Histopathological Study of Thyroid Nodules: Correlation with Fine Needle Aspiration Cytology

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Abstract

Objective*: This study is of paramount importance as it aims to evaluate the diagnostic accuracy of Fine Needle Aspiration Cytology (FNAC) in diagnosing thyroid nodules. By correlating the cytological findings with histopathological outcomes, we can better understand the limitations and advantages of FNAC in clinical practice, a crucial area of research for medical professionals.*

Materials and Methods*: This retrospective study was conducted on 150 patients who underwent thyroidectomy after FNAC at a private hospital in Baghdad. The cytological findings were classified using the Bethesda System for Reporting Thyroid Cytopathology, and the histopathological diagnoses were considered the gold standard for comparison. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated.*

Results*: The findings from FNAC revealed that 70% of the nodules were benign, 15% were suspicious for malignancy, and 10% were malignant. Histopathological examination confirmed malignancy in 20% of cases. The sensitivity and specificity of FNAC were found to be 85% and 92%, respectively. The PPV was 75%, while the NPV was 95%. These results, along with the identification of five false-negative and eight false-positive results, have significant implications for the diagnostic accuracy of FNAC in clinical practice.*

Conclusion*: FNAC remains a highly reliable diagnostic tool for the initial evaluation of thyroid nodules, particularly in ruling out malignancies. However, its limitations in indeterminate cases and false-negative results indicate that additional diagnostic approaches, such as molecular markers or repeat FNAC, may be necessary in complex cases.*

Introduction

Thyroid nodules are a frequent clinical finding, with palpable nodules observed in approximately 4-7% of adults. In comparison, ultrasound screening reveals the presence of nodules in up to 60% of individuals over 60. Although most thyroid nodules are benign, a significant proportion (approximately 5-15%) are malignant, necessitating prompt and accurate diagnosis. The most common forms of thyroid cancer are papillary thyroid carcinoma, follicular carcinoma, and medullary carcinoma, with papillary carcinoma accounting for the vast majority of cases (1).

Fine Needle Aspiration Cytology (FNAC) has become the first-line diagnostic tool in evaluating thyroid nodules due to its minimally invasive nature, cost-effectiveness, and high

diagnostic accuracy (2). FNAC involves extracting cells from the thyroid nodule, followed by cytological examination under a microscope. The results are typically classified using the Bethesda System for Reporting Thyroid Cytopathology, which categorizes results into six groups: non-diagnostic/unsatisfactory, benign, atypia of undetermined significance (AUS), suspicious for a follicular neoplasm, suspicious for malignancy, and malignant. The Bethesda classification provides a standardized framework that aids clinicians in making informed management decisions (3).

FNAC has radically improved the diagnosis of thyroid nodules, but it's not perfect. One problem is when cytological results are uncertain, with AUS, suspected follicular neoplasm, or cross-reference between benign and malignant conditions (4). Furthermore, FNAC is often false-negative or false-positive, making clinical decision-making more difficult. Histopathology after thyroidectomy remains the gold standard for a diagnosis because it enables a more excellent assessment of the nodule's cellular structure and molecular makeup (5).

In this work, we aim to compare FNAC cytological results with the histopathology of thyroidectomy specimens to determine how well FNAC is diagnostically performed and in what areas FNAC may be below the mark. In comparing these two diagnostic approaches, we hope to enable clinicians to discern better the advantages and disadvantages of FNAC for diagnosing thyroid nodules and identify areas where the diagnostic process could be refined.

Materials and Methods

Study Design

A retrospective examination was carried out at [private hospital in Baghdad city] between [2019] and [2023]. The participants included 150 patients who received thyroidectomy after FNAC's initial assessment of thyroid nodules. Participants must have had FNAC, and the histopathology results should be reported in the medical record. Non-compliant patients and patients who had already undergone thyroid surgery were excluded from the study.

