

Diagnostic Accuracy of the Bethesda System of Reporting Thyroid Cytopathology in the Evaluation of Thyroid Nodule in a Tertiary Care Hospital of Kolkata

Sweta Verma¹, Mita Saha Dutta Chowdhury², Souradeep Ray³, Ruma Guha⁴

^{1, 3} Department of Otorhinolaryngology, R.G. Kar Medical College & Hospital, Kolkata, West Bengal, India. ²Department of Ophthalmology, College of Medicine & Sagar Dutta Hospital, Kolkata, West Bengal, India. ⁴Department of Otorhinolaryngology, Chittaranjan National Medical College & Hospital, Kolkata, West Bengal, India.

ABSTRACT

BACKGROUND

Thyroid cancer has the most rapidly increasing incidence of all major cancers in India. The overall prevalence of thyroid malignancy is approximately 1 - 5 % of all cancers in women and less than 2 % in men. Thyroid nodules are a common clinical finding and have a reported prevalence of 4 – 7 % in the general population. The vast majority of these nodules are non-neoplastic or benign and the risk of malignancy varies from 5 to 10 %. Fine needle aspiration cytology (FNAC) is an efficient and reliable means for the evaluation of thyroid nodules. A key challenge for clinicians is to choose which thyroid nodule is to be investigated further and treated. Early detection and treatment of malignant thyroid nodules is associated with excellent outcomes. The aim of our study is to compare and correlate between fine needle aspiration cytology and histopathology of resected specimen and to determine the diagnostic accuracy of TBSRTC (The Bethesda System for Reporting Thyroid Cytopathology) in thyroid nodule.

METHODS

This is a cross sectional validation study conducted in a tertiary care hospital (R.G. Kar Medical College) of Kolkata to find the sensitivity, specificity and diagnostic accuracy of TBSRTC in evaluation of thyroid nodule.

RESULTS

We have observed that TBSRTC is highly sensitive and specific in stratifying the malignancy risk of thyroid nodule.

CONCLUSIONS

It aids the clinician to choose the thyroid nodules which require further evaluation and intervention. It also guides the clinician to decide the operability of thyroid nodule. TBSRTC is highly accurate and is highly specific in stratifying the risk of malignancy of thyroid nodule.

KEYWORDS

TBSRTC, FNAC, Thyroid Nodules, Thyroid Cancer

Corresponding Author:

*Dr. Ruma Guha,
Assistant Professor,
Department of Otorhinolaryngology,
Maya Vila, Plot - 108, Sector - A,
Metropolitan Co-Operative Housing
Society Ltd., PO: Dhapa,
Kolkata – 700105, West Bengal, India.
E-mail: drrumaguhasen@gmail.com*

DOI: 10.18410/jebmh/2021/46

How to Cite This Article:

*Verma S, Chowdhury MSD, Ray S, et al.
Diagnostic accuracy of the Bethesda
system of reporting thyroid
cytopathology in the evaluation of
thyroid nodule in a tertiary care hospital
of Kolkata. J Evid Based Med Health
2021;8(05):241-245. DOI:
10.18410/jebmh/2021/46*

*Submission 04-10-2020,
Peer Review 10-10-2020,
Acceptance 12-12-2020,
Published 01-02-2021.*

*Copyright © 2021 Sweta Verma et al.
This is an open access article
distributed under Creative Commons
Attribution License [Attribution 4.0
International (CC BY 4.0)]*

BACKGROUND

Thyroid cancer has the most rapidly increasing incidence of all major cancers in India. Thyroid carcinoma is found to be the leading cause of death among endocrine cancers after the carcinoma of the ovary. The overall prevalence of thyroid cancer is approximately 1 - 5 % of all cancers in women and less than 2 % in men worldwide.¹ Now days, the incidence of thyroid malignancy is increasing more rapidly than any other malignancy due to the advanced radiological imaging rates (Magnetic resonance imaging- MRI, Computed tomography- CT scan, Ultrasonography). These scans are known to detect even small, non-palpable thyroid nodules, which in the past would never have been identified due to the size being too small to be detected by palpation, and too small to cause any symptoms to the patient. Thyroid malignancy can occur in any age group, although it is most common after age 30, and its aggressiveness increases significantly as the age increases. Females are more likely to have thyroid cancer than males at a ratio of 3:1.²

Thyroid nodules being a common diagnosis, it has a prevalence of 4 – 7 % in the general population.³ The majority of these diagnosed thyroid nodules are non-neoplastic and their risk of malignancy varies from 5 to 10 %.⁴ Fifty percent of people aged 50 and above though have clinically normal thyroid glands and thyroid function but has been diagnosed to have thyroid nodules, and by the age of 90, virtually everyone has nodules. Thyroid malignancy is often found at autopsy of people who died from other causes, never having been diagnosed previously.

