

Original Research Article

Assessment of Cytomorphological Spectrum of Chronic Lymphocytic Thyroiditis with Respect to Cytological Grading, Functional and Radiological Parameters

Ashwini S Khadatkar¹, Supriya D Joshi²

^{1,2}Assistant Professor, Department of Pathology, SMBT Institute of Medical Sciences & Research Centre, Dhamangaon Ghoti, Tal. Igatpuri, Dist Nasik, Maharashtra 422403, India.

Corresponding Author:

Supriya D Joshi, Assistant Professor, Department of Pathology, SMBT Institute of Medical Sciences & Research Centre, Dhamangaon Ghoti, Tal. Igatpuri, Dist Nasik, Maharashtra 422403, India.

E-mail: drjoshisupriya@gmail.com

Received on 04.01.2020

Accepted on 07.02.2020

Abstract

Background: Fine needle aspiration cytology (FNAC) is considered a superior and more cost-effective tool for diagnosis of chronic lymphocytic thyroiditis. Chronic lymphocytic thyroiditis is an autoimmune disorder where in which thyroid follicles are rapidly destroyed. **Aim:** To assess cytomorphological spectrum of chronic lymphocytic thyroiditis with respect to the clinical, biochemical, ultrasonographic, and radionuclide parameters. **Material and Methods:** Hospital based descriptive cross-sectional study was conducted on 172 cases of chronic lymphocytic thyroiditis. **Results:** Majority were females presenting in 3rd to 4th decade. Cases diagnosed on FNAC were 155 and on histopathology were 17. Among FNAC diagnosed cases, commonest clinical presentation was diffuse (65.6%) followed by Nodular (30.9%). Only 50% showed hypothyroidism followed by hyperthyroidism (30%) and majority cases (73.55%) showed grade 2 follicular destruction. Cases diagnosed on histopathology mainly presented as nodules. Cellular changes in follicular & hurthle cells led to false positive diagnosis of neoplasia in 6 cases. Four cases of papillary cancer with thyroiditis were misdiagnosed as goitre and follicular neoplasm on FNAC. **Conclusion:** FNAC remains first line diagnostic modality for thyroiditis. The cytological grades of follicular destruction in thyroiditis can predict functional status. Few cases might be missed due to inherent procedural limitations, changing clinical presentation and associated neoplasms. On FNAC, presence of colloid, follicular hyperplasia and neoplasm could lead to diagnostic pitfalls, hence thorough cytological evaluation and integrated approach is necessary.

Keywords: Hashimoto Thyroiditis; Hurthle cells; TMA; FNAC.

How to cite this article:

Ashwini S Khadatkar, Supriya D Joshi. Assessment of Cytomorphological Spectrum of Chronic Lymphocytic Thyroiditis with Respect to Cytological Grading, Functional and Radiological Parameters. Indian J Pathol Res Pract. 2020;9(1 Part II):109-114.

Introduction

Hakaru Hashimoto described chronic lymphocytic

thyroiditis also known as Hashimoto thyroiditis (HT) in 1912. It is most common form of thyroiditis.¹ Chronic lymphocytic thyroiditis is an autoimmune disorder where in which thyroid follicles are

rapidly destroyed. Initial transient phase of hyperthyroidism is usually followed by a chronic phase of hypothyroidism. Antibody mediated destruction of thyroid follicles and lymphocytic infiltration are characteristic features of initial phase while chronic phase characterized by fibrosis of the thyroid parenchyma along with only minimal residual and atrophic follicles. So, characteristics of hypothyroidism or hyperthyroidism depend on the stage of the disease.²

FNAC is considered a superior and more cost-effective tool.³ As there is increased risk of extra-nodal marginal B cell lymphoma, chances of carcinoma (Between 0.5% & 23.5%) and to avoid overt diagnosis to prevent unnecessary surgery, exact and specific diagnosis is necessary.⁴ Presence of Hurthle cells, follicular cells with fine chromatin, anisonucleosis, mixed population of mature and transformed lymphocytes and giant cells and epithelioid cell collections in cytology are characteristics of chronic lymphocytic thyroiditis. Presence of all or some of these features along with biochemical, radiological and clinical features along with all or few of above mentioned cytological features assist in making a diagnosis.⁵

So this study was planned to assess cytomorphological spectrum of chronic lymphocytic thyroiditis with respect to the clinical, biochemical, ultrasonographic, and radionuclide parameters.

