Original Article

# Improving Bethesda Reporting in Thyroid Cytology: A Team Effort Goes a Long Way and Still Miles to Go…

**Subramanian Kannan, Nalini Raju[1], Vikram Kekatpure[2], Naveen Hedne Chandrasekhar[2], Vijay Pillai[2], A. Renuka Keshavamurthy[3], Moni Abraham Kuriakose[2], Pobbisetty Radhakrishnagupta Rekha[1], Nisheena Raghavan[1], Akhila Lakhsmikantha[1], Srinivas Ramaiah[1], Brijal Dave[1]**

Departments of Endocrinology, Diabetes and Bariatric Medicine, [1]Pathology, [2]Head and Neck Surgical Oncology and [3]Family Medicine, Narayana Health City, Bengaluru, Karnataka, India

## Abstract

**Context:** Fine-needle aspiration cytology is the first step in evaluation of thyroid nodules. Although the Bethesda classification for reporting thyroid cytology has been purported that this uniformity in reporting cytology thereby facilitating clinical decision-making, there are also studies indicating that the reporting percentage and the rates of malignancy in each category vary considerably from center to center making the clinical decision more difficult. **Aim and Materials and Methods:** We looked at our retrospective cytology and histopathology data of thyroid nodules operated between 2012 and 2014 and then prospectively collected data during 2015–2016. In the prospective arm, for every thyroid nodule that was sampled, there was a discussion between the endocrinologist and the cytopathologist on the risk of thyroid cancer (based on the patient's history, examination findings, sonographic pattern, and the cytological appearance). **Results:** We noted that there was considerable improvement in reporting standards with the rates of nondiagnostic cytology dropping from 11% to 5%, an increased reporting of Bethesda Category 2 and 6 which are the definitive strata of benign and malignant nodules (38% to 41% in Category 2 and 7% to 11% in Category 6) with a high specificity (100%). There was a decline in numbers of Category 4 and 5 (13% to 9% in Category 4 and 12% to 3% in Category 5). The reporting prevalence of Category 3 increased from 19% to 27%. **Conclusions:** We conclude that a team approach between the clinician who performs the ultrasound and the reporting cytopathologist improves Bethesda reporting, its predictive value, and thus potentially avoiding unnecessary thyroidectomies in benign thyroid nodules and hemithyroidectomies in thyroid cancers.

**Keywords:** Bethesda, malignancy, thyroid fine-needle aspiration cytology

## Introduction

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)[1] was introduced in 2007 in an attempt to standardize international terminology and to categorize morphological criteria in fine-needle aspirations (FNAs) from patients with thyroid nodules. TBSRTC establishes six diagnostic categories for FNA results and assigns a malignancy risk and recommendations for patient management for each category.[1] Global studies of the incorporation of TBSRTC in diagnostic algorithms for patients with thyroid nodules have concluded that TBSRTC reduces unnecessary thyroidectomies while also ensuring the quality of thyroid malignancy detection.[2] Thyroid surgery can be associated with multiple complications, such as postoperative thyroid hormone imbalance, hypoparathyroidism, recurrent laryngeal nerve injury, bleeding, or infection; thus, there has been an effort to limit unnecessary surgery in asymptomatic patients with benign lesions.[3] Although studies have concluded that the Bethesda criteria appropriately stratify malignancy risk in thyroid nodules,[4-7] controversy continues to exist regarding their accuracy and reliability in decision-making.[8-11] The reasons behind this controversy are variability in the prevalence of cancer in the population studied, the inherent variability in the interpretation of cytology, and bias in the patient selection for surgery.

### Aims

The aim of this study is to evaluate the risk stratification of Bethesda classification of patients who underwent thyroid

Access this article online

Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.IJEM_350_16

**Address for correspondence:** Dr. Subramanian Kannan, 258/A, Bommasandra Industrial Area, Hosur Road, Bengaluru - 560 099, Karnataka, India.
E-mail: subramanian.kannan@gmail.com



**How to cite this article:** Kannan S, Raju N, Kekatpure V, Chandrasekhar NH, Pillai V, Keshavamurthy AR, *et al*. Improving Bethesda reporting in thyroid cytology: A team effort goes a long way and still miles to go…. Indian J Endocr Metab 2017;21:277-81.

FNA at our institution in two arms: a retrospective arm from histopathology records of patients who had undergone thyroid surgery and a prospective arm where patients were evaluated by a single endocrinologist and if chosen to undergo thyroid surgery.

