## Original Research Article

# Diagnostic utility of fine needle aspiration cytology in thyroid lesions

**Farzana Manzoor[1], Arif R. Sheikh[2]\*, Bilal A. Sheikh[1]**

[1]Department of Pathology, Government Medical College, Srinagar, Jammu and Kashmir, India
[2]Department of Medicine, Sher-e-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India

**\*Correspondence:**
Dr. Arif R. Sheikh,
E-mail: ess.arif53@gmail.com

**ABSTRACT**

**Background:** Thyroid fine needle aspiration cytology (FNAC) is an important screening tool and thereby dictates clinical management. The exclusion of non-invasive follicular variant of papillary carcinoma (NIFVPTC) from thyroid malignancies and its reclassification as non-malignant entity i.e., non-invasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP) has added a new dimension. Aim of this study was to study the role of fine needle aspiration cytology in screening thyroid lesions by correlation with histopathological examination and to calculate diagnostic accuracy of FNAC considering NIFTP as non-malignant and compare it with pre NIFTP era.
**Methods:** It was an observational study done over a period of 2 years (2017-2018). It included the cases where FNAC was followed subsequently by histopathology. FNAC results were correlated with histopathological diagnosis established thereof.
**Results:** A total of 107 patients were included in this study. Considering NIFTP as non-malignant, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 92.97%, 100%, 100%, 92.73% and 96.23% respectively, that is significantly higher if authors considered NIFTP as malignant.
**Conclusions:** FNAC plays an indispensable role in making preliminary diagnosis in thyroid lesions. There is a notable increase in diagnostic accuracy of FNAC in thyroid lesions and significant decrease in risk of malignancy by considering NIFTP as non-malignant.

**Keywords:** Diagnostic accuracy, Fine needle aspiration cytology, Thyroid

## INTRODUCTION

The first reports of utility of fine needle aspiration cytology (FNAC) in thyroid lesions dates back to year 1930 by Martin and Ellis.[1] Thyroid nodule is the main indication for FNAC of the thyroid lesions. Palpable thyroid nodules are seen in 4-7% of adults, however, including non-palpable nodules discernable by ultrasonography or at autopsy, the prevalence rises to 20-70%. Given the high prevalence of nodules, combined with impracticality of surgically excising all nodules, FNAC plays an important role as screening test. Around 1980, When FNAC was introduced at the Mayo clinic (around 1980), there was a significant decrease in

percentage of patients requiring thyroid surgery (from 67% to 43%) in 1 year, consequent upon which the percentage of excised malignant nodules increased from 14% to 29%. Since then, the reduction in unnecessary surgery has been even greater: the percentage of excised nodules that are malignant is now 45% to 56%.[2]

The Bethesda system for reporting thyroid cytopathology (TBSRTC), published in 2009, has been widely adopted and used for reporting thyroid FNA samples. As per this system, the thyroid lesions can be divided into 6 broad categories, each category has defined risk of malignancy and treatment approaches.[3-5] The implied cancer risk ranges from 0% to 3% for the "benign" category to

virtually 100% for the "malignant" category.[6] The 2017 revised Bethesda system for reporting thyroid cytopathology reasserted six diagnostic categories, however, risk of malignancy was updated based on post 2010 literature (Table 1).[5]

**Table 1: The 2017 Bethesda system for reporting thyroid cytopathology: implied risk of malignancy and recommended clinical management.**

| Diagnostic category | Risk of malignancy if NIFTP is considered non malignant (%) | Risk of malignancy if NIFTP is considered malignant (%) | Usual management |
|---|---|---|---|
| Nondiagnostic or unsatisfactory | 5-10% | 5-10% | Repeat FNA with ultrasound guidance |
| Benign | 0-3% | 0-3% | Clinical and sonographic follow-up |
| Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS) | 6-18% | 10-30% | Repeat FNA, molecular testing or lobectomy |
| Follicular neoplasm or suspicious for a follicular neoplasm | 10-40% | 25-40% | Molecular testing, lobectomy |
| Suspicious for malignancy | 45-60% | 50-75% | Near total thyroidectomy or lobectomy |
| Malignant | 94-96% | 97-99% | Near total thyroidectomy or lobectomy |

