

A Study to Evaluate Bethesda Grading in Fnac of Thyroid Swellings

Priti Kalani ¹, Angshuman Dutta ^{2*}, Jitendra Tiwari ³, Shiv Kumar ⁴

¹ ENT specialist, Command Hospital Air Force, Bangalore.

² Professor and Head of ENT, Command Hospital Air Force, Bangalore.

³ Resident Radiology, Command Hospital Air Force, Bangalore.

⁴ Graded Specialist Pathology Command Hospital Western Command, Chandimandir, Panchkula.

***Corresponding Author:** Angshuman Dutta, Professor and Head of ENT, Command Hospital Air Force, Bangalore.

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Abstract:

Background: FNAC is a commonly used diagnostic test for preoperative evaluation of thyroid swelling. However, FNAC reporting has its own limitations. The Bethesda classification system was created to guide cytopathological diagnoses and to help identify important correlations with malignancy in the final histological study.

The present study was undertaken to correlate the FNAC findings in thyroid swellings using Bethesda grading with histopathology.

Methodology: This is a prospective study design done in 100 patients of thyroid nodules undergoing surgery. The findings of FNAC as per Bethesda grading and histopathology was correlated and the data analyzed statistically.

Results: Fine Needle Aspiration Cytology using Bethesda grading had a sensitivity of 88.24% and specificity of 96.39%. The accuracy of FNAC was 95% positive predictive value was 83.33% and negative predictive value was 97.56%.

Conclusion: FNAC using Bethesda grading in evaluation of thyroid nodule was extremely reliable with a high specificity 96.39% making it a reliable tool in the diagnosis of a thyroid swelling.

keywords: bethesda; fine needle aspiration cytology; histopathology

Introduction

FNAC is a well-established procedure and is a valuable tool in the diagnosis and management of a patient with thyroid lesions [1]. A major goal of diagnostic workup now is to select those patients for surgery who have a high likelihood of harbouring malignancy in the nodule [2].

The Bethesda system for reporting thyroid cytopathology (TBSRTC) [3] was introduced in 2007 in an attempt to standardize international terminology and to categorize morphological criteria in fine-needle aspirations from patients with thyroid nodules. FNAC is currently the preferred screening test for guiding the diagnosis and treatment of thyroid nodules [4].

TBSRTC is a unified system that complements cytological findings from thyroid FNA and represents a consensus among multiple experts in different areas of medicine. [5] TBSRTC establishes six diagnostic categories for FNA results and assigns a malignancy risk and recommendations for patient management for each category [6]. 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 [7].

The present study is undertaken to compare the diagnostic efficacy of FNAC using Bethesda grading in correlation with histopathology in euthyroid patients having thyroid swelling. The study aims to address the pitfalls in the evaluation of thyroid swelling histology.

Aim

To correlate clinical examination, FNAC vis a vis histopathology in the management of thyroid swelling. The aim is to analyse the cytoarchitecture of clinically palpable thyroid nodule using Bethesda grading and compare results with histopathological examination and to assess its sensitivity and specificity.

Objective

To find out the utility of using BETHESDA grading for FNAC in the evaluation of thyroid swellings with comparison to histopathology which is the gold standard.

Materials and methods

Study setting: This observational study was conducted in the department of ENT at in 100 patients undergoing thyroidectomy over a period of 1 year

Inclusion Criteria:

1. Age – Above 18 years.
2. Patients with thyroid nodule – both benign and malignant.
3. Undergoing Elective surgery (hemithyroidectomy, total thyroidectomy, and lobectomy).
4. Euthyroid.

Exclusion criteria

Statistical methods:

FNAC was considered as primary outcome variables. Histopathology was considered as gold standard. FNAC features was considered as screening tests. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% CI were presented. Reliability of the screening test was assessed by kappa statistic along with its 95% CI and p Value.

Where thyroidectomy is part of other procedures like laryngectomy

Ethical considerations: Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants.

Methodology: After obtaining the informed written consent all the participants were evaluated by through clinical history, clinical examination and FNAC before undergoing thyroidectomy.

Procedure for FNAC: Patient underwent fine-needle aspiration with 23-gauge needle and 10-mL syringe. Fixation in 95% alcohol and one air dried smear from each needle was prepared. Smears staining were done by Papanicolaou and Giemsa method. Finding was recorded as per Bethesda grading for thyroid swelling. Post-surgery histopathology report was collected and compared to FNAC.

