Cyto-histological Study of Thyroid Lesions in An Institute In A Rural Area.

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Abstract

Introduction: Thyroid swellings are a common clinical problem. The Bethesda system of FNAC has been used for the past 5-6 decades for the investigation of thyroid lesions. This system helps in categorising thyroid lesions and also suggests possible management. Histopathology is the gold standard for confirming diagnosis.

Aims and Objectives: To determine the incidence of thyroid lesions according to age and sex. To compare cytological diagnosis according to the Bethesda system of reporting with histological diagnosis and determine accuracy.

Materials and methods: This is a study done over a period of 5 years from January 2016 to December 2020 in the department of pathology in a medical college in a rural area. The number of thyroid aspirations done were 232. Smears were classified as per The Bethesda system. Cytological and histopathological findings were correlated in 50 cases that underwent surgery. Cases with diagnostic discrepancy were reviewed. The sensitivity and specificity, negative predictive value, positive predictive value and diagnostic accuracy values were calculated using standard statistical formulae.

Results: The thyroid lesions on cytology in the nondiagnostic, Benign, Atypia of unknown significance, Follicular neoplasia, Suspicious for malignancy and malignant category were 3.4%, 81.89%, 1.72%, 7.7%, 0.8% and 4.3% respectively. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy in our study was 78%, 84%, 78%, 87% and 84% respectively

Conclusion: The Bethesda system of classification of thyroid lesions on cytology helps in the diagnosis of thyroid lesions and their further management. Histopathological correlation helps in evaluating diagnostic accuracy and helps in quality assurance.

Key words: Thyroid, Bethesda, Correlation, Accuracy

Introduction

Thyroid swellings are a common clinical problem. This is an organ easily accessible for diagnostic fine needle aspiration cytology (FNAC). FNAC has been used for the past 5-6 decades for the investigation of thyroid lesions[1].The Bethesda system of reporting thyroid cytopathology is being followed the world over since its time of inception in 2007 and gained acceptance.

The Bethesda system recommended 6 diagnostic categories which are I-Nondiagnostic, II Benign, III -Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/ FLUS), IV-Follicular neoplasm (FN) or Suspicious for a follicular neoplasm (SFN), V-Suspicious for Malignancy (SM) and VI-Malignant[2]. This system helps in categorising thyroid lesions and their implied risk of malignancy and also guides in clinical management. Histological examination is the gold standard for definitive diagnosis. This study was undertaken to study thyroid lesions in this geographical area and also determine the accuracy of cytological diagnosis

Materials and methods:

This is a study done over a period of 5 years from January 2016 to December 2020 in the department of pathology in a medical college in a rural area after taking ethical clearance.

Inclusion Criteria: All patients with thyroid swellings sent for FNAC were included in the study.

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Exclusion criteria: Patients who refused FNAC and other neck lesions were excluded from the study.

FNAC was done using a syringe with a 22 to 23 gauge needle and the aspirate obtained after multiple passes were smeared on glass slides, stained with Papanicolau (Pap), Haematoxylin and Eosin (H&E) and May Grunwald Giemsa (MGG) and then studied under the microscope and classified as per the Bethesda system of reporting thyroid cytology. Age and sex predilection were determined.77 cases that underwent surgery were studied after appropriate grossing, regular processing and embedding followed by H&E staining. The most common lesion was determined. Following a histological diagnosis both cytology and histopathology was correlated in 50 cases. Cases with diagnostic discrepancy were reviewed. The number of true positive, false positive, true negative, false negative cases were determined and sensitivity and specificity, negative predictive value, positive predictive value and diagnostic accuracy were calculated using standard statistical formulae.

Results:

The total number of thyroid FNACs done was 232. Females outnumbered males in a ratio of 9:1. The most common age group involved was 21- 40 years. On classification of cytological findings as per the Bethesda system, there were 8 cases which were nondiagnostic (ND),191 benign lesions which included multinodular goiter (MNG), colloid cyst, adenomatous goiter, dominant nodule, Hashimotos thyroiditis, lymphocytic thyroiditis. Among the neoplastic category, there were 18 cases of follicular neoplasm, 2 cases of suspicious for malignancy and 10 malignant lesions of which 9 were diagnosed as papillary carcinoma and a case of anaplastic carcinoma. (Table 1)