Thus, thyroid cancers can be clinically insignificant for many patients. A key challenge for clinicians is to find out which ones require evaluation and intervention. Early diagnosis and treatment of malignant thyroid nodules is associated with excellent outcomes. Thyroid malignancy does not always cause symptoms but usually, the first sign is a thyroid nodule and sometimes an enlarged lymph node. However, many adults usually have small nodules in their thyroids, but only under 5 % of these nodules are found to be cancerous.⁵ Fine-needle aspiration biopsy (FNAB) is an efficient and reliable means for the evaluation of thyroid nodules and its diagnostic sensitivity ranges from 89 to 98 % and has a specificity of 92 %.⁶

Over the last three decades, fine needle aspiration (FNA) has become the most accurate, safe, efficient and cost-effective method for the initial screening of thyroid nodules and for guiding the management of these patients with thyroid nodules.

Objectives

1. To find the diagnostic accuracy of TBSRTC in thyroid nodule.
2. To evaluate the role of fine needle aspiration cytology in diagnosing thyroid malignancy.
3. To compare and correlate between fine needle aspiration cytology and histopathology of resected specimen.

METHODS

It is a cross sectional validation study conducted in R. G. Kar Medical College of Kolkata. For a period of one year, over 70 patients presented to outpatient department with complaints related to thyroid gland undergoing FNAC of neck. We had included patients with complaints related to thyroid swelling or mass attending the OPD of the Department of ENT between 18 - 70 years age group, patients with thyroid swelling and also the patients undergoing thyroidectomy.

Sample Size

70 cases

SN = Sensitivity of FNAC from previous study = 92 % (John et al 1987)⁷

e = Precision, usually at 5 % i.e. 0.05

Z = 1.96, Z value for 5 % significance level

Minimum sample size $N = Z^2 * SN * (1-SN) / e^2 = 29$

Hence, minimum sample size of our study for cases should be 29 but to increase the reliability of our study, it is taken as 70.

Fine needle aspiration cytology was done with hypodermic needle of 22 - 23 gauge and results were later classified as per BETHESDA System. Surgery was done as per the diagnosis made. Histopathology of resected specimen was obtained. FNAC was compared with post-operative histopathology to determine the accuracy. FNAC was performed by cytopathologist. Aspiration was performed using disposable 5 / 10 ml syringe using a 23G needle. To reduce contamination of specimen with blood more than 2 - 3 passes were made and non-aspiration technique was used in some patients. All the FNACs done during the study period were correlated with histopathology report in resected thyroid specimen. In some cases, with negative aspirates, FNAC was done under ultrasound guidance. Adequacy of cytological smear was judged by the presence of 5 - 6 groups of well-preserved follicular cells, with each group containing 10 or more cells, according to the Bethesda system of classification of thyroid diseases. Minimum three smears were made for each case and staining was done by haematoxylin & eosin, Papanicolaou and Giemsa stains. Cytology reporting was done according to The Bethesda System for Reporting Thyroid Cytopathology. The cytological findings were correlated with histopathological findings.

Statistical Analysis

Statistical analysis was performed using a computer Statistical Package for Social Sciences (SPSS) program Version 16.0. Results were presented as frequency and percentage. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of fine needle aspiration cytology in evaluation of thyroid nodule were evaluated using categorical tables.

RESULTS

A study of 70 patients with thyroid swelling was done using FNAC (TBSRTC) at R.G. Kar Medical College, Kolkata. Majority of the patients were in 41 - 50 years age group (Figure 1). The youngest was 23-year-old and the eldest was 72-year-old. There was female preponderance in cases of thyroid lesions. Male to female ratio was 1:4.3. In thyroid nodules (70 cases), 57 cases (81.43 %) were females and 13 cases (18.57 %) were males (Figure 2). Benign pathology was observed in 64.29 % cases (Figure 4), among which the commonest was benign nodular goitre (48.57 %) (Table 1). Malignancy accounts for 35.71 % of cases. BETHESDA II has least chance of malignancy and BETHESDA V and VI has highest risk of malignancy (Figure 6). Final confirmation is by histopathological examination (HPE) reporting. HPE is considered as a gold standard in diagnosing thyroid malignancy. The risk of malignancy was found to increase from BETHESDA II to BETHESDA VI when different BETHESDA categories were confronted with results of pathology and risk of malignancy was calculated. Sensitivity and specificity of FNAC for detecting malignancy was 94.44 % & 84.62 % respectively with accuracy of 87.14 % (Table 4).

