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The Bethesda System's Role in Enhancing Thyroid Cancer Diagnosis: A Cytohistological Analysis

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Introduction

Thyroid diseases are prevalent worldwide and accounts for approximately 42 million cases in India. Palpable thyroid nodules are about 4-7% in the middle-aged population and increase with age. FNAC is the first-line of investigation for evaluating the thyroid nodules. It is a quick, easy and cost effective test to differentiate benign from malignant thyroid lesions. Thyroid fine-needle aspiration cytology (FNAC) is essential for the initial evaluation and clinical management of thyroid nodules.

At present, most thyroid FNAC specimens are classified with The Bethesda System for Reporting Thyroid Cytopathology.

This scheme consists of 6 major diagnostic categories, each of which is associated with an implied risk of malignancy (ROM). The ROM represents a fundamental component of TBSRTC that influences subsequent clinical management decisions.

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced at the National Cancer Institute, (NCI) Bethesda, Maryland in 2007. This system categorized the FNAC of thyroid into six diagnostic groups with well-defined cancer risks and clear indications for further clinical management.

Bethesda system was introduced to overcome the ambiguity by introducing six categories to standardise the reporting and ensure uniformity of interpretation.

The study aimed to evaluate the diagnostic utility and reproducibility of "The Bethesda System for Reporting Thyroid Cytopathology".

Keywords: FNAC, Thyroid, Cytopathology, Sensitivity

Aims and Objectives

- To categorize the cytological pattern according to Bethesda System for Reporting Thyroid Cytopathology and correlate them with the histopathological diagnosis wherever possible.
- Calculate the sensitivity, specificity, diagnostic accuracy of thyroid lesions and also the risk of malignancy in each category.

Material and Method

Sample size: Evaluation of 116 consecutive thyroid fine-needle aspiration cytology smears and

thyroidectomy specimens received at Department of Pathology at our institute.

Study design: Retrospective study

Duration: Two-year period from January 2022 to 2024

Patient data, clinical history, investigations and ultrasound reports were retrieved from the requisition forms. Pre FNAC requirements such as informed consent and examination was done prior to the procedure.

Ultrasound guided FNAC was performed whenever necessary. FNAC was performed under aseptic precautions with 23 G needle by direct needling or 10cc syringe and the smears were prepared.

Rapid Onsite Evaluation was performed to determine the adequacy of the samples. Smears were fixed in 95% ethyl alcohol and stained with Haematoxylin-Eosin, Papaniculoau stain, while air-dried smears were stained with Leishman stain. Smears were evaluated by two pathologists and the cytological features were evaluated and the reporting was done according to The Bethesda System of Reporting Thyroid Cytology.

Histopathological specimens wherever available were processed as per standard methods.

Nodules with cytological results of Follicular neoplasm/suspicious for malignancy or malignant diagnosed benign on surgical excision were interpreted as false positive. False negative samples included cases with benign cytology that were found to be malignant upon histopathology. True negative cases were defined as nodules with benign FNA cytology and surgical pathology.

Follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, and malignant cases confirmed to be malignant upon final histology were considered true positive.

The diagnostic values (sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy) and risk of malignancy for FNAs using the Bethesda system were calculated for cases with surgical follow-up.

Result

The age of patients ranged from 20 to 90 years with a mean age of 46 years (SD 14.14) in the study.

The most prevalent age group undergoing thyroid fine needle aspiration in the study was between 30 to 40 years with 33(33%) patients.

Table 1: Age wise distribution of the lesions (N = 116)

Age in years	No of cases (%)
20-30 yrs	8(6.8%)
30-40yrs	33(28.4%)
40-50yrs	29(25%)
50-60yrs	27(23.2%)
60-70yrs	10 (8.6%)
70-80yrs	6(5.17%)
80-90yrs	3(2.5%)

- 5 were males, (4.3%) and 111 were females (95.6%).
- Male-to-Female ratio of 0.04:1.
- Palpable thyroid swelling of any lobe (diffuse or nodular) of both sexes and of any age, with and without USG guided FNAC were included
- The right sided and nodular lesions were more common

Table 2: Gender based distribution of thyroid lesions (n= 116)

Gender	No of cases	Percentage
Male	5	4.31%
Female	111	95.6%
Total	N= 116	100%

The right sided(32.7%) and nodular lesions were more common followed by left sided lesions(24%).

