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# Utility of Bethesda System for Reporting Thyroid Cytology - Five Year Experience in a Tertiary Cancer Centre

**Sangeetha K Nayanar*, MD[1], Manjusha P, MDS[2], Sajith Babu TV; MS (ENT)[3]**
[1]DNB (Pathology), Professor, Department of Oncopathology, Malabar Cancer Centre, (P.O) Moozhikkara, Thalassery, Kannur
[2](Oral Pathology), Fellow in Head & Neck Pathology, Division of Oncopathology, Malabar Cancer Centre, (P.O) Moozhikkara, Thalassery, Kannur
[3]Fellowship in Head & Neck Oncosurgery, Associate Professor, Department of Surgical Oncology, Malabar Cancer Centre, (P.O) Moozhikkara, Thalassery, Kannur

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***Corresponding author**
*Sangeetha K Nayanar*

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**Abstract:** The Bethesda system for reporting Thyroid Cytology (TBSRTC) is useful and reproducible classification system for nomenclature and risk stratification in thyroid lesions. This was the first consensus, systematic approach to Thyroid cytology which resulted in a uniform reporting format easy to be conveyed to the clinician. The aim of the study was to evaluate the utility of Bethesda system and the main objectives were to assess the incidence of the six Bethesda categories and to evaluate the concordance of FNAC reports with histopathology wherever available. This study analysed 403 cases of thyroid cytology for which FNAC was done in our centre during the five year period January 2012-December 2016 and categorised them into the six-tier Bethesda categories. The six categories were as follows Non-diagnostic or unsatisfactory, Benign, Atypia of undetermined significance /follicular lesion of undetermined significance (AUS/FLUS), Follicular neoplasm or suspicious for follicular neoplasm, Suspicious for malignant and Malignant. A cytologic-histologic concordance was done wherever available. More than half the cases were benign (56%). Around 11% were non-satisfactory. The rate of malignancy was 14%. The most common malignancy was Papillary carcinoma. There was a slightly higher incidence of Anaplastic carcinoma in our series. The percentage of cases in the six categories was matching with the reported studies in literature. We noted that there was no overutilization of AUS/FLUS (category III) in our centre.
**Keywords:** Bethesda, thyroid, cytology, utility, malignancy.

## INTRODUCTION

Fine needle aspiration is the most relied on cost-effective technique for the initial rapid evaluation of nodules in the Thyroid gland. Terminologies used by cytopathologists world over in reporting thyroid lesions on FNA were multitude and often confusing to the Physician & Surgeon, leading to potential unwanted surgeries. There was a need for uniform classification and nomenclature of the different non-neoplastic and neoplastic lesions of the thyroid gland. In 2007, a Thyroid Fine Needle Aspiration State of the Art and Science Conference was organised by the National Cancer Institute in Bethesda, Maryland. The meeting addressed the inconsistencies in categorising Thyroid disease and formulated a six tier system with an associated risk of malignancy for each tier, translating directly into clinical management guidelines. This was the first consensus, systematic approach to thyroid cytology which resulted in a uniform reporting format, easy to be conveyed to the clinician. The aim of the study was to evaluate the utility of Bethesda system for reporting thyroid cytology. The main objectives were to assess the incidence of the six Bethesda categories and to evaluate the concordance of FNAC reports with histopathology, wherever available.

## MATERIALS & METHODS

The study design was retrospective and descriptive and the study sample were a total of 403 cases for which FNAC was done in our centre during the five year period January 2012-December 2016. FNA was performed by the Pathologist in OPD and both air dried and alcohol fixed smears were taken and stained by Giemsa & Papanicolau methods respectively. The lesions were reported according to the six tier Bethesda system 2007 (Table-1). Histopathology reports were assessed for those patients where

thyroidectomies were performed and the cytologic-histologic concordance was evaluated.

**Table-1: TBSRTC-recommended diagnostic categories**

| | | |
|---|---|---|
| I | Non-diagnostic or unsatisfactory | *cyst fluid only<br>*acellular specimen<br>*others (obscuring blood clot etc) |
| II | Benign | *Consistent with a benign follicular nodule (includes adenomatous/colloid nodule)<br>* Consistent with lymphocytic (Hashimoto's) thyroiditis in the proper clinical context<br>* Consistent with granulomatous (subacute) thyroiditis |
| III | Atypia of undetermined significance /follicular lesion of undetermined significance | |
| IV | Follicular neoplasm or suspicious for follicular neoplasm | Specify if Hurthle cell(oncocytic )type |
| V | Suspicious for malignant | *Suspicious for papillary carcinoma<br>* Suspicious for medullary carcinoma<br>* Suspicious for metastatic carcinoma<br>* Suspicious for lymphoma |
| VI | Malignant | *Papillary carcinoma<br>*Poorly differentiated(insular)carcinoma<br>*Medullary carcinoma<br>*Undifferentiated(anaplastic) carcinoma<br>*Squamous cell carcinoma<br>*Carcinoma with mixed features(specify)<br>*Metastatic carcinoma<br>*NHL<br>*Others |