### Settings and design

This study was conducted with a retrospective arm (collection of data from hospital records) and a prospective cohort of consecutive patients who underwent fine-needle aspiration cytology (FNAC) by a single endocrinologist.

## Materials and Methods

### Retrospective arm

#### *Study site*

A retrospective registry review of the patients who underwent thyroid surgeries from January 2012 to December 2014 at Mazumdar Shaw Cancer Centre was performed, and details of final histopathology and prior FNA were collected.

#### *Study population and study design*

This is a retrospective review of patient records.

#### *Time frame*

This study was conducted from January 2012 to December 2014.

#### *Inclusion criteria*

Patients who had thyroid surgery at our institution and prior FNA of the thyroid nodule reported in Bethesda format are included in the study. Slides of FNA reports not conforming to the Bethesda format were reviewed by the author (NR) and reported in the Bethesda classification.

#### *Exclusion criteria*

Patients in whom the FNA was done outside or not reported in standardized Bethesda format (with no slides available for review) were excluded from the study. Patients who underwent thyroid surgery without prior thyroid nodule FNA were excluded from the study. Patients with multiple nodules and a lack of clarity from the report on the exact nodule that was sampled were excluded from the study. Patients with thyroid cancer diagnosis made from lymph node FNAC were also excluded from the study.

### Methods

Data were collected from medical and electronic records and tabulated in case program. Data of patient characteristics, nodule size and location, FNA method (ultrasound-guided versus blind), cytology, and their final pathology were collected. Incidental microscopic thyroid cancers (<1 cm) were not categorized as malignant, and the actual histology of the nodule that was biopsied was taken into account. Lesions described as follicular neoplasm of uncertain malignant potential were considered to be benign for study purpose.

### Prospective arm

- Study site: Department of Endocrinology, Head and Neck Surgical Oncology, Mazumdar Shaw Medical Center, Bengaluru
- Duration of study: January 2015 to April 2016
- Inclusion criteria: Patients with thyroid nodules who underwent sonography and FNAC by a single endocrinologist and depending on the results were either counseled on surgery or continued follow-up
- Exclusion criteria: Patients who underwent FNAC outside our institution.

### Intervention

A regular discussion between the endocrinologist and the cytopathologist took place in all the cases in the prospective arm, and the sonographic risk stratification of the thyroid nodule was provided to the cytopathologist.

### Approval

The study was approved by our hospital's Ethics Committee.

### Statistical analysis used

Continuous variables were reported in mean (standard deviation [SD]), median, and range. The reporting percentages of each Bethesda category and the percentage of malignancy in each category were calculated and compared with national studies. The results were compared using the two-sample *t*-test between percents (Microsoft Excel). $P < 0.05$ was considered statistically significant.

## Results

### Retrospective arm

We analyzed 166 thyroid nodule data who had final histopathology; the mean (±SD) age of the patients in the data set was 40 ± 3.5 years (range: 16–72) with 79% females. Among the FNA performed at our institution, 28% ($n = 46$) were performed under ultrasound guidance by the radiologist, and 57% ($n = 94$) were performed blindly by the pathologist. The mean age of the studied patients was 40 ± 13.5 years with 79% of them being women. Benign pathology was detected in 57% ($n = 96$) and malignant in 43% ($n = 70$). The results are summarized in Table 1. As we can note, there was a significantly higher prevalence of malignancy in Bethesda Category 1 (33%) and 2 (16%) compared to literature reports. When we analyzed the patients with Bethesda Category 2 with malignant histopathology, we noted that the mean size of these nodules was 5.95 ± 2.9 cm and they were more likely to cystic nodules. It is possible that inadequate sampling, less sonographic guided needle aspiration, and cystic papillary thyroid carcinomas might have contributed to the high prevalence of malignancy in Bethesda 2.

