Original Research Paper

Volume - 12 | Issue - 05 | May - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pathology

# THYROID CYTOPATHOLOGY REPORTING BY THE BETHESDA SYSTEM: A ONE-YEAR RETROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL IN NORTH EAST INDIA

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**ABSTRACT** **Background:** The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) established a standardized, category-based reporting system for thyroid fine-needle aspiration (FNA) specimens. It has high predictive value, reproducibility, and improved clinical significance. The aim of this study is to analyze the thyroid cytology smears by Bethesda system and to assess the frequency of various categories and to correlate it with previous published studies. **Method and Methodology:** A total of 358 thyroid FNAC samples were examined from January 2019 to December 2019 in the Department of Pathology, Gauhati Medical College. Smears made were both fixed in alcohol and stained by Papanicolaou stain or air dried and stained with Giemsa stain. The FNA smears were reviewed and categorized according to the Bethesda system. **Results:** The study included 285 cases of Benign, 3 cases of AUS, 21 cases of FN, 14 cases of SM, 27 cases of malignancy and 8 cases of ND. Both Benign and AUS are low-risk lesions with low probability of malignancy. FN predicts a higher rate for neoplasm but an intermediate rate for malignancy while SM carries a high risk for malignancy. **Conclusion:** The Bethesda System for reporting thyroid cytopathology proved to be an excellent reporting system and it puts clinician and the cytopathologist on the same page and easier to communicate regarding diagnosis.

**KEYWORDS :** Thyroid FNAC, Bethesda System, Thyroid cytopathology.

## INTRODUCTION

Thyroid nodules are common and may be found in up to 60% of the population. Fine-needle aspiration cytology (FNAC) of thyroid nodules has higher sensitivity and predictive value for diagnosis than any other single diagnostic method. It is a rapid, cost-effective, and very useful method in classifying thyroid nodules as either benign nodules, reducing unnecessary surgery, or malignant nodules requiring surgery. [1]

To achieve standardization of diagnostic terminology, morphologic criteria, and risk of malignancy for reporting of thyroid FNA in 2007, the National Cancer Institute (NCI) organized the NCI Thyroid Fine Needle Aspiration State of the Science Conference which proposed a 6-tier system and named it The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

The study aimed to evaluate the diagnostic utility and reproducibility of "The Bethesda System for Reporting Thyroid Cytopathology" at our institute. [2]

## METHODS AND METHODOLOGY

This was a retrospective study of all cases with thyroid swelling referred to the Department of Pathology, Gauhati Medical College and Hospital. All thyroid FNA smears received from January 2019 to December 2019 in the Department of Pathology, at our institute, were included in the study. Smears made were both fixed in alcohol and stained by Papanicolaou stain or air dried and stained with Giemsa stain.

The FNA smears were reviewed and categorized according to the Bethesda system. The categories under Bethesda System of reporting Thyroid Pathology are I—nondiagnostic, II—benign, III—atypia of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS), IV—follicular neoplasm (FN)/suspicious for follicular neoplasm (SFN), V—suspicious for malignancy (SM), and VI—malignant and the risk for malignancy were 1–4%, 0–3%, 5–15%, 15–30%, 60–75%, and 97–99%, respectively. [3] Statistical analysis were done using MS Excel Sheet and p value <0.05 taken as statistically significant.

## RESULTS

The study included 358 patients with complaints of thyroid swelling evaluated by FNA. The age group of the patients ranged from 8 to 90 years. The male: female ratio was 1: 4.9

**Table 1: Distribution of cases according to the BETHESDA system**

| Serial No | BETHESDA CATEGORY | No of cases | Percentage (n=100) |
|---|---|---|---|
| I | Nondiagnostic/ Unsatisfactory | 8 | 2.2% |
| II | Benign | 285 | 79.6% |
| III | Atypia of undetermined significance (AUS)/ Follicular lesion of undetermined significance (FLUS) | 3 | 0.8% |
| IV | Follicular neoplasm/ Suspicious for follicular neoplasm | 21 | 5.8% |
| V | Suspicious for malignancy (SFM) | 14 | 3.9% |
| VI | Malignant | 27 | 7.5% |
| | Total | 358 | |