## METHODS

It was an observational study done over a period of 2 years (2017-2018). It included the cases where FNAC was followed subsequently by histopathology. Aspiration was done using 23-25-gauge, 30-50 mm fine needle. Smears made were properly stained after air drying with May Grunwald Giemsa (MGG) stain and after wet fixation with papanicolaou stain. FNA sample was considered adequate for evaluation if it contained 6 groups of well visualized follicular cells, with at least 10 cells per group, preferably on a single slide.[6] The surgical specimens were processed in the department, 4-5 micron sections were cut on microtome and stained by Hematoxylin and eosin stain. FNAC results were correlated with histopathological diagnosis established thereof.

### *Statistical analysis*

Data was entered in Microsoft excel spreadsheet. The diagnostic accuracy of FNAC was calculated on www.openepi.com. Tabulation for study was done using SPSS 20.0.

## RESULTS

### *Age and gender*

Of the 107 cases in this study, 23 were male and 84 were female patients with male: female ratio being 1:3.65. The youngest patient was 3.5 months old (thyroglossal cyst)

and oldest patient was 70 years old (follicular adenoma). Maximum number of cases were in the age group of 20-29 years followed by the age group of 30-39 years and 40-49 years (Table 2).

**Table 2: Age and gender distribution of thyroid lesions.**

| Age group (years) | Female (n1=84) | Male (n2=23) | Total (n1+n2=107) |
|---|---|---|---|
| <10 | 2 (2.38%) | 2 (8.69%) | 4 (3.73%) |
| 10-19 | 6 (7.14%) | 3 (13.04%) | 9 (8.41%) |
| 20-29 | 28 (33.33%) | 5 (21.73%) | 33 (30.84%) |
| 30-39 | 20 (23.8%) | 3 (13.04%) | 23 (21.49%) |
| 40-49 | 15 (17.85%) | 4 (17.39%) | 19 (17.75%) |
| 50-59 | 7 (8.33%) | 3 (13.04%) | 10 (9.34%) |
| 60-69 | 5 (5.95%) | 1 (4.34%) | 6 (5.60%) |
| 70-79 | 1 (1.19%) | 2 (8.69%) | 3 (2.80%) |

### *Cyto-histological correlation of thyroid lesions*

The cytologically diagnosed categories in this study included 10 cases of thyroglossal cyst, 16 of colloid goiter (TBSRTC category II), 30 of follicular neoplasm/suspicious for follicular neoplasm (TBSRTC category IV), 1 case suspicious of papillary thyroid carcinoma (TBSRTC category V), 48 of papillary thyroid carcinoma (TBSRTC category VI) and 2 cases of medullary carcinoma (TBSRTC category VI). The subsequent histopathologic diagnosis was consistent with FNAC diagnosis in all cases of thyroglossal cyst, colloid goitre, papillary thyroid carcinoma and medullary

carcinoma. However, of the 30 cases which were reported as follicular neoplasm on FNAC, 19 were diagnosed as follicular adenoma, 4 as follicular carcinoma and 7 as non-invasive follicular variant of papillary thyroid

carcinoma, NIFVPTC (now reclassified as NIFTP) on histopathology and one case which was reported as suspicious of papillary carcinoma on cytology turned out to be colloid goitre on histopathology (Table 3).

**Table 3: Cyto-histological correlation of thyroid lesions.**

| Cytological diagnosis | No. of patients | Histo-pathological diagnosis | No. of patients |
|---|---|---|---|
| Thyroglossal cyst - TBSRTC category II | 10 | Thyroglossal cyst | 10 |
| Colloid goitre - TBSRTC category II | 16 | Colloid goitre | 16 |
| Follicular neoplasm - TBSRTC category IV | 30 | Follicular adenoma | 19 |
| | | Follicular carcinoma | 4 |
| | | NIFVPTC (reclassified as NIFTP) | 7 |
| Suspicious of papillary carcinoma - TBSRTC category V | 1 | Colloid goitre | 1 |
| Papillary carcinoma - TBSRTC category VI | 48 | Papillary carcinoma | 48 |
| Medullary carcinoma - TBSRTC category VI | 2 | Medullary carcinoma | 2 |

