiration Cytology (FNAC) after benign follicular nodule. Fine needle aspiration cytology (FNAC) serves as a crucial diagnostic modality due to its simplicity, safety, and accuracy.

**Objective:** The main objective of this study was to grade chronic lymphocytic thyroiditis on FNAC smears using predefined criteria formulated by Bhatia A et al and to find out its association with clinical parameters.

**Methods:** This cross-sectional study included all the FNAC smears diagnosed with lymphocytic thyroiditis during the five years study period from January 2019 to December 2023. Relevant clinical and pathological data were retrieved from the medical records of the department and all the cases of lymphocytic thyroiditis were graded based on the pre-defined cytomorphological criteria by Bhatia A et al. Pearson chi-square test was employed to determine the association of cytological grading with several clinical parameters.

**Results:** Of the 194 cases of lymphocytic thyroiditis reported in FNAC, females (94%) were commonly affected and majority (49%) were in the age group of 30-50 years. Most cases were clinically hypothyroid (59%) and presented with diffuse swelling (74%) of the thyroid gland. On further cytological grading, most cases (69%) of lymphocytic thyroiditis belonged to grade II. Correlation of cytological grade with thyroid functional status (P value: 0.49), age of patients (P value: 0.46) and clinical presentation (P value: 0.18) were found to be statistically not significant.



Conclusions: Cytological grading of lymphocytic thyroiditis reflects on the autoimmune activity within the thyroid gland and is not significantly related to the age of patient, nature of thyroid swelling or thyroid functional status.

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## 1. Introduction:

Thyroid disorders are the most prevalent endocrine disorders worldwide with varied distribution among different population groups and geographic locations. Surveys show that 3.2% of the Indian population are affected by thyroid related disorders. Easy accessibility for clinical examination along with thyroid hormone assays, ultrasound and Fine Needle Aspiration Cytology (FNAC) have made diagnosis of thyroid disorders easier.[1]

Chronic lymphocytic thyroiditis also known as Hashimoto or autoimmune thyroiditis is found to be the second most common thyroid disorder diagnosed by FNAC after benign follicular nodule. Both these common thyroid lesions belong to category-II in the standard reporting system for thyroid cytology namely The Bethesda System of Reporting Thyroid cytology. Although iodine deficiency was the main cause of hypothyroidism, lymphocytic thyroiditis is the main cause of spontaneous hypothyroidism in iodine adequate areas. Females in the age group of 30-50 years have more predilection for developing lymphocytic thyroiditis.[2] The disease process has a classic destructive autoimmune phenomenon which initially in active phase results in thyrotoxicosis followed by evolution and destructive phase that presents as subclinical or overt hypothyroidism.[3] The pathogenesis of autoimmune destruction was found to be due to production of autoantibodies against certain thyroid specific proteins such as thyroglobulin and thyroid peroxidase along with enzymatic overproduction of reactive oxygen species using Nicotinamide Adenine Dinucleotide Phosphate (NADPH).[4] Most individuals present with a painless, symmetrical enlargement of thyroid gland clinically. Though clinical examination, hormonal profiles and radiology help to assess thyroid enlargement, FNAC remains to be the gold standard, basic and effective

modality to diagnose chronic lymphocytic thyroiditis preoperatively on an outpatient basis with a diagnostic accuracy of 92%.[4] The classic cytology picture of chronic lymphocytic thyroiditis includes the presence of mixed populations of mature and transformed lymphocytes impinging on the thyroid follicular cells along with hurthle cells and occasional epithelioid and giant cells in the background of scant or absent colloid.[5,6]

Though many studies have been carried out on histological grading of thyroiditis by estimating the number of foci of lymphocytes per standard field, there are only few studies which graded thyroiditis on cytology smears and none have been carried out in Chengalpattu district.

## 2. Objectives:

The objective of the present study was to grade lymphocytic thyroiditis based on the evaluation of FNAC smears using a pre-defined criteria developed by Bhatia A et al [7] and to correlate the cytological grades with several clinical parameters like patients' age, nature of thyroid swelling and thyroid functional status. The grading system laid by Bhatia A et al [7] was validated and found to be concordant with many similar studies making it a reliable grading system.

