

Categorization of Thyroid FNAC Using the Bethesda System and Its Histopathological Correlation

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Abstract: Background: Thyroid nodules are common endocrine lesions, with the primary clinical challenge being the identification of malignancy among predominantly benign cases. Fine-needle aspiration cytology (FNAC), reported using the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), provides standardized risk stratification; however, its diagnostic performance requires validation through histopathological correlation. **Methods:** This observational study was conducted over two years at a tertiary care center. A total of 122 patients with thyroid swelling underwent FNAC, of which 83 had subsequent histopathological follow-up. Cytological findings were categorized according to TBSRTC. Cytohistopathological correlation was performed, and the risk of malignancy (ROM) was calculated for each category. The diagnostic performance parameters, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy, were determined using histopathology as the reference standard. **Results:** The majority of cases were categorized as Bethesda Category II (81.15 %). Histopathological examination revealed that 83.13% of the lesions were non-neoplastic and 16.87% were neoplastic, with papillary carcinoma being the most common malignancy. The concordance rates were 89.86% and 78.57% for non-neoplastic and neoplastic lesions, respectively. The ROM increased progressively from Category I (0%) to Category VI (100%). FNAC demonstrated a sensitivity of 78.57%, specificity of 89.85%, PPV of 61.11%, NPV of 95.38%, and an overall diagnostic accuracy of 87.95%. **Conclusion:** FNAC, when interpreted using the Bethesda system, is a reliable and effective initial diagnostic modality for thyroid nodules. Cytohistopathological correlation enhances diagnostic accuracy and highlights the limitations of indeterminate categories. Standardized reporting using the TBSRTC facilitates appropriate clinical management and reduces unnecessary surgical interventions.

Keywords: Bethesda system; Cytohistopathological correlation; Diagnostic accuracy; Fine-needle aspiration cytology; Risk of malignancy; Thyroid nodules.

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INTRODUCTION

Thyroid nodules are among the most common endocrine disorders encountered in clinical practice, with a prevalence of approximately 4 to 7% in the general population and a higher incidence in women [1]. Although the majority of these lesions are benign, the principal clinical challenge lies in identifying the minority that harbor malignancy, as accurate preoperative diagnosis is essential for appropriate management and avoidance of unnecessary surgery.

Fine-needle aspiration cytology (FNAC) is the first-line diagnostic modality for evaluating thyroid nodules because of its simplicity, cost-effectiveness, and minimally invasive nature [2].

However, it has limitations, particularly in follicular-patterned lesions, where capsular and vascular invasion cannot be assessed [3]. Additional factors, such as sampling adequacy and interpretive variability, may also influence diagnostic accuracy.

To enhance reporting consistency and clinical relevance, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced as a standardized six-tier classification scheme linking cytological findings to malignancy risk and management recommendations.[4] This system has improved communication between pathologists and clinicians and enabled more reliable risk stratification across institutions in the past.

Histopathological examination remains the gold standard for a definitive diagnosis. Therefore, cytohistopathological correlation is critical for assessing the diagnostic performance of FNAC, identifying discrepancies, and refining institutional practices. In many regions, including our setting, limited data are available on Bethesda-based reporting with histological follow-up.

Hence, the present study was undertaken to evaluate palpable thyroid lesions using FNAC categorized according to the TBSRTC and to correlate cytological findings with histopathology wherever available. This study also aimed to assess demographic distribution and determine diagnostic concordance, thereby contributing to local evidence on the utility of standardized thyroid cytology reporting.

MATERIALS AND METHODS

This observational study was conducted at the Department of Pathology, Raipur Institute of Medical Sciences (RIMS), Raipur, India, following approval from the Institutional Ethics Committee (IEC/RIMS/2024/040). A retrospective and prospective study design was employed over a two-year period.

Study Population

All patients presenting with palpable thyroid swelling who underwent FNAC and subsequent histopathological evaluation were included. Patients were excluded if consent was not obtained, if their clinical condition precluded participation, or if their histopathological specimens were inadequate due to autolysis or improper fixation.

The minimum sample size was calculated using the standard formula ($n = z^2p(1-p)/d^2$) with a 95% confidence interval ($z = 1.96$), estimated prevalence ($p = 7\%$), and precision ($d = 0.05$), yielding 101 cases. After adding a 10% contingency, the target sample size was 111. A total of 122 FNAC cases were analyzed, of which 83 had histopathological follow-up data.

