



Diagnostic Performance of Fine-Needle Aspiration Cytology in Thyroid Nodules: A Bethesda System-Based Cytohistopathological Study.

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Abstract

Background: Fine-needle aspiration cytology (FNAC), reported using the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), is central to the evaluation and risk stratification of thyroid nodules. This study assessed the cytological spectrum of thyroid lesions according to TBSRTC and evaluated cytohistopathological correlation.

Materials and Methods: This hospital-based cross-sectional study included 90 patients with thyroid swellings who underwent FNAC over one year at a tertiary care teaching hospital in Gujarat. Smears were stained with May-Grünwald-Giemsa and Papanicolaou stains and classified according to TBSRTC. Histopathological correlation was performed in surgically treated cases. Diagnostic performance was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and area under the receiver operating characteristic (ROC) curve. **Results:** The mean age was 38.6 ± 11.8 years, and 80.0% of patients were female. Bethesda II (benign) was the predominant category (64.4%), followed by Bethesda III and VI (8.9% each), IV (6.7%), and I and V (5.6% each). Cytological and histopathological diagnoses showed a significant association ($\chi^2 = 28.64$, $p < 0.001$). FNAC demonstrated 86.7% sensitivity, 93.3% specificity, 86.7% PPV, 93.3% NPV, and 91.1% diagnostic accuracy, with an ROC-AUC of 0.91. **Conclusion:** TBSRTC effectively stratified thyroid lesions and showed strong cytohistopathological concordance. FNAC demonstrated high diagnostic performance and remains a valuable first-line modality for thyroid nodule evaluation.

Keywords: Bethesda system, Cytological patterns, Fine-needle aspiration cytology, Histopathological correlation, Thyroid lesions.



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INTRODUCTION

Thyroid disorders are common endocrine diseases worldwide, and thyroid nodules are increasingly detected because of greater awareness and widespread use of high-resolution imaging. A recent global systematic review of more than 74 million individuals estimated the overall prevalence of thyroid nodules at 24.8%, increasing from 21.5% during 2000–2011 to 29.3% during 2012–2022. Prevalence was higher among women (36.5%) than men (23.5%) and increased with advancing age (1). The prevalence varies with the detection method, with approximately 5–7% of nodules identified by palpation and 20–76% by ultrasonography. Autopsy studies have reported occult thyroid nodules in up to 50–67% of individuals. Although most thyroid nodules are benign, approximately 5–15% are malignant, highlighting the need for accurate and minimally invasive diagnostic evaluation (2). India has a substantial burden of thyroid disease, with an estimated 42 million individuals affected and palpable thyroid nodules reported in 8.5–12.2% of the general population. Although thyroid cancer remains relatively uncommon, with an estimated incidence of 8.7 per 100,000 population per year, the increasing detection of thyroid nodules underscores the need for reliable diagnostic approaches to identify lesions requiring surgical management (3).

Fine-needle aspiration cytology (FNAC) is widely used for the evaluation of thyroid nodules because it is safe, rapid, minimally invasive, inexpensive, and diagnostically accurate. It facilitates differentiation between benign and malignant lesions, helping to avoid unnecessary surgery and identify patients requiring definitive treatment. However, variability in cytological terminology before standardized reporting often resulted in inconsistent interpretation and communication between pathologists and clinicians (4). To overcome these limitations, the National Cancer Institute introduced the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in 2007, with formal publication in 2009. The system classifies thyroid cytology into six categories: I, Nondiagnostic/Unsatisfactory; II, Benign; III, Atypia/Follicular Lesion of Undetermined Significance; IV, Follicular Neoplasm/Suspicious for Follicular Neoplasm; V, Suspicious for Malignancy;

and VI, Malignant. Each category is associated with an estimated risk of malignancy and corresponding management recommendations, improving diagnostic reproducibility and clinical communication (5,6).

TBSRTC has subsequently undergone revisions incorporating advances in thyroid pathology, molecular diagnostics, and malignancy risk estimates. The third edition (2023), together with the 2022 WHO Classification of Thyroid Tumours and subsequent updates, emphasizes risk stratification and individualized management (7). Studies have demonstrated that Bethesda-based reporting improves FNAC standardization and facilitates cytohistopathological correlation. Bethesda Category II generally predominates, whereas Categories III and IV remain diagnostically challenging because of overlapping cytomorphological features and variable malignancy risk. Histopathological examination remains the reference standard for validating cytological diagnoses and assessing malignancy risk across Bethesda categories (8,9). The diagnostic accuracy of thyroid FNAC has been reported to range from 85% to 98%; however, false-positive and false-negative results may occur because of sampling errors, inadequate cellularity, cystic degeneration, overlapping cytomorphological features, and observer variability. Therefore, evaluation of the cytological spectrum using the Bethesda System and correlation with histopathology remain important for diagnostic quality assurance and patient management (10).

