

CYTOPATHOLOGICAL EVALUATION OF THYROID LESIONS BASED ON BETHESDA SYSTEM IN PATIENTS ATTENDING BIRAT MEDICAL COLLEGE AND TEACHING HOSPITAL

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ABSTRACT

More than 50% of the world's population has at least a thyroid nodule. Detail clinical examination and radiology may help in diagnosing thyroid lesions but the management depends upon the cytopathological diagnosis. Optimum use of fine needle aspiration cytology (FNAC) and better understanding of cytomorphological characteristic of thyroid lesions by using Bethesda system, triaging of patients who are to be treated medically or surgically is more accurate. The objective of this present study is cytopathological evaluation of thyroid lesions based on Bethesda System in patients attending Birat Medical College and Teaching Hospital. The objective was also to correlate the cytological findings with histopathological findings where ever possible. A total of 104 patients with thyroid lesions underwent fine needle aspiration cytology in a period of a year (September 1, 2019 to August 31, 2020). Cytological features were evaluated and classified according to the Bethesda system. Histopathological features were evaluated and correlated wherever available. Among 104 patients with thyroid lesions 93 were female and 11 were male. Four cases turned out to be non diagnostic, 85 benign, three Atypia of undetermined significance, three Suspicious for follicular neoplasm and eight Suspicious of malignancy and one Malignant according to Bethesda system. Histopathology specimen was received in 31 patients out of whom 20 (64.5%) patients were reported as colloid nodule, two follicular adenoma, one Hurthle cell adenoma, six papillary carcinoma and two follicular carcinoma. Medullary carcinoma and anaplastic carcinoma were not seen in the patients evaluated. Specificity and sensitivity of fine needle aspiration cytology was 94.7% and 88.9% respectively. Thus reporting thyroid lesions FNAC with Bethesda system allow a more specific cytological diagnosis.

KEYWORDS

Benign, Bethesda system, colloid, fine needle aspiration cytology (FNAC), thyroid lesions

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INTRODUCTION

Thyroid gland is the largest endocrine gland. Enlargement of the thyroid is caused by both neoplastic as well as non neoplastic conditions. Common non-neoplastic lesions of thyroid are goiter, thyroiditis, and Graves' disease and neoplastic conditions are follicular neoplasm, papillary carcinoma, medullary carcinoma and anaplastic carcinoma.¹

More than 50% of the world's population has at least a thyroid nodule.² Majority, around 95% of thyroid nodules are however benign.³ Thus it is very important to distinguish between benign nodules from malignant nodules preoperatively.

There are different diagnostic tests for thyroid lesions like thyroid function test (TFT), ultra sonogram (USG) and fine needle aspiration cytology (FNAC). FNAC is considered as one of the standard diagnostic test in evaluation of thyroid lesions; however other tests like USG and TFT should be used in conjunction with FNAC.⁴ It is cost-effective, simple, safe method for diagnosing thyroid lesions. It is diagnostic test to confirm benign lesions thereby reduces unnecessary surgery.⁵ Its diagnostic importance has increased because of the availability of ultrasound guided techniques which helps in diagnosing deep seated swellings, smaller thyroid swellings and lesions with solid and cystic component.

Numerous studies have proven the role of FNAC in thyroid lesions as the management depends upon the cytopathological diagnosis.² But there was a confusion related to the diagnostic terminology and management of the patients. Multiplicity of the category names, descriptive reports without assigned categories and variable terminology was the reason. This lack of uniform reporting confuses clinicians and results in inconsistent patient management, which is further complicated by lack of universal terminology.⁶ To address these issues, The Bethesda system of Reporting Thyroid Cytopathology (TBSRTC) was introduced in 2007.³ It helps in unifying the terminology and morphologic criteria along with the corresponding risk of malignancy.⁷ It is a uniform reporting system of thyroid FNAC that facilitate effective communication among the cytopathologist, endocrinologists, surgeons, radiologist and other health care providers.² It included six diagnostic categories for thyroid FNAC reporting- Unsatisfactory/ Non diagnostic (ND), Benign, Atypia of undetermined significance/ follicular lesion of undetermined significance (AUS/FLUS), Suspicious of follicular

neoplasm (SFM), suspicious of malignancy (SM) and Malignant.⁷

Detail clinical examination and radiology may help in diagnosing thyroid lesions but the management depends upon the cytopathological diagnosis. Due to the optimum use of FNAC and better understanding of cytomorphological characteristic of thyroid lesions by using Bethesda system, triaging of patients who are to be treated medically or surgically is more accurate. Thus it holds a very important diagnostic significance. The objective of present study is cytopathological evaluation of thyroid lesions based on Bethesda System and to co relate the cytological findings with histopathological findings where ever possible in patients attending Birat Medical College and Teaching Hospital.