Category	Description	Risk of malignancy
I	Nondiagnostic/unsatisfactory	1- 4 %
II	Benign (colloid and follicular cells)	0-3%
III	Atypia of undetermined significance	5%-15%
IV	Follicular neoplasm or suspicious for follicular neoplasm	15-30%
V	Suspicious for malignancy	60-75%
VI	Malignant	97-99%

Fischer test was used to test statistical significance. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

Results

Age group was 19 to 82 yrs. Mean 47.44 Median IQR48.50 (38.00 -56.00) Males 25(25%) and females 75 (75%)

BETHESDA	Frequency	Percentages
BETHESDA 1	4	4.00%
BETHESDA 2	47	47.00%
BETHESDA 3	32	32.00%
BETHESDA 4	6	6.00%
BETHESDA 5	8	8.00%
BETHESDA 6	4	4.00%

Table 1: Descriptive analysis of Bethesda in the study population (N=100)

Among the study population, (4%) had BETHESDA 1, (47%) had BETHESDA 2, (32%) had BETHESDA 3, (6%) had BETHESDA 4 (8%) had BETHESDA 5 and (4%) Bethesda 6.

Histopathology	Frequency	Percentages
Adenomatous goiter	10	10%
Colloid Goiter	27	27%
Follicular Adenoma	12	12%
Follicular Carcinoma	02	2%
Hashimotos Thyroiditis	4	4%
Nodular hyperplasia	28	28%
Nodular hypoplasia thyroid gland	2	2%
Papillary Ca	15	15%

Table 2: Descriptive analysis of Histopathology in the study population (N=100)

FNAC	Frequency	Percentages
Malignant	18	18%Bethesda (IV, V, VI)
Benign	82	82%Bethesda (I, II, III)

Table 3: Descriptive analysis of FNAC in the study population (N=100)

HPE	Frequency	Percentages
Malignant	17	17.00%
Benign	83	83.00%

Table 4: Descriptive analysis of HPE in the study population (N=100)

FNAC	HPE	
	Malignant (N=17)	Benign (N=83)
Malignant (Bethesda IV, V, VI) 18	15/18	3/18
Benign (Bethesda I, II, III) 82	2/82	80/82

Table 5: Comparison of HPE with FNAC (N=100)

×2 value 68.5, P Value (Fischer’s Exact test) :<0.001

FNAC	Number total in each category	Histopathology	
		Benign	Malignant
Bethesda I	04	03	01(25%)
Bethesda II	47	47	00
Bethesda III	31	30	01(3%)
Bethesda IV	06	02	04(67%)
Bethesda V	08	01	07(87%)
Bethesda VI	04	00	04(100%)

Table 6: Correlation between FNAC/Histopathology

X2value:72.2 P value (Fischer’s exact test) <.001

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	88.24%	63.56%	98.54%
Specificity	96.39%	89.80%	99.25%
Positive likelihood ratio	24.41%	7.93%	75.15%
Negative likelihood ratio	.12%	.03%	.45%
Disease prevalence	17.00%	10.23%	25.82%
Positive predictive value	83.33%	61.89%	93.90%
Negative predictive value	97.56%	91.58%	99.32%
Accuracy	95%	88.72%	98.36%

Table 7: Predictive validity of FNAC in predicting HPE malignancy (N=100)

Discussion

Thyroid diseases are the most common endocrine abnormality across the globe. The diagnosis of these diseases is made through clinical evaluation, ultrasonogram, thyroid function tests, fine needle aspiration cytology (FNAC), histopathology and radionuclide scan. FNAC is a well-established procedure and is a valuable tool in the diagnosis and management of a patient with thyroid lesions [8]. FNAC is a valuable adjunct to preoperative screening in the diagnosis of thyroid nodules and in most cases, it can distinguish between neoplastic and non-neoplastic lesions [9] However, FNAC has its own limitations especially in cases where the differentiation between follicular adenoma and carcinoma is difficult. Therefore, the present study correlated the clinical profile, FNAC findings using Bethesda grading with histopathology.

