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DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY USING THE BETHESDA SYSTEM: A CYTOHISTOPATHOLOGICAL CORRELATION STUDY OF THYROID LESIONS

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ABSTRACT

Background: The aim is to correlate FNAC findings categorized according to the Bethesda System with histopathological diagnosis, determine the risk of malignancy in each Bethesda category, and evaluate the diagnostic performance of FNAC in terms of sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy.

Materials and Methods: A hospital-based cross-sectional observational study was conducted in the Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, from January 2019 to June 2020. A total of 130 patients with thyroid swellings underwent FNAC. Histopathological follow-up was available in 97 surgically treated cases, which were included for cytohistopathological correlation. Cytological smears were categorized according to the Bethesda System for Reporting Thyroid Cytopathology. Histopathological diagnosis served as the reference standard for calculating the risk of malignancy, concordance, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy.

Results: Histopathological follow-up was available in 97 of the 130 patients. Overall cytohistopathological concordance was 97.87%, with only two discordant cases. The risk of malignancy was 2.77% in Bethesda Category II, 30.77% in Category IV, and 100% in both Categories V and VI. FNAC demonstrated a sensitivity of 86.67%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.53%, and an overall diagnostic accuracy of 97.87%. No false-positive cases were observed, whereas two false-negative cases resulted from limitations in diagnosing follicular carcinoma and papillary thyroid carcinoma with cystic degeneration. Histopathological examination revealed nodular goitre as the most common benign lesion and papillary thyroid carcinoma as the most common malignant lesion.

Conclusion: FNAC demonstrated excellent cytohistopathological correlation and high diagnostic accuracy in the evaluation of thyroid lesions. The Bethesda System effectively stratified thyroid nodules according to their risk of malignancy and provided reliable guidance for clinical decision-making. Although histopathological examination remains essential for confirmation of selected indeterminate lesions, FNAC continues to be a dependable first-line diagnostic investigation for thyroid nodules.

Keywords: Fine needle aspiration cytology; Bethesda System; Cytohistopathological correlation; Thyroid lesions; Histopathology; Diagnostic accuracy; Thyroid nodules.

INTRODUCTION

Thyroid nodules are one of the most frequently encountered endocrine disorders, with an increasing prevalence owing to widespread clinical examination and advances in imaging techniques. Although the majority of thyroid nodules are benign, distinguishing them from malignant lesions before surgery remains a major clinical challenge. Accurate preoperative diagnosis is essential to avoid unnecessary thyroidectomy while ensuring timely treatment of malignant lesions.[1,2].

Fine needle aspiration cytology (FNAC) has become the investigation of choice for the evaluation of thyroid nodules because it is minimally invasive, safe, inexpensive, rapid, and highly reliable. It serves as the first-line diagnostic modality by differentiating benign from malignant lesions and guiding appropriate clinical management. The widespread use of FNAC has significantly reduced unnecessary surgical procedures while increasing the proportion of malignant lesions identified among patients undergoing thyroidectomy.[3,4].

Before the introduction of standardized reporting, thyroid cytology suffered from considerable interobserver variability and inconsistent terminology, leading to difficulties in communication between cytopathologists and treating clinicians. To overcome these limitations, the National Cancer Institute introduced the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), which classifies thyroid FNAC into six standardized diagnostic categories, each associated with an estimated risk of malignancy and corresponding management recommendations.[1,2,5]

Although FNAC is highly accurate in the diagnosis of most thyroid lesions, certain diagnostic challenges remain. Follicular-patterned lesions, cystic degeneration, inadequate sampling, and overlapping cytological features may result in false-positive or false-negative diagnoses. Consequently, histopathological examination of surgically resected specimens remains the gold standard for confirming the cytological diagnosis and assessing the true diagnostic performance of FNAC.[4,6]

Cytohistopathological correlation plays an important role in evaluating the effectiveness of thyroid FNAC by determining concordance between cytological and histopathological diagnoses. It also facilitates calculation of malignancy rates for individual Bethesda categories and assessment of diagnostic indices such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. These parameters are valuable quality assurance measures for every cytopathology laboratory.[6–8]

Several studies have demonstrated excellent diagnostic performance of the Bethesda System with high specificity and diagnostic accuracy. However, variations in malignancy rates and diagnostic indices have been reported among different institutions because of differences in patient population, sampling techniques, cytopathologist experience, and case selection. Therefore, periodic institutional evaluation of cytohistopathological correlation is necessary to validate the performance of FNAC and ensure consistent reporting standards.[7–10]

The present study was undertaken to correlate FNAC findings categorized according to the Bethesda System with histopathological diagnosis, determine the malignancy risk in each Bethesda category, evaluate the concordance between cytological and histopathological findings, and assess the diagnostic performance of FNAC in terms of sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy.