### Prospective arm

246 FNAC aspirates were assessed prospectively, which included 198 females (80%), with mean (SD) age of 44 ± 13 years. Patients with thyroid bed lesions and lymph node aspirate ($n = 8$) were excluded from further analysis. A total of 77 nodules (32%) had final histopathology assessment out of which 45 nodules (58%) were malignant and 32 nodules (42%) were benign. The Bethesda category of the FNAC results and the prevalence of malignancy in

**Table 1: Comparing the Bethesda percentage and thyroid cancer percentage in the retrospective and the prospective arm**

| Bethesda class | RP arm | Bethesda percentage | Operated | Thyroid cancer | Thyroid cancer percentage | PR arm | Bethesda percentage | Operated | Thyroid cancer | Thyroid cancer percentage | *P* value comparing Bethesda percentage between RP and PR | *P* value comparing thyroid cancer percentage between RP and PR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 18 | 11 | 18 | 6 | 33 | 13 | 5 | 3 | 0 | 0 | 0.02 | <0.01 |
| 2 | 63 | 38 | 63 | 10 | 16 | 102 | 43 | 14 | 0 | 0 | 0.31 | <0.01 |
| 3 | 32 | 19 | 32 | 12 | 38 | 66 | 28 | 16 | 8 | 50 | 0.03 | 0.07 |
| 4 | 21 | 13 | 21 | 11 | 52 | 22 | 9 | 11 | 4 | 36 | 0.20 | 0.02 |
| 5 | 20 | 12 | 20 | 19 | 95 | 8 | 3 | 7 | 7 | 100 | <0.01 | 0.04 |
| 6 | 12 | 7 | 12 | 12 | 100 | 27 | 11 | 26 | 26 | 100 | 0.17 | NS |
| Sum | 166 | 100.00 | 166 | 70 | | 238 | 100 | 77 | 45 | | | |

*P*<0.05 was considered statistically significant. NS: Not significant, RP: Retrospective, PR: Prospective

each category have been presented in Table 1. The rates of nondiagnostic cytology dropped from 11% to 5% ($P = 0.05$). None of the patients categorized as Bethesda 1 or 2 who underwent surgery ($n = 17$) had thyroid cancer ($P < 0.01$). We noted that there was increase in numbers reported as Bethesda category 2 (38%–43%) and 6 (7%–11%) which are definitive categories of benign or malignant nodules, respectively ($P = 0.31$ and $P = 0.17$, respectively). There was a decline in numbers of Category 4 and 5 (13%–9% in Category 4 ($P = 0.2$) and 12%–3% in Category 5 ($P < 0.01$)), thus reducing the rates of diagnostic hemithyroidectomies. The reporting prevalence of Category 3 increased from 19% to 28% ($P = 0.03$). The rates of malignancy in all the categories between the two arms are compared in Table 1 and compared with national literature in Tables 2a and b. We did not have a single case of false negative (malignant pathology reported as benign on cytology) reporting in Category 2 in our prospective arm compared to 16% in our retrospective arm ($P < 0.01$) and an average of 2.1%–7.5% in rest of the literature. While our malignancy rates of Category 3 increased from 38% to 50% ($P = 0.01$), this was on par with the national average of 47%. It is likely that the Category 3 patients chosen to be sent for surgery in the prospective group were likely to have "high-risk" sonographic pattern. On the contrary, our malignancy rates of Category 4 (follicular neoplasm) dropped from 52% to 36% ($P < 0.01$) (national average of 26%) indicating that sonography may not help distinguish between follicular adenoma ($n = 7$), carcinoma ($n = 2$), or follicular variant papillary thyroid cancer ($n = 2$). Our predictive value of malignancy in Category 5 and 6 was much better than national averages (66% and 99.7%, respectively) at 100%.

## Discussion

This exercise of standardizing the procedure of a single person performing the sonography and FNAC and regular discussion with the pathologist in providing them the risk stratification of the thyroid nodules based on American Thyroid Association classification helps in two areas. One it has significantly reduced the numbers of malignancy in the Category 2 (false negative rates). The rates of malignancy in Category 2 have ranged from 2.1% to 7.5% in most of the other Indian studies. We had an extremely high rate of malignancy in Bethesda 2 of 16% in our retrospective arm, but this reduced to 0% in the prospective arm. The other impact the intervention had was the combined rates of Bethesda 4 and 5 reduced significantly ($P < 0.01$) while it increased number of cases being called under Category 2 and 6 (54% versus 45% $P = 0.07$) and still retaining the 100% specificity. This ensures that some of the borderline cases are not labeled as Category 4 or 5 and reduces the rates of diagnostic hemithyroidectomy for these patients with thyroid cancer, and a complete thyroid surgery with neck dissection is performed in the first setting.