**Table-2: BSRTC: implied risk of malignancy and recommended clinical management**

| **Diagnostic category** | **Malignancy risk (%)** | **Usual management** |
|---|---|---|
| Non-diagnostic or unsatisfactory | 1-4 | Repeat FNA with ultrasound guidance |
| Benign | 0-3 | Clinical follow up |
| Atypia of undetermined significance /follicular lesion of undetermined significance | 5-15 | Repeat FNA |
| Follicular neoplasm or suspicious for follicular neoplasm | 15-30 | Surgical lobetomy |
| Suspicious for malignant | 60-75 | Near-total Thyroidectomy or surgical lobectomy |
| Malignant | 97-99 | Near-total Thyroidectomy |

**RESULTS**

Of the total 403, the number of cases under the six categories is given in Table 3. Over half (56 %) were in the Bethesda category II (benign) of which the majority were colloid goitre and the rest were Thyroiditis. Among the cases of Thyroiditis, 17 were Lymphocytic with the remaining three being granulomatous& Hashimoto respectively. Around 13 (3%) were reported as category III (atypia/follicular lesion of undetermined significance)

Of the 41 cases in category IV (follicular neoplasm or suspicious for follicular neoplasm), surgery was done in 34 and the final histopathologic diagnosis is given in Table 4. Total of 80(20%) cases were categorised as malignant (55,14%) and as suspicious for malignancy(25,6%).

The subtypes of thyroid carcinoma reported in Bethesda categories V and VI are given in Table 5. Papillary thyroid carcinoma (PTC) was the most common form of thyroid cancer among the study population (37, 9.5%) followed by of follicular thyroid carcinoma (3.5% ).

**Table-3: Bethesda categories I-VI of study cases**

| | Bethesda categories | N | % |
|---|---|---|---|
| I | Non-diagnostic or unsatisfactory | 45 | 11 |
| II | Benign | 224 | 56 |
| III | Atypia of undetermined significance /follicular lesion of undetermined significance | 13 | 3 |
| IV | Follicular neoplasm or suspicious for follicular neoplasm | 41 | 10 |
| V | Suspicious for malignant | 25 | 6 |
| VI | Malignant | 55 | 14 |

**Table-4**: **Histologic subtype of Bethesda category IV**

| Histopathology | N |
|---|---|
| Colloid goitre | 4 |
| Follicular adenoma | 11 |
| Follicular carcinoma | 14 |
| Follicular variant of Papillary carcinoma | 5 |

**Table-5: Subtypes of thyroid carcinoma reported in Bethesda categories V and VI**

| Subtypes of thyroid carcinoma | N | % |
|---|---|---|
| Papillary carcinoma | 37 | 9.5 |
| Follicular carcinoma | 14 | 3.5 |
| Anaplastic carcinoma | 13 | 3.25 |
| Insular carcinoma | 12 | 3 |
| Medullary carcinoma | 2 | 0.5 |
| Metastatic carcinoma | 2 | 0.5 |

## DISCUSSION

Thyroid nodules are a common clinical scenario and FNA alongside an ultrasound is often the investigation of choice. The implementation of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has standardized nomenclature and categorised thyroid disease into six categories as well as provided its implied risk of malignancy as shown in Tables 1 & 2. Several studies have reported on the efficacy of TBSRTC in generating easily reproducible and clinically meaningful categories of thyroid disease. Using TBSRTC criteria, most thyroid nodules can effectively be organised as either benign or malignant and referred for definitive management without further testing. It was seen that the routine use of TBSRTC has been helpful in effective screening for thyroid lesions [1-3]

In our study, 11% (n 45)were reported as category I (non-diagnostic or unsatisfactory) and 56% (n 224) as category II (benign).The categories I & II patients were predominantly undergoing treatment for visceral malignancies in our centre with the thyroid nodule being noticed incidentally. Around seven cases of category I returned for a repeat FNAC and were re-categorised as II. Others showed mainly degenerated fluid material implying cystic lesions.

Majority of category II were colloid goitres with rest being Thyroiditis. A meta-analysis by Bongiovanni et al showed the cases in this category ranged from 39% to 73.8% [4]. These patients are generally followed by clinical and radiological examination periodically with a repeat FNA if there is any enlargement of the nodule.