The present study aimed to evaluate the cytological spectrum of thyroid lesions according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), determine the distribution of Bethesda categories, and assess their cytohistopathological correlation and diagnostic performance.

MATERIALS AND METHODS

The present study was a hospital-based observational cross-sectional study conducted in the Department of Pathology of a tertiary care teaching hospital in Gujarat over a period of one year. The study aimed to evaluate the cytological patterns of thyroid lesions using the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

A total of 90 patients presenting with clinically or radiologically diagnosed thyroid swellings and referred for fine-needle aspiration cytology (FNAC) during the study period were included. Patients of all age groups and both sexes with thyroid nodules who underwent FNAC and provided informed consent were included in the study. Aspirates that were inadequate for evaluation due to poor cellularity or patients with previously diagnosed thyroid malignancy receiving treatment were excluded from the study.

Relevant demographic and clinical information, including age, sex, presenting complaints, duration of swelling, thyroid function status, and radiological findings, were recorded using a predesigned case record form. Fine-needle aspiration was performed using a 23–25-gauge needle attached to a 10-mL disposable syringe under aseptic precautions. Ultrasound-guided aspiration was performed whenever indicated, particularly in deep-seated, small, or predominantly cystic nodules. Smears were prepared immediately after aspiration and stained using May-Grünwald-Giemsa (MGG) and Papanicolaou (Pap) stains following standard laboratory protocols.

All cytological smears were examined independently by experienced pathologists and classified according to the Bethesda System for Reporting Thyroid Cytopathology (Third Edition) into six diagnostic categories: Category I (Non-diagnostic/Unsatisfactory), Category II (Benign), Category III (Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance), Category IV (Follicular Neoplasm/Suspicious for a Follicular Neoplasm), Category V (Suspicious for Malignancy), and Category VI (Malignant). Histopathological findings of patients who subsequently underwent thyroid surgery were reviewed and correlated with the cytological diagnosis wherever available to assess diagnostic concordance.

The collected data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) version 26.0. Descriptive statistics were expressed as frequencies, percentages, means, and standard deviations. The distribution of thyroid lesions across Bethesda categories was analysed. The association between Bethesda categories and histopathological diagnosis was evaluated using the Chi-square test or Fisher's exact test, as appropriate. Diagnostic indices including sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of FNAC were calculated using histopathological examination as the reference standard. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 90 patients with thyroid swellings were included in the study. The mean age of the study population was 38.6 ± 11.8 years, with the highest proportion of patients belonging to the 31–40 years age group (31.1%). Females constituted the majority of cases (80.0%), resulting in a female-to-male ratio of approximately 4:1, indicating a marked female predominance in thyroid lesions.

Table 1. Demographic Profile of Patients with Thyroid Lesions (N = 90)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
<20	8	8.9
21–30	18	20.0
31–40	28	31.1
41–50	20	22.2
51–60	10	11.1
>60	6	6.7
Mean Age	38.6 ± 11.8 years	
Gender		
Male	18	20.0
Female	72	80.0

According to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), Bethesda Category II (Benign) was the most frequent cytological diagnosis, accounting for 64.4% of all thyroid aspirates, followed by Category III (AUS/FLUS) (8.9%), Category VI (Malignant) (8.9%), Category IV (Follicular Neoplasm/Suspicious for Follicular Neoplasm) (6.7%), Category I (Non-diagnostic/Unsatisfactory) (5.6%), and Category V (Suspicious for Malignancy) (5.6%). These findings indicate that benign thyroid lesions constituted the majority of thyroid swellings evaluated by FNAC.

Table 2. Distribution of Thyroid Lesions According to the Bethesda System (N = 90)

Bethesda Category	Frequency (n)	Percentage (%)
I. Non-diagnostic/Unsatisfactory	5	5.6
II. Benign	58	64.4
III. AUS/FLUS	8	8.9
IV. Follicular Neoplasm/SFN	6	6.7
V. Suspicious for Malignancy	5	5.6
VI. Malignant	8	8.9
Total	90	100.0

Cytohistopathological correlation, available for 45 surgically managed cases, demonstrated a highly significant association between Bethesda cytological categories and histopathological diagnosis ($\chi^2 = 28.64$, $p < 0.001$). Most lesions categorized as benign on cytology were confirmed as benign on histopathology, while the majority of lesions reported as suspicious or malignant were subsequently diagnosed as malignant, reflecting good concordance between cytological and histopathological findings.

