

## The Bethesda system for reporting thyroid cytopathology: a study of 143 patients; with its histopathological correlations in the region of Coimbatore

Kavitha Manoharan<sup>1</sup>, Leelavathy Ganesan<sup>2</sup>, Nithyananthin.V<sup>3</sup>

<sup>1</sup>Assistant Professor, Department of Pathology, Government medical college and ESI hospital. Tamilnadu , India

<sup>2</sup>Assistant Professor, Department of Pathology, Government medical college and ESI hospital. Tamilnadu , India

<sup>3</sup>Assistant Professor, Department of Pathology, Government Theni medical college and hospital. Tamilnadu, India

### Abstract:

**Context:** Fine needle aspiration cytology (FNAC), considered one of the initial diagnostic investigation and easily available screening tests in the evaluation of thyroid lesions. It can effectively categorise patients with neoplastic and non neoplastic thyroid nodules as whether they require surgery or not. The present study aims at classifying the thyroid fine needle aspirations based on the Bethesda system for reporting thyroid cytopathology and to compare the results with histopathology wherever surgery was done. And to evaluate the grey zone lesions of thyroid in FNAC and histopathology. **Methods and Material:** It is a cross-sectional hospital based study done in the department of pathology, Coimbatore medical college. In this study Fine needle aspiration of patients with thyroid lesions, who subsequently underwent thyroidectomy at our institution during the one year study period were included. In the study period, 143 cases of thyroid fine needle aspirations were collected and categorized according to the Bethesda system of reporting thyroid cytopathology, and it was correlated with the histopathological diagnosis. **Statistical analysis:** All the data were entered into Microsoft Excel 2010. Statistical analysis performed using SPSS version 20.0 (statistical package for social sciences). The sensitivity and specificity of The Bethesda system was 20% and 100 % respectively. The positive predictive value was 100% and the negative predictive value was 91.1%. **Conclusions:** A six tier TBSRTC effective in categorizing the thyroid lesions and determining which patients needed surgical treatment or follow –up. However there is a need of further clarity for diagnostic

### INTRODUCTION

Thyroid swelling is one of the commonest neck swelling patients presented with. Fine needle aspiration cytology (FNAC) plays a key role in the evaluation of thyroid swelling. FNAC is a minimally invasive, cost effective Out Patient procedure<sup>1</sup>. Accurate diagnosis is needed for management of the patients with thyroid nodules. FNAC has improved the diagnostic ability and avoidance of surgical treatment in patients with benign thyroid nodular diseases<sup>2</sup>. The various classification schemes adopted by different societies and suggested by several authors include the Papanicolaou Society of Cytopathology in the year 1997<sup>3</sup>, the American Thyroid Association (ATA) in the year 2006<sup>4</sup>

In the year 2007, standardized nomenclature established by National Cancer Institute (NCI) of United states for reporting thyroid fine needle aspirations cytology, which is known as “The Bethesda System of Reporting Thyroid Cytopathology(TBSRTC)”. The aim of this study to evaluating the utility and efficacy of FNAC and to correlate with histopathological pattern of various diseases of thyroid gland.

### MATERIAL and METHODS

This study was a one year cross sectional study conducted in the Department of Pathology of Coimbatore government Medical College Hospital, Coimbatore, Tamilnadu, India. Ethical approval for this study was provided by the Research Ethical Committee of Coimbatore Medical college hospital, Tamilnadu. Total of 143 cases of thyroid lesions where both FNAC and Histopathology was available for the study.

#### Inclusion Criteria

Fine needle aspiration of patients with thyroid lesions, who subsequently underwent thyroidectomy at our institution during the study period were included.

#### Exclusion Criteria

1. Fine needle aspirations of thyroid without further thyroidectomy
2. Thyroidectomy specimens without previous fine needle aspirations.

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Corresponding Author:  
Leelavathy Ganesan  
E-mail; leelavathy8060@gmail.com  
ORCID: 0009-0005-3800-6779  
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Bethesda system. FNAC smears are alcohol fixed and stained with Papanicolaou stain Thyroidectomy

specimens are fixed in 10% buffered formalin overnight. Appropriate bits are taken the next day. Processing was done with histokinete, paraffin blocks made, sections are cut with Leica microtome in 5 μ thickness. Sections are stained with Hematoxylin and Eosin stain and studied and histopathological diagnosis made.

