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Original Research Article

Cyto Histopathological Correlation in Thyroid Lesions: Diagnostic Accuracy and Challenges

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Abstract:

Background: Fine-needle aspiration cytology (FNAC) has been one of the most common diagnostic techniques to assess thyroid lesions using minimal invasiveness and efficiency. It remains a worthwhile tool, although with limitations, primarily with respect to indeterminate categories, and thus warrants careful assessment of its diagnostic performance as well as its own limitations.

Methods: This study analyzed 250 cases of thyroid lesions, correlating FNAC findings categorized using the Bethesda System for Reporting Thyroid Cytopathology with final histopathological diagnoses. The diagnostic accuracy, sensitivity, specificity, and rates of cyto histo concordance were calculated. Discordant cases were examined to identify sources of diagnostic errors.

Results: The overall diagnostic accuracy of FNAC was 91.6%, with sensitivity and specificity of 89.7% and 93.0%, respectively. The highest concordance rates were seen in Bethesda II (94.5%) and Bethesda VI (97.0%) categories. Malignancy rates for indeterminate categories (Bethesda III and IV) were 31% and 40%, respectively, with lower concordance rates (69.0% and 60.0%). Sampling errors and misinterpretation of cytological features were the main causes of discordance. Cyto Histopathological correlation stressed the reliability of FNAC in diagnosing benign and malignant lesions while throwing a challenge in the indeterminate cases.

Conclusion: FNAC is a good diagnostic modality for thyroid nodules but limitations in the indeterminate categories necessitate adjunctive diagnostic strategies, including molecular testing and sophisticated sampling techniques. Cyto Histopathological correlation is crucial for improving diagnostic accuracy and optimal management of the patient.

Keywords: Fine-needle aspiration cytology, thyroid lesions, Cyto Histopathological correlation, Bethesda system, diagnostic accuracy, thyroid nodules.

Introduction

Thyroid lesions represent a significant subset of endocrine disorders, with a rising incidence globally over recent decades. Early and accurate diagnosis of these lesions is critical for initiating appropriate management strategies, thereby improving patient outcomes. Fine-needle aspiration cytology (FNAC) has emerged as a cornerstone in the diagnostic workup of thyroid lesions, offering a minimally invasive, cost-effective, and rapid diagnostic tool [1].

FNAC not only helps differentiate between benign and malignant thyroid lesions but also helps stratify patients who need surgical intervention from those who can be managed conservatively. Though it has its advantages, FNAC is not without its limitations, especially in cases where indeterminate or suspicious cytological findings lead to diagnostic uncertainty [2]. The histopathological examination of surgically excised thyroid tissue remains the gold standard for definitive diagnosis of thyroid malignancies. Despite the fact that several factors may result in discrepancies between cytological and histological diagnoses, such as sampling errors and overlapping cytological features between benign and malignant lesions, inherent classification system limitations exist in the approach used for thyroid cytology classification systems, such as The

Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) [3].

This is because Cyto Histopathological correlation—essentially an analytical approach that correlates preoperative cytological findings with postoperative histopathological diagnoses—is crucial in the process. This not only acts as a quality assurance measure for cytology laboratories but also provides insight into the diagnostic pitfalls and areas of improvement in thyroid cytology [4-6]. Among thyroid malignancies, the most common histological subtype is papillary thyroid carcinoma (PTC), followed by follicular thyroid carcinoma (FTC), medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC). These malignancies often share cytological features with benign conditions such as follicular adenomas or Hashimoto's thyroiditis, making diagnosis challenging. Additionally, new variants of thyroid malignancies, including non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), have complicated the accurate cytological diagnosis [7-8].

This article aims to assess the diagnostic accuracy and challenges of cyto histo correlation in thyroid malignancies, with emphasis on its crucial role in refining diagnostic algorithms and improving the precision of thyroid cancer diagnosis. It identifies common sources of error and explores strategies to address them in an effort to improve the reliability of FNAC and its integration with histopathological analysis, which would lead to better clinical decision-making in the management of thyroid malignancies [9].