In this study, direct FNAC(90%) was performed more frequently than guided FNAC(11%).

Table 3: Distribution of cases according to the Bethesda system

Bethesda Category	Bethesda category percentage	FNA diagnosis	No of cases (N=116)	Percentage
I-Nondiagnostic	3	Cyst fluid Virtually acellular specimen Other (obscuring artefact, drying artifact, clotting artifact)	3 0 0	2.5 0 0
II—Benign	94	Adenomatoid nodule, colloid nodule Lymphocytic thyroiditis Granulomatous thyroiditis	62 32	53 27
III—Atypia of undetermined significance	1	Atypia of undetermined significance-nuclear atypia or AUS-other	1	0.8
IV—Follicular neoplasm	7	Oncocytic (Hurthle cell) type	7	6
V—suspicious for malignancy	7	Papillary carcinoma thyroid Medullary thyroid carcinoma Metastatic carcinoma Lymphoma	7 0 0 0	6 0 0 0
VI—Malignant	4	Papillary carcinoma thyroid High-grade follicular derived carcinoma Medullary thyroid carcinoma Undifferentiated (anaplastic) carcinoma Squamous cell carcinoma Carcinoma with mixed features Metastatic malignancy Non-Hodgkin lymphoma	3 0 0 1 0 0 0 0	2.5 0 0 0.8 0 0 0 0

Benign category was the largest (80%) followed by follicular neoplasm and suspicious for malignant category (7%).

Among benign category ,adenomatoid nodule(62%) was the commonest followed by lymphocytic thyroiditis(32%).

The most common malignancy was papillary carcinoma thyroid(2.5%) followed by anaplastic carcinoma(0.8%).

In the ND category, 3 cases were subcategorized as cyst fluid only. There was no cases in subcategory virtually acellular specimen or other (obscuring blood, clotting artifact, etc.).

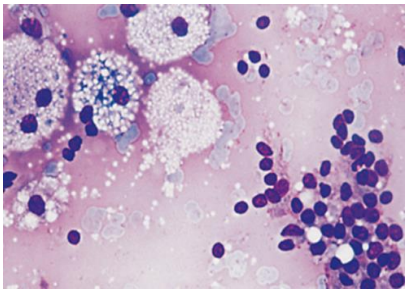

Figure 1: Nodular colloid goitre with cystic change (10x,H & E)

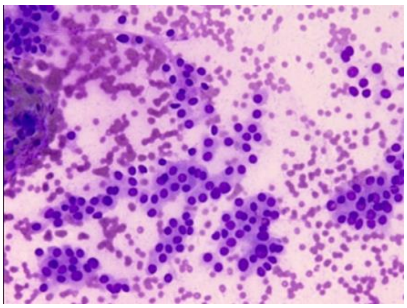

Figure 2: Follicular neoplasm (10x,H & E)

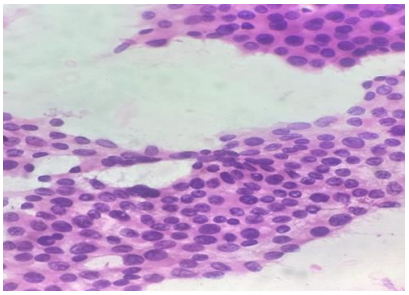

Figure 1: Papillary carcinoma thyroid (10 x, H&E)

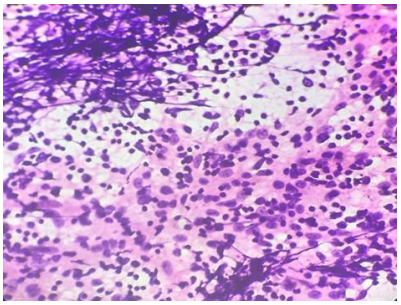

Figure 4: Lymphocytic thyroiditis (10 x, H & E)

