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Original Research Article

"Accuracy of FNAC in thyroid nodule malignancy prediction"

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Abstract: ***Background:*** Thyroid nodules are a common clinical finding, and the primary clinical challenge lies in accurately differentiating benign from malignant lesions to avoid unnecessary surgery while ensuring timely intervention for cancer. Fine-needle aspiration cytology (FNAC) is widely accepted as the first-line diagnostic modality for the evaluation of thyroid nodules. However, variability in its diagnostic accuracy across different cytological categories necessitates continuous evaluation of its performance against histopathological outcomes. This study aimed to assess the diagnostic accuracy of FNAC in predicting malignancy in thyroid nodules using histopathology as the gold standard. ***Methods:*** A retrospective analytical study was conducted on patients with thyroid nodules who underwent FNAC followed by definitive surgical excision and histopathological examination over a defined study period. FNAC results were categorised according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). Cytological diagnoses were correlated with final histopathological findings. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of FNAC for malignancy detection were calculated. Discordant cases were analysed to identify possible causes of diagnostic discrepancies.

Results: A total of 312 patients were evaluated, of whom 294 with diagnostic FNAC were included in the accuracy analysis. Histopathology revealed malignancy in 28.2% of nodules. FNAC demonstrated a sensitivity of 79.2% (95% CI: 68.6–87.2), a specificity of 95.7% (95% CI: 91.9–98.1), a PPV of 82.6%, an NPV of 94.6%, and an overall diagnostic accuracy of 91.5%. There was a strong and statistically significant association between FNAC and histopathology ($\chi^2 = 146.3$, $p < 0.001$). The risk of malignancy increased significantly across Bethesda categories, from 5.4% in Bethesda II to 92.3% in Bethesda VI (trend $p < 0.001$). Indeterminate categories (Bethesda III and IV) showed intermediate malignancy risks of 20.6% and 29.4%, respectively. False-negative cases were predominantly follicular-patterned carcinomas, while false-positive results were mainly due to benign follicular lesions with cytological atypia. ***Conclusion:*** FNAC is a highly accurate and clinically indispensable modality for the preoperative evaluation of thyroid nodules, with excellent specificity and overall diagnostic performance. While it reliably identifies benign and malignant lesions, its reduced sensitivity in follicular-patterned and indeterminate nodules necessitates integration with ultrasound risk stratification and, where available, molecular testing. A multimodal diagnostic approach can further enhance risk prediction and optimise individualised patient management.

Keywords: Thyroid nodules, Fine-needle aspiration cytology (FNAC), Thyroid malignancy, Diagnostic accuracy, Thyroid cancer, Preoperative diagnosis

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INTRODUCTION

Background

1. Thyroid Nodules

1.1 Clinical Importance

Thyroid nodules are one of the most frequent endocrinological clinical findings encountered in daily practice. A thyroid nodule is a lesion characterised by its ability to be differentiated from the adjacent thyroid tissue either by imaging techniques or by feeling it through the skin [1]. Most thyroid nodules are benign, but a small group of them, which is still significant from the clinical point of view, turns out to be malignant. Therefore, an accurate risk assessment is necessary for the management of such patients [2].

The clinical significance of thyroid nodules is that it is necessary to manage the situation where the two competing priorities, "avoiding unnecessary surgery in benign disease" and "ensuring timely surgical intervention in cases of malignancy", are in opposition to each other. Thyroid surgery is, in general, a safe procedure but with risks like recurrent laryngeal nerve injury, hypoparathyroidism, bleeding, and dependence on thyroid hormone for life [3]. Hence, accurate preoperative diagnosis is a must in order to reduce patient morbidity, healthcare expenses, and psychological suffering [4].

The possibility of thyroid nodule cancer varies according to the demographic, clinical, and radiological factors, namely age, sex, exposure to radiation, family history, and ultrasound characteristics, including microcalcifications, irregular margins, hypoechogenicity, and increased vascularity within the nodule [5]. Such characteristics are included in the risk stratification systems like the Thyroid Imaging Reporting and Data System (TI-RADS) that help to determine the necessity of biopsy and other interventions [6].

1.2 Epidemiology

The thyroid nodules' occurrence rate significantly differs based on the detection method used. About 4–7% of adults have palpably detected nodules; on the other hand, high-resolution ultrasonography can find nodules in as many as 50–70% of the patients, especially in those living in areas with a lack of iodine and the elderly [7], [8].