Methods

The present study was conducted to assess the diagnostic accuracy and challenges associated with Cyto Histopathological correlation in thyroid malignancies. The study was designed as a retrospective observational analysis performed in a hospital setting.

Study Population: The patients who had undergone FNAC of thyroid nodules followed by surgery and histopathological examination were taken for this three-year study. The inclusion criteria were those patients who had complete cytological and histopathological records, in addition to adequate FNAC smear along with the appropriate histological specimen. Patients who did not fulfill the inclusion criteria included those with inadequate cytological material or incomplete records and patients who were managed non-surgically. A total number of 250 cases fulfilling the criteria were taken for the study.

Cytological Examination: FNAC was performed using a standard 23-25 gauge needle under ultrasound guidance to ensure representative sampling of the thyroid nodules. On-site smears were prepared and air-dried and stained by Diff quik as well as fixed smear by Papanicolaou stains. The cytological diagnoses were recorded in terms of The Bethesda System for Reporting Thyroid Cytopathology. The cytological categories included: non-diagnostic, benign, AUS, follicular neoplasm, suspicious for malignancy and malignant.

Histopathological Examination: All patients were therefore taken for surgery in the form of hemithyroidectomy or total thyroidectomy depending on clinical and cytological findings. Specimens after the surgery underwent fixation in 10% neutral-buffered formalin, subsequent processing, and embedding in a paraffin block. It was then thin sectioned to stain with hematoxylin and eosin (H&E) for evaluation histopathologically. The classification based on this gold standard in histology was into either benign or malignant lesions, sub-classifying the latter based on guidelines given by the WHO.

Cyto Histopathological correlation: Cyto Histo correlation was done by comparing FNAC diagnoses with the corresponding histopathological findings. Concordance between the two diagnostic modalities was assessed across all categories. Detailed analysis of cases showing discrepancies was done to identify possible sources of error, such as sampling errors, misinterpretation of cytological features, or inherent challenges in specific lesion types. Cases categorized as indeterminate on cytology were specifically evaluated to determine the rate of malignancy in this subgroup.

Statistical Analysis: Data were analyzed using statistical software to determine the diagnostic accuracy metrics, such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic concordance. The malignancy rates related to each Bethesda category were computed. The rates of discrepancies along with their causes were identified and presented. Descriptive statistics were represented in terms of means and percentages, whereas diagnostic performance parameters were reported with 95% confidence intervals.

Results

Patient Demographics and Clinical Characteristics: A total of 250 cases were included in the study, with a mean age of 45.6 ± 12.3 years. The majority of the patients were female (75.2%), with a female-to-male ratio of approximately 3:1. The most common clinical presentation was a palpable thyroid nodule, reported in 82% of cases, followed by compressive symptoms (15%) and incidental findings during imaging studies (3%).

Distribution of FNAC Diagnoses: The cytological diagnoses based on The Bethesda System for

Reporting Thyroid Cytopathology (TBSRTC) are shown in Table 1. The highest number of cases fell under Bethesda Category II (Benign) with 50.8%, followed by Bethesda Category III (Atypia of Undetermined Significance) with 16.8%, and Bethesda Category VI (Malignant) with 14%. The indeterminate categories (Bethesda IV and V) collectively accounted for 22.8% of cases.

Table 1: Distribution of FNAC Diagnoses According to TBSRTC

Bethesda Category	Number of Cases	Percentage (%)
Category I: Non-Diagnostic	12	4.8
Category II: Benign	127	50.8
Category III: AUS	42	16.8
Category IV: Follicular Neoplasm	15	6.0
Category V: Suspicious for Malignancy	30	12.0
Category VI: Malignant	34	14.0
Total	250	100.0

Histopathological Findings and Cyto Histo Correlation: Of the 250 cases, 78 (31.2%) were histologically confirmed as malignant, and the rest 172 (68.8%) were benign. Papillary thyroid carcinoma was the most common histological subtype, which comprised 82.1% of malignant cases, followed by follicular carcinoma, medullary carcinoma, and anaplastic carcinoma with a frequency of 10.3%, 5.1%, and 2.5%, respectively. The cytohisto correlation showed a concordance rate of 87.6%.

