

# EVALUATION OF BETHESDA CATEGORY III AND IV FINE NEEDLE ASPIRATION CYTOLOGY WITH RESPECT TO HISTOPATHOLOGY.



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## INTRODUCTION:

- According to **GLOBOCAN 2018 data**, thyroid cancer ranked 9<sup>th</sup> according to the incidence, accounting for 3.1% of global cancer incidence. [1]
- Females are affected three times more than men, by thyroid disorders with global incidence of 10.2 per 100,000 population. [1]
- Thyroid fine needle aspiration (FNA) reporting is rendered under “The Bethesda system for reporting thyroid cytopathology”, which encompasses six broad categories based on cytological features. Bethesda categories II, V and VI are well established, and hence not subjected to any disagreement in terms of their malignancy rates. [2]
- Category III and category IV lesions belonging to the heterogeneous group including both non-neoplastic and neoplastic lesions, are having controversial data about the risk of malignancies, recurrence and clinical management of nodules in Bethesda categories III and IV, as the reported risks of malignancy vary significantly, from 10% to 30% to 25–40% (including noninvasive follicular thyroid neoplasm with papillary-like nuclear features [NIFTP]), respectively. [3] **Due to paucity in data in Eastern India region about outcome of nodules with category III and IV diagnosis, there is a need for research in this area by cyto-histopathology correlation.**

**AIMS AND OBJECTIVES:** To correlate Bethesda category III and IV of thyroid FNA with corresponding histopathology and thereby estimate the risk of malignancy.

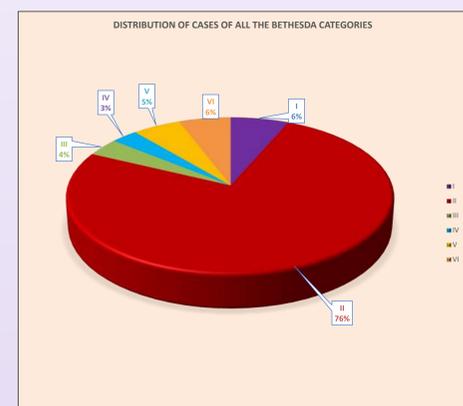
## MATERIAL AND METHODS:

- ❖ **Duration & type of study:** 30 months (January 2018–July 2020), Prospective, hospital based, cross sectional, observational study.
- ❖ **Type of study:** Prospective, hospital based, cross sectional, observational study.
- ❖ **Sample size:** 868 FNA of thyroid were carried out of which 194 patients underwent surgery and histopathology correlation was available.
- ❖ **Inclusion criteria:** All patients clinically suspected &/ or radiologically diagnosed with thyroid swelling who underwent FNA irrespective of age and gender with informed consent.
- ❖ **Exclusion criteria:** Patients who were critically ill/ non-cooperative/ known case of haemorrhagic diathesis.
- ❖ FNA were performed, the reporting was done under the Bethesda system for reporting thyroid cytopathology guidelines and correlation with histopathology done in operated cases.

## RESULTS & OBSERVATIONS :

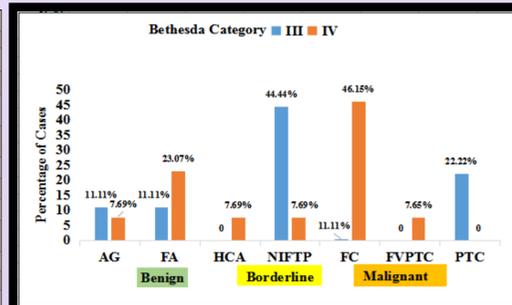
- Out of **868 thyroid FNAs**, 32 cases belonged to **category III** and 26 cases were under **category IV**. (Graph 1)
- Out of these **58 cases**, **Histopathology** analysis could be done in **22 cases** altogether (13 cases of category IV & 9 cases of category III). Out of these majority were malignant (10 cases), followed by benign entities (7 cases) and rest 5 cases had focus with features of NIFTP. (Table 2, Graph 2)
- Risk of malignancy were calculated based on histopathological analysis—33.33% for AUS/ FLUS (Bethesda category III) and 53.85% for FN/ SFN (Bethesda category IV) (Graph 3)
- Out of the total 22 cases in histopathology which were diagnosed under category III and category IV in cytology, all but 3 cases were correlated well.