Thyroid nodules are found to be four times more common in women than in men, and their occurrence is also age-related, with the older population being more affected. Among the various factors contributing to nodule formation, the most important ones are the environmental ones. which include the absence of iodine, exposure to radiation (particularly for children), and the genetic predisposition of individuals [9].

Thyroid nodules have a high frequency in human populations; however, only a small fraction, approximately 5-15%, is found to be cancerous [10]. Among these, papillary thyroid carcinoma is the most frequent histological subtype, followed by follicular, medullary and anaplastic carcinomas [11]. The global increase in thyroid cancer cases is mainly credited to the enhanced diagnosis of small, subclinical papillary cancers through imaging, rather than an actual increase in disease occurrence [12].

Therefore, the epidemiological characteristics of thyroid nodules point out the importance of having safe, simple to use, and reliable methods for diagnosis to tell malignant from benign lesions swiftly.

Ultrasound Features of Thyroid Nodules

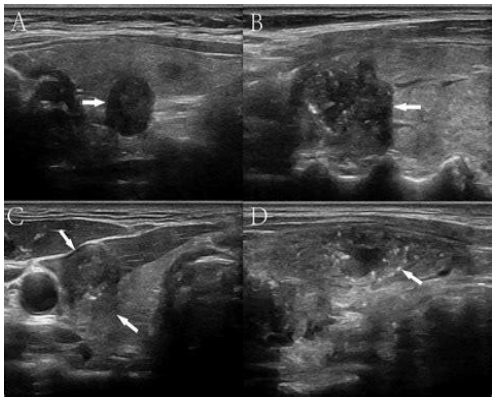

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Fig 1: A Greyscale ultrasonographic image showing a hypoechoic thyroid nodule with irregular and ill-defined margins, representing a suspicious sonographic pattern associated with increased risk of malignancy; **B** Transverse ultrasound view demonstrating a "taller-than-wide" nodule orientation, a well-established predictive feature for thyroid carcinoma; **C** Ultrasound image depicting punctate echogenic foci consistent with microcalcifications within the nodule, highly suggestive of papillary thyroid carcinoma; **D. A colour** Doppler image showing increased central vascularity within the nodule, a finding commonly associated with malignant thyroid lesions.

2. Fine-Needle Aspiration Cytology (FNAC)

2.1 Application and Role in Thyroid Nodule Evaluation

Fine-needle aspiration cytology (FNAC) is a technique that is considered to be very precise, minimally invasive, and cost-effective in the diagnosis of thyroid nodules [13]. This method includes a process where a thin needle (diameter of 23–27 gauge) is used to extract the cellular materials, and then the materials are examined microscopically for cytology.

FNAC is regarded as the top-notch primary diagnostic test for thyroid nodules because of its impressive sensitivity, specificity, and capability to curb needless thyroid operations by as much as half [14, 15]. The method is risk-free, accepted by patients, and linked to negligible complications like slight pain, local bleeding, or, very occasionally, infection [16]. Ultrasound-assisted FNAC has raised diagnostic yield by allowing exact sampling of the doubtful regions inside nodules, especially in the case of tiny, deep, posterior, or complicated cystic-solid nodules [17].

2.2 The Bethesda System for Reporting Thyroid Cytopathology

In order to standardise reporting and to enhance communication between pathologists and clinicians, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was established [18]. It divides FNAC results into six categories, and each of them is linked with a particular malignancy risk and proposed clinical management:

Nondiagnostic / Unsatisfactory
Benign
Atypia of Undetermined Significance (AUS) / Follicular Lesion of Undetermined Significance (FLUS)
Follicular Neoplasm / Suspicious for Follicular Neoplasm
Suspicious for Malignancy
Malignant

Table 1: **The Bethesda System for Reporting Thyroid Cytopathology**

Category	Interpretation	Malignancy Risk
I	Non-diagnostic	1–4%
II	Benign	0–3%
III	AUS/FLUS	5–15%
IV	Follicular neoplasm	15–30%
V	Suspicious for malignancy	60–75%
VI	Malignant	97–99%

This system has significantly improved diagnostic consistency, interobserver reproducibility, and clinical decision-making [19].

2.3 Diagnostic Performance of FNAC

The high diagnostic accuracy of FNAC for thyroid cancer has been shown by several studies, with sensitivity being reported from 65% to 98% and specificity from 72% to 100% [20,21]. FNAC's negative predictive value is very high, which is why it can be considered the best method for ruling out cancer in benign nodules; thus, its high use [22].

