

Evaluation of the Bethesda System of Reporting Thyroid Cytopathology in Correlation with Histopathology

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Abstract

Background: Bethesda system of reporting thyroid cytopathology is a standardized system, improving communication between pathologists and clinicians, leading to more consistent management approaches. The aim of the research work was to study the efficacy of Bethesda System for reporting thyroid fine-needle aspirations in view of offering guidance for patients management and to evaluate the specificity of the system based on the cytology and histopathological correlation.

Methods: All the patients referred for FNAC of thyroid lesions were studied for 2 years and classified them according to Bethesda system. Histopathological correlation was done for all cases which underwent surgical resection.

Results: Out of 280 cases, 64 (22.86%) were of category I, 144 (51.43%) were of category II, 11 (3.93%) were of category III, 43 (15.35%) were of category IV, 09 (3.21%) were of category V, 09 (3.21%) were of category VI. Statistical analysis of this study showed that the sensitivity, specificity, diagnostic accuracy were 95.5%, 84.3%, 89.3%, respectively. The positive predictive value and negative predictive value were 83% and 95.8%, respectively.

Conclusions: The six diagnostic categories of Bethesda system were beneficial for triaging patients for either clinical follow-up or surgical management. Each diagnostic category conveys specific risks of malignancy, which offers guidance for patients management.

Keywords: Bethesda; Cytology; Thyroid.

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Introduction

Fine needle aspiration cytology (FNAC) is the study of cells obtained by a fine needle under vacuum. This procedure has an advantage of being simple, safe, speedy, minimally invasive and cost effective [1]. The whole procedure including fixation and staining is quick and a report can be issued in the same day. Immediate diagnosis relieves patient's anxiety and saves time. Its uses have decreased the number of thyroid surgeries performed and increased the ratio of malignant to benign lesions resected. As a result many thyroid surgeries for benign non-neoplastic diseases have been avoided. Thus FNAC is a well established procedure and is a valuable tool in the diagnosis and management of a patient with thyroid lesions [2].

Fine needle aspiration is the procedure of choice in the preoperative evaluation of thyroid enlargement but it has some limitations as regards variability in its diagnostic terminology. In order to evolve uniform terminology for its use worldwide and to address other issues related to thyroid fine-needle aspiration, The National Cancer Institute (U.S) recently proposed a classification system. This classification system was introduced on October 22 and 23, 2007 in a conference held by National Cancer Institute, at Bethesda, Maryland [3].

Materials and Methods

All the patients referred for FNAC of thyroid lesions in the cytology unit of CAIMS hospital, Karimnagar were studied prospectively for a period of two years. All the patients were clinically examined in detail and a careful palpation of the thyroid gland was done for aspiration. Under aseptic precautions the aspiration was done with 23 G needle. The needle is inserted into the lesion without attachment of a syringe and to and fro movement performed quickly. The material gets collected in the bore by capillary suction. The needle hub was attached to an air filled syringe and the plunger was pushed down to expel the material on a clean labeled glass slide. The same procedure was repeated at different sites varying from 2-6. A minimum of five slides are smeared with the aspirate, two for Leishman stain (air dried) and three for Haematoxylin Eosin (HE). Slides for wet smears were fixed in 95% ethyl alcohol, while the others were air dried. Stained smears are studied under light microscopy and reported based on Bethesda system.

Bethesda System for Reporting Thyroid Cytopathology; recommended diagnostic categories [4].

I. *Nondiagnostic or Unsatisfactory*

- Cyst fluid only
- Virtually acellular specimen
- Other (obscuring blood, clotting artifact, etc.)

II. *Benign*

- Consistent with benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
- Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
- Consistent with granulomatous (subacute) Thyroiditis
- Other

III. *Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance*

IV. *Follicular Neoplasm or Suspicious for a Follicular Neoplasm*

Specify if Hurthle cell (oncocytic) type

V. *Suspicious for Malignancy*

- Suspicious for papillary carcinoma
- Suspicious for medullary carcinoma
- Suspicious for metastatic carcinoma
- Suspicious for lymphoma
- Other

VI. *Malignant*

- Papillary thyroid carcinoma
- Poorly differentiated carcinoma
- Medullary thyroid carcinoma
- Undifferentiated (anaplastic) carcinoma
- Squamous cell carcinoma
- Carcinoma with mixed features (specify)
- Metastatic carcinoma
- Non-Hodgkin lymphoma

The cases were followed by postoperative specimen received from the department of surgery. Specimens were collected in 10% formalin in fresh state and allowed to fix for 24 hours. Detailed gross examination was done and bits were given. Paraffin embedded HE stained sections were obtained and studied under light microscopy.