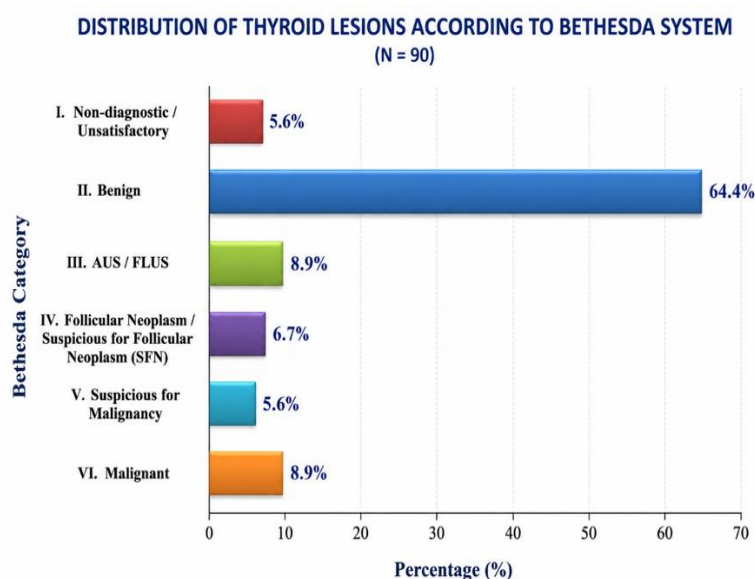


Figure 1: Distribution of Thyroid Lesion According to Bethesda system

Table 3. Cytological Diagnosis and Histopathological Correlation (n = 45*) (*Only operated cases)

Cytological Diagnosis	Histopathology Benign n (%)	Histopathology Malignant n (%)	Total
Benign	23 (92.0)	2 (8.0)	25 (100.0)
AUS/FLUS	4 (66.7)	2 (33.3)	6 (100.0)
Follicular Neoplasm	2 (40.0)	3 (60.0)	5 (100.0)
Suspicious for Malignancy	1 (20.0)	4 (80.0)	5 (100.0)
Malignant	0 (0.0)	4 (100.0)	4 (100.0)
Total	30 (66.7)	15 (33.3)	45 (100.0)
Test of Significance: Chi-square = 28.64, p <0.001*			

The diagnostic performance of FNAC using the Bethesda System was found to be excellent, with a sensitivity of 86.7%, specificity of 93.3%, positive predictive value of 86.7%, negative predictive value of 93.3%, and an overall diagnostic accuracy of 91.1%. The area under the receiver operating characteristic (ROC) curve was 0.91, indicating excellent discriminatory ability of FNAC in differentiating benign from malignant thyroid lesions. Overall, the findings demonstrate that the Bethesda System provides a reliable and standardized framework for reporting thyroid cytology, facilitating accurate diagnosis, effective risk stratification, and appropriate clinical management of patients with thyroid nodules.

Table 4. Diagnostic Performance of FNAC Using Bethesda System (Histopathology as Gold Standard)

Parameter	Value (%)
Sensitivity	86.7
Specificity	93.3
Positive Predictive Value	86.7
Negative Predictive Value	93.3
Diagnostic Accuracy	91.1
Area Under ROC Curve (AUC)	0.91

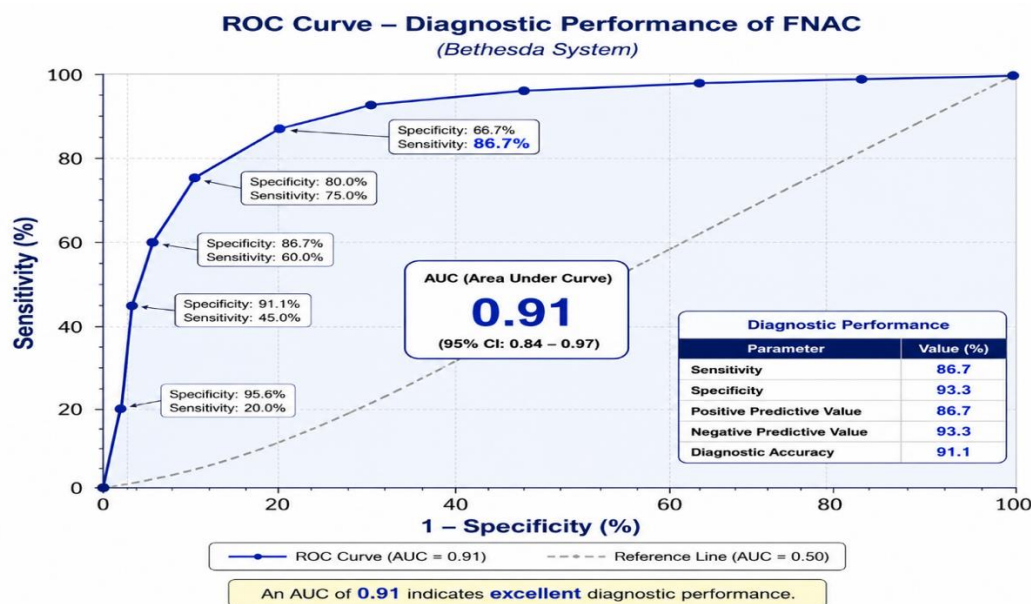


Figure 2: ROC curve: Diagnostic performance of FNAC

DISCUSSION

The present study evaluated the cytological patterns of thyroid lesions according to the Bethesda System among 90 patients with thyroid swellings. The mean age of the study population was 38.6 ± 11.8 years, with the highest proportion of patients (31.1%) belonging to the 31–40 years age group. Females constituted 80.0% of the study population, demonstrating a female predominance of approximately 4:1. Similar demographic findings were reported by Choden et al., who observed that thyroid nodules occurred predominantly in women during the third and fourth decades of life, reflecting the influence of hormonal and autoimmune factors on thyroid disease (11).