**Graph 1: Distribution of cases under Bethesda thyroid FNA categories.**

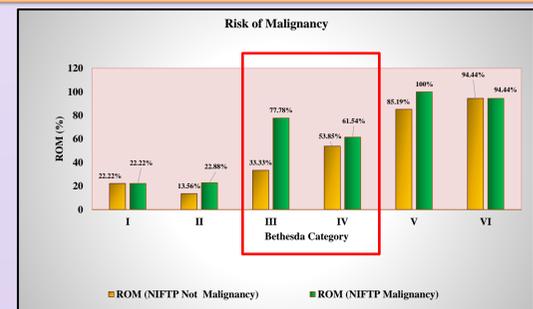


**Table 2, Graph 2: Analysis of Bethesda category III and IV with histopathology**

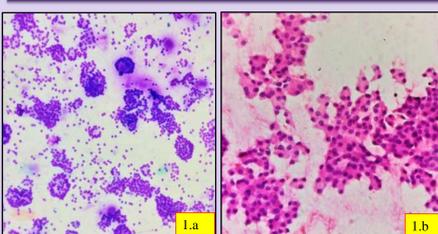
Histopathology categories	Bethesda Category	
	III	IV
<b>Benign</b>		
AG	1 (11.11%)	1 (7.69%)
FA	1 (11.11%)	3 (23.07%)
HCA	0	1 (7.69%)
<b>Borderline</b>		
FA with NIFTP	4 (44.44%)	1 (7.69%)
<b>Malignant</b>		
FC	1 (11.11%)	6 (46.15%)
FVPTC	0	1 (7.69%)
PTC	2 (22.22%)	0
<b>Total cases</b>	<b>9</b>	<b>13</b>



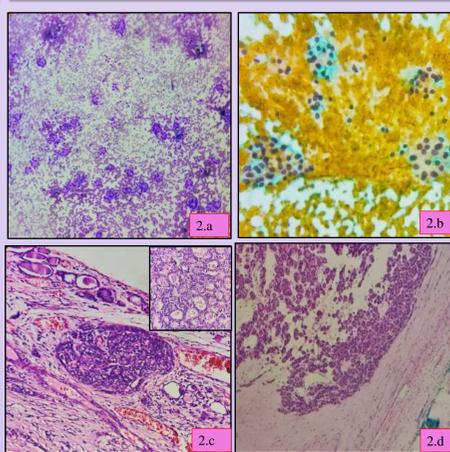
**Graph 3: Risk of malignancy of Bethesda categories in present study**



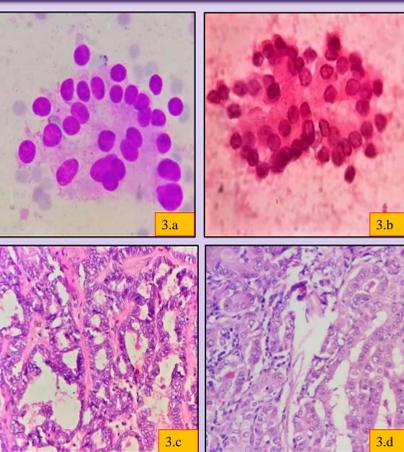
**Fig1: Bethesda IV & Follicular adenoma**



**Fig 2: Bethesda IV & Follicular carcinoma**



**Fig3: Bethesda III & classical PTC**



**Fig4: Bethesda III & NIFTP focus**

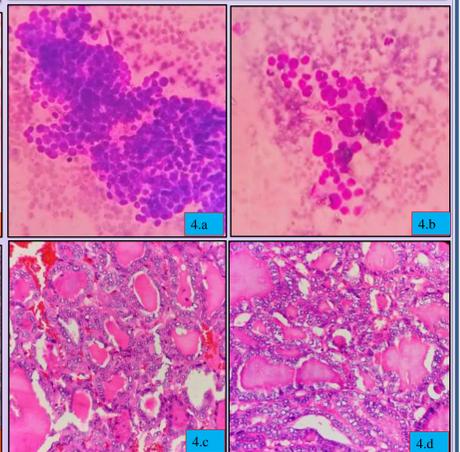


Figure 1: a- (Diff-Quik, 100x), b- (H&E, 100x), c- (PAP, 400x): Cytosmear shows features of Follicular neoplasm ( Bethesda category IV); d (H&E, 40x): closely packed follicles ( inset) in Follicular adenoma.