FNAC Procedure and Cytological Evaluation

For retrospective cases, data were retrieved from the departmental records. In prospective cases, demographic and clinical details were recorded after obtaining informed consent from the patients. FNAC was performed under aseptic precautions using a 23-gauge needle with a 10 to 20 mL syringe. Multiple passes were made as required, and cystic lesions were

aspirated for fluid content. Ultrasound-guided FNAC was performed in selected patients. Smears were prepared immediately and stained with May-Grünwald-Giemsa (MGG) for air-dried preparations and Papanicolaou stain for alcohol-fixed smears. Hematoxylin and eosin staining was performed selectively.

Smear adequacy and reporting were based on the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), which classifies lesions into six categories (I–VI) with defined adequacy criteria and diagnostic implications [4].

Histopathological Examination

Surgically excised specimens were fixed in 10% neutral buffered formalin, routinely processed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Archived slides and blocks were reviewed for retrospective cases, where required. Histopathology was used as the reference standard.

Statistical Analysis

Cytological and histopathological findings were compared to assess the diagnostic concordance. The risk of malignancy (ROM) for each Bethesda category was calculated as the proportion of histologically confirmed malignant cases.

The diagnostic performance parameters, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy, were determined using histopathology as the gold standard. Descriptive statistics were used to summarize the demographic and diagnostic variables. Associations were analyzed using the chi-square test, with $p < 0.05$ considered statistically significant.

RESULTS

Demographic Profile

A total of 122 thyroid FNAC cases were evaluated during the study period, of which 83 underwent surgical excision with histopathological follow-up. The mean age of the participants was 45.16 years. There was a marked female predominance, with a male-to-female ratio of 1:16.1; females accounted for 86.07% of the cases and males for 13.93%.

FNAC distribution by Bethesda category

Cytological evaluation using the Bethesda System demonstrated that most cases were classified as Category II (benign), accounting for 99/122 cases (81.15 %). The remaining cases were distributed as follows: Category I in 7 cases (5.74%), Category III in 2 cases (1.64%), Category IV in 5 cases (4.10%), Category V in 2 cases (1.64%), and Category VI in 7 cases (5.74%).

Among Category I (nondiagnostic) cases, cystic aspirates were the most frequent cause of inadequacy (4/7), followed by blood contamination and scant cellular material.



Table-1: Distribution of Thyroid FNAC Cases According to Bethesda System (n = 122)

Bethesda Category	Number of Cases	Percentage (%)
Category I	7	5.74
Category II	99	81.15
Category III	2	1.64
Category IV	5	4.10
Category V	2	1.64
Category VI	7	5.74
Total	122	100

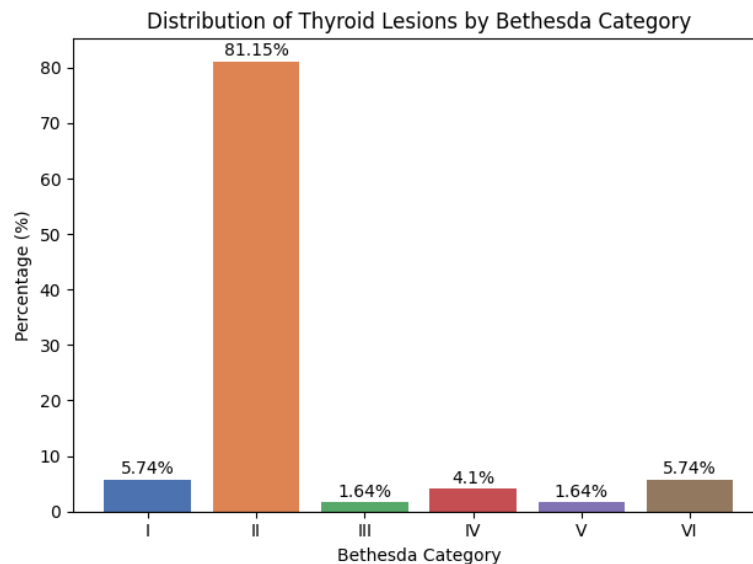


Figure-1: Distribution of Thyroid Lesions According to Bethesda Categories on FNAC