Histopathological Diagnosis	Number	Percentage
Benign nodular goitre	34	48.57
Follicular adenoma	3	4.29
Follicular neoplasm	5	7.14
Lymphocytic thyroiditis	2	2.86
Multinodular goitre	5	7.14
Hurthle cell change	1	1.43
Poorly differentiated (insular variant)	1	1.43
Follicular variant of papillary carcinoma thyroid	13	18.57
Papillary carcinoma thyroid	4	5.71
Medullary carcinoma thyroid	2	2.86
Total	70	100

Table 1. Pathological Diagnosis of Thyroid Nodule

Bethesda	Sensitivity	Specificity	PPV	NPV	OR
II	97.56 %	77.27 %	88.89 %	94.44 %	0.0074
III	80 %	85 %	57.14 %	94.44 %	0.044
IV	46.67 %	97.78 %	87.50 %	84.62 %	38.5
V	52.94 %	100 %	100 %	84.62 %	99.47
VI	11.11 %	100.00 %	100 %	84.62 %	15.70

Table 2. Overall Sensitivity, Specificity, PPV, NPV and OR for Each Category of Bethesda System

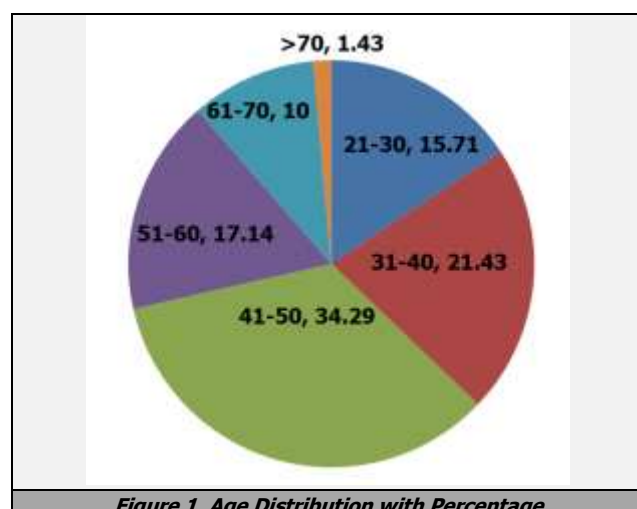


Figure 1. Age Distribution with Percentage

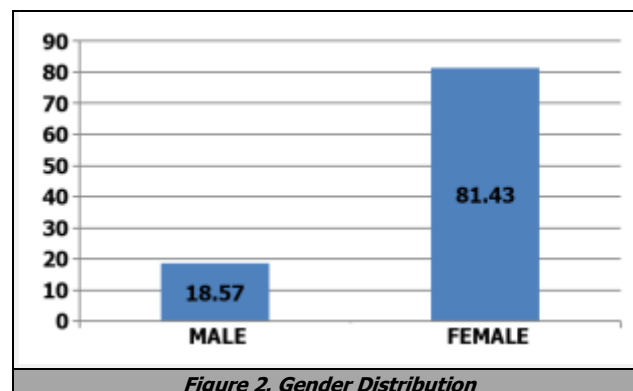


Figure 2. Gender Distribution

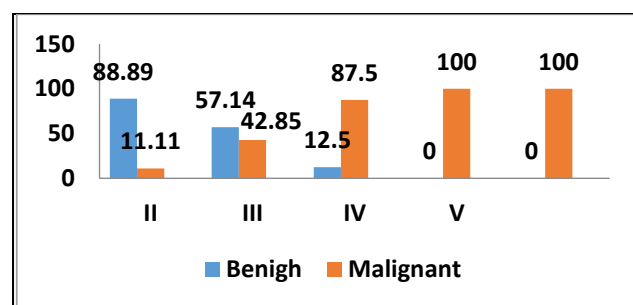


Figure 3. FNAC of Thyroid Nodule as per Bethesda System Correlated with HPE

Histopathology Report		
Bethesda Category	Benign	Malignant
2, 3 (Benign)	44 (TN)	8 (FP)
4, 5, 6 (Malignant)	1 (FN)	17 (TP)