Histopathological analysis was done on 77 cases that underwent surgery. On histological examination, the benign lesions were 49 (63.63%) and neoplastic lesions were 28 (36.25%). The most common lesion was multinodular goiter. Various descriptive terms used for MNG depending on cytological findings were colloid goiter, adenomatous goiter and dominant nodule. The next common nonneoplastic lesion was Hashimotos thyroiditis. The neoplastic lesions included follicular neoplasms, papillary carcinoma and medullary carcinoma. (Table 2)

Table1: FNAC diagnosis as per Bethesda System

TBSRTC category	Number of cases	%
Non Diagnostic	8	3.4
Benign	191	81.89
AUS/FLUS	3	1.72
FN/SFN	18	7.7
SM	2	0.86
Malignancy	10	4.3
Total	232	100

Table 2: Histopathological diagnosis of all cases where surgery done

Diagnosis	No of cases	Percentage
Multinodular goitre	42	54.54%
Hashimotos thyroiditis	7	9.09%
Follicular neoplasm	14	18.18%
Papillary carcinoma	13	16.88%
Medullary carcinoma	1	1.29%
Total	77	100

Table 3: Correlation of cytological diagnosis and histological diagnosis

FNAC Diagnosis	MNG	Thyroiditis	Follicular adenoma	Papillary carcinoma	Medullary carcinoma	Total cases
Benign	23	4	2	1	1	31
FN/SFN	2		8			10
SM				2		2
Malignant	2			5		7

MNG Multinodular goitre, FN Follicular neoplasia, SFN Suspicious for follicular neoplasm.

Fifty cases where both cytological and histological examination was done were correlated.

The histological diagnosis was categorised as nonneoplastic and neoplastic. Bethesda Category I, II and III were considered nonneoplastic and category IV, V and VI were considered neoplastic. The nondiagnostic category and AUS/FLUS were not taken into consideration because none of these cases underwent surgery. Correlating both cytology and histopathology True positives (TP) were 15cases. True negative cases (TN) were 27, False negative (FN) were 4 and False positive (FP) were 4 cases.

Statistical analysis:

Sensitivity(S)

TP/TP+FN x100 = 15/15+4 = 78%

True positives are patients with a positive neoplastic lesion in both cytology and histopathology. False negatives were patients who were diagnosed as having a benign lesion on FNAC but neoplastic on histology

Specificity (SP):

TN/TN+FP x 100 = 27/27+4 = 84%

True negatives were patients with benign nonneoplastic lesions both on cytology and histology. False positives were patients who were diagnosed as having a malignant lesion on cytology but it was benign on histology

Diagnostic accuracy (DA):

TP +TN/FP+FN + TP +TN = 15+27/ 4+4+15+27 = 84%

Positive predictive value (PPV):

TP/TP+FP = 15/15+4 = 78%

Negative predictive value (NPV):

TN/TN+FN = 27/27+4 = 87%

In our study, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 78%, 84%, 78%, 87% and 84% respectively.

Discussion

Thyroid FNAC is a routine diagnostic procedure followed the world over. It is a simple, safe and inexpensive procedure for the management of thyroid lesions. In this study, cytological diagnosis was based on the Bethesda system and correlated with histopathological diagnosis to determine accuracy.

In our study, the female to male ratio was 9:1. Incidence in females outnumbered that in males in all studies [3-10]. The most common age group involved was 21 to 40 years similar to other studies and was closest to the studies done by Nandedkar et al,[3] Sharma et al,[4] Md Iqbal Karim et al,[5] Haider et al[6] and Verma et al[7]. (Table 4)

Table 4: Comparison of incidence of Thyroid lesions as per Age, Sex, Benign and Malignant lesions in various studies and present study

Studies	Age group	F:M	Total cases	Benign	Malignant
Nandedkar et al[3]	21 -40	4.2 :1	171	87.72%	12.2%
Sharma et al[4]	30 -49	7: 1	200	79.5%	20.5%
Karim et al[5]	21 -40	2.2 :1	160	86.85%	13.15%
Haider et al[6]	20 -50	3.5 :1	340	76.3%	23.7%
Verma et al[7]	41 -50	4.3 :1	70	64.29%	35.71%
E Sinna et al[8]	14 -77	5.2 :1	296	53.7%	46.1%
Zhu et al[9]	15 -89	3.1 :1	1122	47.7%	52.4%
Anand et al[10]	7 -85	6.3 :1	646	84.9%	8.1%
Present study	21 -40	9: 1	232	87.01%	12.86%

Table 5: Distribution of lesions as per Bethesda classification in our study in comparison with other studies.

