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Original Research Article

A study of fine needle aspiration cytology findings with thyroid function test, anti-thyroid antibody, and clinical pathological parameters in cases of chronic lymphocytic thyroiditis

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ABSTRACT

Background: Chronic lymphocytic thyroiditis is autoimmune thyroiditis; it is considered as second most common thyroid disorder diagnosed on FNAC following colloid goitre. FNAC is a reliable and efficient method for diagnosing these thyroid lesions. Chronic Lymphocytic thyroiditis frequently affects women, primarily compared to men and is commonly found with hypothyroidism, euthyroidism or every so often with hyperthyroidism. The incidence rate of Hashimoto's thyroiditis is 1–4%, with an occurrence of 30–60/100000 population per year. Autoimmune thyroiditis can be categorised on the cytomorphological features of FNAC.

Materials and Methods: To compare FNAC cytological findings with TFT in Chronic lymphocytic thyroiditis. One hundred ten patients with thyroid swellings were presented for FNAC examination, serology of TFT and Anti TPO antibodies and Ultrasonography during 2020–2021. In addition, fine needle aspiration cytology was performed using non-aspiration or aspiration techniques. TFT and Anti- TPO antibodies were performed on Avion CLX 120 auto analyser based on the Chemiluminescence method.

Results: Out of 110 cases of midline neck swelling presented in our department, Autoimmune Thyroiditis was observed in 43 cases. The most affected age group of lymphocytic thyroiditis was 21–30 years, with the male: female ratio being 1:3. Most of the patients presented with diffuse swelling and few presented with nodular swelling. The Grading of the lymphocytic thyroiditis was done by the criteria used by Bhatia et al Anti-TPO antibody was elevated in 19 cases (26.2%), and TSH was elevated in 28 cases (40.81%). These cases were diagnosed as autoimmune thyroiditis on cytology, clinically and also correlating with radiological findings. Grade 3 lymphoid infiltrate was seen in 53.33% (16/30) cases, and Grade 2, lymphoid infiltrate was seen in eight cases (62.50%). Grade 1 lymphoid infiltrate was seen in five cases (11.63%). Among 43 cases, 28 cases (65.12%) show hypothyroidism, 7 cases (16.28%) show hyper, and 8 cases (18.60%) show Euthyroidism. Among these 43 cases, 26 cases showed diffuse thyroid swelling on ultrasonography, and 7 cases showed solitary nodule.

Conclusion: Grade 3 lymphocytic infiltration statistically correlates with anti-TPO and TSH in conjunction with ultrasonography findings of diffuse enlargement of the thyroid gland. The presence of Hurthle cell change, giant cells, anisonucleosus, and granulomas do not find to be any statistical correlation with lymphocytic thyroiditis as these cases are primarily corresponding to Grade 1 and Grade 2. Through this study, we conclude that FNAC remains the gold standard method despite having different diagnostic modalities accessible for diagnosing thyroid lesions. Grading of FNAC Smears depends on lymphocytic infiltration of the thyroid follicles, along with positivity for antithyroid antibodies (anti-TPO antibody) and TSH. These findings are firmly associated with Chronic Lymphocytic Thyroiditis.

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1. Introduction

Thyroid disorders are one of the most widespread endocrine gland disorders in India. The Incidence of hypothyroidism in India is 30–60/1, 00,000 populations per year with an incidence rate of 1– 4%.[1] The incidence rate of hypothyroidism in women of the reproductive age group is 2–4%.[2] Hakaru Hashimoto described lymphocytic thyroiditis in 1912 for the first time. It is synonymous with Hashimoto thyroiditis and autoimmune thyroiditis. It is an autoimmune disease that affects women more often than men and is associated with hypothyroidism, euthyroidism or not so often with hyperthyroidism. However, most cases show symptoms of hypothyroidism. Autoimmune thyroiditis is the most common type of thyroiditis and the second most common benign thyroid lesion following colloid goitre.[3,4] This condition is most prevalent among the Asian population.[5] It has been observed that iodine supplementation in iodine-deficient regions increases the incidence of lymphocytic infiltration of the thyroid three-fold, with a 40% rise in the incidence of antithyroid antibodies in serum over 0.5 to 5 years.[6] The clinical presentation of autoimmune thyroiditis can range from diffuse to nodular swelling without symptoms.[1] Characteristic cytological features include Hurtle cell changes, an increased number of reactive lymphoid and plasma cells, and the infiltration of lymphocytes into thyroid follicular cells.[7] The most commonly detected autoantibody in the serum is Anti Thyroid Peroxidase Antibody (Anti TPO Ab); however, these may not be present in some cases. Subclinical hypothyroidism can be challenging to diagnose due to a lack of obvious symptoms. The presence of thyroid anti-TPO-Ab in serum is high in most of these patients. We used a predefined set of criteria for grading cytological features on FNAC smears, similar to the method used by Bhatia et al.[7] The main aim is to correlate lymphocyte density with clinical, radiological, and biochemical parameters. The goal was to evaluate the sensitivity and specificity of FNAC, thyroid hormone assay, and Anti-TPO antibody levels preoperatively in patients with thyroid swellings and to determine the incidence of chronic lymphocytic thyroiditis by grading the cytological features of thyroid FNAC according to lymphocyte infiltration and comparing them with TFT and anti-TPO ab levels.