Table 3. Frequency Distribution Table of Thyroid Nodule

TP = True Positive, FP = False Positive, TN = True Negative, FN = False Negative

	Sensitivity	Specificity	Prevalence	PPV	NPV	Accuracy
Bethesda	94.44 %	84.62 %	25.71 %	68 %	97.78 %	87.14 %

Table 4. Overall Sensitivity, Specificity, PPV, NPV And Accuracy of FNAC (Bethesda)

DISCUSSION

FNAC evaluation of a mass lesion in neck was first reported by Kun in 1847.⁸ Scandinavian workers introduced fine needle aspiration. It was later endorsed by the American Thyroid Association. It is considered as one of the standard methods in thyroid nodule evaluation. Most nodules are benign and hence, surgery is not done in those cases. With introduction of fine needle aspiration, there has been a decrease in number of performed thyroidectomies thus, it also decreases the overall cost of care by 25 %. It helps in eliminating unnecessary surgeries and limiting the use of frozen section intraoperatively and hence, it increases the diagnostic yield of cancers. In the 1930s, Memorial Sloan Kettering rediscovered the role of fine needle aspiration from the masses in head and neck region.

The use of large-bore needles for performing aspiration led to frequent complications and seeding of the tumour along the tract of biopsy.⁹ American Association of Clinical Endocrinologists recommends USG guided FNAC for all thyroid nodules which are more than 1 cm in diameter in euthyroid subjects.¹⁰

It has been reported that 9 - 47 % of palpation guided aspiration and 4 to 21 % of USG guided aspiration were inadequate.¹¹

In our study, FNAC is found to have a sensitivity of 94.44 %. Studies by Gharib et al¹² (83 %); Carol et al¹³ (86 %), John et al⁷ (92 %), Khurshidalam et al¹⁴ (92.59 %) are in close conformity with our sensitivity of 94.44 %. Whereas with Mistry et al¹⁵ Kelly. H. Kopald et al,⁸ sensitivity rates of FNAC were on lesser side with 55.3 % and 71 % respectively (Table 5). In literature, it has showed that very few works deal exclusively with thyroid cancer. The majority of them only compares sensitivity of FNAC in thyroid nodule irrespective of the pathological diagnosis of thyroid nodule. Therefore, accuracy and sensitivity varied. Kopald et al.⁸ showed that study done among 62 thyroid cancer patients at the University of California, Los Angeles, FNAC had sensitivity of 71 % whereas false-negative rate was 14.5 % (Table 6, 7). These results may be due to poor test performance therefore ultrasound-guided FNAC was next undertaken to improve diagnostic accuracy and outcomes.

Under "Thy classification" of FNAC, there is a combination of Bethesda category III & IV and has named it as Thy3 grade. Percentage false negativity of FNAC in Mistry et al.¹⁵, Kopald et al.⁸ & our study are 44.7 %, 29 % & 1 % respectively (Table 7).

Kopald et al⁸ study was done before the advent of the Bethesda system of reporting thyroid cytopathology, the cytological results of thyroid malignancy subjects in the Kopald study have been graded according to the TBSRTC.

In study conducted by (Mistry et al)¹⁵ unacceptably high false-negative rates for papillary cancer may be due to the difference of reporting system by cytopathologists for cytology and by the surgeons performing the FNAC. This was explained with the "Thy grading system". Limitations of this study is the variation of varying skill levels and experience of the operators collecting the aspirates.

In the second group (Kopald et al),⁸ he found that 9 cases of follicular neoplasm (Bethesda IV) in FNAC came out to be malignant in histopathological examination which lead to increased percentage of false negatives. It is not possible to distinguish between follicular adenoma and carcinoma with FNAC; histological specimen is required for invasion of the capsule, lymphatics or blood vessels.¹⁶

The reason for low % negativity of FNAC in our study was because aspirations were performed by dedicated cytopathologist with expertise and interest in thyroid disease & use of ultrasound guided FNAC in cases with repeated negative aspirates.

Jarvi et al⁹ showed false-negative rate of 50 % among 20 patients of thyroid neoplasm. The reason for this poor result was due to inexperienced operators. His study showed that FNAC is operator dependent and it always requires a good communication between the surgeon and the pathologist.

