

# Incidence and Malignancy Rate of Bethesda Category III Thyroid Lesions in A Tertiary Hospital

Aneeshya Celes\* and Hilda Fernandes

Department of Pathology, Father Muller Medical College Mangalore

## ABSTRACT

**Background:** The introduction of The Bethesda System for Reporting Thyroid Cytopathology in 2010 provided the opportunity to establish worldwide standard reporting and terminology guidelines diagnostic category in reporting of thyroid FNAC. Indeterminate lesion included in the category III are those with insufficient degree of atypia to qualify for any of the suspicious categories. This study was conducted to determine the incidence and malignancy rate of Bethesda category III thyroid lesions.

**Methods:** A two- and half-year retrospective study was conducted in Father muller medical college. Thyroid lesion which were diagnosed as Bethesda category III on fine needle aspiration cytology during the study period were included. The cytology-histopathological correlation was done where ever available to calculate the incidence and malignancy rate of this category.

**Result:** A total of 1397 cases underwent thyroid FNA during the study period. Out of this, 57 cases were reported as Bethesda category III lesion. The incidence rate of Bethesda category III lesions in the study was 4.08%. Twenty-one cases had histopathology correlation. The malignancy rate was found to be 38.09%.

**Conclusion:** The Bethesda category III still remains a very challenging group with a large and varied range of diagnosis. The risk of malignancy might be higher that what is currently estimated for this category. Sub-classification of this category might help in predicting the nature of lesion better and aid patient management more accurately.

**Keywords:** *Thyroid, Bethesda System, Malignancy Rate*

## Introduction

FNAC is an important diagnostic tool for evaluation of thyroid nodules. It helps avoid unnecessary surgery for patient with benign nodules and conduct appropriate clinical intervention for malignant lesions. The introduction of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in 2010 provided the opportunity to establish worldwide standard reporting and terminology guidelines diagnostic category. Bethesda classification system gives six categories for thyroid lesions in order of increasing rate of malignancy.<sup>1</sup>

Indeterminate lesion which are not clearly benign or malignant has been a walk on the fence for both clinicians and pathologist. Hence, the category III which is labelled as “Atypia of undetermined significance” / “follicular lesion of undetermined significance” is for separating lesions with insufficient degree of atypia to qualify for any of the suspicious categories.<sup>2</sup>

Three to eighteen percentage of the thyroid FNACs come under the category of “AUS”. The risk of malignancy for this category is 5-15 %. Clinical correlation and a repeat FNAC at an appropriate interval is the usual management of this category lesions.<sup>2</sup> The risk of malignancy in this

category is difficult to assess as only few of these cases have a surgical follow up. This study was conducted to determine the incidence and malignancy rate of Bethesda category III lesions diagnosed in FNAC.

## Materials and Methods

A two- and half-year retrospective time bound study was conducted in the department of pathology, Father muller medical college from January 2017 to June 2019. All the thyroid lesion which were diagnosed during routine reporting as Bethesda category III on fine needle aspiration cytology during the time period were included in the study. Records of the cases were retrospectively reviewed and relevant clinicopathological data was extracted. The cytology diagnosis was correlated with histopathological outcome where ever available to calculate the incidence and malignancy rate of Bethesda category III lesions.

**Inclusion Criteria:** All the thyroid lesion which were diagnosed as Bethesda category III on fine needle aspiration cytology during the study period January 2017 to June 2019.

**Exclusion Criteria:** NIL

**Statistical Analysis:** Incidence and malignancy rate of thyroid lesions diagnosed as category III by Bethesda system in fine needle aspiration cytology.

## Result

A total of 1397 cases underwent thyroid FNA during the study period of two and half years. Out of this, 57 cases were reported as Bethesda category III lesion. The age wise distribution of the category III cases is given in Table no.1.

There was a female predominance noted with the male to female ratio being 0.18. A right lobe lesion was slightly more common followed by left lobe. The percentage of B/L lobes with lesion was 12.3%. The least common was isthmus with 5.3% of the cases. One case of category III lesion in the residual thyroid, post subtotal-thyroidectomy was also seen.

Maximum number of cases were in the age group of 41 to 50 years. Out of the 57 cases of category III lesions, 21 cases underwent surgery and histopathology specimen of these cases was available for correlation. Most common diagnosis in histopathology was adenomatous hyperplasia accounting to 28.6% (6 out of 21 cases). This was followed by 19% (4 out of 21) cases of papillary carcinoma and multinodular goitre each. The distribution of the histopathology diagnosis is given in the table 4. Two cases each of follicular carcinoma and papillary microcarcinoma was also seen.

The incidence rate of Bethesda category III lesions in the present study was calculated to be 4.08% (57 out of 1397 cases). The malignancy rate of Bethesda category III thyroid lesions in the study was found to be 38.09% (8 out of 21 cases).