2. Aims and Objectives

1. To investigate the occurrence of hypothyroidism in cases of autoimmune thyroiditis.
2. To examine the relationship between cytomorphological grading, clinical presentation, thyroid function tests (TFT), and Anti-Thyroid Peroxidase Antibody (Anti-TPO Ab) levels in serum in order to improve the diagnosis of autoimmune thyroiditis.

3. Materials and Methods

This study is a retrospective study conducted in the Department of Pathology of ESIC Hospital in Delhi over the course of 2 years (from January 2020 to December 2021). The method used in this study was Fine Needle Aspiration Cytology (FNAC) of the thyroid gland using a non-aspiration/aspiration technique with a 23-gauge needle inserted into a 10 ml syringe. In cases of significant swelling, multiple-point aspirations were carried out. The samples were then air-dried, stained with May-Grunwald-Giemsa (MGG) and evaluated by a single pathologist who used Hamberger's criteria[8] to judge the adequacy of the smears. i.e. at least six clusters of follicular cells on each of two slides prepared from separate aspirations. In cases where the initial sample was unsatisfactory, a repeat aspiration was attempted, but no more than three aspirations were attempted on each patient. The qualitative criteria used for cytological diagnosis included the presence of lymphocytes and plasma cells infiltrating the thyroid follicles, an increased number of lymphocytes in the background, and the presence of Hurthle cell change, multinucleated giant cells, epithelioid cell clusters, and anisonucleosis in the aspirate. The smears were then evaluated and graded quantitatively based on the criteria established by Bhatia et al.[7] Simultaneously, Thyroid function tests (TFT) and Anti-TPO antibody levels were estimated using an automated hormone analyser. These results were then correlated with the patient's clinical presentation, TFT results, and anti-TPO antibody levels

3.1. Bhatia et al grading system[7]

This study used a cytological grading system to categorize the FNAC samples based on the density of lymphocyte infiltration. The grading system used is as follows:

1. Grade I [Mild]: Evidence of a small number of lymphoid cells infiltrating the thyroid follicles and an increased number of lymphocytes in the background.
2. Grade II [Moderate]: Moderate degree of lymphocytic infiltration or few lymphocytic infiltrations with the presence of Hurthle cell changes, giant cells, or anisonucleosis.
3. Grade III [Severe]: Extensive lymphocytic inflammation with formation of germinal centres and limited presence of thyroid follicular cells.

This grading system is used to correlate the cytological features of the FNAC samples with clinical, radiological and biochemical parameters to diagnose and understand the extent of Chronic Lymphocytic Thyroiditis.

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Thyroid function test (TFT) was conducted on 110 patients to determine the blood concentrations of thyroid hormones. The TFT included measurements of T3, T4, and TSH using a Chemiluminescence immunoassay. The reference range for T4 was 5-12 μg/dl, T3 was 80-180 ng/dl, and TSH was 0.5-5 mU/L. Additionally, a few patients who were suspected of chronic thyroiditis were tested for the presence of anti-thyroid peroxidase antibody (TPOAb), with a normal range of 0-60 iu/ml. Depending on the results of these tests, patients were classified as euthyroid, hypothyroid, or hyperthyroid. Additionally, an ultrasound of the thyroid gland (USG) was performed on all patients using a high-resolution ultrasound machine with a 5-10 MHz Broadband linear transducer. This was done by a single sonologist who was blinded to the clinical and biochemical status of the patients.