In our study, out of 358 cases highest number of cases (79.6%) belonged to the benign category followed by the malignant category (7.5%)

**Table 2: Distribution of cases with respect to age**

| Age group | No of cases | Percentage (n=100) |
|---|---|---|
| 1-10 | 2 | 0.5% |
| 11-20 | 20 | 5.5% |
| 21-30 | 65 | 18.1% |
| 31-40 | 94 | 26.2% |
| 41-50 | 87 | 24.3% |
| 51-60 | 54 | 15% |
| 61-70 | 25 | 6.9% |
| 71-80 | 8 | 2.1% |
| 81-90 | 3 | 0.8% |
| Total | 358 | |

In our study, the highest number of cases (26.2%) belonged to the age group of 31-40 years.

**Table 3: Distribution of cases with respect to sex**

| SEX | No of cases | Percentage (n=100) |
|---|---|---|
| Male | 60 | 16.7% |
| Female | 298 | 83.2% |
| Total | 358 | |

**Table 4: Distribution of cases into various lesions**

| Type of lesion | No of cases | Percentage (n=100) |
|---|---|---|
| Non Neoplastic | 293 | 81.8% |
| Neoplastic | 27 | 7.5% |
| Indeterminate | 38 | 10.6% |
| Total | 358 | |

Non Neoplastic: Neoplastic= 10.8 : 1

**Table 5: Subdivision of Benign category (category ii)**

| Serial No | Category | No of cases | Percentage (n=100) |
|---|---|---|---|

| | | | |
|---|---|---|---|
| 1 | Colloid Goitre | 163 | 57.1% |
| 2 | Colloid Goitre with Hurthle cell change | 6 | 2.1% |
| 3 | Adenomatoid nodule | 35 | 12.2% |
| 4 | Multinodular Goitre | 2 | 0.7% |
| 5 | Primary hyperplasia of thyroid (Graves disease) | 1 | 0.3 |
| 6 | Goitre with secondary hyperplasia/ Hyperplastic thyroid disease | 11 | 3.8% |
| 7 | Lymphocytic/ Hashimoto's thyroiditis | 42 | 14.7% |
| 8 | Subacute/ Granulomatous thyroiditis | 25 | 8.7% |
| | **Total** | 285 | |

**Table 6: Subdivision of Neoplastic category**

| Serial No | Category | No of cases | Percentage (n=100) |
|---|---|---|---|
| 1 | PAPILLARY THYROID CARCINOMA | 19 | 39.5% |
| 2 | MEDULLARY THYROID CARCINOMA | 3 | 6.2% |
| 3 | ANAPLASTIC THYROID CARCINOMA | 3 | 6.2% |
| 4 | METASTATIC | 2 | 4.1% |
| 5 | FOLLICULAR NEOPLASM | 15 | 31.2% |
| 6 | HURTHLE CELL NEOPLASM | 3 | 6.2% |
| 7 | HYALINISING TRABECULAR ADENOMA | 3 | 6.2% |
| | **TOTAL** | 48 | |

**Table 7: Comparision of Non- neoplastic cytologic category with respect to age**

| Cytological category | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 81-90 |
|---|---|---|---|---|---|---|---|---|---|
| **Colloid Goitre** | 0 | 7 | 19 | 46 | 43 | 31 | 13 | 4 | 0 |
| **Colloid Goitre with Hurthle cell change** | 0 | 0 | 1 | 3 | 1 | 1 | 0 | 0 | 0 |
| **Adenomatoid Nodule** | 0 | 5 | 8 | 8 | 8 | 3 | 3 | 0 | 0 |
| **Multinodular Goitre** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| **Grave's Disease** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| **Goitre with secondary Hyperplastic Thyroid Disease** | 0 | 0 | 1 | 1 | 2 | 5 | 0 | 1 | 1 |
| **Lymphocytic Thyroiditis** | 1 | 4 | 15 | 8 | 7 | 4 | 2 | 1 | 0 |
| **Granulomatous Thyroiditis** | 0 | 5 | 3 | 8 | 5 | 3 | 1 | 0 | 0 |