## 3. Methods:

### Study design:

This was a cross-sectional study carried out in the department of pathology at a tertiary care centre, during the period of January 2019 to December 2023 after getting ethical approval from the Institutional Ethics committee (IEC Ref No: KIMS/PG/06/09/2023).

**Sample size:**

Purposive sampling technique was used for selection of the desired samples according to the inclusion criteria and a total of 194 cytological smears were reviewed.

**Inclusion criteria:**

All the FNAC cytological smears reported as lymphocytic thyroiditis (Category II of The Bethesda System of Reporting Thyroid cytology) from January 2019 to December 2023 were included in this study.

**Exclusion criteria:**

FNAC cytological smears diagnosed as infectious thyroiditis or thyroid neoplasm were excluded from the study.

**Data collection:**

Relevant clinical, pathological and biochemical data of all cases of lymphocytic thyroiditis reported during the five years study period were retrieved from the medical records of the Department of Pathology. Corresponding FNAC smears stained with Hematoxylin & Eosin (H&E) and May-Grunwald Giemsa (MGG) stains stored in the department of pathology were retrieved, reviewed and the findings were documented. Based on the available thyroid hormone profile, the patients were categorized as euthyroid, hypothyroid and hyperthyroid. The reference range used were T4 (55-135ng/ml), T3 (0.7–2ng/ml) and TSH (0.17-4.05mIU/ml).[6] The cytological smears were further graded as per the pre-defined criteria by Bhatia A et al.<sup>[7]</sup> The grading system formulated by Bhatia A et al<sup>[7]</sup> categorized lymphocytic thyroiditis into three grades:

- Grade I (Mild): Few lymphoid cells infiltrating the follicles and 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 center formation and very few follicular cells left.

**Statistical analysis:**

- Statistical analysis was carried out using SPSS 23.0 and results were expressed in terms of frequency and percentage.
- The correlations were carried out using Pearson chi-square test. P value of less than 0.05 was taken as statistically significant.

**4. Results:**

FNAC is a basic diagnostic tool for diagnosis of thyroid pathology and based on the standard Bethesda System for Reporting Thyroid Cytology, a total of 194 cytological smears diagnosed as category-II lymphocytic thyroiditis were included in the present study. Among the cases studied, 182 were females (94%) with majority of the patients in the age group of 30 to 50 years (n=96; 49%) followed by less than 30 years of age (n=83; 43%). The mean age was 19.5 years, with age ranging from 10 to 68 years clinically (Table 1 and 2).

**Table 1: Gender distribution of Lymphocytic thyroiditis**

Gender	Frequency (n)	Percentage (%)
Females	182	94
Males	12	06
Total	194	100



**Table 2: Age distribution of Lymphocytic thyroiditis**

Age (years)	Frequency (n)	Percentage (%)
<30	83	43
30 to 50	96	49
> 50	15	08
<b>Total</b>	<b>194</b>	<b>100</b>

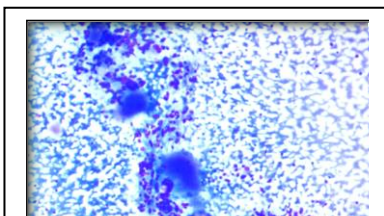
In this study, 143 cases (74%) presented with diffuse thyroid enlargement while only 51 cases (26%) presented with nodular disease. Based on the thyroid hormone profile, 114 cases (59%) were hypothyroid followed by 48 cases (25%) of hyperthyroidism and 32 cases (16%) of euthyroid functional status.

The cytomorphological features of lymphocytic thyroiditis revealed the presence of thyroid follicular

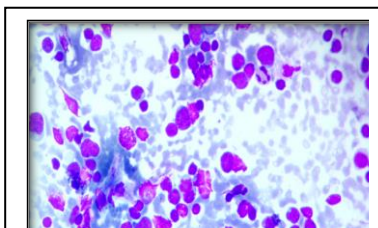
epithelial cells with lymphocytic infiltration and background lymphocytes in all the cases (100%) in the present study. Other features observed were the presence of colloid in 185 cases (95%), hurthle cells with anisokaryosis in 162 cases (84%), giant cells in 49 cases (25%) and germinal centre formation in a single case (Fig 1 to 6; Table 3).

