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Original Research Article

Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in Cat III, IV, V Cases: Validating at a Tertiary Care Centre

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Abstract

Background: The introduction of the Bethesda System of Reporting Thyroid Cytopathology (TBSRTC) represents a major step towards reproducibility, standardization, and greater predictive value of thyroid fine needle aspirates (FNAs).

Materials and Methods: We retrospectively reviewed thyroid FNAs between June 2019 and June 2022, classified them according to the Bethesda System of reporting, found out the distribution of cases in the indeterminate categories III, IV and V, as well as calculated the risk of malignancy (ROM) in each of these categories by follow-up histopathology.

Results: Of the 250 FNA thyroid aspirates, the distribution of Cat III AUS /FLUS (Atypia/follicular lesion of undermined significance) and Cat IV FN/SFN (follicular neoplasm/suspicion for a follicular neoplasm) were 94 cases (38%) and 125 cases (50%) respectively. Cat V SM (suspicious for malignancy) constituted to 31 cases (12%). Risk of malignancy reported on follow-up HPE were AUS/FLUS 9.5%, SFN 26% and SM 78%. The Sensitivity, specificity, positive predictive value and negative predictive value in our study were 82%, 88%, 78% and 90% respectively. The Diagnostic accuracy was found to be 86%.

Conclusion: Surgical follow-up in all indeterminate categories (III&IV) is mandatory to appropriately assess the risk of malignancy associated. NIFTP (Non-Invasive Follicular Thyroid neoplasm with Papillary-like nuclear features) reduced ROM in each of the Bethesda category III, IV and V in our study. Hence, individual institutions need to adjust the cytological criteria based on the occurrence of NIFTP. The high specificity and diagnostic accuracy found in our study recommends TBSRTC to be an effective thyroid FNA classification and provides the clinicians with comprehensible cytopathology reports.

Keywords: Bethesda System of Reporting Thyroid Cytopathology, Risk of Malignancy, Fine-Needle Aspiration.

Introduction

Thyroid nodules are a very common clinical problem encountered by surgeons and pathologists throughout the world [1]. They are seen in about 8.5% of the Indian population. [2] For the initial evaluation of patients with thyroid nodules, FNA has proven to be a cost-effective, rapid, safe and reliable method of investigation. [3,4] FNA plays an instrumental role in the evaluation and workup of thyroid nodules by aiding in the rational triage of patients to surgery or follow up observation [5-7].

In 2007, a conference with one of the objectives being to unify and standardize the diagnostic terminology for the reporting of thyroid cytopathology results was held in Bethesda, Md [8-10]. The recommendations resulting from this conference led to the formation of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). [2,5] It defines the reporting system into 6 different diagnostic criteria with each having different risk of malignancy (ROM) [11,12].

The difficulty in defining the exact diagnosis of thyroid nodules is mainly due to the fact that the probability of malignancy in AUS(Atypia of Undetermined Significance)/FLUS (Follicular Lesion of Undetermined Significance) in FNAC remains unclear [13,14]. The risk of malignancy from Cat III/IV/V with the precise incidence remains variable among different institutions. [7,8] The recent Bethesda reclassification of some thyroid neoplasms as NIFTP (Non-Invasive Follicular Thyroid neoplasm with Papillary-like nuclear features) has impact on the risk of malignancy in each of the Bethesda categories [15].

We performed our study with the aim of validating TBSRTC and to ascertain the risk of malignancy in Bethesda indeterminate categories III, IV, V in our institution.

Materials and Methods

This is a Descriptive Cross-sectional study conducted jointly at the Department of Pathology, ENT and Surgery at Karpagam Faculty of Medical Sciences and Research (KFMS&R), Coimbatore. The study was conducted over a period of 3 years from June 2019 – June 2022. The Study Population included patients with thyroid nodules sent for FNAC with follow up thyroidectomy specimens received for histopathological examination. Cytohistological correlation was done for 250 cases. For FNA, cases were assessed by physical examination and smears were alcohol-fixed, stained with Hematoxylin & Eosin and reporting done based on TBSRTC.

TBSRTC-Cytological Classification:

- I-Non-diagnostic
- II-Benign
- III-Atypia/follicular lesion of undermined significance
- IV-follicular neoplasm/suspicion for a follicular neoplasm
- V-suspicious for malignancy
- VI-malignant

To determine the specificity, sensitivity, positive predictive and negative predictive value of FNAC, we set the following definitions:

- **True Positive:** Positive cases in FNA Bethesda reporting confirmed in HPE.
- **False Positive:** Nodules with cytological results of FN or suspicious for malignancy or malignant with benign diagnosis in the HPE.
- **True Negative:** nodules with benign FNA cytology and surgical pathology.
- **False Negative:** Cases reported as benign in FNA Bethesda that were found to be malignant on histopathology.

IBM SPSS software is used for statistical analysis of results.

Inclusion Criteria:

- FNA thyroid nodules reported as CAT III, IV, V as per TSBRTC.
- FNA cases with surgical follow up (thyroidectomy specimens).

Exclusion Criteria:

- FNA thyroid nodules reported as CAT I, VI as per TSBRTC.
- FNA thyroid cases where histopathological correlation is not available.