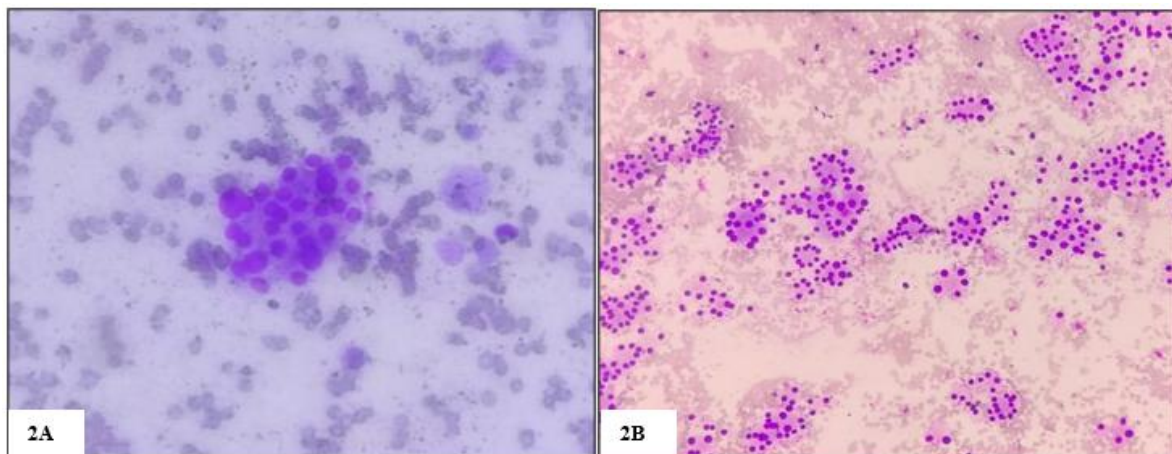


Figure-2: (A) Fine-needle aspiration cytology (FNAC) smear showing follicular cells with Hürthle cell changes (Bethesda Category II; May–Grunwald–Giemsa stain, ×400). (B) FNAC smear showing microfollicular clusters with increased cellularity (Bethesda Category IV; May–Grunwald–Giemsa stain, ×100)

Histopathological findings

Among the 83 cases with histopathological follow-up, 69 (83.13%) were non-neoplastic and 14 (16.87%) were neoplastic cases. Within the non-neoplastic group, colloid/multinodular goiter was the predominant diagnosis (63/69; 91.3%), followed by Hashimoto’s

thyroiditis (5/69; 7.25%) and Graves’ disease (1/69; 1.45%). Among neoplastic lesions, papillary carcinoma was the most common diagnosis (7/14, 50.0%), followed by follicular carcinoma (3/14, 21.4%), follicular adenoma (2/14, 14.3%), and Hürthle cell adenoma (2/14, 14.3%).



Table-2: Overall Histopathological Distribution (n = 83)

Category	Number of Cases	Percentage (%)
Non-neoplastic	69	83.13
Neoplastic	14	16.87
Total	83	100

Table-3: Histopathological Spectrum of Thyroid Lesions (n = 83)

Lesion Type	Number of Cases	Percentage (%)
Non-neoplastic (n=69)		
Colloid goiter/MNG	63	91.3
Hashimoto's thyroiditis	5	7.25
Graves' disease	1	1.45
Neoplastic (n=14)		
Papillary carcinoma	7	50.0
Follicular carcinoma	3	21.4
Follicular adenoma	2	14.3
Hürthle cell adenoma	2	14.3