Nonetheless, FNAC has built-in disadvantages, especially in lesions with a follicular pattern where the criteria for follicular carcinoma, i.e., invasiveness of the capsule and blood vessels, cannot be evaluated through cytology [23]. Therefore, the indeterminate categories (Bethesda III and IV) cause diagnostic ambiguity and usually need a repeat

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FNAC, molecular testing, or surgical diagnosis [24].
False negatives can result from several sources: errors in sampling, changes in the cysts, or difficulties in interpretation. On the other hand, false positives are very uncommon. However, they may happen when a person has Hashimoto thyroiditis or a hyperplastic nodule with atypia [25].

2.4 Integration with Molecular and Radiological Techniques

Current progress includes the use of molecular testing (e.g., BRAF, RAS, and RET/PTC mutations) and gene expression classifiers for better risk categorisation, especially in uncertain nodules [26]. These methods, when used together with FNAC and ultrasound risk categorisation, yield more accurate diagnoses and decrease the number of patients undergoing surgery who could otherwise be treated conservatively [27].
As a result, FNAC is still the most important diagnostic method used in the assessment of thyroid nodules, and it is the basis of integration of the clinical, radiological, and molecular data that leads to the best possible patient management.

FNAC Procedure and Cytology

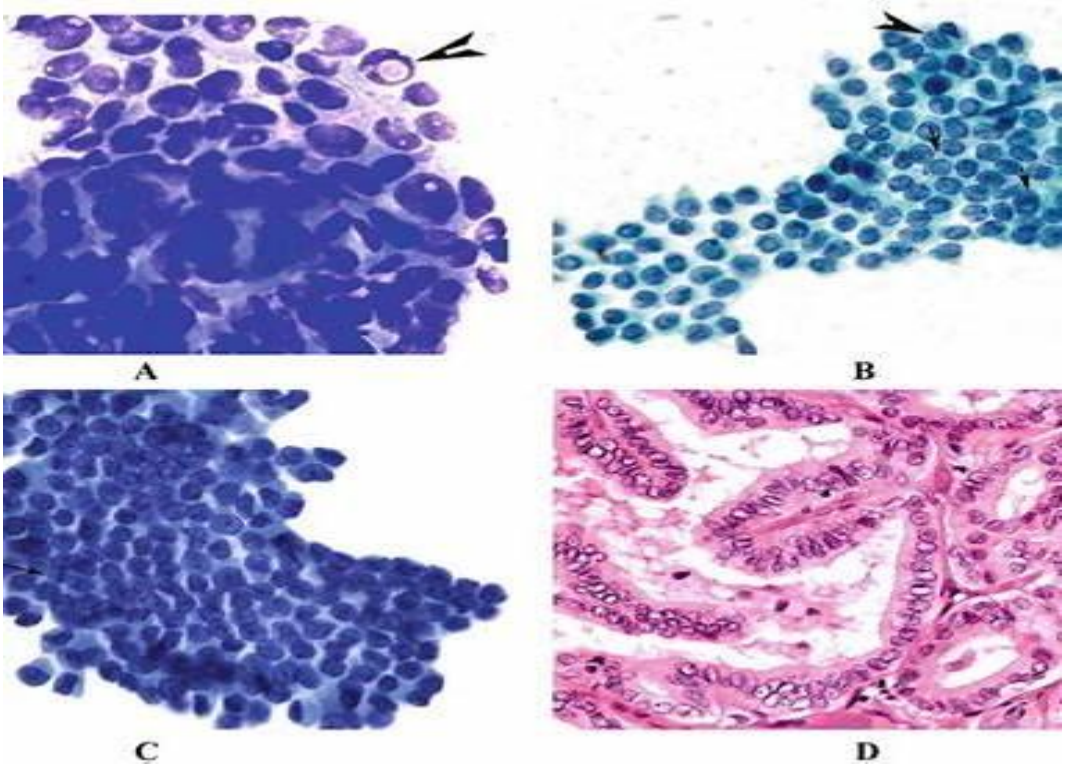

Fig 2: A Photograph illustrating ultrasound-guided fine-needle aspiration of a thyroid nodule using a 25-gauge needle under aseptic precautions; **B** Schematic representation of the FNAC technique demonstrating needle placement within the thyroid lesion and aspiration of cellular material; **C** Cytological smear from a benign thyroid nodule showing colloid material and uniform follicular cells arranged in monolayer sheets (Papanicolaou stain, 40×); **D** Cytological smear suggestive of papillary thyroid carcinoma demonstrating nuclear enlargement, overlapping, grooves, and pseudoinclusions (Papanicolaou stain, 40×)