In the present study, Bethesda Category II (Benign) was the most common cytological diagnosis, accounting for 64.4% of all thyroid aspirates, followed by Category III (8.9%), Category VI (8.9%), Category IV (6.7%), and Categories I and V (5.6% each). These findings are comparable with those reported by Mishra et al., who also found benign lesions to constitute the majority of thyroid aspirates, emphasizing that colloid goitre and benign follicular nodules remain the commonest thyroid lesions encountered in routine cytopathology practice (12).

Cytohistopathological correlation in the present study demonstrated a highly significant association between Bethesda category and histopathological diagnosis ($\chi^2 = 28.64$, $p < 0.001$). Most lesions categorized as benign on FNAC were confirmed histopathologically, whereas lesions categorized as suspicious or malignant showed a high probability of malignancy. Similar observations were reported by Pandey et al., who highlighted that the Bethesda System substantially improves diagnostic reproducibility and facilitates better prediction of malignancy risk across different cytological categories, thereby aiding clinical decision-making (13).

The diagnostic performance of FNAC in the present study was excellent, with a sensitivity of 86.7%, specificity of 93.3%, positive predictive value of 86.7%, negative predictive value of 93.3%, and an overall diagnostic accuracy of 91.1%. These values compare favourably with those reported by Morgan et al., who demonstrated that FNAC possesses high specificity and remains an effective first-line investigation for thyroid nodules, substantially reducing unnecessary thyroid surgeries while accurately identifying lesions requiring operative management (14).

The present findings also closely resemble those of Ko et al., who reported high diagnostic accuracy and excellent cytohistological concordance of thyroid FNAC when interpreted using standardized reporting criteria. Likewise, Jogai et al. observed that most discordant cases occurred in follicular-patterned lesions because cytology cannot reliably differentiate follicular adenoma from follicular carcinoma without histological evidence of capsular or vascular invasion. These studies reinforce the importance of histopathological examination as the gold standard for definitive diagnosis, particularly for indeterminate Bethesda categories (15,16).

The excellent diagnostic performance observed in the present study is further supported by Cai et al., who demonstrated that ultrasound-guided FNAC significantly improves specimen adequacy and diagnostic accuracy, especially in small, cystic, and deep-seated thyroid nodules (17). Similarly, Bamanikar et al. reported that the Bethesda System provides standardized terminology with high specificity and excellent clinicopathological correlation, thereby improving communication between pathologists and treating clinicians (18).

False-positive and false-negative diagnoses remain an inherent limitation of thyroid cytology because of sampling errors and overlapping cytomorphological features. Ergete and Abebe reported that most discordant cases were encountered in indeterminate and follicular-patterned lesions, emphasizing the need for careful clinicoradiological correlation and histopathological confirmation before definitive treatment decisions (19). The present study similarly observed excellent overall concordance while acknowledging that histopathological examination remains indispensable for confirmation of cytological diagnosis in equivocal cases.

Overall, the findings of the present study are consistent with previous national and international literature, demonstrating that the Bethesda System for Reporting Thyroid Cytopathology is a reliable, reproducible, and clinically useful reporting system. The predominance of benign lesions, significant cytohistopathological correlation, and high diagnostic accuracy observed in the present study reaffirm the role of FNAC as the investigation of choice for the initial evaluation and risk stratification of thyroid nodules, facilitating appropriate clinical management while minimizing unnecessary surgical interventions.

CONCLUSION

The present study demonstrated that the majority of thyroid lesions were benign, with Bethesda Category II constituting the largest proportion of cytological diagnoses. Thyroid lesions showed a marked female predominance, and most patients belonged to the third and fourth decades of life. Fine-needle aspiration cytology (FNAC), interpreted according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), exhibited excellent diagnostic performance with high sensitivity, specificity, and overall diagnostic accuracy. A highly significant correlation between cytological and histopathological diagnoses further validated the reliability of the Bethesda System in risk stratification and clinical decision-making. The findings reaffirm that FNAC is a safe, simple, minimally invasive, and cost-effective first-line diagnostic modality for evaluating thyroid nodules, enabling appropriate patient management while minimizing unnecessary surgical interventions.

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