**Statistical Analysis**

Microsoft Excel 2010 used for statistical analysis.. Statistical analysis performed using SPSS version 20.0 (statistical package for social sciences.

**RESULTS**

There were a total of 108 female patients and 35 male patients. The male to female ratio benign 1:3 of all thyroid lesions. Males comprised 24.47% and Females comprised 75.53% of the total cases. Most of the patients belonged to 4th decade 50 (35%), followed by 5th decade of life. Females predominance seen in all the age groups. On following Bethesda classification maximum number of patients belonged to group Category II (83.2%) followed by category IV,I,VI,V,III (9%, 3.5%, 2.1%, 2.1% and 0%) respectively. (Chart 1)

FNAC of thyroid lesions showed maximum number of benign cases belonging to 3rd and 4th decade. Malignant lesions were more common in the wide age group of 21-70 years. Female predominance noted in both malignant and benign category.

Histopathological diagnosis of various thyroid lesions, most cases were of Colloid goitre 72 (50.3%) followed by adenomatous goitre 23 (16.1%).In the malignant group most of the cases were of PTC 12 (8.4%) followed by follicular carcinoma 2 (1.4%).

FNAC and Histopathological correlation of thyroid lesions, out of 119 benign cases on FNAC, 4 cases (3.4% ) turned out to malignant on histopathology and out of 3 cases which were malignant on FNAC, all 3 cases confirmed as malignant in histopathology(Table 1). In our study, we don't have cases in category III, Out of the thirteen cases in

Category IV, 7 cases had non neoplastic diagnosis in histopathology, remaining six cases are malignancy comprised of 1 case of Follicular carcinoma, 1 case of primary lymphoma of thyroid- marginal zone type, and 3 cases of Papillary carcinoma, 1 case of Papillary carcinoma was follicular variant. Statistical analysis done. True positive, true negative, false positive and false negative results were obtained. From those values sensitivity, specificity, positive predictive value, negative predictive value were calculated.

Hence, we conclude the sensitivity and specificity of The Bethesda system was 20% and 100 % respectively. The positive predictive value was 100% and the negative predictive value was 91.1%. (Table II)

**Table 1:** Distribution of patients according to Category (N=143)

Bethesda Categories	Histopathology		Total
	Benign	malignant	
<b>Category I</b> (Non Diagnostic)	5	0	5
Category II (benign)	115	4	119
Category III(Atypia of undetermined significance/AUS)	0	0	0
Category IV(Suspicious of follicular neoplasm/SFN)	7	6	13
Category V (suspicious of malignancy)	1	2	3
Category VI (Malignant)	0	3	3

**Table 2:** 2 x 2 Contingency table comparing Bethesda system with Histopathology (N=138)

Bethesda system	Histopathology		Total
	Carcinoma	Benign	
Carcinoma	3 (TP)	0 (FP)	3
Benign	12 (FN)	123 (TN)	135
TOTAL	15	123	138