Our rates of malignancy in Category 3 and 4 are much higher than the international experiences indicating a referral bias as well as a bias of the treating physician/surgeon in referring specific patients with Category 3 with either clinical suspicion or sonographic suspicion for surgery. The scope of molecular testing in patients with Category 3 and 4 to "rule in" or "rule out" malignancy is still at infancy stages in India. At this point of time in patients in either of these categories, either a repeat FNAC or diagnostic hemithyroidectomy helps in further management. Sonographic risk stratification can better help in choosing patients for surgery. A patient with a low-risk nodule (5%–10% or < 5%) can be carefully followed up, however, if the nodule risk is 10%–15% or greater can probably be referred for surgery.

In a country like India, where there is a dearth of experienced thyroid surgeons, thyroid surgery carries a significant risk of hypoparathyroidism and recurrent laryngeal nerve injury and more importantly making the neck difficult to access in patients who need further surgeries. It is important to utilize the sonography and FNAC results in the best possible way in the evaluation of thyroid nodules. A regular interaction between the endocrinologist, sonologist, and cytopathologist helps the team triage patients better, with more patients with malignancy referred for surgery and follow patients with benign diagnosis without surgery.

**Table 2a: Comparing the prevalence of each category of Bethesda classification in thyroid fine-needle aspiration cytology with national literature**

| | Mondal *et al*.[12] | Garg *et al*.[13] | Bagga and Mahajan[14] | Renuka *et al*.[15] | Mehra and Verma[16] | Arul and Masilamani[17] | Prathima *et al*.[18] | Gupta *et al*.[19] | NHC | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | RP study | PR study |
| Year | 2009-2012 | 2012-2014 | 2004-2008 | 2009-2010 | 2010-2012 | 2012-2015 | 2013 | 2012-2014 | 2012-2014 | 2015-2016 |
| Place | Kolkata | Gujarat | Haryana | Guntur | New Delhi | Perambalur | Kolar | Wardha and Etawah | Bengaluru | Bengaluru |
| Type of study | RP | PR | RP | PR | PR | RP | RP | RP | RP | PR |
| FNA (*n*) | 1020 | 100 | 252 | 564 | 225 | 603 | 178 | 300 | 166 | 238 |
| Percentage of report in each Bethesda category (%) | | | | | | | | | | |
| Bethesda 1 | 1.2 | 6 | 1.6 | 17 | 7.2 | 2.7 | 11.7 | 11 | 11 | 5 |
| Bethesda 2 | 87.5 | 78 | 90.5 | 70.56 | 80 | 65.2 | 77.5 | 78 | 38 | 43 |
| Bethesda 3 | 1 | 4 | 6.7 | 1.95 | 4.9 | 10 | 1.12 | 2 | 19 | 28 |
| Bethesda 4 | 4.2 | 5 | | 4.2 | 2.2 | 10.6 | 3.9 | 3 | 13 | 9 |
| Bethesda 5 | 1.4 | 3 | | 2.6 | 3.6 | 5.3 | 4 | 1 | 12 | 3 |
| Bethesda 6 | 4.7 | 4 | 1.2 | 3.5 | 2.2 | 6.3 | 6 | 5 | 7 | 11 |

FNA: Fine-needle aspiration, RP: Retrospective, PR: Prospective, NHC: Narayana Health City

**Table 2b: Comparing the Bethesda rates and malignancy rates of each of the Bethesda category along with the national literature**

| | Mondal *et al*.[12] | Garg *et al*.[13] | Bagga and Mahajan[14] | Renuka *et al*.[15] | Mehra and Verma[16] | Arul and Masilamani[17] | Prathima *et al*.[18] | Gupta *et al*.[19] | NHC RP study | NHC PR study |
|---|---|---|---|---|---|---|---|---|---|---|
| HPE[#] (*n*) | 323 | 60 | 32 | 85 | 40 | 392 | 60 | | 166 | 77 |
| Percentage of cancer in each category | | | | | | | | | | |
| Bethesda 1 | 0 | 20 | 100 | | 0 | 0 | 33.3 | | 33 | 0 |
| Bethesda 2 | 4.5 | 0 | 4 | 2 | 7.5 | 0.8 | 2.1 | | 16 | 0 |
| Bethesda 3 | 20 | 25 | 50 | 63.6 | 100 | 24.4 | 50 | | 38 | 50 |
| Bethesda 4 | 30.6 | 20 | | | 25 | 28.9 | 25 | | 52 | 36 |
| Bethesda 5 | 75 | 66 | | 62.5 | 50 | 70.8 | 67 | | 95 | 100 |
| Bethesda 6 | 97.8 | 100 | 100 | 100 | 100 | 100 | 100 | | 100 | 100 |