Results

The present study deals with the Bethesda system of reporting (TBSRTC) of the palpable thyroid lesions and determination of the diagnostic accuracy of the TBSRTC with histopathologic correlation. During the period 2120 FNACs are done at different sites, of which 280 were of thyroid, accounting for 13.20%. Among 280 cases who had undergone FNAC, 133 cases were subjected for histopathological study.

Age

Age group of patients referred for thyroid aspirations ranged from 10 years to 72 years. Majority of the patients were in the age group of 21-30 years.

Sex

Majority of the patients were females accounting for 253 (90.36%) of 280 cases forming a male to female ratio of 1: 9.37 (Table1).

Table 1: Age and Sex Distribution of the Patients

Age group	Male	Female	Total
0-10	00	01	01
11-20	01	41	42
21-30	09	87	96
31-40	06	60	66
41-50	06	40	46
51-60	03	13	16
61-70	02	09	11
71-80	00	02	02
Total	27	253	280

Clinical features

Out of 280 cases all patients presented with midline swelling. Enlargement is diffuse and nodular in 120 of cases, diffuse and uniform in 75 of cases, solitary in 85 of cases.

Complications

All patients tolerated the aspiration procedure well. There were no complications following fine needle aspiration.

Nature of the aspirate

Majority of the aspirates were scanty blood mixed to frankly hemorrhagic. However in 32 cases brown or dark brown fluid is aspirated, amount ranging from 0.5ml to 5ml.

Adequacy of the sample

Out of 280 cases satisfactory samples are obtained

in 216 of cases while in remaining unsatisfactory. For considering sample adequate, it required minimum of five to six groups of thyroid follicular cells with minimum of eight to ten thyroid follicular cells.

Cytology

In present study the cases are categorized according to Bethesda system of reporting thyroid cytology. Based on morphology cases are divided in six categories. Out of 280 cases, 64 (22.86%) were of category I, 144 (51.43%) were of category II, 11(3.93%) were of category III, 43(15.35%) were of category IV, 09 (3.21%) were of category V, 09 (3.21%) were of category VI (Table 2).

Table 2: Distribution of cases according to Bethesda system of reporting thyroid cytology

Category	No: of cases	%
Category I	64	22.86
Category II	144	51.43
Category III	11	3.93
Category IV	43	15.35
Category V	09	3.21
Category VI	09	3.21
Total	280	100

In this study most of the cases were categorized under category II (51.43%). In category II out of 144 cases, 93 cases (64.58%) were sub categorized into Benign Follicular Nodules, followed by 51 cases (35.42%) were of Hashimotos thyroiditis, 11 were categorized into Atypia of undetermined significance, 43 cases were diagnosed as Suspicious for Follicular Neoplasm (Fig. 1), out of 43 cases in category IV one case was diagnosed as follicular carcinoma (Fig. 2). 9 cases (100%) were diagnosed as suspicious of Papillary Carcinoma. Out of 9 cases in category VI, 5 cases (55.55%) were diagnosed as Papillary Carcinomas (Fig. 3 & 4), 4 cases (44.44%) as Medullary Carcinomas.

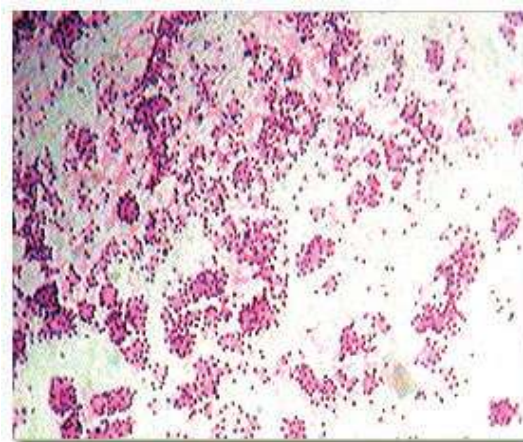


Fig. 1: Follicular neoplasm/Suspicious of follicular Neoplasm: shows a highly cellular aspirate Composed of uniform follicular cells in Crowded clusters, microfollicles. (H&E, X 100)