**Table 1: Age wise distribution.**

Age group	Count	Percentage
11-20	2	3.5%
21-30	7	12.3%
31-40	7	12.3%
41-50	18	31.6%
51-60	11	19.3%
61-70	7	12.3%
71-80	4	7%
81-90	1	1.8%
<b>Total</b>	<b>57</b>	<b>100</b>

**Table 2: Sex wise distribution of cases.**

Gender	Count	Percentage
Female	48	84.2
Male	9	15.8
<b>Total</b>	<b>57</b>	<b>100</b>

**Table 3: Site wise distribution of cases.**

SITE	CASES	PERCENTAGE
Right lobe	24	42.10%
Left lobe	22	38.60%
Isthmus	3	5.30%
B/L lobes	7	12.30%
Residual thyroid	1	1.70%
<b>TOTAL</b>	<b>57</b>	<b>100.00%</b>

**Table 4: Distribution of histopathology diagnosis.**

Histology	Subcategory	Count	percentage
Adenomatous hyperplasia		6	28.6%
Follicular adenoma		1	4.8%
Follicular carcinoma		2	9.5%
Hashimoto		1	4.8%
MNG		4	19%
MNG with Hashimoto		1	4.8%
Papillary carcinoma	Classic	2	9.5%
	Follicular variant	1	4.8%
	Oncocytic	1	4.8%
Papillary microcarcinoma	With Hashimoto	1	4.8%
	With WDUMP	1	4.8%
<b>Total</b>		<b>21</b>	<b>100</b>

**Table 5: Comparison of malignancy rate with other studies in literature.**

Sr.No.	Study Name	Malignancy rate
1.	Present study	38.09%
2.	Guleria et a	35.8%
3.	Garg et al	33.3%
4.	Chandra et al	28.5%
5.	Ho et al	38.6%

## Discussion

The incidence of thyroid carcinoma has been on the higher side in the past few years with the annual rate of increase at 3% in the last 30 years in United states. <sup>(3)</sup> The increase is four times greater in women than in men. Many contemplate that there is true rise in carcinoma over the recent years while many believe that this rise is attributed to better diagnostic tests like ultrasonography and FNAC. <sup>(4)</sup> The diagnosis of thyroid lesions using aspiration cytology was first reported by Martin and Ellis in 1930. <sup>(5)</sup> Since then, FNAC has developed to be a safe, rapid and cost-effective tool in the evaluation of thyroid nodule. Since the introduction of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in 2007, there has been standardization of terminologies used in reporting of thyroid cytology. The Bethesda system used six categories for thyroid cytology reporting. Each category has a list of criteria which aids in making a diagnosis and has a defined range of implied cancer risk. <sup>(6)</sup> The category III in the Bethesda system is the "Atypia of undetermined significance/Follicular lesion of undetermined significance (AUS/FLUS) category and it accounts for 7-18 % of the thyroid diagnosis. <sup>(7)</sup> This category encompasses all specimen which contain cells with architectural and/or nuclear atypia that is not sufficient

to be classified as suspicious for follicular neoplasm, suspicious for malignancy, or malignant. The criteria for this diagnosis include predominant population of microfollicles, predominance of hurthle cells in a sparsely cellular aspirate with scant colloid, air drying artifact, clotting artifact hindering an interpretation of atypia, minor population of cells showing nuclear atypia, presence of atypical lymphoid infiltrate, focal features suggestive of papillary carcinoma etc. <sup>(2)</sup>

The present study showed a predominance of females with category III lesions and the most common age group being 51-60 years. This finding was similar to study done by Mosca et al and Ho et al. <sup>(8,9)</sup> The incidence of Bethesda category III lesion in the present study was 4.08% which was close to studies done by Chandra et al (6.4% ) and Garg et al (6.5 %) while other studies like Guleria et al and Ho et al show the incidence rate to be 11.7% and 8% respectively. <sup>(6,9,10,11)</sup>

On follow-up, histopathology correlation showed majority of the cases as benign ( 61.9%). The most common benign lesion encountered was adenomatous hyperplasia. This finding was consistent with the findings of studies done by Guleria et al, Ho et al and Garg et al. <sup>(9,10,11)</sup> The malignancy rate of Bethesda category III lesion was calculated to be

38.09% which was also comparable to studies done by Ho et al, Garg et al and Guleria et al. <sup>(9,10,11)</sup> The comparison with malignancy rates in other studies are given in table 5. The most common malignancy encountered was papillary carcinoma thyroid and the same was also found in the studies of Ho et al, Garg et al, Guleria et al and Chandra et al. <sup>(6,9,10,11)</sup>

The BSRTC has estimated the risk of malignancy to range from 5% to 15% in AUS/FLUS category and the usual recommended management is repeat FNA. <sup>(6)</sup> However, studies including the present and above-mentioned studies in table 5 have observed a higher malignancy rate in different clinical settings. Therefore, a reconsideration of the malignancy rate of Bethesda category III lesions may be recommended.

The higher malignancy rate in this category may also be due to inter-observer variability in the reporting of the FNAC as all the thyroid FNACs were not reported by a single cytopathologist.

Garg et al and Chandra et al also suggests that subclassifying the category III Lesions into different subgroups may help in reducing the heterogeneity of this category and help in predicting malignancy better which in turn contributes to better patient management. The subcategories used by Garg et al were AUS/FLUS – cannot exclude papillary thyroid carcinoma, AUS/FLUS – cannot exclude follicular neoplasm/Hurthle cell neoplasm, AUS/FLUS – favor benign, AUS/FLUS – not otherwise specified (NOS). <sup>(6,10)</sup>

## Conclusion

The Bethesda category III still remains a very challenging group with a large and varied range of diagnosis. The risk of malignancy might be higher than what is currently estimated for this category. Sub-classification of this category might help in predicting the nature of lesion better and aid patient management more accurately.

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None Declared

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### \*Corresponding author:

Dr. Aneeshya Celes, Father Muller Medical College, Fr Muller Road, Kankanady, Mangalore 575002 Karnataka, India

Email: [anceles@rediffmail.com](mailto:anceles@rediffmail.com)

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