



UTILITY OF CYTODIAGNOSIS IN THE MANAGEMENT OF THYROID LESIONS

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ABSTRACT

Fine needle aspiration cytology (FNAC) has become an accepted and cost effective procedure for preoperative diagnosis of thyroid lesions. Present study was carried out to study the spectrum of thyroid lesions on cytology and to evaluate the diagnostic accuracy of FNAC in palpable thyroid lesions by comparing with histopathology wherever available. Total of 250 cases of thyroid swellings were aspirated over a period of 5 years in a tertiary care hospital. Cytologically, the cases were classified into 5 groups, namely, benign, inadequate, suspicious, malignant and cellular follicular lesions. There were 221 benign cases, 11 malignant, 2 suspicious, 6 inadequate and 10 with cellular follicular lesions. FNAC reports were compared with histopathology results and statistical indices were calculated. The sensitivity, specificity and diagnostic accuracy were 75.86% & 58.82%, 100% & 76.47% and 89.70% & 72.05% respectively considering suspicious cases alternatively as positives and negatives. FNAC is a highly sensitive and specific test with high diagnostic accuracy for preoperative evaluation of patients with thyroid swelling.

KEYWORDS: thyroid, fine needle aspiration, histopathology, accuracy.



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INTRODUCTION

Thyroid gland is unique among the endocrine organs as it is the largest endocrine gland in the body and the first to develop in fetal life.¹ Most common clinical finding in the thyroid gland is thyroid nodule which is defined as any abnormal growth of thyroid cells into a lump within the thyroid.¹ Thyroid nodules are common clinical findings and have a reported prevalence of 4-7% in the general population. Thyroid nodules are common in women.² Fine needle aspiration cytology (FNAC) of the thyroid gland is now a well established, first line diagnostic test for the evaluation of diffuse thyroid lesions as well as of thyroid nodules with the main purpose of confirming benign lesions and thereby, reducing unnecessary surgery.³ The diagnosis of thyroid lesions using aspiration cytology was first reported by Martin and Ellis in 1930.⁴ Clinicians have a variety of tests giving anatomical and functional information about the thyroid gland. Fine needle aspiration cytology (FNAC), by giving direct morphological information has supplanted most other tests for preoperative evaluation of thyroid nodules.⁵ The routine use of FNAC in the assessment of thyroid nodules has reduced the number of patients subjected to thyroidectomy for benign diseases of the thyroid.⁶ Hence, FNAC is considered to be the gold standard in the selection of patients for surgery.⁷ As a result, the incidence of malignancy at thyroidectomy has increased from 5-10% to 30-50% in the recent years.⁸ FNAC has become the dominant method in the evaluation of thyroid nodules as it is a fast, reliable, safe, minimally invasive and cost effective procedure with a high sensitivity and specificity.⁹ The present study was carried out to study the spectrum of thyroid lesions on cytology and to evaluate the diagnostic accuracy of FNAC in palpable thyroid lesions by comparing with histopathology wherever available.

MATERIALS AND METHODS

The present study is a five year analysis of patients referred to a tertiary care hospital for FNAC of thyroid lesions. After obtaining ethical committee clearance from our institution and informed consent from the

patients, FNAC was performed on 250 patients with diffuse or nodular thyroid enlargement and compared with histopathology wherever possible to determine the diagnostic accuracy. All the patients were clinically examined in detail and a careful palpation of the thyroid was done to guide precisely the location for doing aspiration. Details of the procedure were explained to the patients. Aspiration was done with the patient lying comfortably in a supine position and the neck was extended with a pillow under the shoulder so as to make the thyroid swelling appear prominent. Under aseptic precautions, 23gauge needle was inserted into the lesion without attachment to the syringe and to and fro motion performed quickly. The material gets collected in the base by capillary suction. The needle hub was attached to the air filled syringe and the plunger was pushed down to expel the material onto a clean labeled glass slide. In case of cystic nodules, the contents were aspirated with the syringe, centrifuged and slides made from the sediment for cytological analysis. Some of the smears were fixed in 95% ethyl alcohol and stained by Haematoxylin and Eosin (H&E) and Papanicolaou stain, others were air dried and stained with May Grunwald Giemsa stain. Ultrasound (USG) guided aspiration was done wherever necessary. Out of 250 patients, 71 were treated by surgeries like total, subtotal and hemithyroidectomies. Histopathological examination was done. These were fixed in 10% formalin, routinely processed and stained with H&E. Cytological diagnosis was correlated with histopathology and the efficacy of FNAC was estimated using methodology of Galen and Gambino.

