

## A study on Correlation between Cytological Assessment of Thyroid Lesions and Thyroid Function

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### Abstract

**Background and Objectives:** Thyroid dysfunction is a prevalent condition, particularly among females. Fine needle aspiration cytology (FNAC) is widely recognized as the preferred method for evaluating thyroid nodules. The objective of this study was to establish a correlation between cytological findings and hormonal levels in thyroid lesions.

**Materials & Methods:** This retrospective observational study conducted at a tertiary care hospital in India aimed to analyze the data of patients referred for fine needle aspiration cytology (FNAC) of thyroid lesions over a two-year period. The study also included the collection of thyroid function test (TFT) data, specifically measuring triiodothyronine, thyroxine, and thyroid stimulating hormone levels. FNAC results were classified according to the Bethesda System for Reporting Thyroid Cytology (TBSRTC) guidelines, and descriptive statistics were utilized to report the findings.

**Results:** The study included a total of 236 cases, irrespective of gender and age. The mean age of the patients was  $42.6 \pm 5.12$  years. Females were predominant, with a male-to-female ratio of 1:5. The majority of the thyroid lesions (206 cases) were classified as benign, with benign follicular nodules being the most common subtype (154 cases). Among Category II, 129 cases were euthyroid, 47 cases were hyperthyroid, and 60 cases were hypothyroid. Abnormal thyroid function test results were observed in patients with lymphocytic thyroiditis.

**Conclusion:** Relying solely on hormonal status is insufficient for screening thyroid lesions. Cytology serves as the gold standard for diagnosing such lesions, and utilizing the TBSRTC for reporting them offers a rapid and efficient approach.

**Keywords:** Fine needle aspiration cytology, thyroid nodule, thyroid function tests.

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### Introduction

The thyroid gland, situated in the neck and resembling a butterfly in shape, is an endocrine gland. It plays a crucial role by secreting two hormones, namely Triiodothyronine (T3) and Thyroxine (T4).

These hormones are essential for the normal functioning and survival of body cells. The thyroid gland holds significance in processes such as metabolism, growth, development, and maintaining the body's

internal environment. Thyroid dysfunction is a commonly encountered condition in clinical practice, with thyroid disorders being among the most prevalent endocrine disorders worldwide, particularly in females. The gold standard for diagnosing thyroid dysfunction is the assessment of thyroid function tests (TFT), which evaluate the levels of T3, T4, and thyroid stimulating hormone (TSH). TSH, in particular, is considered the primary indicator for the evaluation of thyroid function [1].

Thyroid nodules are prevalent and affect approximately 7% of the population in the United States [2]. The majority of these nodules are non-cancerous (benign). Thyroid nodules have the potential to cause either hyperthyroidism or hypothyroidism. Fine needle aspiration (FNA) is a vital tool in the clinical management of thyroid nodules. The results of FNA play a crucial role in determining whether a thyroid nodule requires close monitoring or surgical removal [2]. The simplicity, diagnostic accuracy, and cost-effectiveness of FNA have established it as the primary diagnostic test in the preoperative assessment of thyroid lesions [3].

The nomenclature utilized in reporting thyroid cytology has displayed significant variation, leading to confusion among clinicians when interpreting cytology reports and subsequently impeding clinical management. In response to these challenges, the National Cancer Institute (NCI) of the United States organized a conference in Bethesda, Maryland, in 2007 [4]. This conference served as a catalyst for the development of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). This standardized system incorporates six categories that cytopathologists can employ to effectively communicate thyroid fine needle aspiration (FNA) interpretations to referring physicians. These terms are universal, concise, unambiguous, and clinically valuable [5].

Hence, the objective of this study was to establish a correlation between cytological findings and hormonal levels measured in thyroid function tests (TFT) among patients with thyroid nodules. Furthermore, the study aimed to evaluate the distribution of different types of thyroid lesions based on the Bethesda system for reporting thyroid cytopathology.

### Material & Methods

This retrospective observational study was conducted by the cytology section of the Department of Pathology at a tertiary care teaching hospital and medical college located in India. Data collection spanned a two-year period from January 2021 to December 2022. Prior to commencing the study, the necessary permission from the institutional ethics committee was obtained to ensure adherence to ethical guidelines [6].