MATERIALS AND METHODS

A hospital-based cross-sectional observational study was conducted in the Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, from January 2019 to June 2020. The study included patients with thyroid lesions who underwent fine needle aspiration cytology (FNAC), and cases with available histopathological examination following surgery were included for cytohistopathological correlation. A total of 130 patients with clinically palpable thyroid swellings underwent FNAC during the study period. Histopathological follow-up was available in 97 cases, which constituted the study population for cytohistopathological correlation and evaluation of diagnostic performance. Ethical approval was taken from the institutional ethical committee. (ref no: GU/HREC/EC/2019/1642)

Inclusion criteria

- Patients presenting with clinically palpable thyroid swelling who underwent FNAC.
- Cases in which subsequent histopathological examination of the thyroid specimen was available.
- Patients of all age groups and both sexes.

Exclusion criteria

- Cases without histopathological follow-up.
- Unsatisfactory or incomplete clinical records.
- Repeat aspirations from the same lesion were excluded.

FNAC procedure: FNAC was performed under aseptic precautions using a 22–23-gauge needle attached to a 10-mL disposable syringe. Aspirated material was smeared onto clean glass slides. Air-dried smears were stained using May–Grünwald–Giemsa stain, while alcohol-fixed smears were stained with Papanicolaou stain. Hematoxylin and Eosin staining was performed whenever required for detailed cytomorphological evaluation.

Cytological evaluation: All aspirates were examined microscopically and categorized according to The Bethesda **System for Reporting Thyroid Cytopathology (TBSRTC)** into six diagnostic categories:

- Category I – Nondiagnostic/Unsatisfactory
- Category II – Benign
- Category III – Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance
- Category IV – Follicular Neoplasm/Suspicious for Follicular Neoplasm
- Category V – Suspicious for Malignancy
- Category VI – Malignant

Histopathological evaluation: Patients who subsequently underwent thyroid surgery had their resected specimens processed according to standard histopathological protocols. Tissue sections were stained with Hematoxylin and Eosin and examined microscopically. Histopathological diagnosis served as the reference standard for comparison with cytological findings.

Cytohistopathological correlation: Cytological diagnoses were correlated with corresponding histopathological findings. Concordant and discordant cases were identified. Malignancy rates for each Bethesda category were calculated based on histopathological confirmation. False-positive and false-negative cases were analyzed to determine the possible causes of diagnostic discordance.

Statistical analysis: Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Categorical variables were expressed as frequencies and percentages. Diagnostic performance of FNAC was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy, considering histopathological diagnosis as the gold standard. A p-value <0.05 was considered statistically significant.

RESULTS

[Table 1] presents the histopathological diagnosis of 97 thyroid lesions that underwent surgical excision. Nodular goitre was the most common histopathological diagnosis, accounting for 37 (38.14%) cases, followed by adenomatous goitre in 15 (15.46%) cases. Papillary thyroid carcinoma constituted 12 (12.37%) cases, making it the most frequent malignant lesion. Follicular adenoma was observed in 11 (11.34%) cases, while Hashimoto's thyroiditis and nodular goitre with cystic degeneration accounted for 7 (7.22%) and 6 (6.19%) cases, respectively. Less common diagnoses included multinodular goitre, follicular carcinoma, follicular variant of papillary thyroid carcinoma, and lymphoma.

[Table 2] demonstrates the correlation between Bethesda cytological categories and histopathological diagnosis. Bethesda Category II showed predominantly benign lesions, with only 2 malignant cases among 72 histologically evaluated cases. Category IV included 13 cases, of which 4 were confirmed as malignant on histopathology. All cases categorized as Bethesda Category V and Category VI were confirmed to be malignant on histopathological examination, indicating excellent concordance in these higher Bethesda categories.