Results

A total of 250 FNA thyroid cases with follow up thyroid resection surgeries available were included. Our study showed female predominance of cases with the female to male ratio being 6.5:1. The age of the patients ranged from 21 to 80 years.

Distribution of cases according to TBSRTC:

Out of 250 cases, the distribution of Cat III AUS/FLUS and Cat IV FN/SFN were 94 cases (38%) and 125 cases (50%) respectively. Cat V constituted to 31 cases (12%).

Out of 94 Cat III cases, 9 turned out to be malignant in HPE and the risk of malignancy being 9.5%. Out of 105 Cat IV cases, 33 cases were diagnosed as malignant in histopathological examination with the risk of malignancy being 26%. A total of 51 cases were diagnosed under Cat V, of which 40 cases were histopathologically confirmed as malignant and the risk of malignancy was estimated as 78%.

Table 1: Distribution of FNAC cases as benign and malignant as per Bethesda Category

Bethesda Category	No. of cases-FNAC	Benign in HPE	Malignant in HPE
Cat III	94	85	9
Cat IV	105	72	33
Cat V	51	11	40
Total	250	168	82

Table 2: Final HPE report in each of the Bethesda Category:

Bethesda Category	MNG	Adenomatous goitre (Hyperplastic Nodule)	Follicular Adenoma/ Hurthle cell Adenoma	Follicular Carcinoma	Papillary Carcinoma	NIFTP	Thyroiditis	Total
III	44	24	5	0	9	3	8	94
IV	21	10	21	5	28	10	10	125
V	1	0	0	0	40	10	0	51

Table 3: Risk of Malignancy (ROM) in each Bethesda Category:

Bethesda Category in FNAC	ROM
III	9.5%
IV	26%
V	78%

The Sensitivity, specificity, positive predictive value and negative predictive value in our study were 82%, 88%, 78% and 90% respectively. The Diagnostic accuracy was found to be 86%.

Discussion

The 6-tiered Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) provides standardized nomenclature for reporting thyroid FNA smears in an effective approach for the diagnosis and management of thyroid nodules. [3,4].

The advantage of this systematic approach is that each Bethesda category has implied risk of malignancy which in turn helps the clinicians to plan the line of management appropriately4. Each category has an implied risk of malignancy ranging from 0%-3% for the benign category to 100% for the malignant category. [5]

The risk of malignancy in Bethesda category III found with our study was 9.6% which is less when compared to the studies by Leena P Naik et al6 (16.7%), 25% in the study done by Acharya et al1, 15.9% in the study conducted by Massimo Bongiovanni et al [3].

The risk of malignancy in Bethesda Category IV in our study was 32% which is in accordance with the studies conducted by Mondal et al [9] (30.6%), Her-Juing Wu et al [8] (22%) and Busra et al [13] (27.6%) but less when compared to the studies done by Acharya et al [1] (40%) and Nandedkar et al [7] (50%).

The risk of malignancy in category V in our study was 78% which is less when compared to Kaumudee et al [5] (100%) and Zarif et al [12] (95%) but in accordance with the studies done by Bongiovanni et al3 (75.2%) and Mondal et al [9] (75%).

The risk of malignancy being relatively low in category IV and V in our study can be attributed to the percentage of NIFTP(Non-Invasive Follicular Thyroid neoplasm with Papillary-like Nuclear features) cases in these categories.

Introduction of NIFTP influences pre-op thyroid FNA. The change in terminology of EFV-PTC as NIFTP could shift the ROM and impact the management algorithm associated with each Bethesda TBSRTC category. [16,17] The study conducted by Andrey Bychkov, Shipra Agarwal et al [17] states that if tumors designated as NIFTP were considered non-malignant, a significant decrease in ROM occurs which is similar to our study results [18].

Table 4: Comparison of Sensitivity specificity PPV NPV and diagnostic accuracy with various other studies

Parameters	Present study	Acharya et al[1]	Nandedkar et al[7]	Zarif et al[12]	Bongiovanni et al[3]
Sensitivity	82%	89.4%	85.7%	88.9%	97%
Specificity	88%	84.9%	98%	75.6%	51%
*PPV	78%	86%	90%	79.7%	56%
*NPV	90%	88%	98%	84.4%	96.3%
*DA	86%	87%	97%	81.5%	68.8%

PPV-Positive Predictive Value
NPV-Negative Predictive Value
DA- Diagnostic Accuracy

The discrepancy in sensitivity, specificity and PPV when compared to other studies may be attributed to the fact that our study was confined to only the indeterminate categories.

Conclusion

The high negative predictive value, specificity and diagnostic accuracy found in our study recommends TBSRTC to be an effective thyroid FNA classification to guide and triage patients for clinical

management in our practice. Surgical follow-up in all indeterminate categories (III&IV) is mandatory to appropriately assess the risk of malignancy associated. Also, the rate of occurrence of NIFTP reduces the risk of malignancy in each of the Bethesda category III,IV and V in our study. Hence, individual institutions need to adjust and refine the cytological criteria based on the occurrence of NIFTP. To conclude, this TBSRTC reporting system provides the clinicians with comprehensible cytopathology reports.

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