**Table 3: Cytomorphological features of Lymphocytic thyroiditis**

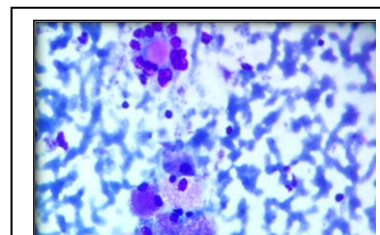
Cytomorphological Features	Frequency (n)	Percentage (%)
Thyroid follicular cells	194	100
Follicular lymphocytic infiltration	194	100
Background lymphocytes	194	100
Hurthle cells with anisokaryosis	162	84
Giant cells	49	25
Presence of colloid	185	95
Germinal centre formation	01	01



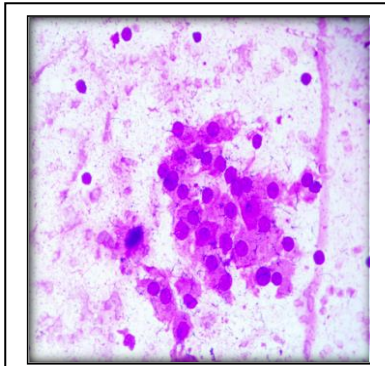
**Figure 1: GRADE-I Lymphocytic thyroiditis showing lymphocytes intermixed with thyroid follicular cells (10x, MGG)**



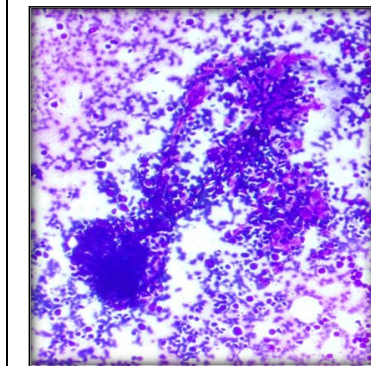
**Figure 2: GRADE-I Lymphocytic thyroiditis showing lymphocytes intermixed with thyroid follicular cells (40x, MGG)**



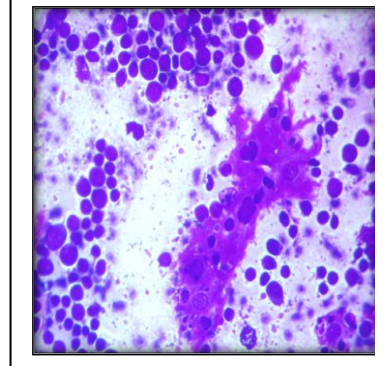
**Figure 3: GRADE-II Lymphocytic thyroiditis showing lymphocytic infiltration with Hurthle cell change (10x, MGG)**



**Figure 4: GRADE-II Lymphocytic thyroiditis showing lymphocytic infiltration with hurthle cell change (40x, MGG)**



**Figure 5: GRADE-III Lymphocytic thyroiditis showing florid lymphocytic inflammation forming lymphoid follicles (10x, MGG)**



**Figure 6: GRADE-III Lymphocytic thyroiditis showing florid lymphocytic inflammation with very few thyroid follicular cells (40x, MGG)**

Based on the cytological grading of lymphocytic thyroiditis proposed by Bhatia A et al,<sup>[7]</sup>135 cases (69%) belonged to grade II followed by 58 (30%) grade I cases. In this study only one case (1%) belonged to grade III category (Table 4).

**Table 4: Cytological grading of Lymphocytic thyroiditis according to Bhatia A et al<sup>(7)</sup>**

Cytological grade	Frequency (n)	Percentage (%)
Grade I	58	30
Grade II	135	69
Grade III	01	01
Total	194	100

Among the 96 patients in the age group of 30 to 50 years, 70 cases (73%) belonged to cytological grade II while 26 cases (27%) belonged to Grade I cytological category. The age distribution of patients with

lymphocytic thyroiditis was correlated with cytological grade which showed statistically insignificant association (P value: 0.46) in this study (Table 5).