FNAC Procedure

FNAC was delivered under ultrasound guidance using a 22-gauge needle to ensure nodule target exactness. At least two attempts were made on each node to acquire sufficient cytological samples. The excised solution was immediately splashed on glass slides and set into 95 percent ethanol to stain with Papanicolaou or air-dried to stain with Giemsa. Each specimen was examined by an experienced cytopathologist and categorized according to the Bethesda System for Reporting Thyroid Cytopathology, which includes the following classifications:

1. **Non-diagnostic/Unsatisfactory**: Inadequate sampling or poor cell preservation
2. **Benign**: Indicating a non-cancerous lesion, such as colloid goiter or thyroiditis
3. **Atypia of Undetermined Significance (AUS)** or **Follicular Lesion of Undetermined Significance (FLUS)**: Cytological atypia that is insufficient for a clear benign or malignant diagnosis

4. **Suspicious for a Follicular Neoplasm**: Suggesting possible follicular carcinoma but requiring histological confirmation
5. **Suspicious for Malignancy**: High suspicion of malignancy but not definitive
6. **Malignant**: Cytological evidence suggestive of thyroid cancer

Histopathological Examination

Following thyroidectomy, the excised thyroid specimens were processed, fixed in 10% formalin, and embedded in paraffin. Thin sections of the tissue were cut and stained with hematoxylin and eosin (H&E) for histopathological examination. The histopathological diagnoses were categorized as benign (e.g., colloid goiter, adenoma, thyroiditis) or malignant (e.g., papillary thyroid carcinoma, follicular carcinoma, medullary carcinoma). Histopathological findings were considered the gold standard for diagnosis.

Statistical Analysis

Statistical analysis was conducted using SPSS software version [Insert Version]. The diagnostic performance of FNAC was assessed by calculating the sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy, using the histopathological findings as the reference standard. Sensitivity was defined as the proportion of true positive (malignant) cases identified by FNAC, and specificity was defined as actual unfavorable (benign) cases. The PPV represented the proportion of positive FNAC results confirmed as malignant on histopathology. In contrast, the NPV represented the proportion of negative FNAC results confirmed as benign. Statistical significance was set at $p < 0.05$.

Results

Patient Demographics

The study population included 150 patients, with a female predominance of 110 females (73%) and 40 males (27%), reflecting the higher incidence of thyroid nodules in women. The age of the patients ranged from 18 to 75 years, with a mean age of 42 ± 12 years. The demographic characteristics of the study population are presented in Table 1.

Table 1: Demographic Characteristics of the Patients

Characteristic	Value (n = 150)
Mean Age (years ± SD)	42 ± 12
Age Range (years)	18 – 75
Male	40
Female	110

FNAC Results

Of the 150 FNAC samples, 105 (70%) were categorized as benign, 10 (7%) as AUS/FLUS, 8 (5%) as suspicious for a follicular neoplasm, 15 (10%) as suspicious for malignancy, and 7 (5%) as malignant. Additionally, 5% of cases (7 patients) were considered non-diagnostic due to insufficient sampling or poor slide preparation.

Table 2: FNAC Results

FNAC Category	Number of Cases (n = 150)	Percentage (%)
Non-diagnostic/Unsatisfactory	7	5
Benign	105	70
AUS/FLUS	10	7
Suspicious for a Follicular Neoplasm	8	5
Suspicious for Malignancy	15	10
Malignant	7	5

Histopathological Findings

Histopathological examination of the thyroidectomy specimens confirmed that 120 cases (80%) were benign, and 30 (20%) were malignant. Among the malignant cases, 20 were diagnosed as papillary thyroid carcinoma, seven as follicular carcinoma, and three as medullary carcinoma (Fig. 1, 2, 3). Table 3 provides a breakdown of the histopathological findings.