The performance metrics for FNAC are tabulated in Table 2. Overall sensitivity, specificity, positive predictive value, and negative predictive value were at 89.7%, 93.0%, 86.3%, and 94.6%, respectively.

Table 2: Diagnostic Performance of FNAC in Thyroid Malignancies

Metric	Value (%)
Sensitivity	89.7
Specificity	93.0
Positive Predictive Value (PPV)	86.3
Negative Predictive Value (NPV)	94.6
Diagnostic Accuracy	91.6

Analysis of Discrepancies: Discrepancies between FNAC and histopathology were observed in 31 cases (12.4%). The most common source of discordance was in the indeterminate categories (Bethesda III and IV), where the malignancy rate was 31% and 40%, respectively. Sampling errors accounted for 45% of the discordant cases, while misinterpretation of cytological features contributed to 35%. The remaining 20% of errors were attributed to overlapping cytological features of benign and malignant lesions.

Malignancy Rates by Bethesda Category: The risk of malignancy for each Bethesda category is given in Figure 1. Malignancy rates increased stepwise from Category I (non-diagnostic, 8.3%) through to Category VI (malignant, 100%).

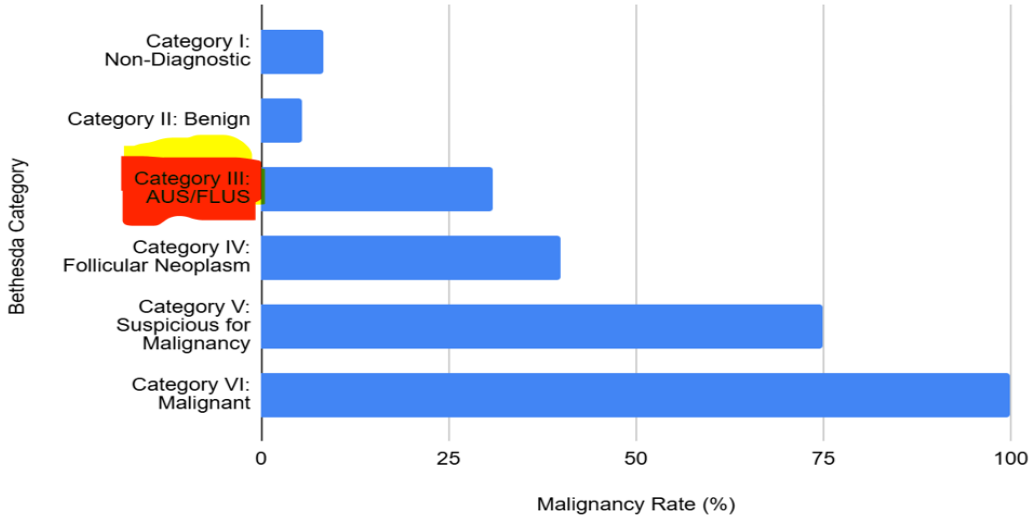

Figure 1: Malignancy Rates by Bethesda Category

(Bar graph illustrating the percentage of malignancy for each Bethesda category.)

Cyto Histo Correlation Trends: Figure 2 shows the cyto histo concordance rates by Bethesda categories. The highest concordance rates were seen in benign (Category II) and malignant (Category VI) categories, whereas the lowest concordance rates were observed in indeterminate (Category III and IV) cases.