Materials and Methods

An observational hospital based descriptive cross-sectional study was conducted for duration of two and half years at department of pathology. Institutional Ethics Committee (IEC) permission was taken before commencement of study. Total 172 cases of chronic lymphocytic thyroiditis of any age and gender; diagnosed on cytology (FNAC) or histopathology (where prior FNAC was done) were included in study. Cases of acute or subacute thyroiditis and those who not given consent were excluded. Confidentiality of identity of study participants was maintained.

Written informed consent was taken from each study participants after giving detailed information about study procedure in local language. Standard operating definitions and protocols required for diagnosis were formulated before start and followed till end of study. Information about demographic variables and symptoms was collected. General and systemic clinical examination were done in details

to check clinical presentation. Thyroid function tests (TFTs) and ultrasonography was done in all cases. Anti-thyroid microsomal antibodies (AMA) levels were done in 48 cases and Thyroid scan (Technetium scan) done in 21 cases.

May-Grunwald-Giemsa, Papanicolaou/Eosin & Haematoxylin stains were used. Repeat aspiration was done if sample was not satisfactory, but not more than 2 aspirations per patient. To avoid observer bias, the smears were examined by two expert cytologists independently and findings were confirmed. Presence of lymphocytes and plasma cells infiltrating the thyroid follicles, increased number of lymphocytes in the background with or without lymphoid follicles, multinucleated giant cells, Hurthle cell change, anisonucleosis and epithelioid cell clusters on FNAC was diagnostic criteria for diagnosis.⁶ The grading of the thyroiditis was done on fine needle aspiration cytology (FNAC) by the criteria used by Bhatia et al.⁶

Data was entered in Microsoft Excel 2007 and analysed with SPSS v.16. Tables and images were used at appropriate places to present data. Mean, standard deviation, frequency and proportions were used to describe study findings. Association was checked by chi-square test at 5% level of significance.

Results

Study conducted on 172 cases of Chronic Lymphocytic Thyroiditis (CLT) diagnosed on cytology or histopathology (where prior FNAC was done). Out of 172 cases, 17 cases diagnosed on histopathology while 155 cases on FNAC. Out of total 172 cases, 8.14% were male and 71.86% were females with male to female ratio of 0.09:1. Most of male cases were of age 41 or more while in female cases, most were of age 21 to 40 years. Very few cases were reported of age below 10 years. Among 155 cases diagnosed with FNAC, 65.5% had diffuse thyroiditis, 30.9% had nodular and 3.8% had solitary thyroid nodule (STN) while those diagnosed on histopathology, nodular USG findings were present in 52.94% cases followed by STN (29.41%). Among 155 cases diagnosed with FNAC, 43.87% had hypothyroidism, 25.16% had hyperthyroidism and 16.13% were normal on Thyroid function tests (TFTs). Among 17 cases diagnosed on histopathology, most presented as nodular (52.94%) and STN (29.41%). Majority were Euthyroid (41.18%) followed by hyperthyroid (29.41%) (Table 1).

Table 1: Demographic, clinical and functional profile of study participants (*n* = 172).