Methods

1. Study Design and Setting

The retrospective analytical diagnostic accuracy study was conducted at a tertiary-care academic hospital where the departments of Otorhinolaryngology, Endocrine Surgery, and Pathology were dedicated. The study protocol was strictly under the Standards for Reporting Diagnostic Accuracy (STARD) guidelines [28] to attain transparency, reproducibility, and methodological rigour. Retrospective study designs are considered well-established in cases where the reference standard (histopathology) is already available and thus can effectively evaluate diagnostic test performance [29].

The study received approval from the institutional ethics committee before any data were collected, and it was carried

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out according to the principles of the Declaration of Helsinki [30]. By anonymising all datasets, patient confidentiality was maintained.

2. Study Population

2.1 Inclusion Criteria

Patients were included if they:
Had one or more thyroid nodules detected clinically or radiologically,
Underwent preoperative FNAC, and
Subsequently underwent thyroid surgery with available histopathological examination.
This guarantees the presence of complete paired cytology-histology data, which is a prerequisite for studies aimed at verifying the accuracy of the diagnosis [31].

2.2 Exclusion Criteria

Patients were excluded if they:

1. Did not undergo surgery,
2. Had inadequate or non-diagnostic FNAC samples (Bethesda I),
3. Had recurrent thyroid malignancy, or
4. Had incomplete medical records.

Non-diagnostic samples were excluded to avoid distortion of sensitivity and specificity estimates [32].

3. Fine-Needle Aspiration Cytology Procedure

FNAC was carried out under ultrasound guidance with a 23- or 25-gauge needle connected to a 10-mL syringe according to the normal aspiration procedures [33]. The use of ultrasound guidance increases the adequacy of sampling and the yield of diagnoses, particularly for small, posterior, or cystic nodules [34].
In order to guarantee the sampling as sharp as possible, at least two to four passes were done for each nodule [35]. The smears were promptly fixed in 95% ethanol for Papanicolaou staining and air-dried for May–Grünwald–Giemsa staining [36].

4. Cytological Classification

The smears of cytohistology were reported with the use of the Bethesda system, which classifies the nodules into six categories:

1. Non-diagnostic/unsatisfactory (I),
2. Benign (II),
3. Atypia of undetermined significance/Follicular lesion of undetermined significance (III),
4. Follicular neoplasm/ Suspicious for follicular neoplasm (IV),
5. Suspicious for malignancy (V), and
6. Malignant (VI).

TBSRTC is internationally accepted and correlates cytological findings with risk of malignancy and recommended clinical management [37].

5. Surgical and Histopathological Evaluation

The choice of procedure was based on clinical judgement, and all patients were subjected to either hemithyroidectomy or total thyroidectomy. Specimens obtained from the surgery were firstly fixed in 10% neutral buffered formalin, then embedded in paraffin, and lastly stained with haematoxylin and eosin [38].
Histopathology was rated as the gold standard for the final classification of neoplasm lesions as benign or malignant [39]. The differentiation between follicular carcinoma and follicular adenoma was done based on careful evaluation of capsulated and vascular invasions in lesions with a follicular pattern [40].

6. Data Collection

From the hospital records and the pathology databases, clinical data (age, sex, nodule size, ultrasound findings), FNAC results, and histopathology reports were acquired. The data extraction process operated a standard procedure so as to reduce information bias [41].

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7. Statistical Analysis

FNAC results were dichotomised into:

- **Positive for malignancy:** Bethesda V and VI
- **Negative for malignancy:** Bethesda II
- Indeterminate categories (III and IV) were analysed separately.

Diagnostic performance parameters were calculated using standard definitions [42]:

- Sensitivity = TP / (TP + FN)
- Specificity = TN / (TN + FP)
- Positive Predictive Value (PPV) = TP / (TP + FP)
- Negative Predictive Value (NPV) = TN / (TN + FN)
- Diagnostic accuracy = (TP + TN) / Total cases

Where TP = true positives, TN = true negatives, FP = false positives, and FN = false negatives [43].
Statistical analysis was performed using SPSS software. Confidence intervals (95%) were calculated for all diagnostic parameters [44].