Figure 2: a- (Diff-Quik, 100x), b- (PAP, 400x): cytology of FN (Bethesda category IV), c ( H&E, 100x): Follicular carcinoma having LVI with neoplastic follicles (inset), d (H&E, 100x): Capsular invasion.

Figure 3: a- (Diff-Quik, 400x), b- (H&E, 400x) : Cytosmear showing follicular arrangement with mild nuclear atypia, with nuclei showing focal groundglass appearance and mild overlapping, nuclear grooving—AUS /Bethesda category III), c-d- (H&E, 400x): Features of papillary thyroid carcinoma, classical variant.

Figure 4: a (Diff-Quik, 400x), b- (H&E, 400x): Cytology of AUS/ FLUS (Bethesda category III), c-d- (H&E, 400x) Focus with NIFTP (score 3)

## DISCUSSION:

- The FN/ SFN category presents as the greatest uncertainty, as follicular carcinoma resemble as benign follicular neoplasms at individual cellular level, therefore limiting the ability of pathologist to accurately diagnose these nodules unless tissue demonstrates any vascular or capsular invasion.
- The Bethesda category III (AUS/ FLUS) includes in it a subset of lesions that are not easily classified as benign, suspicious or malignant.
- In the present study, out of 9 cases in Bethesda category III, majority of the cases has focus with features of NIFTP (4 cases), followed by malignant cases (3 cases) and 2 cases of benign entities. In a study by Konkay et al. out of 15 cases in category III, on histopathology correlation, malignant entities were slightly higher (8 cases) than that of benign (7 cases). [4]
- In this study, Bethesda category IV cases on histopathological correlation were found to be slightly more malignant (7 cases) comprising of mostly follicular carcinoma (6 cases) and single cases of Follicular variant of PTC, meanwhile the rest six cases were follicular adenoma ( 3 cases) and one case each of adenomatoid goiter, Hurthle cell adenoma and NIFTP. These findings were well correlated with study done by Konkay et al. which had 3 cases of category IV amongst which 2 cases turned out to be malignant on histopathology and third case was of nodular Hashimoto thyroiditis. [4]
- In the present study, there were total 20 cases which had focus with features of NIFTP, amongst which 20% were rendered as category III in cytology and 5% were rendered as category IV which was in close association with study conducted by Kim et al. where cytologic diagnoses of cases with NIFTP were majorly in category III (56%) and 8% in category IV. [5]
- Risk of malignancy were more in category IV than category III.

## Conclusion:

Bethesda category IV confers higher risk of malignancy than Bethesda category III. Correlation of the cytology with corresponding histopathology helps in determining the ROM and leads to different approaches in choosing the best therapies. The surgical specimens for which the cytology diagnosis is given in these two categories must be vigilantly grossed so as not to miss the suspicious foci and thereby rendering the correct histopathology diagnosis and instilling proper treatment to the patient.

## REFERENCES:

1. GLOBOCAN 2018
2. Bongiovanni M, Crippa S, Baloch Z, Piana S, Spitale A, Pagni F, Mazzucchelli L, Di Bella C, Faquin W. Comparison of 5-tiered and 6-tiered diagnostic systems for the reporting of thyroid cytopathology: a multi-institutional study. Cancer Cytopathol. 2012;120(2):117–25.
3. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009;19(11):1159–65
4. Konkay K, Kottu R, Yootla M, Hulikal N. Fine-needle aspiration cytology of nodular thyroid lesions: A 1-year experience of the thyroid cytopathology in a large regional and a University Hospital, with histological correlation. Thyroid Res Pract 2019;16(2):60.
5. Kim M, Kim JE, Kim HJ, Chung YR, Kwak Y, Park SY. Cytologic diagnosis of noninvasive follicular thyroid neoplasm with papillary-like nuclear features and its impact on the risk of malignancy in the Bethesda system for reporting thyroid cytopathology: An institutional experience. J Pathol Transl Med 2018;52(3):171–8.