Table 3: Histopathological Findings

Histopathological Diagnosis	Number of Cases (n = 150)	Percentage (%)
Benign (e.g., colloid goiter, adenoma)	120	80
Malignant	30	20
- Papillary carcinoma	20	13.3
- Follicular carcinoma	7	4.7
- Medullary carcinoma	3	2

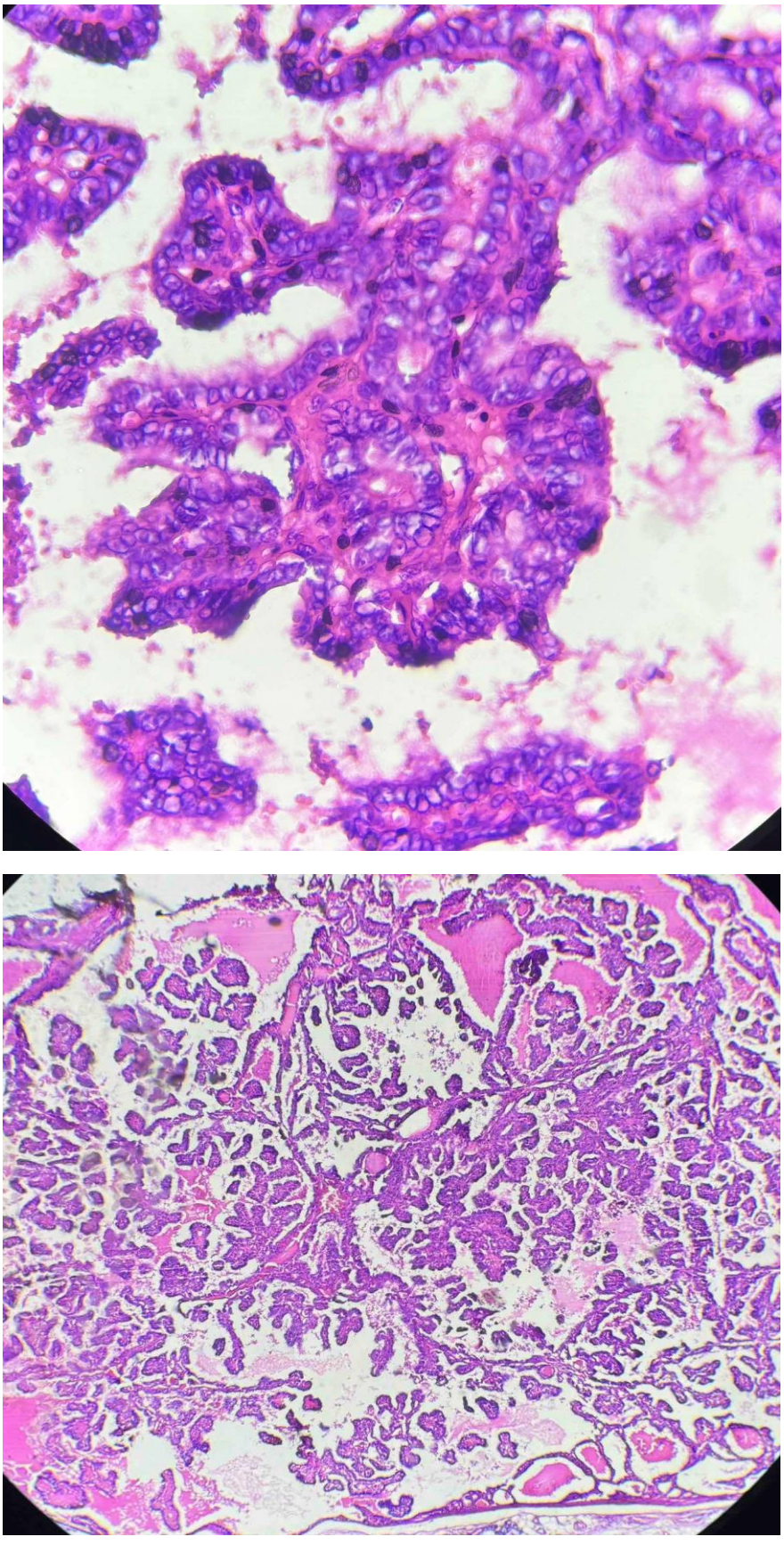
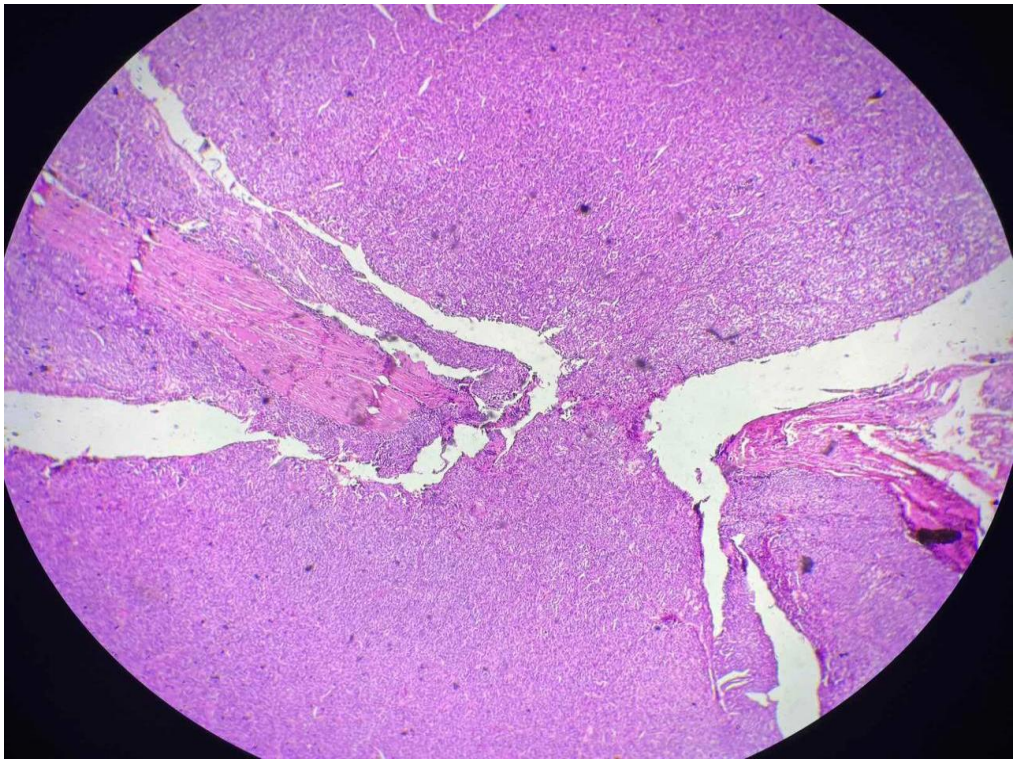
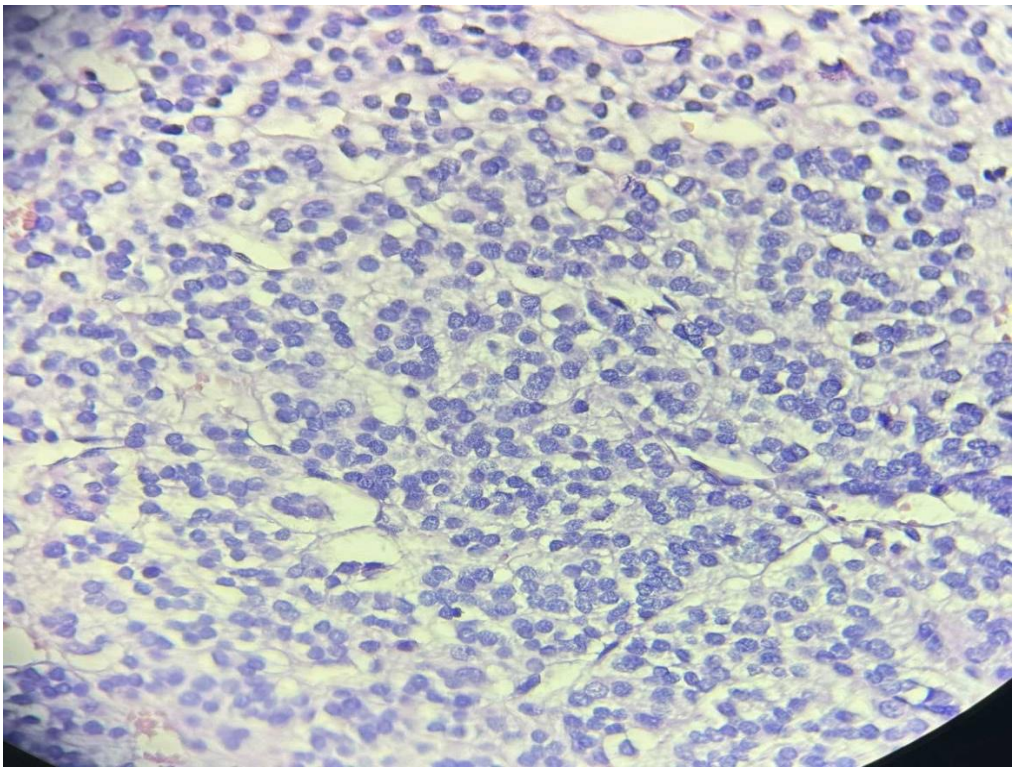