4. Results

Patients included in this study were in age 11-70 years (Mean) with a male: female ratio of 1:3. The Highest no of patients was seen in the age group of 21 to 30 with the majority of patients being females 33(%). (Table 1) shows the Age and sex distribution of Autoimmune thyroiditis. Female preponderance has been observed in this study. Duration of thyroid swelling varied from patient to patient. In this study, the majority of patients (68.8%) reported experiencing midline neck swelling for a duration of 1-3 years. The shortest reported duration was eight months, while three patients had swelling for less than three years. The most commonly reported symptoms among patients were a pain in the swelling and rapid growth, both at a rate of (40.6%), followed by discomfort while swallowing (25%). Clinically, 16 patients were found to have a multi-nodular goitre, and 14 cases had solitary thyroid nodules. Through examination, it was determined that eight patients were euthyroid, seven were hyperthyroid, and 28 were hypothyroid. Table 2 illustrates the cytological grading of Hashimoto's thyroiditis, with five (32.5%) patients being classified as grade 1 due to mild lymphocytic infiltration of the gland (Figure 1). Additionally, eight patients (41.25%) were classified as grade 2, characterized by moderate lymphocytic infiltration with evidence of follicular destruction, Hurthle cell change, and giant cells (Figures 2 and 3). Lastly, 30 (26.24%) patients were classified as grade III, characterized by dense lymphocytic infiltrates with germinal centres and very few remaining follicular cells (Figure 4). The ultrasonography findings of patients with autoimmune thyroiditis show diffuse enlargement of the thyroid gland seen in 26 cases, multinodular goitre was seen in eight cases, a solitary nodule was seen in seven cases, and two cases show normal study. Twenty cases show a significant increase in high TSH levels, while anti-TPO antibody increased in 15 cases of grade 3 autoimmune thyroiditis. In contrast, five patients did not show any increase in TSH and anti-TPO antibodies.

Table 1: Age & sex distribution of autoimmune thyroiditis cases

Age Interval (Years)	Male N (%)	Female N (%)	Total Cases N (%)
0 – 10	0 (0.0%)	0 (0.0%)	0 (0.0%)
11 – 20	0 (0.0%)	2 (4.7%)	2 (4.7%)
21 – 30	7 (16.3%)	22 (51.2%)	29 (67.4%)
31 – 40	3 (7.0%)	6 (14.0%)	9 (20.9%)
41 – 50	0 (0.0%)	2 (4.7%)	2 (4.7%)
51 – 60	0 (0.0%)	1 (2.3%)	1 (2.3%)
61 – 70	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	10 (23.3%)	33 (76.7%)	43 (100%)

Table 2: Cytomorphological grading of Hashimoto's thyroiditis cases

Grades of Hashimoto's Thyroiditis	Number of Cases N (%)
1	5 (11.63%)
2	8 (18.60%)
3	30 (69.77%)
Total	43 (100%)

Table 3: Comparison of cytological grades of Hashimoto's thyroiditis with biochemical values

Grades	Euthyroid N (%)	Hypothyroid N (%)	Hyperthyroid N (%)
1	1 (2.33%)	3 (6.98%)	1 (2.33%)
2	2 (4.65%)	5 (11.63%)	1 (2.33%)
3	5 (11.63%)	20 (46.51%)	5 (11.63%)
Total	8 (18.60%)	28 (65.12%)	7 (16.28%)

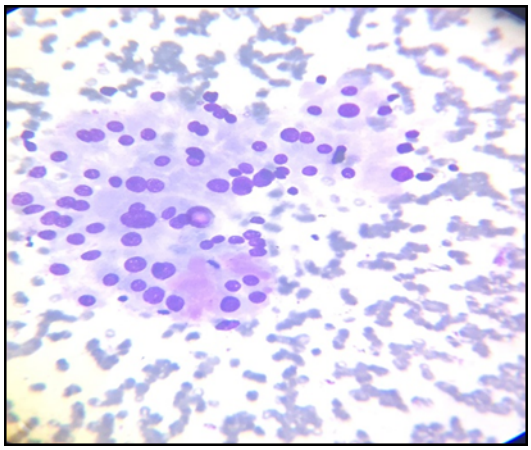

Fig. 1: Grade 2 Lymphocytic thyroiditis with Hurthle cell 400X

Table 4: Comparison of cytological grades of Hashimoto's thyroiditis with ultrasonography findings