MATERIALS AND METHODS

A cross sectional hospital based study was conducted in Department of Pathology Birat Medical College with approval from ethical committee from Birat Medical College. All patients attending Birat Medical College with thyroid lesions undergoing FNAC for a period of one year from 1st September 2019 to 31st August 2020 were evaluated. In hyperextended position FNAC was done using 24-26 gauge needle attached to 10 ml syringe under asptic conditions. Two to three passes were made. In the patients where swelling was not palpable, USG guided FNAC was done. The material aspirated was immediately transferred into glass slides half of which was air dried and half was fixed in ethyl alcohol for Giemsa stain and Papanicolaou (PAP) stain, respectively. Cytological features were evaluated by two pathologists under the microscope (Motic BA 210) and subsequently classified according to the Bethesda system.

Histopathological specimens wherever available were processed, microtomed and subsequently were stained by Hematoxylin and Eosin stain. Histopathological features were also evaluated by two pathologists. Data was entered in Microsoft excel. Frequencies of cases in each Bethesda categories were noted. Correlation with histopathological finding was done wherever available

RESULTS

During the study period, 104 patients with thyroid swelling underwent FNAC out of which 93 were female and 11 were male. The age ranged from 10 to 73 years with mean age of 37.3 years.

Among these cases, four turned out to be ND, 85 benign, three AUS/FLUS, three SFN and eight SM and one Malignant (Table 1).

Table1: Cytopathological diagnosis according to the Bethesda system.

Diagnostic category	n	%
ND	4	3.9
Benign	85	81.7
AUS/ FLUS	3	2.9
SFN	3	2.9
SM	8	7.7
Malignant	1	0.9
Total	104	100

About 46 patients (44.23%) of patients were diagnosed as goiter, which included nodular goiter along with cystic degeneration. Suspicious of follicular neoplasm and Suspicious for Hurthle cell neoplasm (Fig. 1) was also seen in 1.92% and 0.9% cases respectively. Eight cases showed suspicious for malignancy and one malignant lesion showed papillary (Fig. 2) carcinoma.

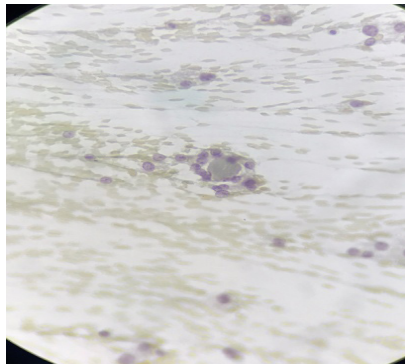


Fig.1: Hurthle cell neoplasm with cells arranged in follicle with inspissated colloid (PAP stain,40X)

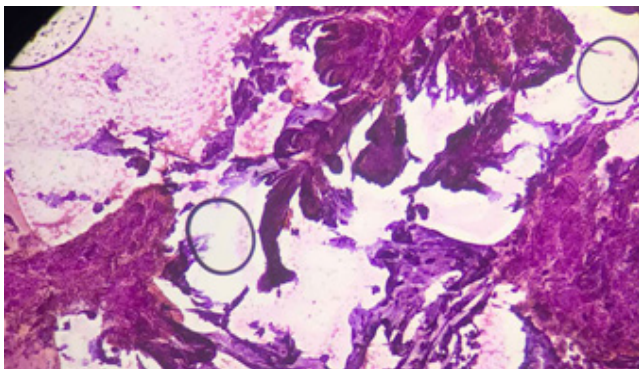


Fig. 2: Papillae formation (PAP stain,10X) with subset showing cells with nucleomegaly, nuclear crowding, clearing and grooving (40X)

Out of 104 cases histopathology was received in 31 patients out of whom 20 (64.5%) patients were reported as colloid nodule, two follicular adenoma, one Hurthle cell adenoma (Fig. 3), six papillary carcinoma and two follicular carcinoma. Medullary carcinoma and anaplastic carcinoma were not seen in the patients evaluated.