Characteristics		FNAC (<i>n</i> = 155)		Histopathology (<i>n</i> = 17)	
Age and Gender wise distribution		Male (<i>n</i> = 12)	Female (<i>n</i> = 143)	Male (<i>n</i> = 2)	Female (<i>n</i> = 15)
Age groups (years)	0 to 10	0	2	0	0
	11 to 20	1	16	0	0
	21 to 30	1	41	0	4
	31 to 40	2	42	0	6
	41 to 50	5	19	2	4
	>50	3	23	0	1
Clinical and functional profile		No.	%	No.	%
USG findings	Diffuse	101	65.5	3	17.65
	Nodular	48	30.9	9	52.94
	Solitary thyroid nodule	6	3.8	5	29.41
Functional status	Hyperthyroid	39	25.16	5	29.41
	Hypothyroid	68	43.87	1	5.88
	Euthyroid	25	16.13	7	41.18
	Not done	23	14.84	4	23.53

Among FNAC group cases, out of 68 hypothyroid cases, 63.24% had diffuse pattern on USG followed by nodular pattern (35.29%) and STN (1.47%). Among 39 cases with hyperthyroidism diagnosed on FNAC most had diffuse pattern (66.67%)

and nodular pattern (30.77%). Among 17 cases diagnosed on histopathology, 7 cases had normal TFTs but out of that, 71.43% had nodular thyroid while 5 had hyperthyroidism showing diffuse or nodular pattern. (Table 2)

Table 2: Association between USG findings and functional status of study participants.

Groups	No.	Hypothyroid		Hyperthyroid		Euthyroid		Not done	
		%	No.	%	No.	%	No.	%	No.
FNAC group (<i>n</i> = 155)	Diffuse	43	63.24	26	66.67	15	60	17	73.91
	Nodular	24	35.29	12	30.77	9	36	3	13.04
	Solitary Thyroid Nodule	1	1.47	1	2.56	1	4	3	13.04
	Total	68	100	39	100	25	100	23	100
Histopathology group (<i>n</i> = 17)	Diffuse	0	0	2	40	1	14.29	0	0
	Nodular	0	0	2	40	5	71.43	2	50
	Solitary Thyroid Nodule	1	100	1	20	1	14.29	2	50
	Total	1	100	5	100	7	100.00	4	100

Out of 155 cases diagnosed on FNAC, 31 cases (20%) were of Grade I, 114 (73.55%) cases were of Grade II and 10 (6.45%) cases were of Grade III. In Grade I, few lymphoid cells infiltrating the follicles/increase number of lymphocytes in background were seen. In Grade II, moderate lymphocytic infiltration with hurthle cell change/giant cells/ anisonucleosis could be seen. In Grade III, florid lymphocytic inflammation with germinal center formation and very few follicular cells left. Out of 155 cases diagnosed on FNAC, Hurthle cells found in 40.65% cases and granulomas in 12.26% cases. Two case operated for hashitoxicosis. Four

cases of Papillary Cancer with thyroiditis were misdiagnosed as goitre (3) and follicular neoplasm (1) on FNAC. (Fig. 1 and 2).

Out of 31 cases with FNAC Grade I, 41.94% had hypothyroid, 25.81% had hyperthyroid and 19.35% had euthyroid. In 114 cases with FNAC Grade II, 42% had hypothyroid followed by hyperthyroid (26.32%). Most Grade III cases (70%) had hypothyroidism. Nodular pattern on USG was most common (71.43%) in Grades III of FNAC. Diffuse pattern was most common finding on USG in Grade I (48.39%) and Grade II (71.93%). (Table 3)