The p value is <0.0001 which is statistically highly significant

**Table 8: Comparision of Neoplastic cytologic category with respect to age**

| Cytological category | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 81-90 |
|---|---|---|---|---|---|---|---|---|---|
| **Follicular neoplasm/Suspicious for follicular neoplasm** | 0 | 1 | 3 | 7 | 6 | 1 | 2 | 0 | 1 |
| **Suspicious for malignancy** | 0 | 0 | 4 | 6 | 2 | 1 | 1 | 0 | 0 |
| **PTC** | 0 | 0 | 5 | 5 | 4 | 3 | 1 | 1 | 0 |
| **MTC** | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 |
| **ATC** | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| **Metastatic** | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |

The p value is 0.27 which is statistically not significant

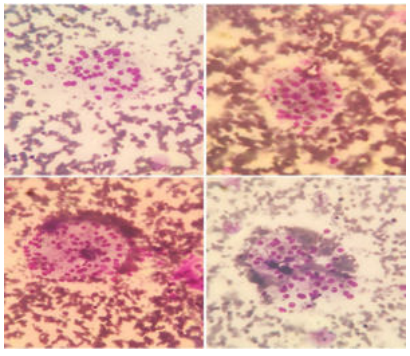


**Fig 1: Colloid Goitre**

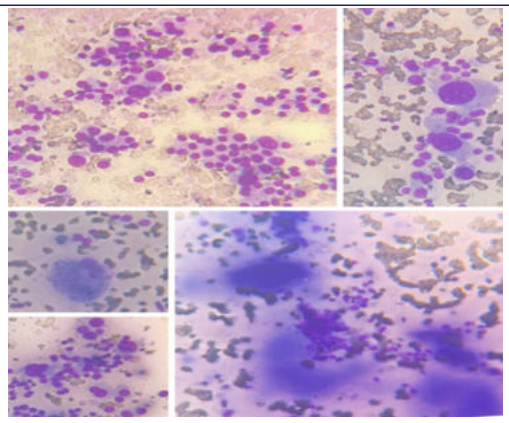


**Fig 2: Colloid Goitre with hyperplastic change**

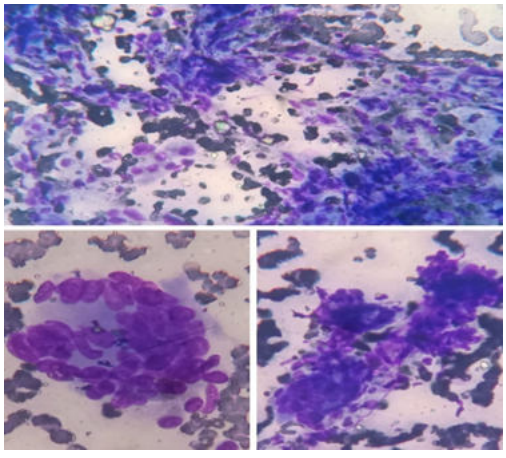


**Fig 3: Granulomatous Thyroiditis**

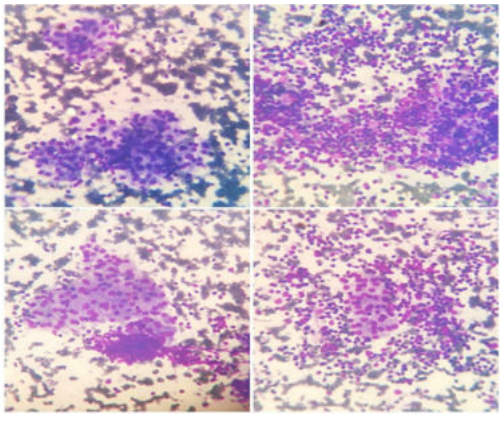


**Fig 4: Lymphocytic Thyroiditis**

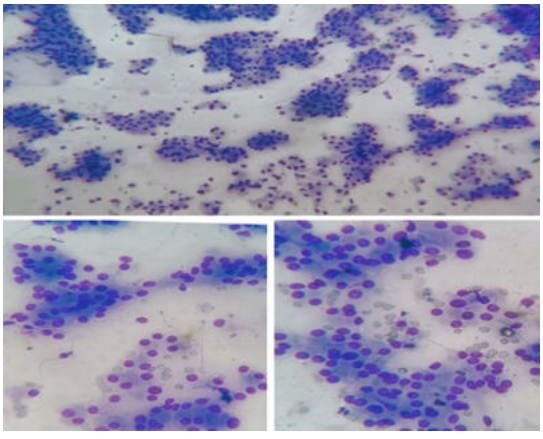
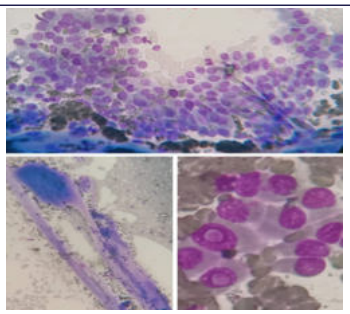


**Fig 5: Follicular Neoplasm**

(a)



(b)

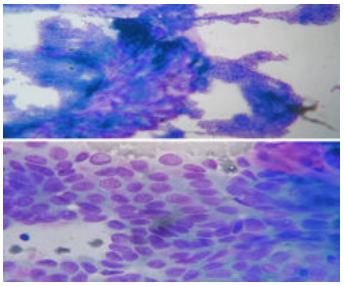


**Fig 6 (a,b): Papillary Thyroid Carcinoma**

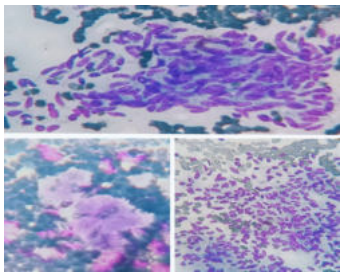


**Fig 7: Medullary Thyroid Carcinoma**

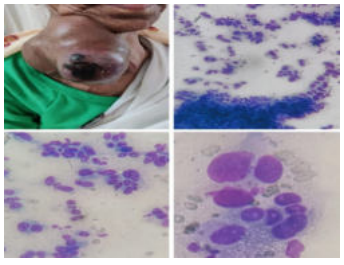