Grades	Diffuse Thyroiditis N (%)	Goitre N (%)	Thyroid Nodule N (%)	Normal Study N (%)
1	2 (4.65%)	1 (2.33%)	1 (2.33%)	1 (2.33%)
2	4 (9.30%)	2 (4.65%)	1 (2.33%)	1 (2.33%)
3	20 (46.51%)	5 (11.63%)	5 (11.63%)	0 (0.00%)
Total	26 (60.47%)	8 (18.60%)	7 (16.28%)	2 (4.65%)

Table 5: Cytomorphological grading of autoimmune thyroiditis

Grade	Cytomorphological Features	% Present study
Grade 0	No lymphoid cells present	0
Grade 1	Evidence of a small number of lymphoid cells infiltrating the thyroid follicles and an increased number of lymphocytes in the background	5
Grade 2	A moderate degree of lymphocytic infiltration or few lymphocytic infiltrations with the presence of Hurthle cell changes, giant cells, or anisonucleosus	8
Grade 3	Extensive lymphocytic inflammation with formation of germinal centres and limited presence of thyroid follicular cells.	30

Table 6: Correlation between cytomorphological grading of chronic lymphocytic thyroiditis with increased anti-TPO Ab level and TSH level

Cytological Grade	TSH (Normal) N (%)	TSH (Increased) N (%)	TSH (Decreased) N (%)	Anti-TPO (Normal) N (%)	Anti-TPO (Elevated) N (%)
Grade 1	1 (1.43%)	3 (4.29%)	1 (1.43%)	1 (1.43%)	1 (1.43%)
Grade 2	2 (2.86%)	5 (7.14%)	1 (1.43%)	2 (2.86%)	3 (4.29%)
Grade 3	5 (7.14%)	20 (28.57%)	5 (7.14%)	5 (7.14%)	15 (21.43%)

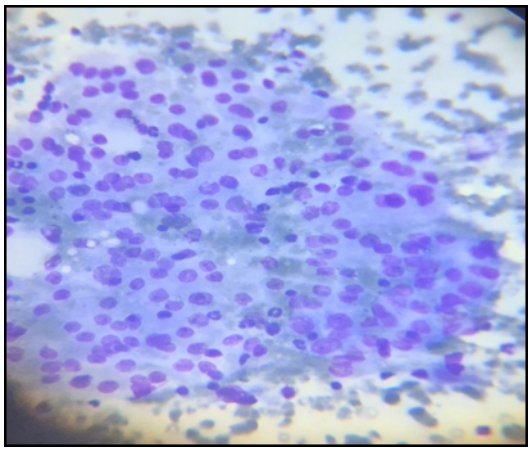

Fig. 2: Grade 1 Lymphocytic thyroiditis 400X

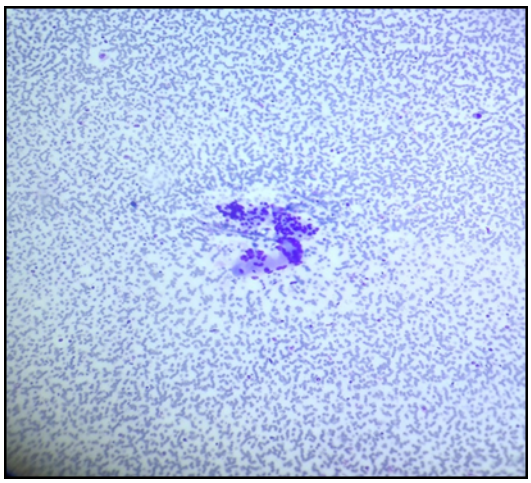

Fig. 3: Giant cell and, granuloma 100X

5. Discussion

The thyroid is a vital endocrine gland that produces three hormones: triiodothyronine (T3) and thyroxine (T4) which are thyroid hormones, and calcitonin which is a peptide hormone. These hormones play a crucial role in regulating the metabolic rate, protein synthesis, growth, and development in children. They also play a vital role in normal reproduction and pregnancy. Autoimmune thyroiditis is a common cause of hypothyroidism. If left undiagnosed and untreated, it can lead to various complications such as abnormal sexual development, menstrual irregularities, infertility, sub-fertility in women of reproductive age group, and miscarriages and congenital malformations during pregnancy.[9,10] With an increasing prevalence of autoimmune thyroiditis, especially in women of childbearing age, the diagnosis of subclinical hypothyroidism can be challenging. The presence of elevated levels of thyroid autoantibodies in the blood is often seen in these cases, making cytological and serological evaluations essential for proper diagnosis and

