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Association of Anti-TPO and Anti-TG Antibody Levels with Cytological Categorisation of Thyroiditis

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Abstract:

Background: Thyroiditis represents a heterogeneous group of inflammatory thyroid disorders with overlapping clinical, biochemical, and cytomorphological features. Autoimmune thyroiditis, particularly Hashimoto's thyroiditis, is commonly associated with circulating antithyroid antibodies, notably anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies. Fine-needle aspiration cytology (FNAC) remains the diagnostic cornerstone for thyroiditis, especially in cases with equivocal clinical or serological findings.

Objectives: To evaluate the association between anti-TPO and anti-TG antibody levels and cytological categorisation of thyroiditis and to correlate cytomorphological patterns with clinical and biochemical parameters.

Methods: This hospital-based prospective observational study included 150 cytologically proven cases of thyroiditis evaluated at Patna Medical College and Hospital over a two-year period. Clinical features, thyroid function tests, antithyroid antibody levels, and FNAC findings were analysed and correlated.

Results: Hashimoto's thyroiditis constituted the predominant cytological diagnosis (82%), followed by De Quervain's thyroiditis (18%). Elevated anti-TPO and anti-TG antibody levels were significantly associated with cytological features of Hashimoto's thyroiditis, including lymphocytic infiltration, Hurthle cell change, plasma cells, and follicular cell anisonucleosis. Granuloma formation was strongly associated with De Quervain's thyroiditis. Subclinical hypothyroidism was identified in 40.7% of cases.

Conclusion: Anti-TPO and anti-TG antibodies show a strong association with cytological patterns of autoimmune thyroiditis. FNAC remains the gold standard for accurate categorisation of thyroiditis, particularly in seronegative or early disease. A multidisciplinary diagnostic approach enhances diagnostic accuracy and clinical management.

Introduction

Thyroiditis comprises a heterogeneous group of inflammatory disorders of the thyroid gland characterised by variable clinical presentation, biochemical abnormalities and cytomorphological patterns [1]. These disorders include acute suppurative thyroiditis, subacute granulomatous thyroiditis (De Quervain's thyroiditis), painless lymphocytic thyroiditis and chronic autoimmune thyroiditis, of which Hashimoto's thyroiditis is the most prevalent [2]. The inflammatory process in thyroiditis may be transient or progressive, and patients may present with euthyroid, hyperthyroid or hypothyroid states depending on the phase of the disease [3]. This variability often complicates diagnosis based solely on clinical and biochemical parameters.

Hashimoto's thyroiditis is an autoimmune disorder resulting from a breakdown in immune tolerance to thyroid autoantigens, leading to gradual destruction of thyroid follicles and eventual thyroid failure [4]. It is the most common cause of hypothyroidism in iodine-sufficient regions and shows a marked female predominance [5]. The immunopathogenesis involves both humoral and cell-mediated immune mechanisms, with circulating antithyroid antibodies playing a central role. Among these, anti-thyroid peroxidase (anti-TPO) antibodies are considered the most sensitive and specific marker of autoimmune thyroid disease, while anti-thyroglobulin (anti-TG) antibodies act as supportive but less specific indicators [6].

Anti-TPO antibodies are directed against thyroid peroxidase, an enzyme essential for iodination and coupling reactions in thyroid hormone synthesis. These antibodies are capable of fixing complement and mediating antibody-dependent cell-mediated cytotoxicity, thereby contributing directly to follicular cell destruction [7]. Anti-TG antibodies, although commonly present in autoimmune thyroiditis, are less clearly implicated in direct tissue injury and may also be detected in other autoimmune conditions and even in a proportion of healthy individuals [8]. Despite their widespread use, the relationship between antibody titres and morphological severity of thyroiditis remains inconsistent across studies.

Fine-needle aspiration cytology (FNAC) is widely regarded as the gold standard diagnostic modality for thyroiditis, particularly in resource-limited settings and in patients with seronegative disease or atypical biochemical profiles [9]. FNAC allows direct assessment of characteristic cytomorphological features such as lymphocytic infiltration, Hurthle cell change, plasma cells, follicular cell anisonucleosis, epithelioid cells, giant cells and granuloma formation, which facilitate accurate categorisation of thyroiditis subtypes [10]. Understanding the association between serological markers and cytological patterns may enhance diagnostic accuracy and guide clinical management.