[#]Final histopathology. RP: Retrospective, PR: Prospective, NHC: Narayana Health City

## Conclusions

A team approach to thyroid nodules in the risk stratification of thyroid nodules helps in reduce inadequate sampling (Bethesda 1), reduce false-negative rates in Bethesda 2, reduce the prevalence of reporting in Bethesda Category 4 and 5, and increase more definitive reporting (Bethesda 2 and 6) without losing specificity. This helps avoiding unnecessary diagnostic surgery for benign nodules and subject patients with malignant nodules to more complete surgery in the initial setting.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

## References

1. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid 2009;19:1159-65.
2. Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, *et al.* Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A synopsis of the National Cancer institute thyroid fine-needle aspiration state of the science conference. Diagn Cytopathol 2008;36:425-37.
3. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: An appraisal. Ann Intern Med 1993;118:282-9.
4. Cesur M, Corapcioglu D, Bulut S, Gursoy A, Yilmaz AE, Erdogan N, *et al.* Comparison of palpation-guided fine-needle aspiration biopsy to ultrasound-guided fine-needle aspiration biopsy in the evaluation of thyroid nodules. Thyroid 2006;16:555-61.
5. Pinchot SN, Al-Wagih H, Schaefer S, Sippel R, Chen H. Accuracy of fine-needle aspiration biopsy for predicting neoplasm or carcinoma in thyroid nodules 4 cm or larger. Arch Surg 2009;144:649-55.
6. Robitschek J, Straub M, Wirtz E, Klem C, Sniezek J. Diagnostic efficacy of surgeon-performed ultrasound-guided fine needle aspiration: A randomized controlled trial. Otolaryngol Head Neck Surg 2010;142:306-9.
7. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993;328:553-9.
8. Yoon JH, Kwak JY, Moon HJ, Kim MJ, Kim EK. The diagnostic accuracy of ultrasound-guided fine-needle aspiration biopsy and the sonographic differences between benign and malignant thyroid nodules 3 cm or larger. Thyroid 2011;21:993-1000.
9. Solorzano CC, Carneiro DM, Ramirez M, Lee TM, Irvin GL 3rd.

Surgeon-performed ultrasound in the management of thyroid malignancy. Am Surg 2004;70:576-80.
10. Shimamoto K, Satake H, Sawaki A, Ishigaki T, Funahashi H, Imai T. Preoperative staging of thyroid papillary carcinoma with ultrasonography. Eur J Radiol 1998;29:4-10.
11. Stulak JM, Grant CS, Farley DR, Thompson GB, van Heerden JA, Hay ID, *et al.* Value of preoperative ultrasonography in the surgical management of initial and reoperative papillary thyroid cancer. Arch Surg 2006;141:489-94.
12. Mondal SK, Sinha S, Basak B, Roy DN, Sinha SK. The Bethesda system for reporting thyroid fine needle aspirates: A cytologic study with histologic follow-up. J Cytol 2013;30:94-9.
13. Garg S, Desai NJ, Mehta D, Vaishnav M. To establish Bethesda system for diagnosis of thyroid nodules on the basis of FNAC with histopathological correlation. J Clin Diagn Res 2015;9:EC17-21.
14. Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? Indian J Cancer 2010;47:437-42.
15. Renuka IV, Saila Bala G, Aparna C, Kumari R, Sumalatha K. The Bethesda system for reporting thyroid cytopathology: Interpretation and guidelines in surgical treatment. Indian J Otolaryngol Head Neck Surg 2012;64:305-11.
16. Mehra P, Verma AK. Thyroid cytopathology reporting by the Bethesda system: A two-year prospective study in an academic institution. Patholog Res Int 2015;2015:240505.
17. Arul P, Masilamani S. A correlative study of solitary thyroid nodules using the Bethesda system for reporting thyroid cytopathology. J Cancer Res Ther 2015;11:617-22.
18. Prathima S, Suresh TN, Harendra Kumar ML, Bhaskaran A. Impact of the Bethesda system in reporting thyroid cytopathology. Thyroid Res Pract 2016;13:9-14.
19. Gupta V, Bhake A, Dayal S. Pattern and frequency of thyroid pathologies among thyroid cytology specimen in rural part of central India: A retrospective secondary data analysis. Thyroid Res Pract 2015;12:93-5.