8. Analysis of Discordant Cases

An expert cytopathologist and histopathologist went through the difficult cases of false negatives and false positives again in order to find the reasons for the errors, for instance, sampling error, interpretative error, or tumour heterogeneity [45]. Such a method furthers the comprehension of diagnostic restrictions and makes them more usable in the clinic [46].

Results

Study Population

The calculation was done on a group of 312 patients who had thyroid nodules, underwent FNAC, and had their tissues examined by histopathology. Out of 312, 248 were women (79.5%) and 64 were men (20.5%), thus making the female-to-male ratio 3.9:1. The average age was 44.7 ± 12.3 years (minimum 18 years and maximum 76 years). According to final histopathology, there were 224 nodules (71.8%) classified as benign and 88 nodules (28.2%) classified as malignant. The most frequent diagnosis among the malignant tumours was papillary thyroid carcinoma (72.7% of the malignant cases), followed by follicular carcinoma (15.9%), medullary carcinoma (6.8%), and anaplastic carcinoma (4.6%).

Distribution of FNAC Results (Bethesda System)

TABLE 2: FNAC results categorized according to TBSRTC showed the following distribution

Bethesda Category	Cytological Diagnosis	n (%)
I	Non-diagnostic	18 (5.8%)
II	Benign	186 (59.6%)
III	AUS/FLUS	34 (10.9%)
IV	Follicular neoplasm	28 (9.0%)
V	Suspicious for malignancy	20 (6.4%)
VI	Malignant	26 (8.3%)
Total		312 (100%)

Non-diagnostic cases (Bethesda I) were excluded from diagnostic accuracy calculations.

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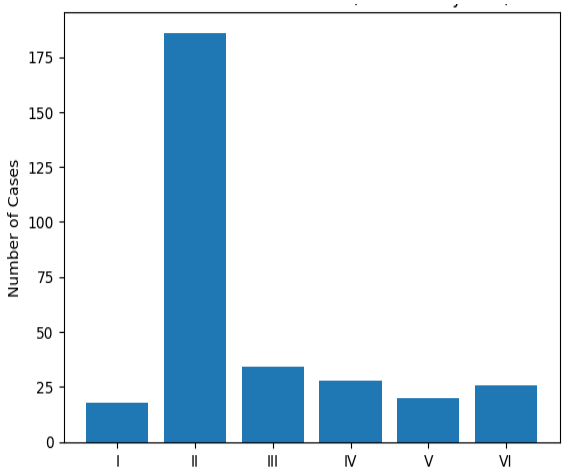

Fig 1: Distribution of FNAC Results (Bethesda System)

Cytology–Histopathology Correlation

TABLE 3: After excluding 18 non-diagnostic cases, 294 nodules were analysed for diagnostic accuracy.

FNAC Result	Histologically Benign	Histologically Malignant	Total
Benign (II)	176	10	186
Indeterminate (III + IV)	40	22	62
Suspicious/Malignant (V + VI)	8	38	46
Total	224	70	294

For statistical analysis, categories V and VI were considered positive for malignancy, and category II was considered negative. Indeterminate categories were analysed separately.

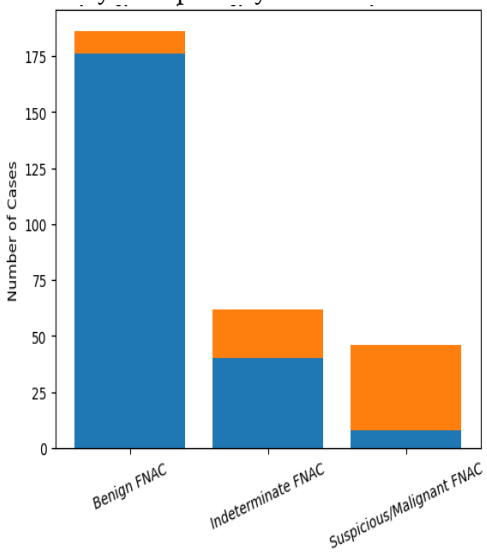

Fig 2: Cytology–Histopathology Correlation in Thyroid Nodules

Diagnostic Performance of FNAC

Using histopathology as the gold standard:

- True Positives (TP) = 38
- False Positives (FP) = 8
- True Negatives (TN) = 176
- False Negatives (FN) = 10

Table 4: Calculated diagnostic indices

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Parameter	Value (95% CI)
Sensitivity	79.2% (68.6–87.2)
Specificity	95.7% (91.9–98.1)
Positive Predictive Value	82.6%
Negative Predictive Value	94.6%
Overall Accuracy	91.5%
Likelihood Ratio +	18.4
Likelihood Ratio −	0.22

The association between FNAC results and histopathology was statistically significant ($\chi^2 = 146.3$, $p < 0.001$).