Figure 1. Papillary thyroid carcinoma

Figure 2. Follicular thyroid carcinoma





Correlation Between FNAC and Histopathology

Of the 150 cases, 105 were benign on FNAC, and 102 were confirmed benign on histopathology. In the remaining 3 cases, histopathology revealed malignancy (false-negative cases). Conversely, 7 cases diagnosed as malignant on FNAC were confirmed as malignant on

histopathology. However, 8 cases suspicious of malignancy or a follicular neoplasm on FNAC were confirmed benign (false-positive cases). The sensitivity, specificity, PPV, NPV, and overall accuracy of FNAC in diagnosing thyroid nodules were calculated and are presented in Table 4.

Table 4: Diagnostic Performance of FNAC

Parameter	Value (%)
Sensitivity	85
Specificity	92
Positive Predictive Value	75
Negative Predictive Value	95
Overall Diagnostic Accuracy	90

Discussion

It shows that FNAC can detect thyroid nodules at high diagnostic accuracy. The results show that FNAC has reasonable specificity and NPV, which makes it an extremely valuable marker for excluding malignancy in thyroid nodule patients. Our paper's corresponding high specificity (92%) and NPV (95%) agree with the other studies that found FNAC to be a consistent method for detecting benign, malignant nodules. These findings indicate that FNAC can reduce unnecessary surgeries in benign nodules, with positive patient outcomes and low healthcare costs.

FNAC in the Diagnosis of Thyroid Nodules

Fine Needle Aspiration Cytology (FNAC) has been used extensively to assess thyroid nodules because of its minimal invasiveness, affordability, and diagnostic yield. Since FNAC can discriminate between benign and malignant lesions, it is a vital part of the preoperative management of thyroid nodules (6,7).

In our case, FNAC had high specificity (92%) and negative predictive value (95%), reflecting its power to exclude malignancy. They are consistent with some studies where the NPV value for FNAC has been high, indicating that a positive FNAC result strongly predicts a positive histopathology result (8,9,10). It’s a crucial distinction for practitioners since clinicians can now manage benign thyroid nodules safely without operating. A group led by (11), who developed the Bethesda System for Reporting Thyroid Cytopathology, reported comparable specificity and NPV for FNAC across a large population, suggesting it can be used to guide clinical decision-making.

However, FNAC’s sensitivity in our work was 85%, which means it failed to find 15% of malignant nodules with FNAC. Such false-negative results might result from sampling problems, cystic degeneration, or simply the inability of cytology to distinguish certain thyroid cancers, such as follicular carcinoma. The low sensitivity suggests that, though FNAC is

suitable for diagnosing benign disease, it might be inaccurate in a minority of malignant nodules (12). This requires vigilant monitoring, especially in patients with abnormal ultrasound examination or symptoms, even with a normal FNAC (13,14).