**Fig 8: Anaplastic Thyroid Carcinoma**

## DISCUSSION

The goal of thyroid FNA is to successfully differentiate benign from malignant lesions and to triage patients requiring surgery. The six-tired Bethesda system provides standardized nomenclature for reporting thyroid FNA smears which enables better communication and understanding between clinicians and pathologists. The advantage of this systematic approach is that each of the six Bethesda categories has implied risk of malignancy which helps the clinicians to plan appropriate therapy necessary for the patient. [4]

This paper shows the one-year experience in reporting thyroid aspirations by The Bethesda System of Reporting Thyroid Cytopathology in North East India. The Bethesda System of Reporting Thyroid Cytopathology does not recommend surgery for Non Diagnostic, Benign and Atypia/ Follicular lesion of undetermined significance categories. In the Follicular Neoplasm/ Suspicious for Follicular Neoplasm, Suspicious for Malignancy and Malignant categories, excision of nodules or partial/complete Thyroidectomy was done in all cases as per The Bethesda System of Reporting Thyroid Cytopathology recommendations.

The present study had 8 (2.2%) cases in Non Diagnostic/ Unsatisfactory category which was matching with The Bethesda System of Reporting Thyroid Cytopathology consensus. The clinical management plan for non-diagnostic cases is a repeat FNA with ultrasound guidance, which is mostly diagnostic. However, for persistently non-diagnostic cases, a limited excision is recommended. [5] All of the cases in our study were advised to be reaspirated after a minimum period of 3 months. The 3-month interval was recommended to prevent false positive interpretations due to reactive or reparative changes.