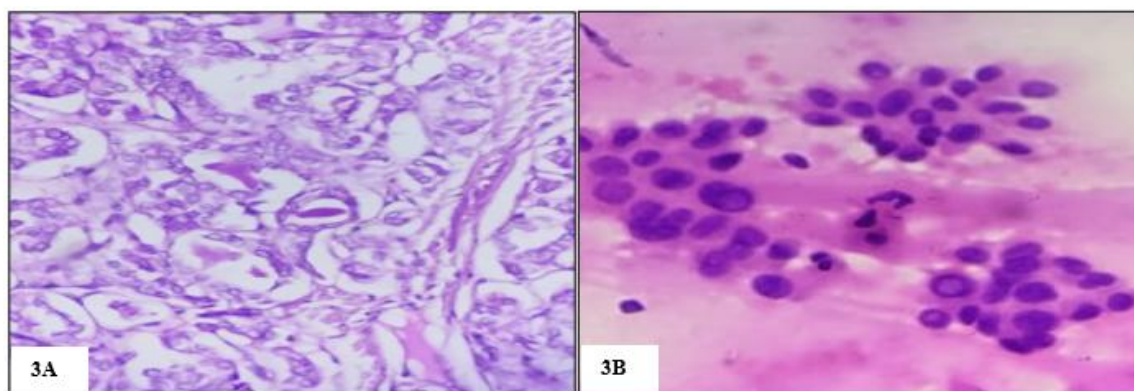


Figure-3: (A) Histopathology showing papillary carcinoma with arborizing papillae and psammoma bodies (hematoxylin and eosin stain, ×100) (B) FNAC smear showing nuclear features of papillary carcinoma, including intranuclear inclusions (Bethesda Category VI; hematoxylin and eosin staining, ×400)

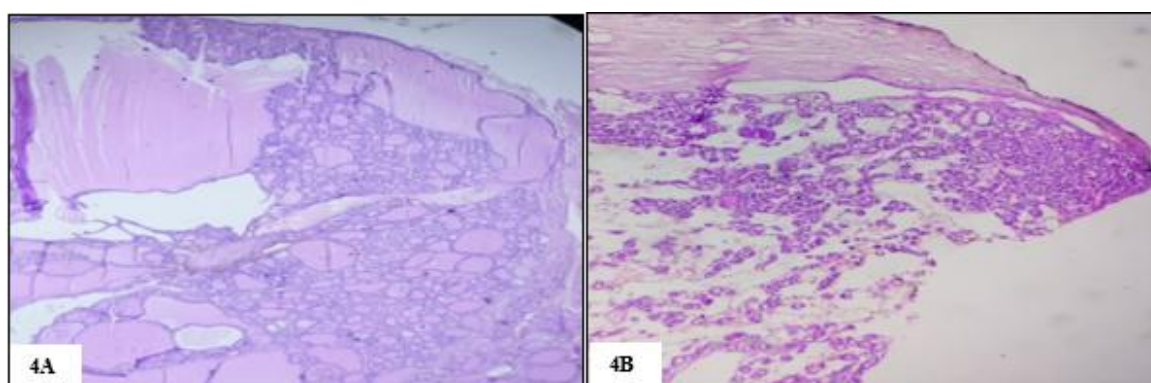


Figure-4: (A) Histopathology of colloid goiter showing variably sized follicles filled with colloid (hematoxylin and eosin staining, ×100). (B) Histopathology of minimally invasive follicular carcinoma (hematoxylin and eosin staining, ×100)

Cytohystopathological correlation

Cytohystopathological correlation was performed in 83 cases with available surgical follow-up data (Table 4). In Bethesda Category II (n=65), 62 cases were concordant and three were discordant. The discordant cases were diagnosed as follicular adenoma (n=1) and Hürthle cell adenoma (n=2) on histopathology. In Category IV (n=5), four cases were concordant and one

was discordant. In Category V (n=2), one case was concordant and one was discordant. All five cases in Category VI were concordant with the histopathological findings. Bethesda Category III included 2 cases, which were diagnosed as multinodular goiter (n=1) and papillary carcinoma (n=1). In Category I (n=7), histopathological follow-up was available in four cases, all of which were non-neoplastic.



Table-4: Cytohistopathological Correlation of Thyroid Lesions (n = 83)

Bethesda Category	Cases with Follow-up (n)	Non-neoplastic (n)	Neoplastic (n)	Concordant (n)	Discordant (n)	Concordance (%)
Category II	65	62	3	62	3	95.38
Category IV	5	1	4	4	1	80.00
Category V	2	1	1	1	1	50.00
Category VI	5	0	5	5	0	100.00

Concordance was observed in 62 of 69 non-neoplastic cases (89.86%) and 11 of 14 neoplastic cases (78.57%).

Discordance was observed in 7 non-neoplastic and 3 neoplastic cases ($p = 0.236$).