The main purpose of TBSRTC was to eliminate the ambiguity and to follow uniformity in the reporting of thyroid FNAs thereby enabling ease of communication among pathologists and clinician and to plan appropriate treatment for the patients. It consists of a six-category classification system associated with increased risk of malignancy. This classification system ensures the uniformity of information shared among pathologists, clinicians, and surgeons, and it provides better correlations between malignancy and cytological results, thus enabling more appropriate management. “The Bethesda System for Reporting Thyroid Cytopathology” (TBSRTC) includes definitions, diagnostic/morphologic criteria, explanatory notes, and a brief management plan for each diagnostic category. It is a six-category scheme of thyroid cytopathology reporting. Each category has an implied cancer risk,

which ranges from 0% to 3% for the “benign” category to virtually 100% for the “malignant” category. It uses three categories, AUS/FLUS, SFN/Hurthle cell neoplasm and SFM, to report thyroid aspirates that fall between benign and malignant. As a function of these risk associations, each category is linked to evidence based clinical management guidelines. A retrospective study done by Arul P et al [10] in which total number of 483 thyroid FNACs out of which 209 cases of Solitary thyroid nodule (STN) were chosen for this study. FNACs diagnoses were compared with histopathological diagnoses. Among 209 FNACs, 88 (42.1%) had non-neoplastic lesions, 6 (2.9%) had atypia of undetermined significance/follicular lesions of undetermined significance (AUS/FLUS), 52 (24.9%) had follicular neoplasm/suspicious for a follicular neoplasm (FN/SFN), 33 (15.8%) were suspicious for malignancy and 18 (8.6%) had malignant cytology. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of FNAC in STN cases were 94.4%, 97.6%, 95.8%, 98.1% and 93.2% respectively. Study concluded that FNAC reporting using Bethesda system for reporting thyroid cytopathology highly correlated with the histopathological diagnosis and results were comparable with published data. The FNAC diagnosis helps in triaging patients with STN and identifies those who require surgical intervention. It is a simple, convenient, cost effective, sensitive, specific, safe and accurate initial diagnostic method for the preoperative evaluation of STN.

In our study among the study population, (32%) had BETHESDA III Atypia of undetermined significance, (6%) had BETHESDA IV suspicious for follicular neoplasm (8%) had BETHESDA V suspicious for malignancy and 4% Bethesda VI. In our study the sensitivity was

88.24%, specificity 96.39% positive predictive value was 83.33% negative predictive value was 97.56% and accuracy was 95%. In our study no repeat FNAC was done and all patients including Bethesda I and II underwent surgery owing to cosmetic reasons.

On comparing histopathological examination (HPE) with FNAC (table 5) out of 100 cases. 18 were labelled as malignant by FNAC and 82 were labelled as benign by FNAC. On histopathology 83 were found to be benign and 17 cases to be malignant.

Out of Bethesda (IV, V, VI) in FNAC, 15 were labelled as malignant by HPE and 3 were benign by HPE (table 5). The correlation of FNAC by Bethesda grading with histopathology was statistically significant (P value <0.001). Out of Bethesda 82 (I, II, III) in FNAC, 2 were labelled as malignant by HPE and 80 were benign by HPE. (Table 5)

Present study	61.54	94.87	80	88.10	86.54
Nautilya et al12	78.9	96.29	93.75	95.23	95
Sikder et al13	68.75	100	100	87.18	90
Mangshettyetal14	90	100	100	96.9	97.56
Gupta et al15	80	86.6	-	-	84

Table 8: Comparing the results of FNAC of present study with previous studies.

The sensitivity and specificity ratios for FNAC in published series range between 65% - 98% for sensitivity and 73-100% for specificity [13,16]. The current study showed sensitivity 88.24% and specificity 96.39% respectively which is comparable with the studies above.

The reason for varied range of sensitivity and specificity is due to the differences in the categorization of "FN/SFN which is Bethesda IV, suspicious for malignancy which is Bethesda V. "AUS/FLUS" Atypia of undetermined significance which is Bethesda III is a heterogeneous subjective category which shows wide interobserver variability.

In addition, some authors categorize follicular lesions as histopathological benign, while others categorize these lesions as malignant [13,16]. The present study there were 12 follicular adenoma and 2 were follicular carcinoma.