**Table 5: Correlation between age of patients and cytological grade of Lymphocytic thyroiditis**

Age (years)	Grade I n (%)	Grade II n (%)	Grade III n (%)	Total n (%)	Pearson chi-square test
<30	29 (35)	53 (64)	01 (01)	83 (43)	P value- 0.46
30 to 50	26 (27)	70 (73)	0	96 (49)	



> 50	03 (20)	12 (80)	0	15 (08)	
<b>Total</b>	58 (30)	135 (69)	01 (01)	194 (100)	

Among the patients with diffuse thyroid enlargement, majority (69%) belonged to cytological grade II while 73% of patients with nodular thyroid enlargement belonged to cytological grade II category. However the

association between clinical presentation and cytological grade of lymphocytic thyroiditis was found to be statistically insignificant (P value: 0.18) in the current study (Table 6).

**Table 6: Correlation between Clinical presentation and cytological grade of Lymphocytic thyroiditis**

Clinical presentation	Grade I n (%)	Grade II n (%)	Grade III n (%)	Total n (%)	Pearson chi-square test
Diffuse thyroid enlargement	45 (31)	98 (69)	0	143 (74)	P value- 0.18
Nodular thyroid enlargement	13 (25)	37 (73)	01(2)	51 (26)	
<b>Total</b>	58 (30)	135 (69)	01 (1)	194 (100)	

In the present study, majority (59%) of the patients presented with hypothyroidism and among them, 66% belonged to cytological grade II followed by 33% in grade I and 1% in grade III cytological categories. The

statistical association between thyroid functional status and cytological grade of lymphocytic thyroiditis was not significant (P value: 0.49) in this study (Table 7).

**Table 7: Correlation between thyroid functional status and cytological grade of Lymphocytic thyroiditis**

Thyroid functional status	Grade I n (%)	Grade II n (%)	Grade III n (%)	Total n (%)	Pearson chi-square test
Hypothyroid	38 (33)	75 (66)	01 (1)	114 (59)	P value- 0.49
Hyperthyroid	14 (29)	34 (71)	-	48 (25)	
Euthyroid	6 (19)	26 (81)	-	32 (16)	
<b>Total</b>	58 (30)	135 (69)	01 (1)	194 (100)	



## 5. Discussion:

Hashimoto thyroiditis also known as chronic lymphocytic thyroiditis is an autoimmune condition characterized by antibody mediated destruction of thyroid follicles and is the most common cause of hypothyroidism among adult females especially in coastal areas with adequate iodine diet.[8] FNAC is a basic and effective diagnostic modality in the clinical evaluation of patients with thyroid enlargement.

A total of 194 cases diagnosed as category-II lymphocytic thyroiditis using the Bethesda System for reporting thyroid cytology were included in the study. The most common age group was 30 to 50 years (49%) with mean age of 19.5 years. This was almost similar to the studies by Singh BK et al [8] from Assam, North East India and Anila KR et al [9] from Kerala, South India. However Ashraf D et al [6] from North India reported majority of patients in the age group of 16-30 years in their study. Thus there was a difference in the prevalence of lymphocytic thyroiditis in different geographical locations. The probable underlying etiology is attributed to iodine deficiency in non-coastal regions among the younger age group while excess intake of iodine is implicated in the iodine sufficient coastal areas among elderly females. The female to male (F:M) ratio in the present study was 15:1 which was in close concordance to the studies by Singh BK et al [8] and Ashraf D et al. [6]

Majority of patients in this study presented clinically with diffuse enlargement (74%) of thyroid gland which was almost similar to the studies by Ashraf D et al [6], Anila KR et al [9] and Shetty A et al.[10] The diffuse enlargement of thyroid gland was attributed to the variations in dietary iodine intake and late stage of clinical presentation. Nodular thyroid enlargement occurs in the initial phase of lymphocytic thyroiditis. However most of the patients present in the advanced stage with diffuse thyroid swelling. [6,11] In this study, nodular disease was observed in 26% of patients who were picked up in the early stage of disease without any significant biochemical alterations in the serum thyroid hormonal profile.

Based on the thyroid hormonal status, hypothyroid state was observed in majority (59%) of the patients in the current study which was similar to studies done by Ashraf D et al [6], NS Divya et al [3], Gupta et al [12] and Kumar R et al.[13] On the contrary, Jayaram G et al [14] from New Delhi reported 55% of euthyroid patients while Anila KR et al [9] from Kerala reported 65% of euthyroid patients. Thus there was a difference in the thyroid functional status of the patients with lymphocytic thyroiditis in different geographic locations.