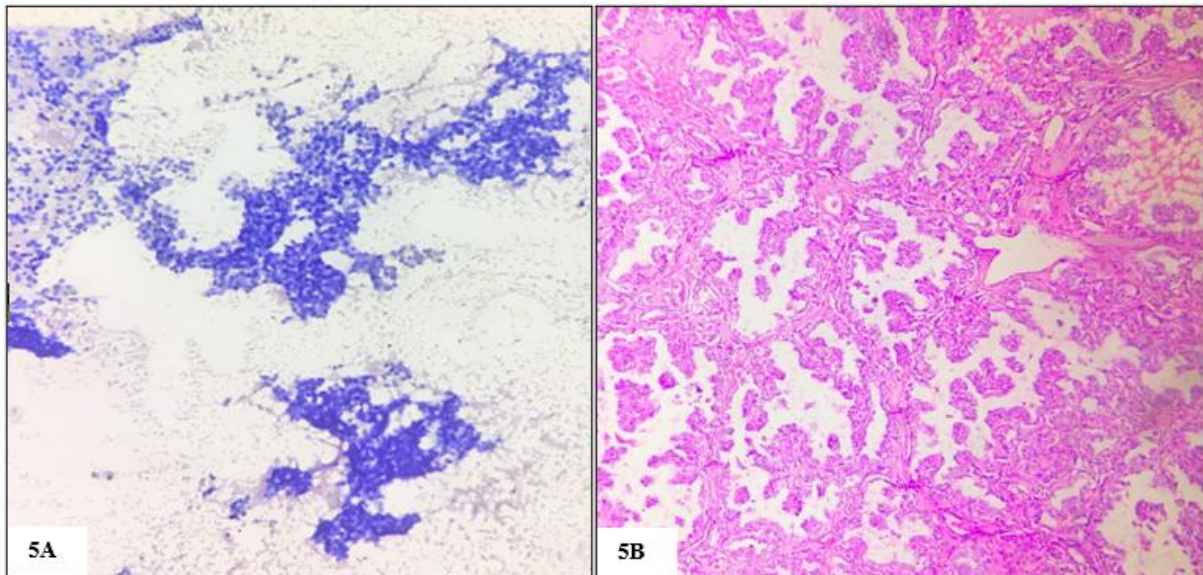


Figure-5: (A) FNAC smear showing papillary clusters with fibrovascular cores and characteristic nuclear features. (B) Corresponding histopathology showing papillary carcinoma with similar characteristics.

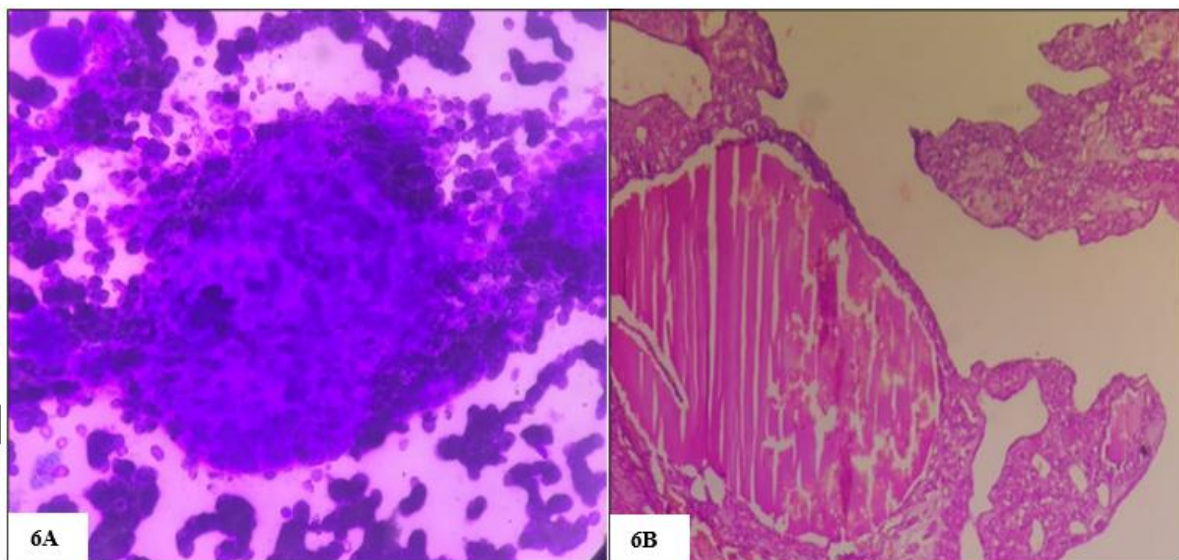


Figure-6: (A) FNAC smear showing papillaroid clusters with nuclear crowding and overlap. (B) Histopathological examination showing colloid goiter with papillary hyperplasia.

