DIAGNOSTIC ACCURACY OF THE FINE-NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS OF SOLID SOLITARY THYROID NODULE

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ABSTRACT

Objective: To determine the diagnostic accuracy of fine needle aspiration cytology (FNAC) for solid solitary thyroid nodules, using histopathology as the reference standard.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of ENT, Lady Reading Hospital (MTI), Peshawar, from 01 October 2024 to 31 March 2025.

Methodology: Adults (≥18 years) with a solitary, predominantly solid thyroid nodule on ultrasonography underwent ultrasound-guided FNAC followed by surgical excision and histopathology. Cytology was reported using the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). For diagnostic accuracy analysis, Bethesda II was considered benign (test negative) and Bethesda V–VI malignant (test positive); non-diagnostic (Bethesda I) and indeterminate categories (Bethesda III–IV) were excluded from the primary 2×2 analysis. Cytology and histopathology were interpreted independently with blinding to each other's reports. Sensitivity, specificity, PPV, NPV, and accuracy were calculated with 95% confidence intervals (CI).

Results: A total of 110 patients were included; mean age was 45.81±16.24 years, and 63 (57.3%) were males. Histopathology confirmed 50 (45.5%) malignant and 60 (54.5%) benign nodules. FNAC showed sensitivity 84.00% (95% CI: 71.50–91.67), specificity 88.33% (95% CI: 77.79–94.22), PPV 85.71% (95% CI: 73.29–92.91), NPV 86.89% (95% CI: 76.17–93.23), and accuracy 86.36% (95% CI: 78.69–91.63).

Conclusion: In this single-centre surgical cohort, FNAC demonstrated good diagnostic performance for solid solitary thyroid nodules; however, false-negative and false-positive results occurred, so FNAC should be interpreted alongside clinical and ultrasound risk features, with repeat sampling or alternate techniques when suspicion persists.

Keywords: Fine needle aspiration cytology; Thyroid nodule; Histopathology; Diagnostic accuracy; Sensitivity; Specificity.

INTRODUCTION

Thyroid nodules are common; high-resolution ultrasonography can detect nodules in up to two-thirds of adults, whereas palpation identifies approximately 4–7%.[1] In patients presenting with solitary thyroid nodules, the risk of malignancy is clinically important and has been reported to be 36.9% in a published study, underscoring the need for reliable preoperative diagnostic tools such as FNAC for timely risk stratification and management.[2]

Fine needle aspiration cytology (FNAC) is widely used for initial risk stratification due to its minimally invasive nature, low cost, and diagnostic yield.[3] The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) standardizes reporting into six categories with defined malignancy risks, improving reproducibility and clinical communication.[4,5,6] Meta-analyses show FNAC generally has high specificity with variable sensitivity depending on population mix, adequacy, and handling of indeterminate categories.[7] A prospective study by Gupta M et al. evaluating solitary thyroid nodules demonstrated that FNAC had a sensitivity of 80% and a specificity of 86.6% when correlated with histopathology, supporting its value as an important preoperative diagnostic tool while also highlighting the possibility of false-negative and false-positive results.[8] However, diagnostic performance can vary across centres due to sampling technique, smear adequacy, and interpretive expertise.[9,10,11]

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In resource-limited settings such as Pakistan, local performance estimates are important for clinical decision-making and to contextualize false-negative and false-positive outcomes.[12] Therefore, this study evaluated FNAC accuracy against histopathology for solid solitary thyroid nodules at a tertiary care hospital.

METHODOLOGY

After ethical approval from the Institutional Review Board of Lady Reading Hospital (MTI), Peshawar (Ref. No. 596/LRH/MTI), this cross-sectional validation study was conducted in the Department of ENT from 01 October 2024 to 31 March 2025. Patients aged ≥18 years with a clinically and ultrasonographically confirmed solitary thyroid nodule were enrolled using non-probability sequential sampling.

A solid solitary thyroid nodule was operationally defined as a single discrete thyroid lesion on ultrasound with predominantly solid composition (≥80% solid component) in an otherwise non-nodular thyroid gland, with no additional nodules identified on the same examination. Patients with multinodular goitre, previous thyroid surgery, or current/past thyroid-suppressive therapy were excluded.

Sample size was calculated using the Buderer method, incorporating expected sensitivity of 80% and specificity of 86.6% from Gupta et al[8]., and an anticipated malignancy prevalence of 36.9%[2] from a published study on solitary thyroid nodules, with 95% confidence level and 10% absolute precision. The required sample size was 109 patients; therefore, 110 patients were included in the study.

All patients underwent ultrasound-guided FNAC using a 23-gauge needle under aseptic technique. Smears were stained and reported by consultant cytopathologists using TBSRTC categories I–VI. For the primary diagnostic accuracy analysis, Bethesda II was treated as benign (test negative) and Bethesda V–VI as malignant (test positive). Non-diagnostic (Bethesda I) and indeterminate categories (Bethesda III–IV) were excluded from the primary 2×2 analysis and documented separately.

All enrolled patients underwent surgical excision followed by histopathological examination, which served as the reference standard. Cytology and histopathology were interpreted independently; histopathologists were blinded to FNAC categories at the time of reporting to reduce interpretive bias. Inter-observer reliability was assessed by independent second review of a random subset of smears, and agreement was quantified using Cohen's kappa.