The study encompassed patients of all genders and age groups who presented with diffuse or nodular thyroid swelling. Comprehensive demographic and clinical information was recorded using a pre-approved and pre-validated data sheet. Thyroid function tests (TFT), specifically measuring the levels of T3, T4, and TSH hormones, were documented for each patient.

Fine needle aspiration (FNA) was performed on all patients using a 22 or 23-gauge needle, following standard procedures and aseptic precautions. Smears were immediately prepared from the aspirates and fixed using methanol. Staining was carried out utilizing H&E and PAP stains. The evaluation of smears was conducted by a pathologist and categorized according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

Thyroid function tests (TFT) profiles, including T3, T4, and TSH, were performed using the Siemen's Advia Centaur CP Chemiluminescence immunometric assay method. Reference

ranges for the hormone levels were as follows: T3 (triiodothyronine) - 0.6-1.81 ng/ml, Free T3 (triiodothyronine) - 2.18-3.98 pg/ml; T4 (thyroxine) - 4.5-12.6 µg/dl, Free T4 (thyroxine) - 0.76-1.46 ng/dl; TSH - 0.55 - 4.78 µIU/ml [7].

Statistical analysis: The data collected for this study was organized and analyzed using Microsoft Excel 2016. Descriptive statistics, including measures such as mean, standard deviation, and percentage, were employed to report the findings.

## Results

During the two-year study period, a total of 236 patients with thyroid lesions, regardless

of age and sex, were referred for fine needle aspiration cytology (FNAC) from the ENT/Surgery outpatient department or were admitted to the ward. The mean age of the patients was  $42.6 \pm 5.12$  years. The distribution of thyroid lesions demonstrated a higher prevalence among females, with 197 females and 39 males, resulting in a male-to-female ratio of 1:5.

The distribution of the 236 cases of thyroid FNAC was categorized according to the guidelines of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and is presented in Table 1. The majority of thyroid lesions, specifically 206 cases (87.8%), were classified as benign.

**Table 1: Thyroid cases as per The Bethesda System for Reporting Thyroid Cytology**

Category	Cytology diagnosis	N	%
I	Non-diagnostic or Unsatisfactory	8	3.5
II	Benign Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)	154	65.6
	Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context	48	20.5
	Consistent with granulomatous (subacute) thyroiditis	4	1.7
III	Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	10	4.1
IV	Follicular Neoplasm or Suspicious for a Follicular Neoplasm	4	1.6
V	Suspicious for Malignant	5	2.2
VI	Malignant. Papillary carcinoma of thyroid.	3	1.2
	<b>Total</b>	<b>236</b>	<b>100</b>

Table 2 shows the Correlation of TFTs with TBSRTC categories. Majority (154) of the patients were Euthyroid.

**Table 2: Correlation of TFTs with TBSRTC categories**

TFT	TBSRTC categories						Total
	I	II	III	IV	V	VI	
Euthyroid	4	129	14	3	4	0	154
Hyperthyroid	3	47	0	0	0	0	50
Hypothyroid	0	60	0	2	0	1	63
<b>Total</b>	<b>7</b>	<b>205</b>	<b>14</b>	<b>5</b>	<b>4</b>	<b>1</b>	<b>236</b>

## Discussion

Thyroid swelling is a prevalent endocrine disorder, particularly among females on a

global scale. With advancements in diagnostic tools, early detection of these swellings has become feasible. Whether presenting as diffuse or nodular

enlargement, thyroid swelling prompts a series of investigations aimed at ruling out neoplastic conditions or thyroiditis. Fine needle aspiration cytology (FNAC) serves as the primary diagnostic procedure, followed by additional investigations such as ultrasound (USG), thyroid function tests (TFT), thyroid scans, and antibody level assessments to guide appropriate management [8].