CONCLUSIONS

FNAC plays an important role in establishing pathological diagnosis of thyroid malignancy & is superior to clinical

assessment and in most cases curtails the need for other diagnostic modalities. The Bethesda System of Reporting Thyroid Cytopathology is a systematic method of reporting thyroid cytopathology and is a useful adjunct in pre-operative diagnosis, management and in predicting the risk of developing malignancy. Histopathology is the gold standard for diagnosis of thyroid malignancy. Ultrasound guided FNAC is useful in reducing the sampling error and false negatives rates when dealing with thyroid cancer. FNAC is highly sensitive and specific in stratifying the malignancy risk of thyroid nodule as per TBSRTC and it aids the clinicians to choose the thyroid nodules that require further evaluation and intervention.

Recommendations

Multiple aspirations should be done in order to obtain representative material from different areas of the thyroid gland in order to minimise negative aspirates. Ultra sound guided FNAC should be resorted to, in multiple non diagnostic repeat aspirates and in situations where there is a strong clinical suspicion of malignancy (small focus) which is not being picked up with routine FNACs. To avoid false negative results in cases of poorly cellular and excessive hemorrhagic smear, one can use liquid-based cytology in cases of thyroid neoplasm. H & E, Papanicolaou and Giemsa stains are to be routinely used in all thyroid FNACs to reduce the false negative diagnosis and to improve the preoperative diagnostic accuracy in detecting thyroid cancer. To obtain maximum benefit from the procedure, a close cooperation between a committed and trained cytopathologist and an experienced clinician is essential.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

- [1] Melak T, Mathewos B, Enawgaw B, et al. Prevalence and types of thyroid malignancies among thyroid enlarged patients in Gondar, Northwest Ethiopia: a three years institution based retrospective study. BMC Cancer 2014;14: Art No. 899.
- [2] Types of Thyroid cancer. National Cancer Institute <http://www.cancer.gov/cancertopics/wyntk/thyroid/page4>. Accessed on Feb 24, 2012.
- [3] Enomoto K, Enomoto Y, Uchino S, et al. Follicular thyroid cancer in children and adolescents: clinicopathologic features, long-term survival and risk factors for recurrence. Endocrine Journal 2013;60(5):629-635.
- [4] Sharma C. Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant cases. Journal of the Egyptian National Cancer Institute 2015;27(3):147-153.

- [5] Witt RL. Thyroid cancer: current diagnosis, management and prognostication an issue of North American Clinics of Otorhinolaryngology. The clinics: internal medicine. Vol. 47-4. 1st edn. Elsevier Publication 2014.
- [6] Pinchot SN, Al-Wagih H, Schaefer S, et al. Accuracy of fine-needle aspiration biopsy for predicting neoplasm or carcinoma in thyroid nodules 4 cm or larger. Arch Surg 2009;144(7):649-655.
- [7] Boey J. Investigations for thyroid - a critical assessment. Journal of Hong Kong Medical Association 1987;39(1):54-57.
- [8] Kopald KH, Layfield LJ, Mohrmann R, et al. Clarifying the role of fine-needle aspiration cytologic evaluation and frozen section examination in the operative management of thyroid cancer. Arch Surg 1989;124(10):1201-1205.
- [9] Jarvi K, Mokka R, Vorne M. Problems of cancer diagnosis in thyroid nodules. Acta Chir Scand 1988;154(2):93-96.
- [10] Gharib H, Papini E, Valcavi R, et al. American association of clinical endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Prac 2006;12(1):63-102.
- [11] Goudy SL, Flynn MB. Diagnostic accuracy of palpation guided and image guided fine needle aspiration biopsy of the thyroid. Ear Nose Throat J 2005;84(6):371-374.
- [12] Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med 1993;118(4):282-289.
- [13] Lewis CM, Chang KP, Pitman M, et al. Thyroid fine-needle aspiration biopsy: variability in reporting. Thyroid 2009;19(7):717-723.
- [14] Khurshidalam. Clinical study of neoplastic thyroid swellings with particular reference to surgical management. JK-Practitioner 2007;14(1):6-11.
- [15] Mistry SG, Mani N, Murthy P, et al. Investigating the value of fine needle aspiration cytology in thyroid cancer. Journal of Cytology 2011;28(4):185-190.
- [16] Bouknight AL. Thyroid Physiology and thyroid function testing. Otolaryngol Clin North America 2003;36(1):9-15.