Indeterminate Cytology and the Challenge of AUS/FLUS

A critical drawback of FNAC, as evidenced by our study, is that it does not definitively diagnose most cases diagnosed as indeterminate (AUS/FLUS). About 7 % of FNAC results in our group were of AUS/FLUS, as cytological data can often take much work to understand. In the Bethesda System, AUS/FLUS is a condition for which cytological characteristics are ambiguous (not diagnosed as benign or malignant). They might be caused by slight nuclear atypia, low cell count, or characteristics not necessarily associated with a follicular neoplasm (15,16).

Management of variable thyroid nodules remains controversial. Although the risk of cancer in AUS/FLUS nodules varies by study population and institution, the estimated figure is 5 to 15%. For this reason, most doctors will recommend FNAC repeats, molecular tests, or diagnostic lobectomy for a more precise diagnosis. Molecular testing has emerged as a valuable complement to cytology, and gene expression classification systems and mutational analysis can refine risk assessment in unresolved situations. Such diagnostic tests could save millions of otherwise unnecessary surgeries on benign nodules (17,18).

False-Positive and False-Negative Results

The fact that there was false-positive or false-negative in our study sometimes shows the limitations of FNAC. We found eight false positives (5%) and five false negatives (3%).FNAC false-positives, when nodules appear normal but they turn out to be suspicious or malignant, can result in unnecessary surgery and anxiety. These mistakes are usually induced by hyperplastic or inflammatory changes mimicking the cell characteristics of tumors – for example, in Hashimoto's thyroiditis, where the proliferation of lymphocytes leads to nuclear changes analogous to papillary carcinoma (19,20). Several false positives in our work were related to the architectural atypia of follicular carcinoma and stellate nodules with high numbers of Hurthle cells that are also difficult to distinguish cytologically (21,22).

False-negative FNAC is, on the other hand, a clinical hazard, as malignant nodules can be missed and treated over time. Inadequate sampling, nodule cystic degeneration, or well-differentiated cancer with no evident cytological characteristics of malignancy are some of the common causes of false-negative findings. In our group, three false negatives had initially been identified as benign on FNAC and were later identified as papillary thyroid carcinoma on histopathology. It also shows the need for complete clinical and ultrasonographic review before FNAC, especially in patients with a history of radiation exposure or familial thyroid cancer, which may require additional diagnostic and treatment interventions despite positive cytology (23,24).

Correlation with Histopathology

Histopathological examination remains the gold standard for diagnosing thyroid nodules, providing detailed architectural and cellular information that FNAC cannot offer. In our study, FNAC results were compared with histopathological findings following thyroidectomy, and a strong correlation was observed between the two diagnostic methods in most cases. Among the

150 cases, 102 of the 105 benign FNAC results were confirmed benign on histopathology, resulting in an NPV of 95%. Similarly, 7 cases diagnosed as malignant on FNAC were confirmed to be malignant on histopathology, yielding a PPV of 75%.

The discordant results (false-positive and false-negative cases) point to the inherent limitations of FNAC, particularly in the context of indeterminate or suspicious cytological findings (25). While FNAC is highly accurate in identifying benign and malignant nodules, its diagnostic performance decreases in the indeterminate categories, where histopathological confirmation is often required to make a definitive diagnosis (26). That's in line with the literature, where FNAC doesn't do an excellent job of delineating follicular adenomas and follicular carcinomas, which sometimes share cytological similarities (27,28). This makes histopathology vital to distinguish capsular or vascular invasion, which characterizes follicular carcinoma (29).

Conclusion

Our investigation showed a positive relationship between Fine Needle Aspiration Cytology and histopathology when measuring thyroid nodules.FNAC remains vital to the diagnostic process, offering high specificity and negative predictive value to inform clinical decision-making.FNAC does a great job distinguishing benign from malignant nodules, but its indecisive nature suggests that the multimodal solution requires molecular testing and imaging.

Thyroid nodules must be managed according to clinical, cytological, and radiological evidence, especially if the outcome is unclear. Continuing studies and developments in molecular diagnostics and imaging could enable better diagnosis and risk stratification of thyroid nodules. Finally, it is to give each patient a customized treatment plan that minimizes surgeries and diagnoses thyroid malignancies as early as possible.

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