Data were analysed in IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Sensitivity, specificity, PPV, NPV, and accuracy were calculated using 2×2 contingency tables and reported with 95% confidence intervals. Association between FNAC category and histopathology was tested using the Chi-square test or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 110 patients with solid solitary thyroid nodules were included. Mean age was 45.81±16.24 years; 63 (57.3%) were males and 47 (42.7%) were females. FNAC classified 61 (55.5%) nodules as benign and 49 (44.5%) as malignant, while histopathology confirmed 60 (54.5%) benign and 50 (45.5%) malignant nodules (Table 1).

On cytohistological correlation, 53/61 cytologically benign nodules were histologically benign and 8/61 were malignant (false negatives 13.1%). Among 49 cytologically malignant nodules, 42 were confirmed malignant and 7 were benign on histopathology (false positives 14.3%) (Table 2). FNAC showed sensitivity 84.00% (95% CI: 71.50–91.67), specificity 88.33% (95% CI: 77.79–94.22), PPV 85.71% (95% CI: 73.29–92.91), NPV 86.89% (95% CI: 76.17–93.23), and overall accuracy 86.36% (95% CI: 78.69–91.63).

Table-1: Baseline Characteristics of Study Participants (n = 110)

Variable	Value
Age (years)	45.81 ± 16.24
Gender	
– Male	63 (57.3%)

– Female	47 (42.7%)
FNAC Diagnosis	
– Benign	61 (55.5%)
– Malignant	49 (44.5%)
Histopathological Diagnosis	
– Benign	60 (54.5%)
– Malignant	50 (45.5%)

Table-2: Comparison of FNAC with Histopathology in Diagnosis of Solid Solitary Thyroid Nodule (n=110)

FNAC Result	Histopathology Results		Total	Statistics
	Benign	Malignant		
Benign	53 (48.2%)	8 (7.3%)	61 (55.5%)	P Value = < 0.001 Sn = 88.33% Sp = 84.00% PPV = 86.89% NPV = 85.71% Accuracy = 86.36%
Malignant	7 (6.4%)	42 (38.2%)	49 (44.5%)	
Total	60 (54.5%)	50 (45.5%)	110 (100.0%)	

Table-3: Gender-wise Comparison of Cytology and Histopathology in Diagnosis of Solid Solitary Thyroid Nodule (n=110)

Gender	Cytology Result	Histopathology Result		Total	Statistics
		Benign	Malignant		
Male	Benign	35 (89.7%)	4 (16.7%)	39 (61.9%)	P Value = < 0.001 Sn = 89.7% Sp = 83.3% PPV = 89.7% NPV = 83.3% Accuracy = 87.3%
	Malignant	4 (10.3%)	20 (83.3%)	24 (38.1%)	
	Total	39 (100.0%)	24 (100.0%)	63 (100.0%)	
Female	Benign	18 (85.7%)	4 (15.4%)	22 (46.8%)	P Value = < 0.001 Sn = 85.7% Sp = 83.3% PPV = 81.2% NPV = 86.9% Accuracy = 84.4%
	Malignant	3 (14.3%)	22 (84.6%)	25 (53.2%)	
	Total	21 (100.0%)	26 (100.0%)	47 (100.0%)	

DISCUSSION

This study evaluated FNAC performance for solid solitary thyroid nodules using histopathology as the reference standard. FNAC demonstrated good overall accuracy (86.36%), with sensitivity 84.00% and specificity 88.33%, supporting its use as a practical first-line investigation in tertiary care settings.[13]

The major clinical issue in thyroid cytology is balancing missed malignancies (false negatives) against unnecessary surgery (false positives). In our cohort, false negatives occurred in 8/61 (13.1%) cytologically benign nodules, while false positives were 7/49 (14.3%) among cytologically malignant nodules. False-negative FNAC is commonly related to follicular-patterned lesions and well-differentiated carcinomas where cytology cannot assess capsular/vascular invasion, and also to sampling error in heterogeneous nodules.[14]

False-positive cytology may result from overlap between malignant cytomorphology and benign inflammatory/hyperplastic conditions such as Hashimoto's thyroiditis and cellular nodular

hyperplasia, contributing to cytohistological discordance.[15,16] These findings emphasize the importance of ultrasound guidance, adequacy assessment, and experienced cytopathology reporting.

Standardized reporting using TBSRTC improves communication and risk-based management, and meta-analyses show FNAC generally has high specificity with variable sensitivity depending on inclusion of indeterminate categories and local practice patterns.[13] Adjunct strategies such as repeat FNAC, core-needle biopsy for repeatedly non-diagnostic/indeterminate nodules, and imaging adjuncts (e.g., elastography) can reduce uncertainty but are often limited by cost and availability in low-resource settings.[17,18] Emerging evidence also suggests artificial-intelligence approaches may improve standardization of imaging interpretation, though implementation and validation challenges remain.[19,20]

This study has limitations. It is a single-centre study using non-probability sampling and includes a surgical cohort only, which may inflate malignancy prevalence and limits generalizability to all ultrasound-detected nodules. Exclusion of non-diagnostic and indeterminate Bethesda categories from the primary 2×2 analysis may overestimate diagnostic indices. Larger multicentre studies with explicit handling of Bethesda III–IV categories are recommended.

CONCLUSION

In this cross-sectional validation study of a single-centre surgical cohort, FNAC demonstrated good diagnostic accuracy for solid solitary thyroid nodules. However, clinically relevant false-negative and false-positive results were observed. FNAC should be interpreted in conjunction with ultrasound risk features and clinical suspicion and repeat sampling or alternative diagnostic approaches should be considered when discordance is suspected.

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