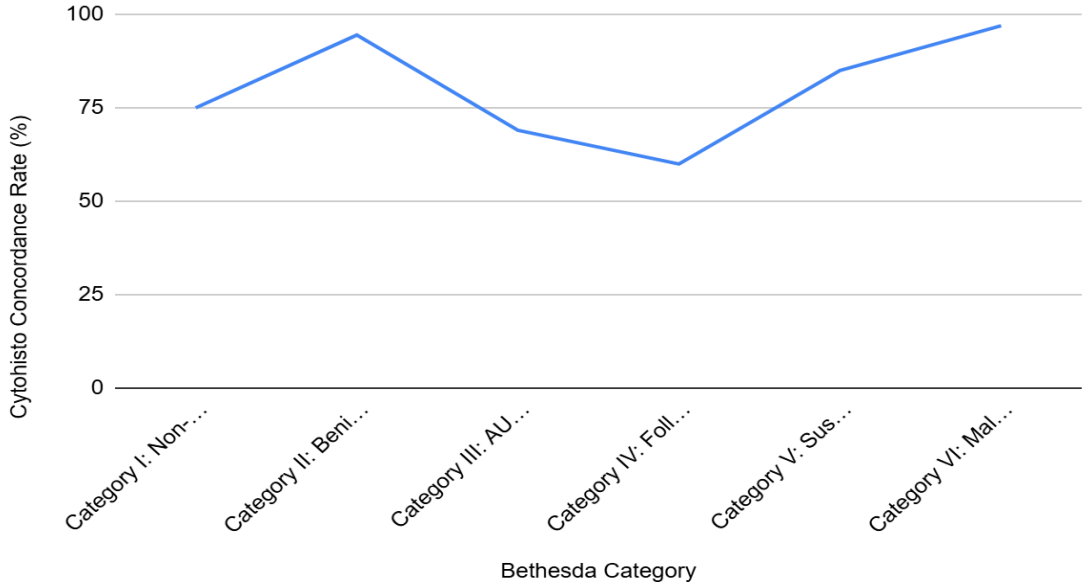

Figure 2: Cytohisto Concordance across Bethesda Categories

(Line graph comparing FNAC diagnosis with histopathological outcomes.)

These results will highlight the robust diagnostic accuracy of FNAC for thyroid malignancies while underlining the challenges that indeterminate cytological findings raise. Enhanced sampling techniques, ancillary diagnostic tools, and molecular testing might reduce the uncertainty that these cases create regarding diagnosis.

Discussion

FNAC has been considered a valuable adjunct in the diagnostic workup of thyroid nodules for decades. Its minimally invasive nature, rapidity, and cost-effectiveness have established it as the first line of investigation in the majority of thyroid lesions. Nonetheless, its diagnostic accuracy, though excellent, is not perfect, as shown in this study and supported by studies in the past.

The present study involving 250 cases with cyto histo correlation gave an overall diagnostic accuracy of 91.6% for FNAC with sensitivity of 89.7% and specificity of 93.0%. According to Gowardhan and Valand (2024), "FNAC being a reliable modality with the sensitivity and specificity being comparable to fine-needle aspiration cytology has been recognized to be one of the important investigations in the management plan.". Our results further support the robustness of FNAC, especially in the accurate categorization of benign (Bethesda II) and malignant (Bethesda VI) lesions, where concordance rates were highest. Sharma (2015) made similar observations while emphasizing the high accuracy of FNAC in these categories and noted significant challenges in the indeterminate groups [10,11].

The indeterminate categories, atypia of undetermined significance (AUS) and follicular neoplasm (Bethesda III and IV), present a diagnostic dilemma, as evidenced by the malignancy rates of 31% and 40%, respectively, in our study. These rates fall within the range reported by Sharma (2015) and Chang et al. (1997), who pointed out the challenge of distinguishing follicular-patterned lesions based on cytology alone. This diagnostic uncertainty often arises from the overlapping cytological features between benign and malignant follicular lesions, and thus, requires histological examination for a definitive diagnosis. These categories also had the lowest Cyto Histopathological concordance rates in this study, and thus, underline the inherent limitations of FNAC in such cases [11,12].