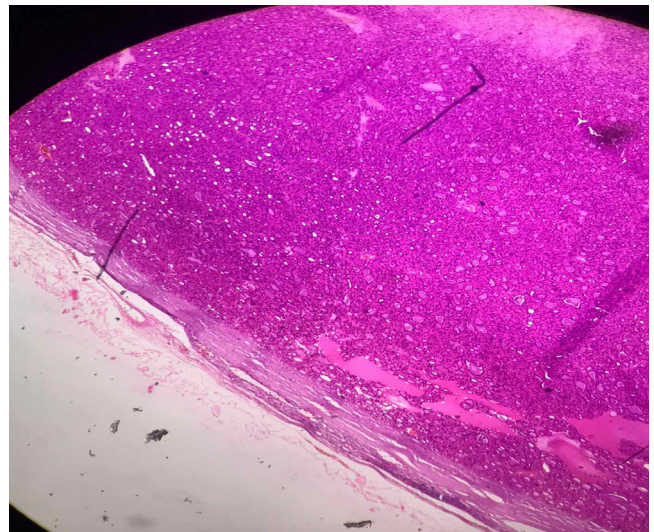


Fig. 3: Hurthle cell adenoma showing encapsulated tumor comprising predominantly of Hurthle cells. (H&E stain 10X)

Out of four cases reported as ND, one case was available for histopathological follow up which was reported as colloid nodule with cystic change. Out of 85 cases reported as benign, 19 cases were available for histopathological follow up. Eighteen cases were benign and one case was reported as papillary carcinoma. Thus risk of malignancy was 5.3%. There were three cases of AUS/FLUS out of histopathology was available in 2 cases which showed follicular adenoma. Thus the risk of malignancy was 0% in this study.

Three cases reported for SFN showed, Hurthle cell adenoma and two follicular carcinoma respectively with 66.66% risk of malignancy. Out of the 8 cases reported as suspicious for malignancy, histopathology was available in 5 out of which 4 cases showed papillary carcinoma and one showed colloid nodule with hyperplastic foci. Risk of malignancy was 80%. One malignant reported case was found to be papillary carcinoma in histology. Risk of malignancy was 100% (Table 2).

In the present study positive predictive value and negative predictive value were 88.88% and 94.73% respectively. Specificity and sensitivity were 94.7% and 88.88% respectively. (Table3).

Table 2: Cytological and histopathological diagnosis of thyroid lesions.

Bethesda category	FNAC diagnosis (n)	Histopathological diagnosis (n)
Category 1 (ND)	ND (4)	colloid nodule with cystic change (1)
Category 2 (Benign)	Colloid nodule including secondary changes (46) Thyroiditis (35) De Quervian's thyroiditis (2) Autoimmune thyroiditis (2)	colloid nodule (18) papillary carcinoma (1)
Category 3 (AUS/FLUS)	AUS (3)	Follicular adenoma (2)
Category 4 (SFN)	SFN (2) SFN Hurthle cell type (1)	Follicular carcinoma (2) Hurthle cell adenoma (1)
Category 5 (SM)	SM (8)	Colloid nodule with hyperplastic foci (1) Papillary carcinoma (4)
Category 6 (Malignant)	Papillary carcinoma (1)	Papillary carcinoma (1)
Total	104	31

Table 3: Cyto histopathological correlation of thyroid lesions

FNAC Diagnosis	FNAC cases (n)	Surgical biopsy (n)	Correct FNAC diagnosis	FN	FP
Benign	88	19	18	1	
Malignant	12	11	10		1
Unsatisfactory	4	1			
Total	104	31	28	1	1

FN: False negative, FP: False positive

DISCUSSION

In any thyroid lesions FNAC is the first line diagnostic test for triaging the patients as to who require surgery and who do not. Due to lack of standardized system of reporting, pathologist have been using different terminologies and diagnostic criteria thereby creating confusion among clinicians in the interpretation of cytopathology report and ultimately affecting the management. Reporting thyroid lesions FNAC with Bethesda system allow a more specific cytological diagnosis.⁸ In this study all the patients undergoing thyroid FNAC were reported as per Bethesda system and was compared it with histopathological finding wherever possible.