Table-5: Correlation of Cytological and Histopathological Diagnosis (n = 83)

Histopathology	Concordant (n)	Concordant (%)	Discordant (n)	Discordant (%)	Total (n)
Non-neoplastic	62	89.86	7	10.14	69
Neoplastic	11	78.57	3	21.43	14

$p = 0.236$

Malignancy risk by category

The risk of malignancy (ROM) was calculated for each Bethesda category based on histopathological follow-up (Table 6). The ROM values were as follows: Category I, 0% (0/4); Category II, 4.62% (3/65); Category III, 50.00% (1/2); Category IV, 80.00% (4/5); Category V, 50.00% (1/2); and Category VI, 100.00% (5/5).

Table-6: Risk of Malignancy Across Bethesda Categories (n = 83)

Bethesda Category	Cases with Follow-up (n)	Malignant Cases (n)	Risk of Malignancy (%)
Category I	4	0	0.00
Category II	65	3	4.62
Category III	2	1	50.00
Category IV	5	4	80.00
Category V	2	1	50.00
Category VI	5	5	100.00
Total	83	14	—

Chi-square test: $\chi^2 = 34.38, p < 0.001$

Diagnostic performance of FNAC

The diagnostic performance of FNAC for detecting malignant thyroid lesions was evaluated using histopathology as the reference standard (Tables 7 and

8). Sensitivity was 78.57%, specificity 89.85%, positive predictive value (PPV) 61.11%, negative predictive value (NPV) 95.38%, and overall diagnostic accuracy 87.95%.

Table-7: Diagnostic Performance of FNAC for Malignant Thyroid Lesions (n = 83)

FNAC Result	Malignant (Histopathology)	Non-malignant (Histopathology)	Total
Positive for malignancy	11	7	18
Negative for malignancy	3	62	65
Total	14	69	83

Table-8: Diagnostic Indices

Parameter	Value (%)
Sensitivity	78.57
Specificity	89.85
Positive Predictive Value	61.11
Negative Predictive Value	95.38
Diagnostic Accuracy	87.95

DISCUSSION

The present study evaluated the diagnostic utility of fine-needle aspiration cytology (FNAC) in thyroid lesions with cyto-histopathological correlation. A total of 122 thyroid FNAC cases were analyzed, of which 83 underwent histopathological follow-up. These findings reaffirm the role of FNAC as a primary diagnostic modality for thyroid nodules when interpreted using the Bethesda System.

Demographic Profile

The mean age of the patients in the present study was 45.16 years, with the majority of cases occurring in the middle-aged group. A similar age distribution has been reported by Pijush *et al.* [5] and Malukani *et al.* [6], indicating that thyroid lesions are most commonly encountered in the fourth to sixth decades of life. A marked female predominance (male: female ratio =

1:16.1) was observed, which aligns with the findings of Sameep *et al.* [8], Arul *et al.* [9], and Saranyu *et al.* [10], reflecting the higher prevalence of thyroid disorders among women.

Bethesda Category Distribution

In the present study, most cases were classified as Bethesda Category II (81.15 %). This predominance of benign lesions is comparable to observations by Malukani *et al.* [6], Mondal *et al.* [7], and Sameep *et al.* [8].

The relatively low proportion of nondiagnostic cases (5.74%) is similar to that reported by Sameep *et al.* [8] and Arul *et al.* [9], whereas higher rates have been described by Saranyu *et al.* [10] and V. Gupta *et al.* [11]. The lower rate in the present study may be



attributed to the improved sampling techniques and selective use of ultrasound-guided FNAC.

The proportion of indeterminate categories (III to V) in this study was low, consistent with the findings of Mondal *et al.* [7] and Malukani *et al.* [6], possibly reflecting strict adherence to the diagnostic criteria and efforts to minimize equivocal reporting.