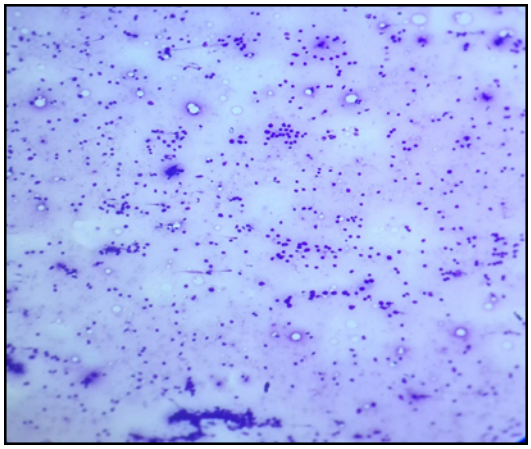

Fig. 4: Grade 3 Lymphocytic thyroiditis 100X

treatment. Autoimmune thyroiditis is characterized by the infiltration of T and B lymphocytes, which attack thyroid antigens and can lead to the destruction of the thyroid gland's follicular structure and replacement with fibrosis. Autoimmune thyroiditis is a common cause of hypothyroidism, especially in women of childbearing age. The disease's active phase can present as thyrotoxicosis, but it can also progress to subclinical or overt hypothyroidism. The exact cause of autoimmune thyroiditis is not fully understood, but it is thought to be influenced by factors such as iodine deficiency, medication, infection, smoking, and stress. Furthermore, autoimmune thyroiditis has an increased risk of developing into malignancy, particularly extra nodal marginal B-cell lymphoma and papillary carcinoma.[11,12] Autoimmune thyroiditis is a condition that requires ongoing monitoring, as it can have a significant impact on a patient's health. In our study, we evaluated 110 cases and found that the most common age group among patients was 21-30 years, which aligns with previous research by Ashwin et al.[13] who also found a high incidence in the 20-40 age range. The typical presentation in our study was diffuse thyroid swelling 26 (60.47%) which bears resemblance with studies by Kartha S et al[14] (66%) and Ashwin et al[13] (50.81%). Grading of autoimmune thyroiditis was done per the criteria described in (Table 5). The majority of our cases belonged to Grade 3, 30 (69.77%). On analysing the TSH levels, we found 20 (28.57%) patients to be hypothyroid, which was in concordance with a study by Rathi et al,[15] Ashwin et al,[13] and P Agrawal et al[16] who observed hypothyroidism in 56.1%, 50% and 50% cases, respectively. However, Bhatia et al[7] reported hypothyroidism in 73.6% of patients. In our study, Anti-TPO Antibody was raised in 15 (21.43%), 3 (4.29%) and 1 (1.43%) cases of Grade 3, Grade 2 & Grade 1 categories of autoimmune thyroiditis, respectively. Similarly, the study conducted by Neelam Sood et al[17] found elevated levels of Anti-TPO Antibody and TSH in a high percentage of cases across all grades of autoimmune thyroiditis, with 91.67%, 94.12% and 96.16% of patients in Grade 1, Grade 2 and Grade 3 respectively showing elevated levels.

6. Conclusion

Hashimoto's thyroiditis is an autoimmune disorder that affects females more frequently than males and is typically found in individuals in their 20s and 30s. The most common clinical feature is hypothyroidism, which may be the initial presentation. The results of fine-needle aspiration cytology (FNAC) are often associated with abnormal biochemical findings in higher grades of Hashimoto's thyroiditis. The preliminary stages of the disease, characterized by diffuse thyroiditis (Grade 1), can occur before overt thyroid failure and is a strong predictor of the autoimmune process, even when the disorder is not suspected clinically. Grade 3 lymphocytic infiltration statistically correlates with thyroid peroxidase (TPO) and thyroid-stimulating hormone (TSH) levels. The study also found that anti-TPO and TSH levels, along with ultrasonographic findings of diffuse thyroid enlargement, are significant indicators of the disease. However, the presence of prominent Hurthle cell changes, giant cells, and granulomas did not statistically correlate with anti-TPO and TSH levels. A combination of cytological grading of Hashimoto's thyroiditis, ultrasonography, and biochemical levels can help detect subclinical hypothyroidism and guide treatment.

7. Source of Funding

None.

8. Conflict of Interest

None.

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