Sensitivity = TP/(TP+FN) - 20%

Specificity = TN/(TN+FP) - 100%

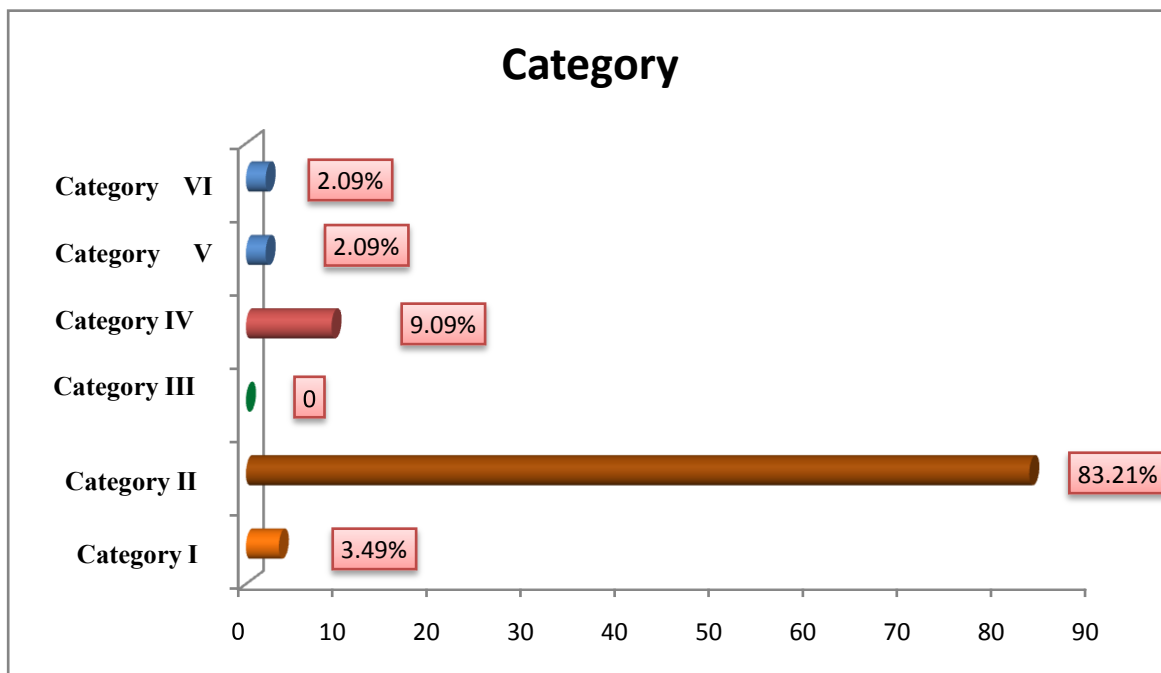
Positive Predictive Value = TP/(TP+FP)- 100%

**Table 3:** Comparison of incidence of Bethesda categories

Study	BethesdaI	BethesdaII	BethesdaIII	BethesdaIV	BethesdaV	BethesdaVI
Ji Hye Park et al	13.3%	40.6%	9.1%	0.4%	19.3%	17.3%
Vickie YJo et al	18.6%	59%	3.4%	9.7%	23%	7%
Mondolet al	1.2%	87.5%	1%	4.2%	1.4%	4.7%
Presentstudy	3.4%	83.21%	0%	9.1%	2.1%	2.1%

**Table 4:** Comparison of malignancy rates

Study	BethesdaI	BethesdaII	BethesdaIII	BethesdaIV	BethesdaV	BethesdaVI
Vickie YJo et al	8.9%	1.1%	17%	25.4%	70%	98.1%
Yassaet al	10%	0.3%	24%	28%	60%	97%
Mondol et al	0%	4.5%	20%	30.6%	75%	97.8%
Yang et al	10.9%	7.3%	13.5%	32.2%	64.7%	98.6%
Presentstudy	0%	3.4%	0%	46%	66%	100%



**Chart 1:** Percentage distribution of the sample according to Bethesda

**DISCUSSION**

A total of 143 cases of thyroid swelling aspirations followed by histopathological diagnosis were included in the study. The findings in cytology and histopathological were compared and scrutinized. Female to male ratio is 3:1. The age range was between 9-80 years with youngest and oldest patient being a case of colloid goitre. The highest number of cases were seen in the age group of 31-40 years (34.96%) followed by the age group of 41-50 years (27.27%). In our study thyroid lesions are more prevalent in females, and it was comparable with other studies (Naz et al<sup>5</sup>, Ji Hye Park et al<sup>6</sup>, Melo Cribe et al). In the study of Melo Cribe et al<sup>7</sup> the ratio of female to male ratio was higher.

**Fine Needle Aspiration Cytology**

In the Bethesda system of reporting thyroid FNAC on our 143 thyroid aspirates, which included Non- diagnostic (Category I) 5 cases (3.49%), Benign (Category II) 119 cases (83.21%), AUS (Category III) NIL cases, FN (Category IV) 13 cases (9.09%), SM (Category V) 3 cases (2.09%) and Malignant (Category VI) 3 cases (2.09%). Our study didn't correlate with the other studies conducted by Vickie Y Jo et al<sup>8</sup>, & Ji Hye Park et al<sup>9</sup>, because the category I lesions in our study were lower than the their studies (Table III). There were no lesions in category III in the present study. Her-Junig Wu H et al. (2011)<sup>10</sup> where they reported NonDiagnostic (20.1%), Benign (39%), AUS (27.2%), FN (8.4%), SM (2.6%) and Malignant (2.7%) on 1328 thyroid aspirates. This discrepancy can be explained because of huge difference in the sample size.