The benign category in our study had 285 cases (79.6%) with colloid goitre being the predominant group followed by Lymphocytic Thyroiditis. This was quiet similar with the study done by Anand Kumar Verma et al 80%. [6] The recommended treatment for this category is follow up but few patients from our study underwent surgery due to cosmetic and pressure symptoms.

The classification of "indeterminate" lesions (those not clearly benign or malignant) in thyroid cytopathology has long been a source of confusion for both pathologists and clinicians. The general category AUS/FLUS is reserved for specimens that contained cells (follicular, lymphoid, or other) with architectural and/or nuclear atypia that is not sufficient to be classified as suspicious for a follicular neoplasm or suspicious for malignancy. The atypia is more marked than can be ascribed confidently to benign changes. [6] We had 3 cases (0.8%) in group Atypia of Undetermined significance (AUS)/ Follicular lesion of Undetermined Significance (FLUS) which was close with the study done by Bakiarathana Anand et al (1.2%). [7] The recommended management for an initial AUS/FLUS interpretation is the clinical correlation and, for most cases, a repeat FNA at an appropriate interval. A repeat FNA usually results in a more definitive interpretation.

Follicular Neoplasm/ Suspicious for Follicular Neoplasm category had 21 cases (5.8%) with subcategory Follicular neoplasm cases being 15, Hurthle cells neoplasm cases being 3 and Hyalinising Trabecular Adenoma cases being 3 respectively. The meta-analysis done by Bongiovanni M et al showed that the percentage of cases classified into this category ranged from 1.2% to 25.3% with an overall value of 10.1%. [8] This difference can be due to geographical variation and loss of follow up of patients. Usual management option includes Lobectomy. The drawback of FNAC is that capsular or vascular invasion cannot be known in this category and thus we cannot categorise into adenoma or carcinoma.

Suspicious for Malignancy category had 14 cases (3.9%), 9 of which were suspicious for Papillary carcinoma, 2 was suspicious for Medullary carcinoma, 2 was suspicious for Anaplastic carcinoma and 1 Metastatic. The meta-analysis done by Bongiovanni M et al showed FNA cases in this category ranged from 1.4% to 6.3% with an overall value of 2.7%. [8] Committee V of the NCI Thyroid Fine Needle Aspiration State of the Science Conference has provided guidelines for indications of ancillary studies, specific ancillary studies to be performed, and sample preparation for each study. Immuno histochemistry panels have been suggested for suspicious malignancies which include Medullary carcinoma (calcitonin, thyroglobulin, CEA, and chromogranin), Anaplastic carcinoma (pan-cytokeratin), and Metastatic carcinoma (TTF-1). Dedicated passes are also needed for studies to detect genetic alterations such as BRAF mutation or RET/PTC chromosomal rearrangements, which are very promising for the diagnosis of papillary carcinoma. [6]

The reported rate of malignancy included in the meta analysis done by Bongiovanni M et al ranged from 2% to 16.2% with an overall value of 5.4% [8]. The present study had 27 (7.5%) cases in the malignant category, 19 of which were Papillary thyroid carcinoma, 3 were Medullary thyroid carcinoma and 3 were Anaplastic thyroid carcinoma and 2 were of Metastatic carcinoma respectively. The management option includes Total Thyroidectomy.

## CONCLUSION

Thyroid FNA smears reported using the Bethesda system helped in achieving more precise cytological diagnosis. The Bethesda system has an added advantage of predicting the risk of malignancy which enables the clinician to plan for follow-up or surgery and also the extent of surgery. [7]

The Bethesda System of Reporting Thyroid Cytopathology is a very useful standardized system that enhances the diagnostic accuracy of thyroid FNAC and improves the quality of reporting by decreasing the diagnostic discrepancies and leads to more consistency in management plans. [9] However further study with larger number of sample is recommended for more accuracy of the result.

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