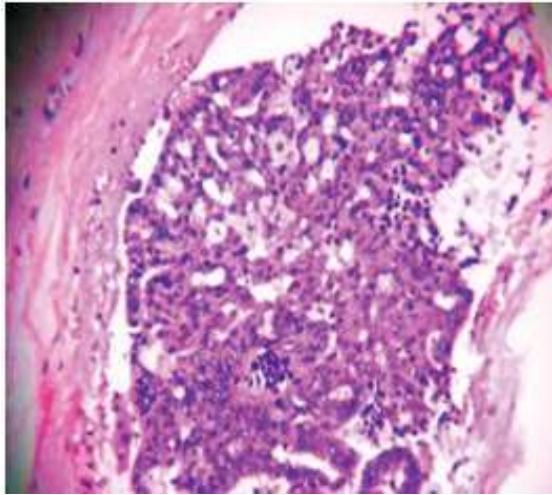


Fig. 2: Microscopy Follicular Carcinoma: shows thyroid follicles with vascular invasion. (H&E, X 400)



Fig. 3: Macroscopy-total thyroidectomy specimen shows grey brown areas filled papillae with colloid, papillary areas (arrow) are also seen.

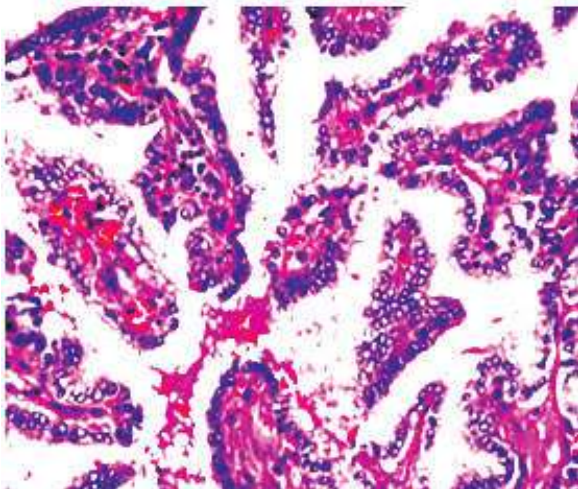


Fig. 4: Microscopy; Papillary Carcinoma: with round to focal oval nuclei, with overlapping, overcrowding.(H&E, X 400)

Out of 64 cases, 33 cases were undergone surgery in category I, out of 144 cases 62 cases underwent surgery in category II, out of 11 cases 5 cases are biopsied in category III, out of 24 cases 11 cases underwent surgery in category IV, out of 9 cases 6 cases in category V and out of 9 cases, 3 cases of category VI were received in histopathology and correlating with histopathological diagnosis (Table 3).

Table 3: Cases with histopathological correlation

Bethesda categories	Histopathological diagnosis	No.of cases	%
Category I	Multinodular goiter with hemorrhage, cystic change, fibrosis	24	72.72
	Follicular adenoma with extensive cystic change	7	21.21
	Papillary carcinoma with cystic change	2	6.06
Category II	Multinodular goitre	51	82.25
	Hashimoto thyroiditis	02	03.22
	Toxic goiter	02	03.22
Category III	Follicular adenoma	01	20
	Papillary carcinoma	01	20
Category IV	Follicular adenoma	08	33.33
	Hurthle cell adenoma	02	8.33
	Follicular carcinoma	01	4.16
Category V	Papillary carcinoma	04	66.66
Category VI	Papillary carcinoma	01	33.33
	Medullary carcinoma	01	33.33

In our study using Bethesda System of Reporting Thyroid Cytology, we found that the sensitivity, specificity, diagnostic accuracy were 95.5%, 84.3%, 89.3%, respectively. The positive predictive value and negative predictive value were 83% and 95.8%, respectively.