[Table 3] shows the risk of malignancy for each Bethesda category based on histopathological follow-up. The malignancy risk was 2.77% in Bethesda Category II and increased to 30.77% in Category IV. Bethesda Categories V and VI demonstrated a malignancy risk of 100%, whereas no evaluable cases were available in Categories I and III for risk estimation. The increasing malignancy risk across higher Bethesda categories confirms the effectiveness of the Bethesda System in stratifying thyroid nodules according to their malignant potential.

[Table 4] summarizes the diagnostic performance of FNAC using histopathology as the gold standard. FNAC demonstrated a sensitivity of 86.67% and a specificity of 100%. The positive predictive value was 100%, while the negative predictive value was 97.53%. The overall diagnostic accuracy was 97.87%, with no false-positive cases identified and only two false-negative cases. These findings indicate excellent diagnostic reliability of FNAC in the evaluation of thyroid lesions.

[Table 5] presents the concordance between cytological and histopathological diagnoses. Among the 97 cases with histopathological follow-up, 95 (97.87%) showed complete agreement between FNAC and histopathological diagnosis, whereas only 2 (2.13%) cases demonstrated discordance. This high concordance rate reflects the strong diagnostic agreement between cytological interpretation using the Bethesda System and final histopathological diagnosis.

[Table 6] describes the discordant cases identified during cytohistopathological correlation. Both discordant cases represented false-negative diagnoses. One case diagnosed cytologically as a follicular neoplasm was confirmed as follicular carcinoma on histopathology because capsular and vascular invasion, essential for diagnosing follicular carcinoma, cannot be assessed by cytology alone. The second case was reported as a benign goitrous lesion on FNAC but was diagnosed as papillary thyroid carcinoma on histopathological examination, most likely due to cystic degeneration and sampling error that obscured the characteristic cytological features of malignancy. These findings highlight the known limitations of FNAC and emphasize the importance of histopathological confirmation in selected cases.

Table 1: Histopathological diagnosis of thyroid lesions (n = 97)

Histopathological diagnosis	Number (n)	Percentage (%)
Nodular goitre	37	38.14
Adenomatous goitre	15	15.46
Papillary thyroid carcinoma	12	12.37
Follicular adenoma	11	11.34
Hashimoto's thyroiditis	7	7.22
Nodular goitre with cystic degeneration	6	6.19
Multinodular goitre	3	3.09
Follicular carcinoma	1	1.03
Follicular variant of papillary thyroid carcinoma	1	1.03
Lymphoma	1	1.03
Total	97	100.00

Table 2: Correlation between Bethesda category and histopathological diagnosis

Bethesda category	Histopathology available	Benign	Malignant	Malignancy rate (%)
I	0	0	0	—
II	72	70	2	2.77
III	0	0	0	—
IV	13	9	4	30.77
V	4	0	4	100.00
VI	5	0	5	100.00
Total	94*	79	15	—

Table 3: Risk of malignancy according to Bethesda category

Bethesda category	Histopathology available	Malignant cases	Risk of malignancy (%)
I	0	0	—
II	72	2	2.77
III	0	0	—
IV	13	4	30.77
V	4	4	100.00
VI	5	5	100.00

Table 4: Diagnostic performance of FNAC using histopathology as the gold standard

Diagnostic parameter	Value
Sensitivity	86.67%
Specificity	100.00%
Positive Predictive Value (PPV)	100.00%
Negative Predictive Value (NPV)	97.53%
Overall Diagnostic Accuracy	97.87%
False-positive rate	0.00%
False-negative cases	2
Concordance	97.87%

Table 5: Concordance between cytological and histopathological diagnosis

Correlation	Number of cases	Percentage (%)
Concordant diagnosis	95	97.87
Discordant diagnosis	2	2.13
Total	97	100.00

Table 6: Discordant cases observed on cytohistopathological correlation

Case	Cytological diagnosis (FNAC)	Histopathological diagnosis	Type of error	Probable reason
1	Follicular neoplasm / benign follicular lesion	Follicular carcinoma	False negative	Capsular and vascular invasion cannot be assessed on cytology
2	Goitrous lesion (Category II)	Papillary thyroid carcinoma	False negative	Cystic degeneration leading to inadequate sampling and overlapping cytological features

DISCUSSION

Fine needle aspiration cytology (FNAC) is the most widely accepted first-line investigation for the evaluation of thyroid nodules because it is simple, minimally invasive, cost-effective, and highly reliable. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has standardized thyroid cytology reporting by providing uniform diagnostic categories with defined risks of malignancy and recommended clinical management. The present study assessed the cytohistopathological correlation of thyroid lesions categorized according to the Bethesda system and evaluated the diagnostic performance of FNAC using histopathology as the gold standard.