104 patients with thyroid lesions were evaluated. In this study the age of the patients ranged from 10 to 73 years with female preponderance (89.4%). Similar observations

were noted by Swarkar *et al.*⁹ Muratli *et al.*¹⁰, Sinna *et al.*¹¹ and Hajmoochehri *et al.*¹²

The inadequate rate in this study was 3.9% which is similar to the study by Bhartiya *et al.*¹³ Ali³ suggested that the rate of ND should be below 10%. Minimum number of 5-6 groups with at least ten cells is recommended for adequacy. Diagnoses of thyroiditis and in lesions with abundant thick colloid do not require minimum number of follicle cells.¹⁴ Any lesions with inadequate number of atypical cells or atypical pattern should not be interpreted as ND.¹⁵ Thyroid cyst with cystic macrophages and no follicular cells should be interpreted as cyst fluid only.

Many of the cases of ND category in this study showed cyst fluid only. USG guided FNAC from solid areas in predominantly cystic lesions increases the accuracy and ultimately reduces the need of unnecessary surgery.¹⁶ Hence

prior clinical and radiological finding is very important to determine the modality of FNAC and to increase the accuracy.

In the present study 96.15% (n=100) cytological smears were satisfactory for evaluation which is similar to study by Nandedkar *et al*⁵ and Sangalli *et al*.¹⁷

Most of the cases were in category 2 that correlates well with studies conducted by Sawarkar *et al*⁸, Mehrotra *et al*⁹, Yang *et al*¹⁵ and Mondal *et al*.¹⁸ The reason of majority of benign cases is that most of the cases come directly to the Medical College without any referral. Hence, the study group could be a representative of general population. On the other hand lower incidence of benign cases were seen in study by Jo *et al*¹⁹ and Yassa *et al*.²⁰

There were less number of cases 2.9% (n=3) diagnosed under category AUS/FLUS in the present study. This could be due to efforts in practice to avoid ambiguity and keep the use of AUS/FLUS to a minimum. Study by Jo *et al*¹⁹ and Yassa *et al*²⁰ reported 3.4% and 4% of cases of AUS/AFLUS respectively. However, Mondal *et al*⁸ reported lower percentage of AU/AFLUS (1%) could be because they strictly adhered to the diagnostic criteria and because of large sample size. About three percent (2.9%) of cases were diagnosed as SFN. Higher cases (10.52%) were seen in study by Nandedkar *et al*.⁵

In present study 7.7% (n=8) patients were categorized as suspicious of malignancy. Lower prevalence were seen in study by Nandedkar *et al*⁵ and Mondal *et al*⁸ who reported 1.9% and 1.8% respectively. This difference could be due to lower sample size in this study.

Out of 104 thyroid FNAC, 31 patients underwent surgery. By the Bethesda categorization in six categories and corresponding cytohistopathological correlation, malignant risk of each category was obtained in 31 cases.

On histology 8 out of 31 cases were malignant. One case was diagnosed as benign on cytology making false negative with malignant risk of 5.3%. This patient was diagnosed as colloid nodule with cystic change in cytology. Cystic neoplasm in thyroid is a common diagnostic pitfall in cytology.¹³ One case was reported as SM (Bethesda category 5) in FNAC but histopathological evaluation showed Colloid nodule with hyperplastic foci. False positive in this case could be due to aspiration from hyperplastic foci (hypercellular) of colloid nodule which led to over diagnosis. The AUS/FLUS category included two cases which were both benign on histopathology with 0%

malignancy rate. Similar finding was seen in study by Nandedkar *et al*.⁵ In the SFN category, two out of three patients had malignancy. The remaining case was diagnosed as adenoma. There is no reliable cytological feature that distinguishes follicular adenoma from follicular carcinoma and distinction between the two is based solely on demonstration of histologic evidence of capsular/vascular invasion.¹⁴

Histopathology of five out of eight cases of SM was received. One patient of this category was diagnosed as colloid nodule with cystic change in histology that brought down the risk of malignancy to 80%. USG guided FNAC from the solid areas have seen to reduce the sampling error on these type of cases.²¹

In the present study, sensitivity of the thyroid cytology was 88.88% which is similar to the study by Nandedkar *et al*⁵ and Aviranthan *et al*.²²

Specificity of thyroid cytology was 97.7% similar to that of Arvantham *et al*.²² Larger population of study would provide a better sensitivity and specificity of FNAC using Bethesda system. Positive predictive value and Negative predictive value in this study was 88.9% and 94.7% which was similar to the study by Reddy *et al*⁴ and Saddique *et al*.²³

In conclusion, this study showed that reporting of thyroid lesions cytopathology using Bethesda system is standardized initial modality for diagnosing thyroid lesions and triaging patients who require surgery or not. However a study over larger population would provide more information about the merits and demerits of the Bethesda system.

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