Discussion

Fine needle aspiration sample of a thyroid nodule should be representative of underlying lesion, in order to provide useful diagnostic information. Fine needle aspiration reduces the rate of unnecessary thyroid surgery in patients with benign nodules and detects those with thyroid cancers who have to be surgically treated.

Before the routine use of thyroid fine needle aspiration, the percentage of surgically resected thyroid nodules that were malignant was 14%. 5 With current thyroid fine needle practice, the percentage of resected nodules that are malignant surpasses 50% [6].

Historically, terminology for thyroid fine needle aspiration has varied from one laboratory to another, creating confusion and hindering the sharing of data among multiple institutions. For clarity of communication and uniformity of terminology National Cancer Institute hosted "The NCI thyroid FNA state science conference". The conclusions regarding terminology and morphologic criteria from this meeting led to The Bethesda Thyroid Atlas Project and formed the frame work for TBSRTC.

In the present study, thyroid lesions are categorized according to The Bethesda System of Reporting Thyroid Cytology and correlated with histopathology wherever available to determine its diagnostic accuracy. The present study deals with fine needle aspiration cytology of thyroid performed in 280 patients of which 133 of them underwent surgery subsequently. In the present study, age of the patients ranged from 10 years to 72 years with a median age of 32 years. Age distribution of the present study is comparable to Mitra et al. [7].

The number of males in the present study is 27 (9.6%) and the females are 253 (90.36%) with a male to female ratio 1:9. Sex distribution is similar to study done by Tabaqchali et al. [8]. According to Bethesda system of reporting thyroid cytology there are six diagnostic categories. Of 280 cases, 133 cases are subjected for histopathology, of these 59 cases are not correlated with histopathology; this is due to secondary degenerative changes like hemorrhage, cystic change, fibrosis.

In our study using Bethesda System of Reporting Thyroid Cytology, we found that the sensitivity, specificity, diagnostic accuracy were 95.5%, 84.3%, 89.3%, respectively. The positive predictive value and negative predictive value were 83% and 95.8%, respectively. Study done by Bongiovanni M et al. [13] showed results of meta-analysis as sensitivity, specificity, diagnostic accuracy were 97%, 50.7%, 68.8%, respectively (Table 4 & 5). The positive predictive value and negative predictive value were 55.9% and 96%, respectively. Yang et al. [14] reported sensitivity and specificity were 94% and 98.5%, respectively. Sensitivity and specificity were similar to the study done by yang et al. diagnostic accuracy in study differs significantly from Bongiovanni et al. [13]. Reddy P et al. [17] reported positive predictive value and negative predictive value 80% and 93.5% respectively, which is similar to our study.

Table 4: Comparison of percentage of distribution of fine needle aspiration diagnosis among published studies. [9,10,11,12]

Diagnostic category	Present study	Vickie Y. Jo et al.	Yassa et al.	Yang et al.	Nayar and Ivanovic
I	22.86	18.6	7	10.4	5
II	51.43	59	66	64.6	64
III	3.93	3.4	4	3.2	18
IV	15.35	9.7	9	11.6	6
V	3.21	2.9	9	2.6	2
VI	3.21	7	5	7.6	5

Table 5: Comparison of percentages of follow-up malignancy among published studies [9,10,11,12]

Diagnostic category	Present study	Vickie Y. Jo et al.	Yassa et al.	Yang et al.	Nayar and Ivanovic
Nondiagnostic	6.06	8.9	10	10.7	9
Benign	3.22	1.1	0.3	0.7	2
Atypical follicular lesions of indetermined significance	20	17	24	19.2	6
Suspicious for follicular neoplasm	8.33	25.4	28	32.2	14
Suspicious for malignancy	66.66	70	60	64.8	53
Malignant	66.66	98.1	97	98.4	97

Conclusion

FNA is a safe and rapid procedure. The current results indicate that FNA provides an accurate diagnosis of thyroid lesions. The six diagnostic categories were beneficial for triaging patients for either clinical follow-up or surgical management. Each diagnostic category conveys specific risks of malignancy, which offers guidance for patient management. The current results indicate that FNA provides an accurate diagnosis of thyroid malignancy. Definitive diagnosis are given on cytology and unnecessary surgeries are avoided. Universal application of the new standardized nomenclature may improve interlaboratory agreement and lead to more consistent management approaches.

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