Cytological diagnosis was classified as

1. Benign: Smears with large quantity of colloid and several groups (generally six or more) of normal appearing follicular cells with or without the presence of histiocytes. The benign lesions include colloid/ nodular goiter (CG/NG) and thyroiditis.
2. Cellular follicular proliferation (Follicular Lesion): When the smears show a profusion of follicular cells distributed in follicular structures or sheets with small quantity of colloid. Two cytological

categories are included in this group: a) Cellular follicular lesion favouring hyperplastic or adenomatous nodule b) Follicular neoplasm: If oxyphilic cells dominated a diagnosis suspicious of Hurthle cell neoplasm was made. In cases of follicular/ Hurthle cell neoplasm (FN/HN), histological evaluation was advised because the criteria for malignancy in these lesions are based on histological evidence of capsular/ vascular invasion.

3. Suspicious: When the smears show low cellularity but marked loss of cohesion. An aspirate was also labeled as suspicious when it showed some but not all features of papillary carcinoma such as fragments exhibiting papillary or pseudopapillary configuration, calcified bodies or nuclear clearing. All suspicious cases were advised surgery.
4. Malignant: The aspirates contained groups of cells with features considered diagnostic of primary thyroid cancer (papillary, medullary or anaplastic subtypes) or disease metastatic to thyroid.
5. Insufficient: Smears showing a minimum of six clusters of well preserved follicular cells with each group containing atleast ten cells were considered adequate. Aspirate considered insufficient had only blood or cyst fluid or scattered thyroid cells fewer than the above mentioned number without colloid.¹⁰

Statistical analysis

True positive (TP) and True negative (TN) cases are those which are diagnosed correctly as malignant and benign respectively. False positive (FP) cases consist of those cases which are benign but wrongly diagnosed as malignant. False negative refers to those cases which are malignant but are diagnosed as benign on cytology.¹¹ Sensitivity, specificity and accuracy were analyzed according to the standard criteria by Galen and Gambino.¹⁰

RESULTS

Thyroid enlargement, whether diffuse or nodular, leads to a battery of investigations like ultrasound (USG), thyroid function tests (TFTs), thyroid scan and FNAC, of which

FNAC is the most useful first line of investigation for early diagnosis and treatment of thyroid lesions. A total of 250 patients with thyroid lesions were subjected to FNAC during the five year study period. Of these, 71 patients underwent surgery and histopathological examination was done. Ages of the patients ranged from 10- 73 years with the peak age incidence being 20-40 years (54%). Females outnumbered the males with a male to female (M:F) ratio of 1: 7.06. Table 1 shows the age and sex distribution of the patients. All the patients presented with swelling in the thyroid region. Commonest symptom was dysphonia (7.93%) and hyperthyroidism (7.93%) followed by dysphagia (6.09%) and hypothyroidism (3.66%). Thyroid profile was available in 56 patients of which 7 were hyperthyroid, 6 were hypothyroid and the rest were euthyroid. FNAC results were interpreted as inadequate in 6 (2.4%), benign in 221 (88.4%), suspicious in 2 (0.8%), malignant in 11 (4.4%), cellular follicular lesion favouring adenomatoid nodule in 2 (0.8%), FN in 7 (2.8%) and HN in 1 case. Table 2 shows the detailed FNAC diagnosis in 250 cases. Histopathology was available in 71 cases (28.4%). Table 3 shows the correlation between FNAC and histopathology. Among 221 non neoplastic lesions diagnosed by cytology, histopathological studies were possible in 46 cases. The histopathological diagnosis remained the same in 37 cases and differed in 9 cases. Of these 9 cases, follicular adenoma (FA) was seen in 2 cases, papillary carcinoma (PC) in 5, follicular variant of PC (FVPC) in 1 and follicular carcinoma (FC) in 1. Out of 21 neoplastic lesions, histopathology was available in 20 cases and the diagnosis remained the same in 16 cases. It differed in 4 cases of cytologically diagnosed FN which turned out to be FVPC in 3 cases and dyshormonogenetic goiter (DG) in 1 case. Six aspirates were inadequate for evaluation even on repeated aspiration. Histopathological correlation was available in three cases and all were diagnosed as CG/NG. Two cases were diagnosed as suspicious for malignancy. On histopathology, one was a case of PC and the other was a case of multinodular goiter with chronic thyroiditis. For statistical analysis, the 6 inadequate cases were excluded. All cellular follicular lesions were considered as suspicious as no definite information (either