**Table 4: Cytohistological correlation to diagnose malignant lesions of thyroid (if NIFTP is considered malignant, pre NIFTP era).**

| Cytological diagnosis | No. of patients | Histopathological diagnosis | No. of patients |
|---|---|---|---|
| Benign | 55 | Benign | 44 |
| | | Malignant | 11 |
| Malignant | 51 | Benign | 0 |
| | | Malignant | 51 |

**Table 5: Cytohistological correlation to diagnose benign and malignant lesions of thyroid (if NIFTP is considered non-malignant, NIFTP era).**

| Cytological diagnosis | No. of patients | Histopathological diagnosis | No. of patients |
|---|---|---|---|
| Benign | 55 | Benign | 51 |
| | | Malignant | 4 |
| Malignant | 51 | Benign | 0 |
| | | Malignant | 51 |

**Table 6: Comparison of sensitivity, specificity, PPV, NPV and diagnostic accuracy considering NIFTP as malignant or non-malignant.**

| | If NIFTP is considered malignant (%) | If NIFTP is considered non malignant (%) |
|---|---|---|
| Sensitivity | 82.25% | 92.97% |
| Specificity | 100% | 100% |
| PPV | 100% | 100% |
| NPV | 80% | 92.73% |
| Diagnostic Accuracy | 89.6% | 96.23% |

***Cytohistological correlation to diagnose malignant lesions of thyroid***

On cytology 55 cases were categorized as benign. Considering NIFTP as malignant (pre NIFTP era), 11 cases (22%) subsequently proved as malignant on histopathology. However, only 4 proved malignant (7.27%) if NIFTP is considered as non-malignant (NIFTP

era). Among the 11 cases, 7 cases were NIFVPTC (reclassified as NIFTP) and 4 cases were that of follicular carcinoma. All the 51 cases categorized as malignant on cytology were subsequently confirmed as malignant on histopathology (Table 4 and 5).

This results in overall sensitivity, specificity, positive predictive value (PPV); negative predictive value (NPV)

and diagnostic accuracy as 82.25%, 100%, 100%, 80% and 89.6% respectively if NIFTP is considered malignant. However, if NIFTP is considered as non-malignant (NIFTP), the sensitivity, specificity, PPV, NPV and diagnostic accuracy in this study turns out to be 92.97%, 100%, 100% ,92.73 % and 96.23% respectively, depicting significant increase in diagnostic accuracy of FNAC in NIFTP era (Table 6).

**Table 7: Risk of malignancy (ROM) in various cytologically diagnosed thyroid lesions.**

| Cytologic diagnosis | ROM if NIFTP is considered malignant (pre NIFTP era) (%) | ROM if NIFTP is considered non-malignant (NIFTP era) (%) |
|---|---|---|
| Colloid goiter (TBSRTC category II) | 0 | 0 |
| Follicular neoplasm/ suspicious for follicular neoplasm (TBSRTC category IV) | 36.6 | 13.3 |
| Papillary carcinoma and medullary carcinoma (TBSRTC category VI) | 100 | 100 |

*Risk of malignancy*

Regarding the risk of malignancy (ROM) in this study, it was not applicable in TBSRTC category I and III as authors had no cases of these two categories. ROM was 0% for TBSRTC category II, 36.6% and 13.3% for TBSRTC category IV considering NIFTP as malignant and non-malignant respectively. The ROM for TBSRTC category VI was 100% and for TBSRTC category V, ROM cannot be commented on due to small sample size (single case) (Table 7).