The present study evaluates the association of anti-TPO and anti-TG antibody levels with cytological categorisation of thyroiditis and correlates cytomorphological findings with clinical and biochemical parameters.

Materials and Methods

This hospital-based prospective observational study was conducted in the Department of Pathology at a tertiary-care teaching hospital over a period of two years. A total of 150 patients with cytologically proven thyroiditis were included. Patients with thyroiditis associated with benign or malignant neoplasms and those with non-inflammatory thyroid lesions were excluded from the study.

All patients underwent detailed clinical evaluation, including documentation of presenting symptoms, pattern of thyroid

enlargement and evidence of thyroid dysfunction. Thyroid function tests comprising serum T3, T4 and TSH were performed in all cases. Subclinical hypothyroidism was defined by elevated serum TSH levels with normal T3 and T4 concentrations.

FNAC was performed under aseptic precautions using 23–25 gauge needles with aspiration or non-aspiration techniques. Ultrasound guidance was employed where indicated. Multiple passes were obtained, and smears were prepared and stained with Giemsa and Papanicolaou stains. Cytological evaluation focused on identifying lymphocytic infiltration, Hurthle cells, plasma cells, follicular cell anisonucleosis, epithelioid cells, giant cells and granuloma formation. FNAC diagnoses were categorised into Hashimoto's thyroiditis and De Quervain's thyroiditis based on established cytomorphological criteria (9,10).

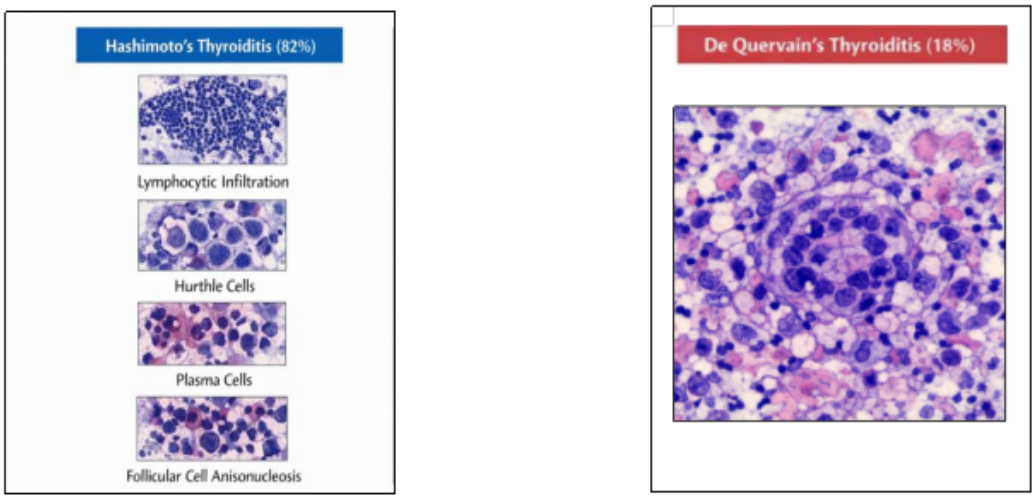

Figure 1. Representative cytomorphological features observed on fine-needle aspiration cytology in the two major categories of thyroiditis identified in the study. Hashimoto's thyroiditis, which constituted the majority of cases, is characterised by dense lymphocytic infiltration, Hurthle cell change, presence of plasma cells and follicular cell anisonucleosis. In contrast, De Quervain's thyroiditis demonstrates granulomatous inflammation with epithelioid histiocytes and multinucleated giant cells. The figure illustrates the distinct cytological patterns that facilitate accurate cytological categorisation of thyroiditis and support correlation with underlying immunological mechanisms.

Antithyroid antibody estimation, including anti-TPO (antimicrosomal antibody) and anti-TG antibody levels, was performed after cytological confirmation using standard immunoassay techniques. Statistical analysis was undertaken to assess associations between cytological features, FNAC diagnosis and antibody levels, with p values <0.05 considered statistically significant.