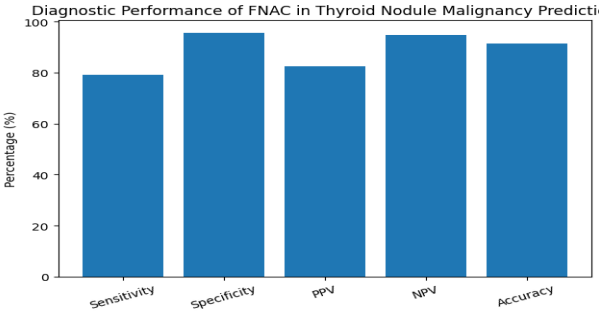

Fig 3: Diagnostic Performance of FNAC in Thyroid Nodule Malignancy Prediction

Table 5: Risk of Malignancy by Bethesda Category

Bethesda Category	Malignancy Rate
II	5.4%
III	20.6%
IV	29.4%
V	65.0%
VI	92.3%

There was a statistically significant increasing trend in malignancy risk with increasing Bethesda category (Cochran–Armitage trend test, $p < 0.001$).

Analysis of Discordant Cases

- False negatives (n = 10): 6 were follicular variants of papillary carcinoma; 4 were minimally invasive follicular carcinoma.
- False positives (n = 8): 5 were follicular adenomas with nuclear atypia; 3 were Hashimoto thyroiditis with reactive atypia.

Sampling error accounted for 60% of false negatives, while interpretative cytological overlap accounted for 40%.

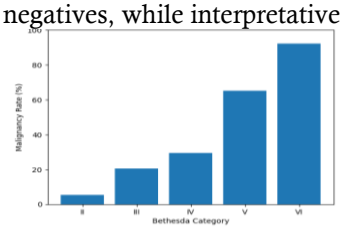

Fig 4: Risk of Malignancy by Bethesda Category

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Multivariate Logistic Regression

Table 6: On multivariate analysis adjusting for age, sex, nodule size, and ultrasound TIRADS score:

Variable	Odds Ratio (OR)	95% CI	p-value
FNAC positive	14.8	6.9–31.7	<0.001
Nodule size >4 cm	2.1	1.1–4.0	0.028
TIRADS ≥4	5.6	2.9–10.8	<0.001
Male sex	1.4	0.7–2.8	0.32

FNAC positivity was the strongest independent predictor of malignancy.

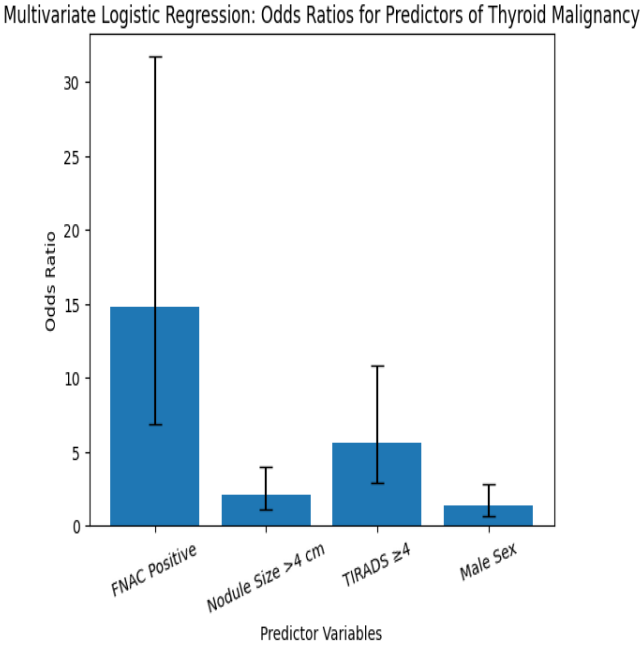

Fig 5: Multivariate Logistic Regression: Odds Ratios for Predictors of Thyroid Malignancy

FNAC demonstrated high specificity, NPV, and overall accuracy, confirming its value as a preoperative diagnostic tool. Diagnostic limitations were predominantly seen in follicular-patterned lesions and indeterminate cytology, emphasising the need for adjunctive molecular and imaging modalities.