Studies	I	II	III	IV	V	VI	Total Cases
Nandedkar et al[3]	4.25%	82.6%	0.82%	9.48%	1.15%	1.98%	606
Sharma et al[4]	5.5%	74%	-	5.5%	2.5%	12.5%	200
Karim et al[5]	5%	78.1%	8.75%	5%	3.13%	5%	160
Haider et al[6]	10.6%	59.4%	6.3%	7.9%	7.9%	7.9%	340
E Sinna et al[8]	7.1%	33.1%	13.5%	16.5%	10.1%	19.5%	296
Zhu et al[9]	14.8%	17.1%	15.8%	2.3%	11.6%	38.5%	1122
Anand et al[10]	13.8%	75.9%	1.2%	3.7%	2.6%	2.8%	646
Upadhyaya et al[11]	2.8%	61.5%	-	11.9%	4.6%	19.3%	109
Arul et al[12]	5%	44.5%	2,9%	21.5%	15.3%	10.8%	483
Sukumaran et al[13]	6.04%	12.5%	4.43%	13.3%	4.03%	59.68%	248
Mehra et al[14]	7.2%	80%	4.9%	2.2%	3.6%	2.2%	225
Present study	3.4%	81.89%	1.72%	7.7%	0.86%	4.3%	232

In our study (n=224) 96% of the smears were adequate for diagnosis and only (n=8) 3.45% were inadequate. The nondiagnostic category ranged from 2.8% to 14.8% in various studies[3-6, 8-14]. Our study was closest to studies done by Nandedkar et al[3], Upadhyaya et al[11] and Arul et al[12]. In the nondiagnostic category most of the smears were unsatisfactory because they were obscured by blood and had less number of cells or had only macrophages and did not meet the criteria for adequacy. A smear with fewer cells but abundant colloid can be considered adequate in the case of a predominantly macrofollicular colloid goiter[2]. It is suggested that such cases have to be re-aspirated under ultrasound guidance[2].

Benign lesions in our study were 87.01% (n=191) which was similar to studies done by Nandedkar et al[3], Anand et al[10] but differed from studies done in West Asia and East Asia by EA Sinna et al[8] and Zhu et al[9] respectively and in one study done in India by Sukumaran et al[13]. In their studies, the malignant lesions were comparatively higher than benign lesions. Our hospital is a tertiary hospital and not a referral hospital therefore the number of malignant lesions were probably less and similar to the study done by Nandedkar et al[3].

In our study, there were only 3 (1.72%) cases of category III. The smears showed atypical nuclear features and were therefore included in this category. Atypia in endocrine cells is considered a normal feature. The number of cases in the AUS/FLUS category ranged from 0.82% to 15.8% in various studies. Our findings were closest to studies done by Nandedkar et al[3] and Anand et al[10].

In our study, neoplastic lesions were 30 cases (12.86%) and of these 18 (7.7%) were cases of follicular neoplasm, 2 (0.86%) cases of suspicious for malignancy and 10 (4.3%) cases of malignant lesions of which 9 were papillary carcinoma and one case of Anaplastic carcinoma. The incidence of neoplastic lesions ranged from 9.1% to 52.4% in various studies. The incidence of neoplastic lesions in our study was closest to that of Nandedkar et al[3] and Anand et al[10]. The most common malignancy in all studies including ours was papillary carcinoma.

A histopathological diagnosis was made in 77 cases that underwent surgery and both cytological and histological diagnosis was available only in 50 cases for correlation. Most of the cases with a benign diagnosis on FNAC did not undergo surgery.

Of the 50 cases according to the Bethesda system 31 of them were classified as benign of which 23 were Multinodular goiter and 4 were thyroiditis and considered true negative. There were 2 cases of benign follicular neoplasm and one case each of papillary carcinoma and medullary carcinoma on histopathology and were considered as false negative. The reason in these cases diagnosed as follicular neoplasms on histology was that there were larger number of macrofollicles, flat sheets of benign cells and colloid and the microfollicles were overlooked on cytology. In the case of papillary carcinoma, the lesion was cystic and the papillary focus would have been missed on needling, this being one of the most common reasons for a missed diagnosis of malignancy (Fig 1, Fig 2).