Results

The study population consisted predominantly of females (96.7%), with a female-to-male ratio of approximately 29:1. The majority of patients belonged to the 21-40-year age group, reflecting the higher prevalence of autoimmune thyroid disorders in younger and middle-aged women. Hashimoto's thyroiditis was the most frequent cytological diagnosis, accounting for 82% of cases, while De Quervain's thyroiditis constituted 18%.

Clinically, tiredness was the most common presenting symptom, followed by menstrual irregularities, weight changes and cold intolerance. Subclinical

hypothyroidism was detected in 40.7% of patients, indicating early thyroid dysfunction in a substantial proportion of cases.

Mean serum T3, T4 and TSH values demonstrated wide variability, consistent with the fluctuating functional states observed in thyroiditis. Anti-TPO antibody levels showed a markedly elevated mean value, while anti-TG antibody levels were also significantly raised, though with greater inter-individual variation.

Table 1. Association between cytological features and FNAC diagnosis of thyroiditis

Cytological feature	Hashimoto's thyroiditis (n=123)	De Quervain's thyroiditis (n=27)	p value
Lymphocytic infiltration	112 (91.1%)	7 (25.9%)	<0.001
Hurthle cells	86 (69.9%)	0	<0.001
Plasma cells	24 (19.5%)	0	0.005
Follicular cell anisonucleosis	43 (35.0%)	0	<0.001
Giant cells	48 (39.0%)	20 (74.1%)	0.001
Granuloma	0	27 (100%)	<0.001

Cytomorphological analysis revealed lymphocytic infiltration as the most common finding, present in 79.3% of cases. Hurthle cell change was observed in 57.3% of patients and was strongly associated with Hashimoto's thyroiditis. Plasma cells and follicular cell anisonucleosis were noted exclusively in Hashimoto's thyroiditis. Granuloma formation and prominent giant cells were seen in all cases of De Quervain's thyroiditis and were absent in Hashimoto's thyroiditis.