In our study, of 100 cases on microscopic evaluation by HPE (table 2), 10 (10%) were with adenomatous goiter, 27 (27%) were with colloid goiter, 12 (12%) were with follicular adenoma, 2 (2%) were with follicular carcinoma, 4 (4%) were with Hashimoto thyroiditis, 28 (28%) were with nodular hyperplasia, 2 (2%) were with nodular hypoplasia thyroid gland and 15 (15%) were with papillary carcinoma.

Baloch NM et al. (2008) [17] described 40 patients of indeterminate follicular lesions on FNAC. Of these 25 (62%) had carcinoma on histopathology of which 13 had follicular variant of papillary, 8 had papillary and 4 had follicular carcinoma on final histopathology report.

Goldestein RE et al. (2002) [18] described 74 follicular neoplasms without atypia, only 5 (6.8%) were malignant. Also, there were 9 patients of follicular neoplasm with atypia out of which 4 (44.4%) were malignant

The FNAC findings had sensitivity of 88.24% (63.56CI to 98.54%) in predicting final HPE malignancy. Specificity was 96.39% (95% CI 89.80% to 99.25%), positive predictive value was 83.33% (95% CI 61.89% to 93.90%), negative predictive value was 97.56% (95% CI 91.58% to 99.32%), the total diagnostic accuracy was 95% (95% CI 88.72% to 98.36%), positive likelihood ratio was 24.41 (95% CI 7.93 to 75.15) and negative likelihood ratio was 0.12 (95% CI 0.03 to 0.45).

Basharath, et al in 11 study showed FNAC with high specificity (96.29%), sensitivity (78.9%), positive predictive value (93.75%), negative predictive value (95.23%) and accuracy (95%).

The present study showed comparable sensitivity.

on histopathology, in their study out of 15 lesions of atypia, 3 (20%) were malignant and out of 25 highly suspicious for malignancy (84%) proved to be malignant on histopathology.

Ohuri NP et al. (2010) [19] described 117 cases of follicular lesions of undetermined significance/ atypia of undetermined significance of which 29.9% had neoplastic outcome and 17.1% were carcinomas on histopathology. In his study, among 46 undetermined FNACs [12 AUS and 34 FL] on histological follow-up 41.7% were carcinomas, 24.9% were adenomas and 33.4% were non-neoplastic lesions in AUS and 20.8%, 58.9% and 11.7% were carcinomas, adenomas and non-neoplastic lesions respectively in FL.

Comparison of percentages of malignancy on histopathology with FNAC

It has been reported that the risk of malignancy in the Bethesda categories is 1-4%, 0-3%, 5-15%, 15-30% and 60-75% in I-V, respectively.

In our series out of 31 cases Bethesda III AUS 30 were benign and 01 was malignant on histopathology, of 06 cases of follicular neoplasm Bethesda IV ;02 were benign and 04 were follicular carcinoma. Of 08 cases of Bethesda V 01 was benign and 07 were carcinoma (12.5%). FNAC of cases Bethesda VI and II 47 and 4 respectively had 100% correlation with their histopathological diagnosis. Out of 4 cases of Bethesda I 03 were benign and 01 was malignant.

In our study the incidence of malignancy seen on histopathology was 25% in Bethesda I, 3% in Bethesda III, 67% in Bethesda IV, 87% in Bethesda V, 100% in Bethesda VI which was slightly in variance to the risk of malignancy as proposed by Bethesda.

Diagnostic Category	Bethesda1	Bethesda2	Bethesda3	Bethesda4	Bethesda5	Bethesda6
Our Study	25	0	3	67	87	100
Yassa 20	10	.3	24	28	60	97
Mondol21	0	4.5	20	30.6	75	97.8
Mufti22	20	3.1	50	20	80	100
Jo23	8.9	1.1	17	25.4	70	98.1
Kapila24	33.3	11.4	18.6	35.3	61.3	96.5

Table 9: Comparing the results of FNAC of present study with previous studies.

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.

Conclusion

The Bethesda system for thyroid cytology correlates adequately with final histopathological diagnosis in our study. In conclusion, for the

interpretation of aspiration cytology of thyroid lesions TBSRTC is a useful tool that enhances the diagnostic accuracy of FNA, exhibits an adequate diagnostic correlation with the final histopathological examination and enables a comparison of results between different institutions.

Funding

Nil

Conflict of Interest

Nil

Ethical approval

Study was approved by Institutional Ethical Committee

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