Figure 1: Gross appearance of a cystic nodule with Papillary carcinoma

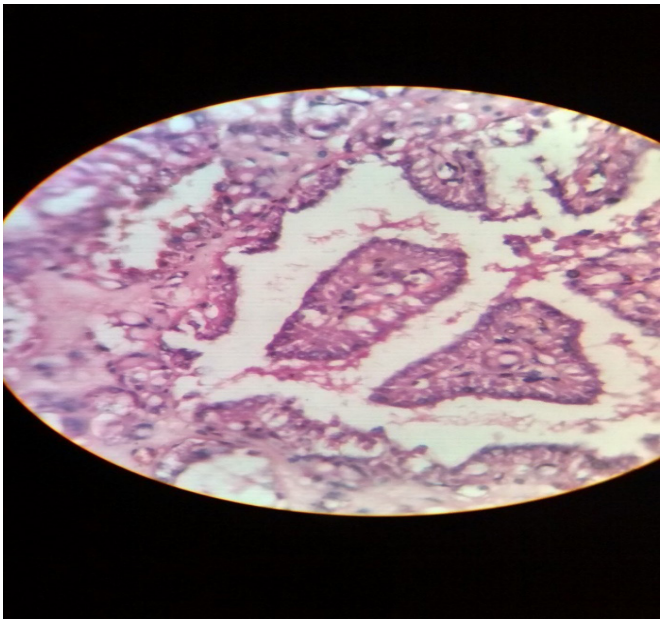

Figure 2: Papillary processes in a papillary carcinoma H&E 40x

The most common cause for false negative diagnosis

by FNAC was the presence of an unsampled microcarcinoma in an adenomatous goiter[9]. In the case of medullary carcinoma, our diagnosis was of a benign spindle cell lesion on cytology because there was high cellularity with spindle cells and the amyloid in the background was mistaken as fibrocollagenous stroma (Fig 3, Fig 4).

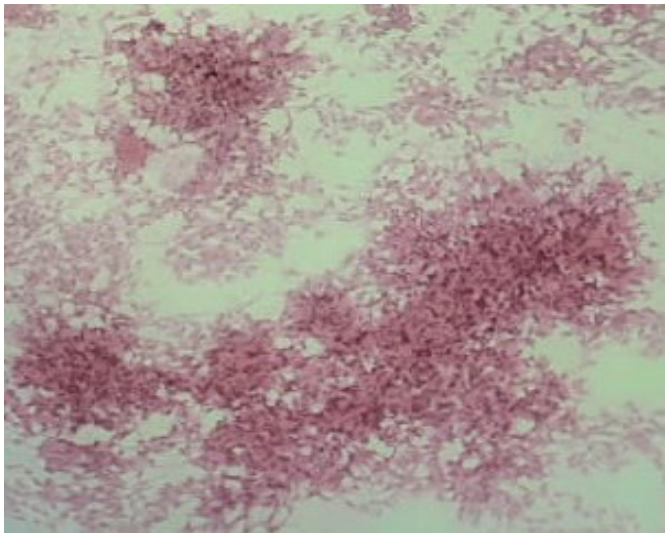

Figure 3: Smear showing high cellularity with spindle cells in Medullary carcinoma of Thyroid H&E 10X

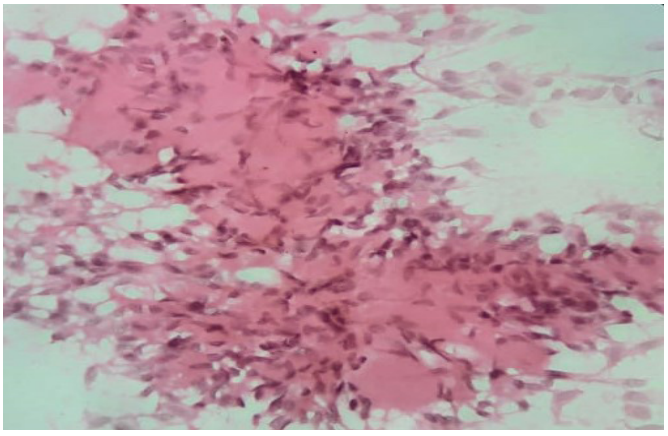

Figure 4: Amyloid in Medullary Carcinoma on FNAC H&E 40X

This brings to the fact that an experienced cytopathologist and correct technique are essential for a good and accurate diagnosis. False negative results can occur due to sampling error and rarely by misinterpretation[4,9,12].

Our false negative rate was 21% False negative rates varied from 1.85% to 22% in various studies done by Haider et al[4], Arul et al[12] Sukumaran et al[13], Asli Muratli[15] and Bagga et al[16].