The Grading system proposed by Bhatia A et al [7] categorised lymphocytic thyroiditis into three grades namely, Grade I, Grade II and Grade III based on the cytological features. The present study showed that majority of the patients belonged to grade II (69%) followed by grade I (30%) and grade III (1%) which was concordant to similar studies by Ashraf D et al [6] and Singh BK et al.[8] However, Anila KR et al [9] from Kerala reported majority (45%) of grade I cases while Sood N et al [15] from New Delhi reported majority (40%) of grade III cases.

The cytomorphological features of lymphocytic thyroiditis observed in the present study were similar to the studies by Ashraf D et al [6] and Iha et al.[16] The additional features reported by Ashraf D et al [6] and Iha et al [16] were the presence of granulomas and plasma cells. Granulomas were observed in 7% of cases in the study by Ashraf D et al [6] and 16% of cases in the study by Iha et al.[16] Ashraf D et al [6] reported the presence of plasma cells in 11% of cases while Iha et al [16] reported plasma cells infiltrate in 29% of cases.

In the present study, the predominant cytological grade observed among patients of all age groups was Grade II. This reflects on the lack of association between age distribution of patients and cytological grade of lymphocytic thyroiditis. Thus statistical analysis revealed insignificant (P value: 0.46) results in this study. No other similar correlation studies have been reported in literature.



In general, patients with early-stage of lymphocytic thyroiditis may present with nodular disease without altered TSH levels despite having elevated antithyroid antibodies.[6] In the present study, 78% of patients belonging to cytological grade I and 73% of patients in cytological grade II presented with diffuse thyroid swelling while the single case in cytological grade III showed nodular enlargement of thyroid. This shows that cytological grade does not reflect on the duration or stage of lymphocytic thyroiditis. Thus the association between nature of thyroid enlargement and cytological grade of lymphocytic thyroiditis was not statistically significant (P value: 0.18) which was in concordance with the study by PP Kartha et al.[5]

In the studies by Anila KR et al [9] and Singh BK et al [8], there was no statistically significant association between cytological grade based on cytomorphological features of lymphocytic thyroiditis and thyroid functional status similar to the present study. Charanjeet Ahluwalia et al [17] reported a significant correlation between hurthle cell change and T3 hormone levels (P value : 0.041) alone. However there was no significant correlation with other cytomorphological features in the study by Charanjeet Ahluwalia et al.[17] Thus the cytological grading of lymphocytic thyroiditis gives an overall picture about the autoimmune destruction occurring within the thyroid gland and it does not necessarily reflect on the functional status of the thyroid gland. [6]

### Limitation(s):

In the present study, serum anti-thyroid antibodies like anti-Thyroid Peroxidase (anti-TPO) data were not available for majority of the patients. Also radiological investigations like Radioactive Iodine Uptake (RAIU) studies or ultrasound findings were not taken into consideration. Further studies can be carried out by incorporating the serum anti-TPO levels and radiological findings. This will provide additional information on the association of cytological grade of lymphocytic thyroiditis with serum anti-TPO levels and radiological findings thereby enabling early diagnosis and appropriate treatment for the patients.

### Conclusion(s):

Diagnosis of lymphocytic thyroiditis is a multidisciplinary approach by taking into consideration clinical, biochemical, cytological and radiological parameters. Cytological grading of lymphocytic thyroiditis is a novel approach and studies have been carried out to find out the utility of cytological grade and its clinical significance in several regions worldwide. In Chengalpattu district of Tamil nadu, no similar studies have been reported in literature. Thus in this study carried out for the first time in Chengalpattu district, it was observed that cytological grading of lymphocytic thyroiditis reflects on the severity of autoimmune activity within the thyroid gland based on cytomorphological features. However, cytological grade was not significantly associated with age of patients, nature of thyroid swelling or thyroid hormonal profile similar to other studies in literature.

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### Conflict of interest:

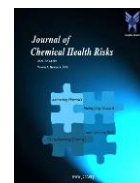
The authors declare that there is no conflict of interest.

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