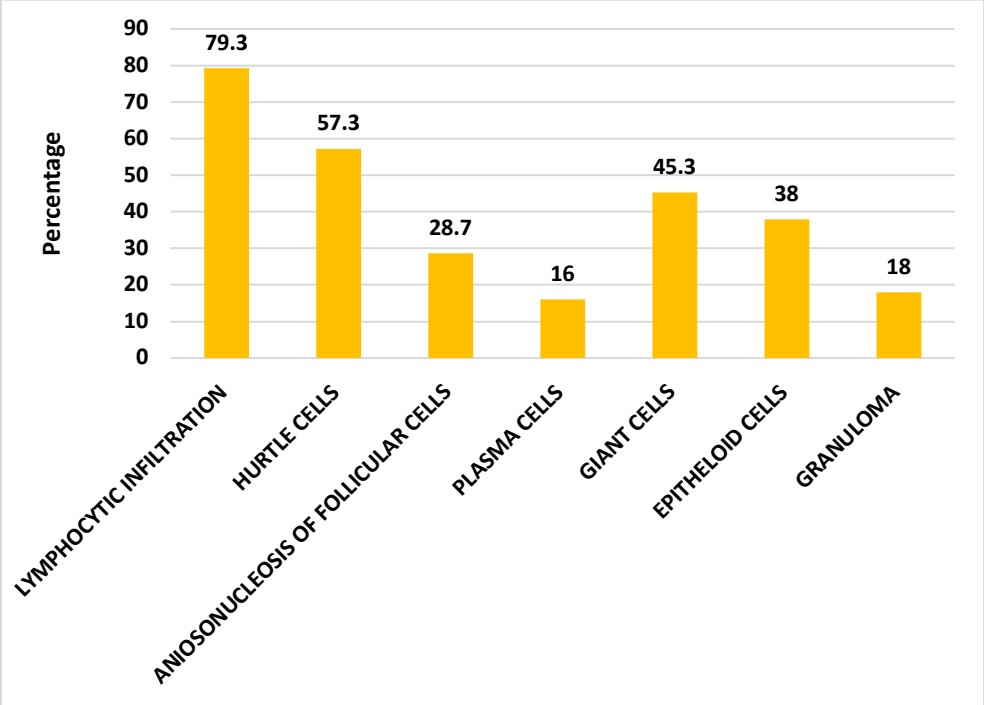

Figure 1. Distribution of cytomorphological features observed on fine-needle aspiration cytology in patients with thyroiditis. Lymphocytic infiltration was the most frequent cytological finding, followed by Hurthle cell change and giant cells. Plasma cells, epithelioid cells, follicular cell anisonucleosis and granuloma were observed in varying proportions, reflecting the diverse cytomorphological patterns underlying different subtypes of thyroiditis.

Statistical analysis demonstrated a significant association between elevated anti-TPO and anti-TG antibody levels and cytological features of Hashimoto's thyroiditis, particularly lymphocytic infiltration, Hurthle cell change, plasma cells and follicular cell anisonucleosis ($p < 0.001$). Granuloma formation showed a strong and exclusive association with De Quervain's thyroiditis.

Discussion

Thyroiditis represents a diagnostic challenge due to overlapping clinical manifestations and biochemical findings among its subtypes. FNAC has significantly improved the diagnostic evaluation of thyroid lesions by providing a rapid, minimally invasive and highly accurate method for morphological assessment [9]. The predominance of Hashimoto's thyroiditis in the present study is consistent with earlier reports describing autoimmune thyroiditis as the most common inflammatory thyroid disorder in iodine-sufficient regions [4,10].

The marked female predominance observed in this study aligns with the known epidemiology of autoimmune thyroid diseases, which are influenced by hormonal, genetic and immunological factors [5]. The concentration of cases in the reproductive age group underscores the clinical relevance of early diagnosis, particularly in women, due to the potential impact on fertility and pregnancy outcomes.

The strong association between elevated anti-TPO antibody levels and cytological features of Hashimoto's thyroiditis reinforces the pathogenic role of these antibodies. Anti-TPO antibodies correlate with disease activity and severity because of their ability to fix complement and induce antibody-dependent cytotoxicity, leading to follicular cell damage [6,7]. In the present study, high anti-TPO levels were consistently associated with lymphocytic infiltration and Hurthle cell change, reflecting chronic immune-mediated injury.

Anti-TG antibodies, while less specific, also demonstrated a significant association with autoimmune cytological patterns. Their presence supports the diagnosis of autoimmune thyroiditis, particularly when interpreted alongside anti-TPO antibodies and cytological findings [8]. However, their variability and lower specificity highlight the importance of FNAC in establishing a definitive diagnosis.

Granuloma formation and multinucleated giant cells were exclusively associated with De Quervain's thyroiditis, reflecting its granulomatous inflammatory pathogenesis, often triggered by viral infections [2]. The mutually exclusive cytological patterns observed between Hashimoto's thyroiditis and De Quervain's thyroiditis emphasise the diagnostic value of FNAC in distinguishing these entities, especially when clinical features overlap.

The detection of subclinical hypothyroidism in over 40% of patients highlights the importance of early recognition and follow-up. Many patients with autoimmune thyroiditis may remain asymptomatic or minimally symptomatic for prolonged periods before progressing to overt hypothyroidism [3,11]. In such cases, reliance on serology alone may miss early disease, particularly in seronegative individuals, reinforcing the continued relevance of cytological evaluation.

Overall, the findings of this study support a multidisciplinary diagnostic approach integrating clinical assessment, thyroid function testing, antithyroid antibody estimation and FNAC for accurate categorisation and management of thyroiditis.

Conclusion

Anti-TPO and anti-TG antibody levels show a strong association with cytological categorisation of thyroiditis. Hashimoto's thyroiditis is characterised by elevated

antithyroid antibody titres and distinctive cytomorphological features, whereas De Quervain's thyroiditis demonstrates granulomatous inflammation independent of antibody elevation. FNAC remains the gold standard diagnostic modality and should be integrated with clinical, biochemical and serological assessments to ensure accurate diagnosis and optimal patient management.

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