benign or malignant) could be communicated to the clinician based on cytologic findings. So the total number of suspicious cases were 12 out of 250 (including 2 suspicious cases showing some form of cytologic atypia and 10 cellular follicular lesions). Four of these cases turned out to be malignant. Analysis of the data

considering the suspicious cases (12 in number) alternatively as positive and negative showed.

1. Sensitivity of 75.86% and 58.82%
2. Specificity of 100% and 76.47%
3. Diagnostic accuracy of 89.70% and 72.05%

Table 1
Age and sex distribution of patients

Age	Males	Females	Number of patients
10-19	5	21	26
20-29	8	56	64
30-39	9	62	71
40-49	4	46	50
50-59	2	23	25
60-69	2	9	11
70-79	1	2	3
Total	31	219	250

Table 2
Distribution of lesions on FNAC

Diagnosis	Total	Percentage%
Benign	221	
Nodular/Colloid G	161	64.4%
Hashimoto's thyroiditis	60	24%
Inadequate	6	2.4%
Suspicious	2	0.8%
Malignant	11	4.4%
Papillary carcinoma	7	
Follicular carcinoma	2	
Anaplastic carcinoma	2	
Cellular follicular lesions	10	4%
Adenomatoid nodule	2	
Follicular neoplasm	7	
Hurthle cell neoplasm	1	

Table 3
Analysis of FNAC diagnosis and histopathology results in 71 patients

FNAC diagnosis	Histopathology diagnosis									Total
	NG/CG	HT	DG	AN	HN	FA	PC	FC	Anaplastic carcinoma	
NG/CG	30	0	0	0	0	1	6	1	0	38
HT	0	7	0	0	0	1	0	0	0	8
Inadequate	3	0	0	0	0	0	0	0	0	3
Suspicious	1	0	0	0	0	0	1	0	0	2
Malignant	0	0	0	0	0	0	7	2	1	10
Adenomatoid nodule(AN)	1	0	0	1	0	0	0	0	0	2
FN/HN	0	0	1	0	1	3	3	0	0	8
Total	35	7	1		1	5	17	3	1	71

Figure 1
Colloid Goiter: Abundant colloid showing the cracking artifact (H&E, 400x)



Figure 2
Hashimoto's Thyroiditis: Smear showing cluster of follicular cells and numerous lymphocytes (MGG, 400x)

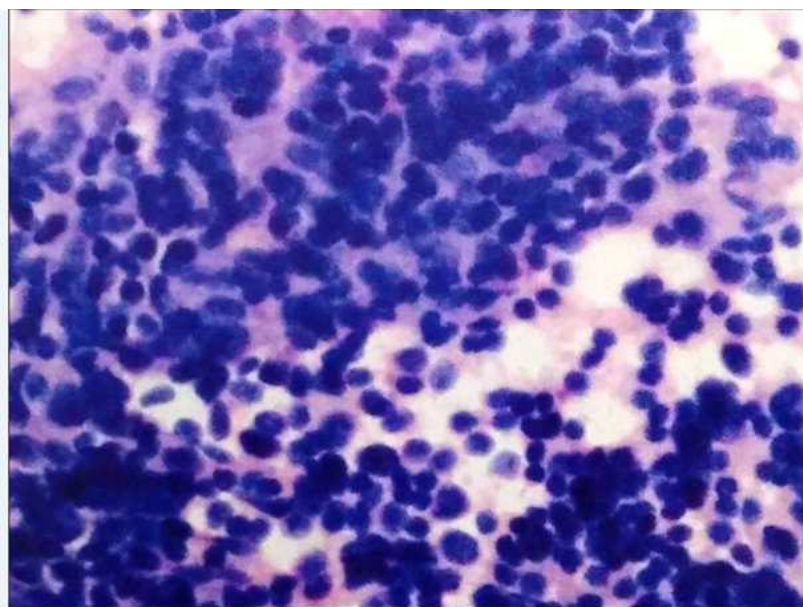


Figure 3

Papillary carcinoma: Highly cellular smear showing follicular cells in sheets and papillary pattern with vascular core (H&E, 400x) Inset shows intranuclear inclusions (MGG, 400x)