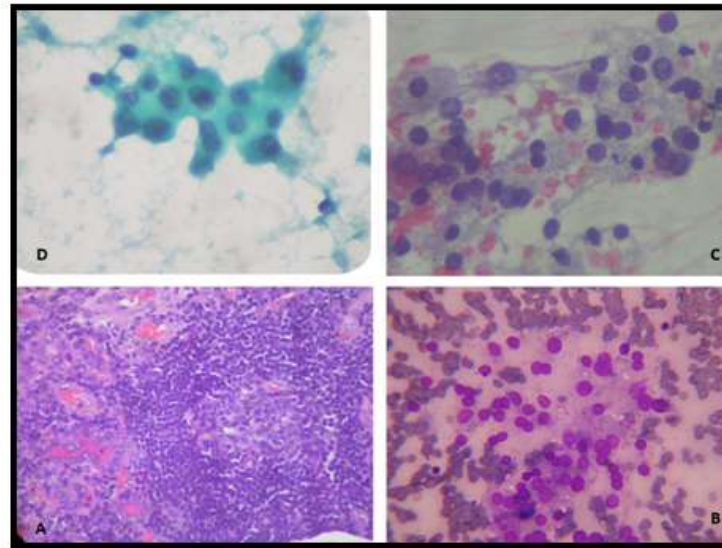


Fig. 1: Characteristics features. (A- Classical morphology; B- Hashitoxicosis with fire flares; C-Anisonucleosis, lymphocytes in follicles; D-Hurthle cell.)

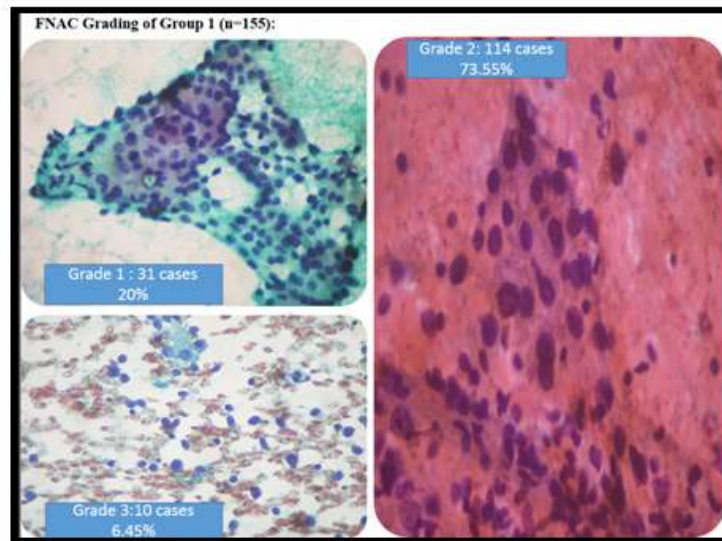


Fig. 2: FNAC grading of study participants ($n = 155$):

Table 3: Association between FNAC grades and functional status and USG findings of study participants.

Groups	No.	Grade I		Grade II		Grade III	
		%	No.	%	No.	%	No.
Functional status	Hyperthyroid	8	25.81	30	26.32	1	10
	Hypothyroid	13	41.94	48	42.11	7	70
	Euthyroid	6	19.35	18	15.79	1	10
	Not done	4	12.90	18	15.79	1	10
	Total	31	100.00	114	100.00	10	100
USG findings	Diffuse	15	48.39	82	71.93	4	57.14
	Nodular	11	35.48	32	28.07	5	71.43
	Solitary Thyroid Nodule	5	16.13	0	0.00	1	14.29
	Total	31	100.00	114	100.00	10	100.00

Relationship between antithyroid microsomal antibodies (AMA), Tc (Technetium) scan and functional status, USG findings shown in table no.4. Out of total 48 cases tested for AMA, 41 were AMA positive. Out of that, 61% had hypothyroid, 20% had hyperthyroid and 20% were normal on TFTs. Diffuse pattern was seen in 75.6% cases of AMA +ve

patients. Out of 21 cases in which Tc scan was done, increased uptake was seen in 17 cases, decreased in 03 cases and normal in 1 case. Among 17 cases of increased uptake, 12 had hyperthyroidism and 4 had hypothyroidism on TFTs. Diffuse pattern (11 cases) dominates over nodular pattern (6 cases) in cases with increased Tc uptake (Table 4).