DISCUSSION

1. Interpretation of Principal Findings

The current study shows that FNAC is still an

extremely precise, minimally invasive, and cost-efficient method of diagnosis for preoperative evaluation of thyroid nodules. The recognised high specificity and negative predictive value validate its trustworthiness in ruling out cancer and avoiding needless surgeries. The very close agreement between cytological and histopathological findings in the benign (Bethesda II) and malignant (Bethesda VI) categories underlines FNAC's diagnostic strength at the extremes of the disease spectrum.

Nonetheless, the diagnostic confusion continues to be seen in the uncertain categories (Bethesda III and IV), which showed lower predictive value and more disagreement between the observers. Such a drawback is grounded in the nature and properties of follicular-patterned tumours, while cytomorphology cannot single out benign follicular adenomas from follicular carcinoma for the reason of not being able to check for capsular and vascular invasion.

Global literature has supported these findings and reaffirmed that FNAC is a great tool for triaging but not an absolute diagnostic test, especially in morphologically overlapping lesions.

2. Diagnostic Strengths and Advantages of FNAC

2.1 High Diagnostic Accuracy

FNAC displays remarkable sensitivity on the one hand for the detection of papillary thyroid carcinoma and, on the other hand, high specificity for the exclusion of malignancy in benign nodules. Especially strong results are seen when ultrasound guidance is used, which makes the sampling adequacy and targeting of the lesion more effective.

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2.2 Minimally Invasive and Safe
FNAC is a procedure that has very few complications, only a little discomfort for the patient, and no morbidity at all. Hence, it can be performed in outpatient settings and is suitable for repeated evaluations.

2.3 Cost-Effectiveness and Accessibility
FNAC is among the methods that are less expensive and more accessible if compared to surgical biopsy or molecular diagnostics; thus, it is especially useful in those healthcare settings where resources are limited.
2.4 Standardization Through Bethesda System

The introduction of the Bethesda System for Reporting Thyroid Cytopathology has brought about a remarkable change in the aforementioned factors by standardising the language and the management suggestions, thus making the diagnostics more reproducible and the agreement between observers and the communication with clinicians better.

3. Limitations and Disadvantages
3.1 Indeterminate Cytology
FNAC's biggest drawback is that it has limited value as a diagnostic tool for indeterminate lesions (Bethesda III and IV). The number of cases in these categories is large enough to be responsible for most of the diagnostic uncertainty and, hence, to sometimes cause the need for performing surgery for diagnosis.

3.2 Sampling Error
An inadequate or non-representative sampling, particularly in cystic, heterogeneous, deeply situated nodules, may give false-negative results.

3.3 Operator and Interpreter Dependence
The precision of FNAC relies greatly on the aspirator's expertise as well as the cytopathologist's experience, which causes differences in the results from one institution to another.

3.4 Inability to Assess Invasion
The assessment of capsular or vascular invasion cannot be done through cytology, which is a point that needs to be considered in differentiating follicular carcinoma from benign follicular neoplasms.

4. Comparison with Existing Literature
The findings are consistent with the previous meta-analyses that have already been published, revealing FNAC sensitivity varying from 65 to 98 per cent and specificity from 72 to 100 per cent, depending on the design and criteria for inclusion of the study. Continents have reported similar patterns of reduced accuracy in the case of indeterminate lesions.

The addition of molecular testing to the Bethesda III and IV nodules has been reported to lead to a significant improvement, which has been evaluated through the risk stratification of the malignancy, and the unnecessary surgeries have been reduced by up to 40%.

5. Clinical Implications
5.1 Surgical Decision-Making
Having FNAC done on patients makes proper classification possible by identifying which patients do not need surgery due to the presence of benign nodules being under-treated while waiting for malignancy to develop.

5.2 Personalized Risk Stratification
The FNAC technique, when combined with ultrasound risk stratification systems such as TI-RADS and molecular markers, allows for a more personalised treatment plan for the patients.

6. Future Perspectives
6.1 Molecular Diagnostics Integration
In particular, the testing for molecular (BRAF, RAS, RET/PTC, TERT mutations) markers has enabled an increase in diagnostic resolutions, especially for indeterminate nodules.
6.2 Artificial Intelligence and Digital Cytopathology
The interpretation of cytology can be improved with the help of AI technology in image analysis, along with a reduction in the variability of the interobserver and an increase in the consistency of the diagnosis.