As per the guidelines outlined by the American Thyroid Association, the initial assessment of thyroid swellings should include the measurement of serum thyroid-stimulating hormone (TSH) levels. Further evaluation becomes necessary in cases where overt or subclinical hyperthyroidism is detected. It is worth noting that a higher serum TSH level is typically associated with an elevated risk of malignancy in thyroid nodules, as well as a more advanced stage of thyroid cancer [9].

The average age observed in this study was 40.8 years, which aligns with similar studies conducted by Thakor T et al. [9], Patel CB et al [10], Jain V et al. [11], and Das MK et al. [12], where the mean age at presentation ranged from 39.6 years to 41.3 years. The male-to-female ratio in our study was 1:4.8, which is consistent with the findings of Thakor T et al. [9] and Jain V et al. [11], who reported male-to-female ratios of 1:5.3 and 1:6.2, respectively.

Table 2 presents the distribution of cases based on the TBSRTC categories in our study compared to previously published studies [3, 5, 10, 11, 13]. Interestingly, we observed a variation in the distribution of cases across the six-tier Bethesda system compared to the studies mentioned in Table 2. Specifically, the percentage of cases in the benign category was higher in our study, while the percentages in the non-diagnostic and Atypia or Follicular Lesion of Undetermined Significance categories were lower. Several factors may contribute to the higher number of cases in the benign category. Firstly, our institute attracts a diverse population as patients come directly

without referral, making it more representative of the general population. Therefore, this demographic diversity is reflected in our study. Additionally, our institute offers easy accessibility to FNAC procedures, particularly for economically disadvantaged individuals, as the test is performed at a minimal cost.

In our study, the most common thyroid lesions categorized as Bethesda category II were benign follicular nodules, and a majority of these cases were found to be euthyroid. This finding aligns with the previous studies where they reported a similar proportion of euthyroid cases among Bethesda category II lesions [11, 12].

In the present study, the majority of patients diagnosed with lymphocytic thyroiditis demonstrated hypothyroidism on hormonal assay. This finding suggests that these patients were in an advanced stage of the disease at the time of diagnosis, indicating the presence of a destructive phase of the disease. These findings were consistent with the results reported in several previous studies [15, 16, 17, 18].

The incidence of malignancy in Hashimoto's thyroiditis (HT) has been reported to range from 0.4% to 28% in previous studies [19, 20]. Among the neoplasms associated with HT, papillary thyroid carcinoma (PTC) and primary thyroid lymphoma are the most commonly encountered [19]. Consistent with these observations, our study also identified one case of HT with PTC-micro-carcinoma.

Thyroid lesions often present with overlapping clinical, radiological, and hormonal parameters, making thyroid function tests (TFTs) less reliable when used alone [14]. In cases where the diagnosis is equivocal, antibody testing can provide valuable information. However, it should be noted that approximately 7% to 33% of cases of Hashimoto's thyroiditis (HT) may be negative for antibodies. This discrepancy can be attributed to the fact

that localized immune destruction may occur earlier than detectable serological changes. Therefore, cytological evidence emerges as a superior diagnostic tool compared to hormonal and serological findings [16, 21, 22].

Our study had a few limitations that should be considered. Firstly, not all cases of fine needle aspiration cytology (FNAC) had complete biochemical parameters for correlation, which could have provided more comprehensive insights. Secondly, due to the high cost of certain diagnostic tests, some patients were unable to undergo all the recommended investigations. This limitation may have affected the completeness of our data. Lastly, the number of cases included in the study was limited, as many of the thyroid lesions did not require surgical intervention. This restricted sample size may have influenced the generalizability of our findings.

### Conclusions

This study confirms that cytology remains the gold standard for diagnosing thyroid lesions. Hormonal status alone is insufficient for screening thyroid lesions. Accurate sampling and ultrasound-guided FNAC can reduce indeterminate, false-positive, and false-negative diagnoses. In equivocal cases, a combination of cytomorphology, clinical features, thyroid hormonal profile, antibody testing, and ultrasound features aids in diagnosis. Surgical indications should consider multiple factors, including cytology, medical history, physical examination, laboratory tests, and ultrasonography. Further studies correlating FNAC results with surgical confirmation can strengthen the evidence for cytological diagnosis.

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