Table 4: Association between AMA test and Tc scan results and functional and USG status of study participants

	+ve (%)	AMA (n = 41)		Tc scan (n = 21)	
		Increased (n = 17)	Decreased (n = 03)	Normal (n = 01)	
Functional status	Hyperthyroid	19.5	12	1	0
	Hypothyroid	60.97	4	2	0
	Euthyroid	19.5	1	0	1
USG status	Diffuse	75.6	11	1	0
	Nodular	24.4	6	2	1
	Solitary Thyroid Nodule	0	0	0	0

AMA: Antithyroidmicrosomal antibodies; Tc: Technetium scan

Discussion

Hashimoto Thyroiditis (HT) is an immunologically mediated inflammatory disease. It happens due to sensitization of CD4+ T-helper cells to thyroid antigens. After this thyroid destruction occurs due to CD8+ T-cell mediated cytotoxicity, cytokine mediated cell death, and antibody dependent cell-mediated cytotoxicity caused due binding of antithyroglobulin, antithyroid antibodies, antithyroid stimulating hormone (TSH) receptor antibodies and antithyroid peroxidase to thyrocyte surface.⁷ Study done by Anila et al.⁷ reported, age range of 5 to 74 years, 91.66% females with male to female ratio of 0.091:1 and 31 to 40 years as most common age group. Another study done by Bhatia et al.⁶ reported age range of 6 to 60 years and 92.1% females. Findings of these studies were comparable with present study as it reported, age range of 8 to 65 years, 71.86% females, and 21 to 40 years as most common age group. In present study, among 155 cases diagnosed on FNAC, diffuse (65.5%) and nodular (30.9%) were common patterns on USG while among histopathologically diagnosed group nodular (52.94%) and STN (29.41%) were common patterns. Studies done by Anila et al.⁷ and Bhatia et al.⁶ reported similar trend but slightly higher proportions of diffuse pattern, 77% & 89.47% respectively. Kumar et al.⁸ reported 81.8% diffuse and 18.2% nodular cases.

In current study, on cytology, FNAC Grade II was most common which found in 73.55% cases followed by Grade I in 20%. Study done by Bhatia

et al.⁶ reported, Grade II in 44%, Grade I in 38% and Grade III in 17.33% cases. Anila et al.⁷ reported, Grade II in 36.67%, Grade I in 45% and Grade III in 18.33% cases. Kumar et al.⁸ also reported highest cases from grade I group (61%). Current study reported higher percentage of grade II cases than these studies. Cibas et al.⁹ reported, the FNAC smears were characterized by cellular aspirate with numerous dispersed, heterogeneous lymphoid cells and few follicular cells. Bhatia et al.⁶ reported cytological characteristic findings which include lymphocytic infiltration of the inter-follicular space, invasion of follicles by the lymphocytes giving a 'fire-flare appearance' characterized by eosinophilic vacuolated cytoplasm and later, total destruction of follicles. Study done by Jayaram et al.¹⁰ showed, hurthle cells in 56% cases, granulomas in 16% cases and giant cells in 39% cases which was comparable with present study findings.

Anila et al.⁷ found no correlation between the cytological grades of thyroiditis and serum values of ATG, ATPO, and TSH. Present study also did not find any association between these two factors. Features of hypothyroidism on TFTs were commonest presentation in all three grades. Singh et al.¹¹ reported that the grading of thyroiditis and lymphocytic infiltration showed no correlation with the clinical severity of lymphocytic thyroiditis. Sood et al.¹² reported, significant association between cytological Grades III and TFTs status. Ekambaram et al.¹³ and Rathi et al.³ reported similar findings in their study. Studies done by Kumar et al.⁸ and Bhatia et al.⁶ reported hormonal imbalance in 72% and 98% cases. Present study reported comparable

finding. But study done by Nguyen et al.¹⁴ reported lower rate of hormonal imbalance (35%). AMA levels raised in 83.6% and 65.71% cases in studies done by Kumar et al.⁸ and Bhatia et al.⁶ while in present study it was raised in 89.66% cases.

In current study, in patients diagnosed on histopathology, none showed classical presentation. Presence of abundant colloid, macrophages and hyperplastic changes were misinterpreted as spectrum of goitre. Cellular changes in follicular & hurthle cells led to false positive diagnosis of neoplasia in 6 cases 4 cases of Papillary ca with thyroiditis were misdiagnosed as goitre (3) and follicular neoplasm (1) on FNAC. Kocjan et al.¹⁵ reported, a diagnostic accuracy rate of FNAC of 92%. They commented that likelihood to misdiagnosis when cytology smears show evidence of hyperplasia (in case of Grave's disease) or in cases where the colloid is abundant.