Histopathological Spectrum

Histopathological evaluation demonstrated that non-neoplastic lesions constituted the majority (83.13%), with colloid or multinodular goiter being the most common diagnosis (91.3%). These findings are comparable to those reported by Pijush *et al.* [5] and Manoj *et al.* [12], in which benign thyroid lesions predominated. Among neoplastic lesions, papillary carcinoma was the most frequent malignancy (50%), followed by follicular carcinoma and adenoma. A similar pattern was described by Sameep *et al.* [8] and Manoj *et al.* [12], where papillary carcinoma was the predominant thyroid malignancy.

Cytohistopathological Correlation

The present study demonstrated concordance rates of 89.86% for non-neoplastic lesions and 78.57% for neoplastic lesions. These findings are comparable to those reported by Pijush *et al.* [5], Malukani *et al.* [6], and Usha *et al.* [1].

Discordant cases in the benign category were mainly due to follicular-patterned lesions, such as follicular adenoma and Hürthle cell adenoma, which represent a recognized limitation of FNAC due to the inability to assess capsular and vascular invasion. Similar observations have been reported by Bamanikar *et al.* [13] and Manoj *et al.* [12], highlighting the diagnostic challenge of differentiating follicular adenoma from carcinoma on cytology. The variability observed in indeterminate categories (III to V) is consistent with the findings of Saranyu *et al.* [10], where these categories showed heterogeneous histopathological outcomes.

Risk of Malignancy (ROM)

The risk of malignancy in the present study was 0% for Category I, 4.62% for Category II, 50% for Category III, 80% for Category IV, 50% for Category V, and 100% for Category VI.

These findings are broadly comparable to those reported by Mondal *et al.* [7], Saranyu *et al.* [10], and Sameep *et al.* [8], who demonstrated an increasing trend in malignancy risk across the Bethesda categories. The relatively higher malignancy rate observed in Category IV in the present study compared with some reports may be attributed to the smaller sample size and selection bias toward surgically managed cases.

Diagnostic Performance of FNAC

In the present study, FNAC demonstrated a sensitivity, specificity, and diagnostic accuracy of 78.57 %, 89.85%, and 87.95 %, respectively. These values are comparable to those reported by Saranyu *et al.* [10], Pijush *et al.* [5], and Manoj *et al.* [12]. The high negative predictive value (95.38%) observed in the present study supports the reliability of FNAC in excluding malignancies. The relatively lower positive predictive value (61.11%) may be attributed to false-positive interpretations, particularly in follicular-patterned lesions, as also noted by Malukani *et al.* [6].

Clinical Implications

The findings of the present study support the role of FNAC as an effective first-line diagnostic tool for thyroid disease. The Bethesda System facilitates standardized reporting and risk stratification, thereby aiding clinical decision-making.

However, indeterminate categories and follicular-patterned lesions continue to pose diagnostic challenges, as also highlighted in studies by Bamanikar *et al.* [13] and Saranyu *et al.* [10], emphasizing the need for careful interpretation and appropriate histopathological correlation.

Overall, the findings reinforce the role of FNAC with Bethesda-based reporting as a reliable and clinically relevant tool for the evaluation of thyroid nodules.

Limitations

The study was conducted at a single tertiary care center, which may limit its generalizability. Histopathological correlation was available only for surgically managed cases, introducing a selection bias. The absence of molecular testing and small sample size in certain Bethesda categories may have affected risk stratification.

CONCLUSION

FNAC, when reported using the Bethesda system, is a reliable and effective method for the initial evaluation of thyroid nodules in the Indian population. It provides an accurate differentiation between benign and malignant lesions and supports clinical decision-making.

Cytohistopathological correlation is essential for assessing diagnostic accuracy, particularly in indeterminate lesions. The use of standardized reporting systems, such as the TBSRTC, should be encouraged in routine practice. Overall, FNAC with Bethesda-based reporting serves as a valuable diagnostic tool that guides appropriate patient management and minimizes unnecessary surgical interventions.

Ethics Approval & Consent: The study was approved by the Institutional Ethics Committee (IEC No. IEC/RIMS/2024/040). The requirement for informed



consent was waived for retrospective data, whereas written informed consent was obtained for prospective cases.

Conflicts of Interest: The authors declare no conflict of interest

Data Availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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