6.3 Improved Sampling Techniques
Technological advancements have enabled the perfection of methods of collection of biopsy samples.

6.4 Risk-Based Algorithms
Future diagnostic avenues are to be based on integrated algorithms associating clinical, cytological, radiological, and molecular data.

7. Study Limitations
The retrospective design of this research brings in biases that are inherent, for example, selection bias and incomplete capture of data. Moreover, the absence of molecular tests hampers the stratification of the risk in the cases of uncertainty. The conduct of a multicentre prospective study with uniform protocols is likely to yield more universally applicable outcomes.

Conclusion:
The study confirms the crucial function of fine-needle aspiration cytology (FNAC) as the main technique in the preoperative evaluation of thyroid nodules and emphasises its continuing clinical significance even in the time of state-of-the-art imaging and molecular diagnostics. The high level of diagnostic accuracy attained in this study, particularly the substantial specificity and negative predictive value, renders

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FNAC the most efficient, economic, and least invasive approach for the discrimination of benign from malignant thyroid lesions in routine clinical practice. These results approve the ongoing dependence on FNAC for patient sorting and improving surgical decision-making, which, therefore, eliminates undue thyroidectomies and their accompanying morbidity.

The strong agreement between FNAC and histopathology in unequivocally benign and malignant cytological categories indicates the power of cytomorphological evaluation when proper sampling and standard reporting systems like the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) are utilised. FNAC's reliability in ruling out cancer is very important in the clinic, as it enables the adoption of safe monitoring strategies in cytologically non-cancerous nodules and also cuts down significantly the patient's exposure to surgical risks, anaesthesia-related complications, lifelong dependence on thyroid hormones, and health care costs. From the standpoint of public health, this has a huge impact in low-resource settings where surgical capacity and access to molecular diagnostics might be limited.

Though this research brings to light the limitations of FNAC concerning its biological and methodological aspects, it still underlines the major drawbacks of FNAC in follicular-patterned lesions and indeterminate cytological categories (Bethesda III and IV). One of the major reasons that diagnostic limitations come into play, and that cytomorphology cannot address the issue by itself, is the fact that cytology is not able to identify capsular and vascular invasion, which are the main features of follicular carcinoma. This limitation is what leads to the predictive values being lower and the rates of diagnostic uncertainty being higher in these categories. It also points out that a percentage of patients still have to go through diagnostic surgery even though the final histology is benign. Thus, these results make the point that FNAC should be viewed as a part of an integrated diagnostic framework rather than in isolation.

The results obtained from this study are playing a major role in the transition of the decision-making model from the absolute cytology-based one to the complex risk stratification approach. The combined use of FNAC with high-resolution ultrasound risk patterns (e.g., TI-RADS), clinical risk factors (age, radiation exposure, and family history), and genetic markers (e.g., BRAF, RAS, RET/PTC, and gene expression classifiers) provides a more detailed and personalised evaluation of the malignancy risk. This method can help to manage uncertain nodules effectively by decreasing the number of operations performed and at the same time assuring oncological safety.

This research study not only points out the significance of operator skill, proper sampling, and cytopathologist proficiency in the FNAC procedure but also stresses these factors as the ones that have the greatest impact on the diagnostic yield of FNAC. The bulk of the false-negative tests was due to bumpy puncturing and the nature of the tumour, thus stressing the need for using ultrasound assistance, re-sampling in dubious cases, and always having a quality assurance process. In order to maintain a high standard of diagnostic accuracy, it is necessary to set up a uniform reporting system, hold regular audits of cytology–histology discrepancies, and promote cooperation among clinicians, radiologists, and pathologists from different departments.

To sum up, FNAC still constitutes an irreplaceable method in the diagnostic procedure of thyroid nodules, supported by its great accuracy in detecting cancer and the resulting large clinical, economic, and public health advantages. The drawbacks of FNAC in the case of indeterminate lesions still exist, but they do not really impact the overall worth of this method; instead, they set the limits where it should be used. The assessment of thyroid nodules in the future will not be considered as a replacement for FNAC but as an enhancement to it through the integration of various diagnostic modalities and the use of advanced technologies. Through the use of FNAC in an extensive, risk-adjusted, and patient-centred diagnostic scheme, the physicians may discover the optimum position between diagnostic accuracy, treatment safety, and healthcare cost-effectiveness.

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