The incidence of malignancy rates according to the Bethesda

system(TBSRTC) for category II is 0-3%, category III is 5-15%, category IV is 15 -30%, category V is 60-75%, category VI is 97-99%. In our study the percentage of malignancies in each category

was in accordance to TBSRTC categories except category IV (Table III). In category IV, present study had higher incidence of malignancy (46%).

In this study out of 119 benign lesions of thyroid, colloid goitre was the most common lesion (58.8%). Papillary thyroid carcinoma was the most common malignant thyroid lesion (100%). Study done by Naggada H.A et al<sup>11</sup> (2006) and Fernandes H et al. (2009)<sup>12</sup> described nodular colloid goiter was the most common benign lesion, and Papillary thyroid carcinoma was the most common malignant neoplasm in thyroid.

**Cyto-histopathological correlation of thyroid lesions**

In the study Category IV had 13 cases, out of which 7 cases turned out to be benign in histopathology, among the remaining 6 cases, 4 cases were Papillary carcinoma, 1 case each of Follicular Carcinoma and Lymphoma.

Category V had 3 cases, among them one case was Multinodular goiter, one was follicular carcinoma and the remaining one was Follicular variant of Papillary carcinoma. Category VI had 3 cases of Papillary carcinoma and there was 100% histopathological correlation in the malignancy category (Table I).

Bakhos et al<sup>13</sup> (2000) observed 22 cases of false negative cases out of 543 cases of histopathological confirmation. They also quoted the commonest cause of false negative were cystic degeneration in papillary carcinoma. Settakorn et al<sup>14</sup> (2001) observed adenomatous goitre was misdiagnosed as follicular adenoma and vice versa.

Literature shows the false positive rates are 6 to 8%<sup>15</sup>. In our study it was nil. In this study the sensitivity and specificity of the Bethesda system(TBSRTC) was 20% and 100 % respectively. The positive predictive value was 100% and the negative predictive value was 91.1% (Table IV).

#### Grey- zone lesions

Baloch NM et al (2008)<sup>15</sup> described 40 patients of indeterminate follicular lesions on FNAC. Of these 8 were papillary thyroid carcinoma,13 patients had follicular variant of papillary, 4 had follicular carcinoma on histopathology. L.Foppiani et al (2003)<sup>16</sup> found no cancers in all the operated nodules with cytological diagnosis of FL .

Ohuri NP et al. (2010)<sup>17</sup> observed 117 cases of FL/AUS, 29.9% shows neoplastic outcome and 17.1% were carcinomas on histopathology.

In study, among 13 undetermined FNACs [nil AUS and 13 FL] on histological follow-up shows 53.84% had non neoplastic diagnosis (4 cases adenomatous goitre, 2 cases of Hashimoto's thyroiditis and 1 case of nodular goiter) and Remaining 46.16% were carcinoma (six cases comprised of 1 case of Follicular carcinoma, 1 case of primary lymphoma of thyroid- marginal zone type, and 4 cases of Papillary carcinoma. One case of Papillary carcinoma was follicular variant). In this study out of 3 suspicious for malignancy 2 (66.6%) were malignant on histopathology .<sup>[6]</sup>

#### CONCLUSION

Thyroid swellings are still an enigma to the surgeon and the pathologist. Diagnostic accuracy of cytopathology is proven by the present study with 100% specificity and 100% PPV. Thus, as a screening test before surgery, FNAC still needs to be followed as a routine procedure for successful patient management. Adequacy rate of the present study is 96%. This can be further enhanced by further imaging technique like ultrasound. Category I and II in the non neoplastic category of The Bethesda system have more accurate categorization index. Similarly category V and VI had precision in the diagnosis. This indicates that there are clearcut distinctions between the two ends of the spectrum of non neoplastic and neoplastic lesions. A six tier TBSRTC effective in categorizing the thyroid lesions and determining which patients needed surgical treatment or follow - up .However in our category III had no cases and category IV had high discordant rate. This suggest that there is need of further clarity for diagnostic categorization in this grey zone. It could be further refined by applying more advanced immunocytochemical and molecular genetic analysis to these patients falling in the grey zone. Further studies involving larger sample size and with specialized techniques is the need of the hour for patients with thyroid swelling .

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<sup>2</sup>Assistant Professor, Tuberculosis and Respiratory Disease, ASMC, Shahjahnpur, Uttar Pradesh, India