Discordant cases were analyzed in detail to identify contributory factors in 12.4% of our cohort. The most common cause of discordance was sampling errors, accounting for 45% of these cases. This is in agreement with Bakhos et al. (2000), who reported that inadequate or unrepresentative sampling significantly undermines the diagnostic utility of FNAC. Misinterpretation of cytological features,

seen in 35% of discordant cases in our study, represents another major pitfall. For instance, nuclear atypia or overlapping nuclear features may result in over diagnosis or underdiagnosis. Al-Rikabi et al. (1998) and Machała et al. (2018) have also reported similar challenges, pointing out the importance of experienced cytopathologists and ancillary techniques to enhance the accuracy of diagnosis [13-15]. Our study found a malignancy rate of 75% in cases classified as suspicious for malignancy (Bethesda V), which is within the ranges reported in The Bethesda System for Reporting Thyroid Cytopathology and supports the results of Gowardhan and Valand (2024).

The high malignancy rate in this category supports the recommendation for surgical intervention, as also noted by Chang et al. (1997). The low malignancy rates in Bethesda II at 5.5% confirm the role of FNAC in identifying nodules that can be managed conservatively, thereby reducing the burden of unnecessary surgeries [10,12].

FNAC is not a standalone diagnostic modality, and integration of clinical, radiological, and molecular data can significantly enhance its diagnostic performance. For example, molecular testing for mutations like BRAF, RAS, and RET/PTC has been demonstrated to decrease diagnostic uncertainty in indeterminate categories. Sharma (2015) and other researchers have supported the use of molecular markers as an adjunct to cytology in challenging cases. In addition, advancements in ultrasound-guided FNAC techniques have helped reduce sampling errors, as reported by Al-Rikabi et al. (1998) [11,14]. In the study, the cyto histo concordance rates of Bethesda II and VI categories were quite high, standing at 94.5% and 97.0%, respectively, showing the success of FNAC in straightforward cases. However, a relatively lower concordance rate in the case of indeterminate categories was noted as 69.0% for Bethesda III and 60.0% for Bethesda IV, which requires more cautious approaches. Gowardhan and Valand (2024) have identified similar trends wherein the measures for quality control along with the training for cytopathologists need to be robust enough to prevent any discrepancies at the diagnostic end [10].

The study will contribute to the literature existing as of date in affirming the diagnostic usefulness of FNAC in thyroid malignancies but while revealing its drawbacks and limitations. While our results are in agreement with Sharma (2015) and Chang et al. (1997), the study also emphasizes the changing role of Cyto Histopathological correlation as a quality assurance measure. Through systematic analysis of discordant cases, valuable insights can be gained to enhance diagnostic algorithms and optimize patient outcomes [11,12]. While FNAC is indeed a cornerstone in the evaluation of thyroid lesions, its limitations, mainly in indeterminate cases, call for the incorporation of other diagnostic modes. Future research should include molecular techniques, refining cytological criteria, and the exploration of novel diagnostic tools to further improve the accuracy and reliability of thyroid cytology.

Conclusion

Fine-needle aspiration cytology still remains a staple in the diagnosis of thyroid lesions, especially with high sensitivity and specificity values for benign as well as malignant cases. Despite this, its disadvantages, especially for indeterminate categories, underscore the necessity for more complementary diagnostic procedures, such as molecular testing, and better techniques for sampling in order to gain higher accuracy with reduced diagnostic uncertainty. Cyto Histopathological correlation, therefore, remains a valuable tool to assess the performance of FNAC, identify any diagnostic discrepancies, and improve quality assurance in cytopathology. The present study's findings further reinforce the role of FNAC as an essential diagnostic modality while underlining the importance of a multidisciplinary approach in optimizing patient care and outcomes for thyroid lesions.

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