None of the cases categorised as AUS/FLUS underwent surgery. Coming to the benign neoplastic lesions there were 8 cases of follicular neoplasms on histology. Two of the cases were diagnosed as nodular goiter on cytology and one of them turned out to be a parathyroid adenoma. Most of the follicular neoplasms prove not to be neoplasms but a hyperplastic proliferation of follicular cells in a multinodular goiter[2].It is very difficult to differentiate parathyroid adenoma from a follicular neoplasm because no cytologic criteria clearly distinguish parathyroid adenoma from follicular neoplasms[1]. This could have been because the parathyroid gland is closely associated with the thyroid and presented clinically as a thyroid swelling and the needle would have aspirated the normal adjacent thyroid. A case of parathyroid adenoma was also found in a study done by Aili Guo et al[17].

Of the 2 cases diagnosed as suspicious for papillary carcinoma on cytology, both were malignant on histology similar to a study by Nandedkar et al. In both these cases smears showed pattern A type which is associated with patchy nuclear changes where benign follicular cells were detected along with cells with nuclear enlargement, nuclear grooves, nuclear membrane irregularity and or nuclear moulding usually without a trace of intranuclear inclusions[18].

There were 9 cases of papillary carcinoma on cytology but 2 of them were reported as nodular goiter on histology. These smears showed moderate cellularity with few papillae and very occasional cells showing intranuclear grooves which can also be seen in other conditions. Some of the follicular cells showed degenerative changes giving a false impression of grooving. Histology showed papillary hyperplasia. Benign thyroid hyperplastic nodules show follicular cells with small dark nuclei in a honeycomb pattern however focal nuclear atypia, oval shape, chromatin clearing and overlapping can be seen in hyperplastic nodules leading to diagnostic difficulties[9].

The false positive cases were 4 in number. The false positive rate was higher in our studies and this is because of interpretative error. Our false positive rate was 12.9%. The false positive rates ranged from 0%- 15.5% in various studies[13,15,16]. The higher false negative rates are mostly because of interpretative errors rather than sampling errors[9].

In our study, the sensitivity, specificity, positive predictive value, negative predictive values and diagnostic accuracy were 78%, 84%, 78%, 87% and 84% respectively. Sensitivity ranged from 72.4% to 98.35 in various studies. Specificity ranged from 30.9% to 100% in various studies. Diagnostic accuracy ranged from 89% to 98% in various studies.(Table 6)

Table 6: Comparison of Sensitivity(S), Specificity (SP), Positive predictive value (PPV), Negative Predictive value (NPV) and Diagnostic Accuracy (DA) with other studies

Studies	S	SP	PPV	NPV	DA	Total No
Nandedkar et al[3]	85.7%	98.6%	97.1%	90%	98%	171
Sharma et al[4]	84%	100%	90%	-	-	40
Haider et al[6]	49.2%	84.2%	74.7%	63.5%	67.2%	303
Verma et al[7]	94.44%	84.62%	87.14%	68%	97.78%	70
E Sinna et al[8]	92.8%	94.2%	93.6%	94.9%	91.8%	296
Zhu et al[9]	98.35%	30.9%	94.9%	58.3%	93.55%	1122
Anand et al[10]	72.4%	94.3%	87.9%	84%	89.2%	100
Upadhyaya et al[11]	75%	100%	93.57%	100%	92%	109
Arul et al[12]	94.4%	97.6%	95.8%	98.1%	93.2%	209
Mehra et al[14]	78.57%	81.25%	64.71%%	89.66%	-	40
Muratli et al[16]	87.1%	64.6%	76.1%	79.5%	77.3%	126
Present study	78%	87%	78%	87%	84%	50

Our study included only 50 cases where both cytological and histopathological diagnosis was correlated. Sensitivity was lower because of a higher false negative rate[4]. Specificity and diagnostic accuracy were closest to studies done by Anand et al[10] and Sharma et al[4].Our values probably differ widely from other studies because the number of cases in our study were comparatively lower and our institute is a teaching hospital where diagnostic FNAC was done by people with varying experience both in sampling and also in interpretation.

In conclusion, FNAC is a relatively safe and simple procedure aiding in the diagnosis of thyroid lesions and their further management. Diagnostic errors are unavoidable due to overlapping cytological features among the various lesions. However, the pitfalls in diagnosis and sampling need to be addressed so that institutions can improve upon their diagnostic accuracy and allow for better management of patients. Improvement of technique and being aware of and updating knowledge for better interpretation and greater accuracy is also a measure of quality.

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