**DISCUSSION**

FNAC though an old tool to diagnose thyroid lesions is turning indispensable with new developments in the field of thyroid pathology. In this study, females outnumbered males and maximum number of cases were in the age group of 20-49 years. These observations are agreeable with most of the previous studies, thereby reaffirming the already well-known fact that thyroid lesions are frequently seen in middle aged females.[7-11]

Cytologically diagnosed cases included 26 cases of TBSRTC category II (10; thyroglossal cyst and 16; colloid goiter), 30 cases of TBSRTC category IV (follicular neoplasm/suspicious for follicular neoplasm), 1 case of TBSRTC category V (suspicious for papillary carcinoma) and 50 cases of TBSRTC category VI (48; papillary carcinoma and 2; medullary carcinoma). There was not a single case either of TBSRTC category I (non-diagnostic/unsatisfactory) or category III (atypia of undetermined significance/follicular lesion of undetermined significance) in this study which is in concordance with lower percentage of these cases reported in literature.[10,12] This can be explained by small sample size, strict adherence to adequacy criteria, application of ultrasound guided FNAC, repeat aspirations and multiple passes done by the cytopathologists, thereby reaching to the unambiguous

diagnosis and hence avoiding unnecessary surgical intervention.

**Table 8: Comparative statistical values on cyto-histological correlation of thyroid lesions.**

| Author (year) | Sensitivity (%) | Specificity (%) | Diagnostic accuracy (%) |
|---|---|---|---|
| Settakorn et al[15] | 85.7% | 92.5% | 90.4% |
| El hag et al[7] | 85.7% | 97.6% | 94% |
| Mazeh et al[16] | 87% | 89% | 75% |
| Sangali et al[17] | 93.4% | 74.9% | - |
| Kumar et al[18] | 77% | 100% | 97.7% |
| Haberal et al[19] | 92.6% | 91.6% | 96.5% |
| Handa et al[8] | 97% | 100% | 98.48% |
| Sharma R et al[20] | 89.47% | 86.11% | 87.83% |
| Rajbhandari et al[21] | 96% | 100% | 92.85% |
| Bamanikar et al[9] | 50% | 100% | 94.2% |
| Nandedkar et al[10] | 85.7% | 98.6% | 97.1% |
| Present study (pre NIFTP era) | 82.85% | 100% | 89.6% |
| Present study (NIFTP era) | 92.97% | 100% | 96.23% |

The cases diagnosed as thyroglossal cyst and colloid goiter (TBSRTC category II) on cytology showed consistent results on histopathology. Of the 30 cases which were reported as follicular neoplasm/suspicious for follicular neoplasm (TBSRTC category IV) on cytology, 19 were diagnosed as follicular adenoma, 4 as follicular carcinomas and 7 as NIFVPTC (now reclassified as NIFTP) on histopathology. This discrepancy could be explained under following points: 1. The well-known fact

that the capsular and vascular invasion are the sine qua non of follicular carcinoma which can be established on surgical resection specimen only. 2. Follicular lesions of thyroid have overlapping cytomorphologic features and cannot be accurately distinguished by FNAC alone. This fallacy has also been reported in previous studies.[13,14]

There was 1 false positive case in this study which was reported as suspicious of papillary carcinoma (TBSRTC category V) on cytology and turned out to be colloid goiter on histopathology which could be due to the reason that benign conditions may show nuclear changes of papillary carcinoma. 50 cases diagnosed as TBSRTC category VI showed consistent results on follow up histopathology.

In the present study, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy vis-a-vis the prior studies are shown in table 8. The values obtained in this study mirrored the earlier studies.[8-10,17,19,21] Having said that a conclusive diagnosis of follicular adenoma versus follicular carcinoma is impossible on cytologic features alone and after the introduction of NIFTP as non-malignant entity, the predictive diagnostic accuracy of FNAC in this study reaches to 100%.

The observed risk of malignancy for TBSRTC category II was 0%, for TBSRTC category IV 36.6% (pre-NIFTP era) and 13.3% (NIFTP era) and for TBSRTC category VI 100%. This falls in the range of values given by the revised 2017 Bethesda system.[5]

## CONCLUSION

FNAC is the valuable screening tool for classifying the thyroid lesions into 6 diagnostic categories with its prime ability to reliably distinguish benign and malignant lesions. This study showed the notable increase in diagnostic accuracy of FNAC in thyroid lesions and significant drop in risk of malignancy for Bethesda category IV lesions in NIFTP era vis-a-vis pre NIFTP era.

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