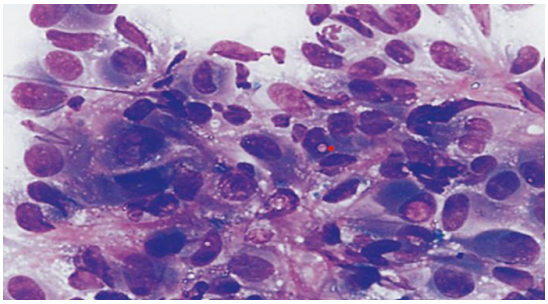

Figure 5: Anaplastic carcinoma thyroid , 40x

Table 4: Cytohistological correlation

Cytopathological categorization	Number of cases in cytopathology	No of cases received in histopathology	Benign	Malignant	Risk of malignancy (%)
I-Nondiagnostic	3	0	0	0	0
II—Benign	94	15	13	2	13
III—Atypia of undetermined significance	1	0	0	0	0
IV—Follicular neoplasm	7	0	0	0	0
V—suspicious for malignancy	7	2	0	2	100
VI—Malignant	4	2	0	2	100

Out of 116 cases that were cytologically studied, histopathological specimens of 19 cases were received and studied. In benign category,15 cases were received for histopathology ,in which 13 cases were diagnosed as benign and 2 cases were malignant with an implied risk of malignancy of 13%.

The two malignant cases were classic micropapillary carcinoma of thyroid and follicular variant of papillary carcinoma thyroid. Among benign cases, nodular colloid goitre with cystic change was the most frequently observed histopathological finding, occurring in 9 cases and remaining 3 were lymphocytic thyroiditis.

In malignant category, Papillary carcinoma thyroid was the most common malignancy (5%) followed by non invasive follicular thyroid neoplasm with papillary like features(1%). Risk of malignancy was assessed for 116 cases with surgical follow-up.

Histopathological correlation was available for 15 out of 94 cases in the category II, in which 2 turned out to be malignant with 13% ROM.

In category V, out of 7cases histopathological correlation was available for 2 cases and was confirmed to be malignant, leading to a 100% ROM .

For the category VI, 2 out of 4 cases had histopathological correlation, and the 2 were confirmed to be malignant, giving ROM of 100%.

Histopathological corelation were not available for the category I, III and IV thus preventing the assessment of the Risk of Malignancy.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 66%, 100%, 100%, and 86%, respectively.

The overall diagnostic accuracy was 89%, calculated using the formula (TP + TN) / (TP + TN + FP + FN).

Discussion

The six-tired Bethesda system provides standardized nomenclature for reporting thyroid FNA smears which enables better communication and understanding between clinicians and pathologists.

The goal of thyroid FNA is to successfully differentiate benign from malignant lesions and to triage patients requiring surgery.

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.

The age group of the patients ranged from 20 to 90 years with a mean of 46 years. The male: female ratio was 0.04: 1. In a study by Gupta et al the age group of the patients ranged from 7 to 85 years with a mean of 41.78 years and male: female ratio was 1: 6.3.

Table 5: Comparison of Our Study Values (in Percentage) with Findings from Other Studies

	Our study	Silverman et al	Gupta et al	Ko et al.
Sensitivity	66%	93	80	78.4
Specificity	100%	96.5	86.6	98.2
PPV	100%	88.9	80	99
NPV	86%	96.5	86.6	66.3

Table 6: Comparison of ROM in our study with other studies

Category	Present study	Mondal et al	Yassa et al
Non diagnostic	0%	0%	10%
Benign	13%	4.5%	0.3%
Atypia of undetermined significance	0%	20%	24%
Follicular neoplasm	0%	30.6%	28%
Suspicious for malignancy	100%	75%	60%
Malignant	100%	97.8%	97%

Conclusion

Thyroid FNA smears reported using the Bethesda system helped in achieving more precise cytological diagnosis. Our study substantiates greater reproducibility among pathologists using TBSRTC for reporting thyroid FNA.

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.

Limitation

- Benign and malignant lesions share overlapping features which makes it difficult for definitive diagnosis.
- Reliability of the study is compromised by the limited availability of histopathological correlation and pathological findings.

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