Conclusion

FNAC remains first line diagnostic modality for thyroiditis. The cytological grades of follicular destruction in thyroiditis can predict functional status. Few cases might be missed due to inherent procedural limitations, changing clinical presentation and associated neoplasms. On FNAC, presence of colloid, follicular hyperplasia and neoplasm could lead to diagnostic pitfalls, hence thorough cytological evaluation and integrated approach is necessary.

References

1. Kini SR. Thyroiditis. In: Kini SR, ed. *Thyroid Cytopathology*, first edition. Riverwoods, Illinois: Lippincott Williams and Wilkins 2008:294-5.
2. Chandanwale SS, Gore CR, Bamanikar SA, Gupta N, Gupta K. Cytomorphologic spectrum of Hashimoto's thyroiditis and its clinical correlation: A retrospective study of 52 patients. *Cytojournal* 2014;11:9.
3. Rathi et al. Cytomorphological Aspects of Hashimoto's Thyroiditis: Our Experience at a Tertiary Center. *Clinical Medicine Insights: Pathology* 2014;71-5. doi: 10.4137/CPath.S13580.
4. Pearce EN, Farewell AP, Braveran E. Thyroiditis. *N Engl J Med* 2003;348:2646.
5. Gurkan DE, Kiyak G, Bozkurt B. Correlation of thyroid fine-needle aspiration with final histopathology: a case series. *Minerva Chirurgica* 2013;68:191-97.
6. Bhatia A, Rajwanshi A, Dash RJ, et al. Lymphocytic thyroiditis—is cytological grading significant? A correlation of grades with clinical, biochemical, ultrasonographic and radionuclide parameters. *Cytojournal* 2007;4:10.
7. Anila KR, Nayak N, Jayasree K. Cytomorphologic spectrum of lymphocytic thyroiditis and correlation between cytological grading and biochemical parameters. *J Cytol* 2016;33:145-9.
8. Kumar N, Ray C, Jain S. Aspiration cytology of Hashimoto's thyroiditis in an endemic area. *Cytopathology* 2002;13:31-9.
9. E.S. Cibas. "Thyroid," in *Cytology: Diagnostic Principles and Clinical Correlates*, E. S. Cibas and B. S. Ducatman, Eds. Saunders, an imprint of Elsevier, Philadelphia, Pa, USA, 3rd edition, 2009. pp.264-65.
10. Jayaram G, Iyengar KR, Sthaneshwar P, et al. Hashimoto's thyroiditis-A Malaysian perspective. *J Cytol* 2007;24:119-24.
11. Singh N, Kumar S, Negi VS, et al. Cytomorphologic study of Hashimoto's thyroiditis and its serologic correlation: A study of 150 cases. *ActaCytol* 2009;53:507-16.
12. Sood N, Nigam J. Correlation of Fine Needle Aspiration Cytology Findings with Thyroid Function Test in Cases of Lymphocytic Thyroiditis. *Journal of Thyroid Research; Volume 2014, Article ID 430510*, 5 pages.
13. Ekambaram M, Kumar B, Chowdhary N, et al. Significance of eosinophils in diagnosing Hashimoto's thyroiditis on fine-needle aspiration cytology. *Indian J PatholMicrobiol* 2010;53:476-9.
14. Nguyen GK, Ginsberg J, Crockford PM, et al. Hashimoto's Thyroiditis: Cytodiagnostic accuracy and pitfalls. *DiagnCytopathol* 1997;16:531-6.
15. Kocjan G. Lymphoid infiltrate. In: Schroder G, editor. *Fine Needle Aspiration Cytology-Diagnostic Principles and Dilemmas*. 1st ed. Germany: Springer; 2006.p.99-101.