Around 3% of our cases were categorised as III i.e- atypia of undetermined significance/ follicular lesion of undetermined significance (n 13).The main criteria for labelling a smear as III was the presence of nucleomegaly, sometimes focally and the presence of a follicular pattern. A study by Ohori & Schoedel where the review of AUS/FLUS category showed a wide variation in frequencies ranging from 0.7% to 18% [5]. Other studies have reported that there is an increase in usage of this category more than recommended. This points to the fallacies of inter-observer variation. Mathew T Olson and Syed Z Ali inferred that a finding of “nuclear atypia” co notated a higher risk of malignancy than other cytologic types of AUS atypia [6]. A recent update suggests that this category can serve as a key parameter for quality control and a regular monitoring of the rate of AUS/FLUS in the laboratory can check its over usage [7].

The criteria prescribed for reporting under TBSRTC category IV are significant alteration in the follicular cell architecture, characterized by cell crowding, micro follicles, dispersed isolated cells and scant or absent colloid [7]. In our study, among the Bethesda IV category histopathology reports of thyroidectomies were available in 34 out of 41.The histologic breakup of the remaining can be seen in Table 4. The predominant type was Follicular carcinomas (14, 34%). According to literature around

15-30% of cases called Bethesda IV finally prove to be malignant.

Our study showed total of 25 cases (6%) in category V(suspicious for malignant) and 55 cases (14%) in Bethesda category VI (malignant).The commonest type reported in both categories combined was Papillary thyroid carcinoma (37, 9.5%) as depicted in Table-5. The reported rate of malignancy in a meta-analysis ranged from 2% to 16.2% with an overall of 5.4% and a risk of malignancy of 98.6% [4].

Literature review shows that 80 % of thyroid malignancies are Papillary carcinomas [9]. The management option in such cases is Near Total Thyroidectomy. Data on histologic concordance was only available in twelve cases of Papillary carcinomas and two cases of Medullary carcinomas. Among PTC, the encapsulated follicular variant which has recently been designated as non-invasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP) has been shown to have overlapping nuclear features with invasive follicular variant of PTC and therefore cannot be reliably diagnosed on cytology. It is hence recommended to consider this diagnosis in indeterminate cases of thyroid cytology [10].

We found that the incidence of Anaplastic carcinoma was slightly high (3.25%) in our centre compared to few other reports. Anaplastic carcinoma was diagnosed primarily and conclusively on cytology.

A nationwide multicenter survey by the Korean Society of Endocrine Pathologists from 42,132 cases of 16 institutes showed a mean distribution of six categories as follows: 11.1% non-diagnostic, 62.3% benign, 9.7% AUS, 0.9% FN, 6.7% SM, and 9.1% malignancy [1].

In a study by Arul et al, of total 603 FNACs, 16 (2.7%) were non-diagnostic, benign were 393 (65.2%), AUS/FLUS were 60 (10%), FN/SFN were 64 (10.6%), suspicious for malignancy (SM) were 32 (5.3%), and malignant were 38 (6.3%) [8].

Results of a study recounting the Australian experience with 2076 thyroid nodules in 1410 patients were as follows: 266 (12.8%) non-diagnostic, 1551 (74.7%) benign, 97 (4.7%) AUS/FLUS, 98 (4.7%) FN/SFN, 16 (0.8%) suspicious for malignancy and 48 (2.3%) malignant [11].

There has been a popular opinion that a risk based stratification based on clinical, radiological and molecular aspects should be the new line of approach in thyroid disease [7]. An international panel composed of sixteen cyto-pathologists and endocrinologists with special interest in thyroid cytology, including several co-authors of the 2010 TBSRTC Atlas, was created to analyze the current worldwide impact of TBSRTC, to report on the current state of TBSRTC based upon a review of the published literature, and to provide possible recommendations for a future update of TBSRTC. They evaluated that TBSRTC is a huge success for its distinct categorisation which is clinically relevant and for the clarity of communication afforded. Latest molecular advances and American Thyroid Association 2015 guidelines has been incorporated as modifications to the existing system. The key recommendations are included in the TBRSTC II to be published in 2018 [12, 13].

## CONCLUSION

In our study we have found that the Bethesda system for reporting Thyroid Cytology (TBSRTC) is useful, reproducible and guides the clinician towards definitive management plans it allows for ease in efficient communication as well as decision making in management. The rate of AUS/FLUS in our centre was comparatively on the lower side of published ranges thereby suggesting that there has been no overuse of this Bethesda category. The malignancy values reported in our centre were comparable with the results of other published data.

## ACKNOWLEDGEMENTS

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