Histopathological follow-up was available in 97 of the 130 patients who underwent FNAC. Overall concordance between cytological and histopathological diagnosis was 97.87%,

demonstrating excellent agreement between FNAC and final histopathological diagnosis. Similar high concordance rates have been reported by Sharma et al., Bhatta et al., Jeelani et al., and Reddy et al., confirming that Bethesda-based reporting provides reproducible and clinically reliable cytological diagnoses.[11–14]

The present study demonstrated a progressive increase in malignancy risk with increasing Bethesda category. Bethesda Category II showed a malignancy risk of only 2.77%, whereas Category IV demonstrated a malignancy risk of 30.77%. All cases categorized as Bethesda Categories V and VI were confirmed as malignant on histopathological examination, resulting in a malignancy risk of 100% in both categories. These findings closely correspond with the expected malignancy risks described in the Bethesda System and are comparable to those reported by Reddy et al. and Jeelani et al., who also observed increasing malignancy rates across successive Bethesda categories.[13,14]

The diagnostic performance of FNAC in the present study was excellent, with a sensitivity of 86.67%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.53%, and an overall diagnostic accuracy of 97.87%. These results are comparable with previous institutional studies. Sharma et al. reported similar high specificity and diagnostic accuracy, while Bhatta et al. documented sensitivity of 85.7%, specificity of 92.3%, and overall diagnostic accuracy of 90%. Likewise, Reddy et al. observed high specificity and diagnostic accuracy using the Bethesda System, supporting its usefulness as an effective preoperative diagnostic tool.[11–13]

No false-positive diagnosis was encountered in the present study, indicating excellent specificity of FNAC in identifying malignant thyroid lesions. However, two false-negative cases were identified. One case diagnosed cytologically as a follicular neoplasm was subsequently confirmed as follicular carcinoma on histopathology. This discrepancy is expected because cytological examination cannot demonstrate capsular or vascular invasion, which are essential criteria for diagnosing follicular carcinoma. The second false-negative case involved papillary thyroid carcinoma that was initially interpreted as a benign goitrous lesion on FNAC. Cystic degeneration and inadequate sampling likely contributed to the absence of characteristic nuclear features in the cytological smears. Similar causes of false-negative diagnoses have been described by Bhatta et al. and Jeelani et al., who emphasized sampling error and overlapping cytomorphological features as major limitations of thyroid FNAC.[12,14]

Histopathological examination confirmed nodular goitre as the most common benign lesion and papillary thyroid carcinoma as the predominant malignant lesion. This histopathological distribution is consistent with observations reported in previous studies, where benign thyroid lesions constitute the majority of thyroid nodules while papillary thyroid carcinoma remains the most frequent thyroid malignancy. These findings further validate the cytological diagnosis obtained using the Bethesda System.[13,14]

The findings of the present study reaffirm that the Bethesda System is an effective classification system for predicting malignancy risk and guiding appropriate clinical management. The excellent cytohistopathological concordance and high diagnostic indices observed in this study are comparable with those reported in published literature and support the continued use of FNAC as the primary investigation for thyroid nodules. Although histopathological confirmation remains necessary in selected Bethesda categories, particularly follicular-patterned lesions, FNAC continues to provide a dependable preoperative diagnosis in the majority of patients.[15]

CONCLUSION

The present study demonstrated excellent cytohistopathological correlation between FNAC and histopathological diagnosis of thyroid lesions, with an overall concordance of 97.87%. The risk of malignancy increased progressively across successive Bethesda categories, and all cases classified as Bethesda Categories V and VI were confirmed as malignant on histopathology.

FNAC showed high diagnostic performance, with a sensitivity of 86.67%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.53%, and an overall diagnostic accuracy of 97.87%. The few discordant cases were attributable to the inherent limitations of cytology, particularly in follicular neoplasms and cystic papillary thyroid carcinoma.

Overall, the Bethesda System for Reporting Thyroid Cytopathology is a reliable, standardized, and reproducible reporting system that accurately predicts the risk of malignancy and demonstrates excellent agreement with histopathological findings. The results of the present study support the continued use of FNAC as the primary diagnostic investigation for thyroid nodules while emphasizing the importance of histopathological confirmation in selected indeterminate lesions.

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