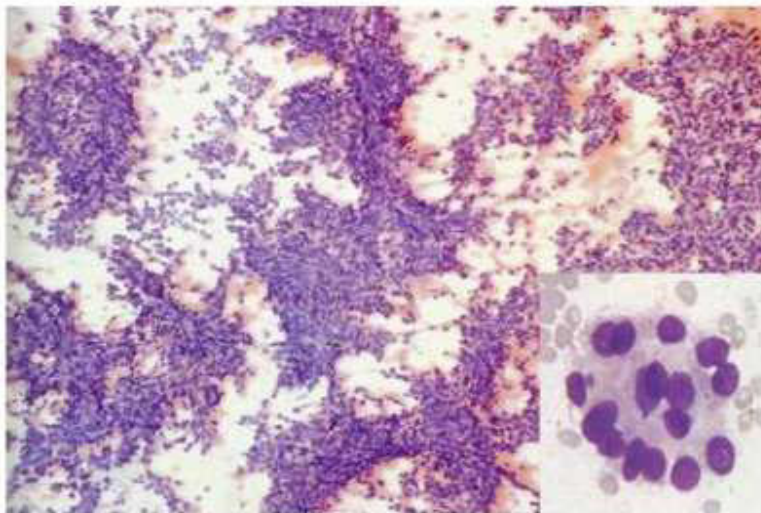


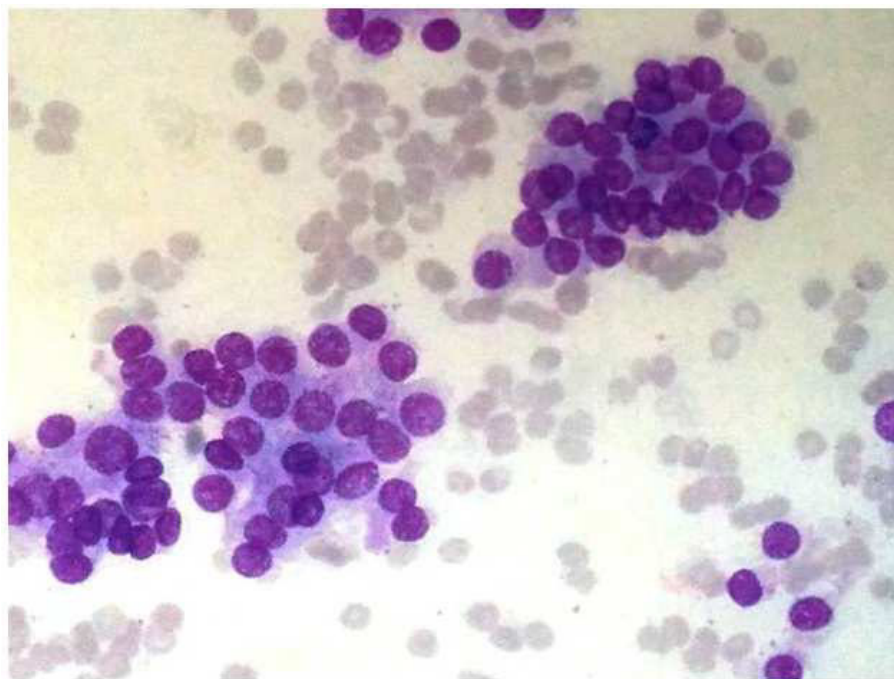
Figure 4

Anaplastic carcinoma: Cluster of pleomorphic plump spindle cells resembling malignant fibrous histiocytoma (H&E, 400x)



Figure 5

Follicular neoplasm: Smear showing repetitive follicular pattern. Follicular cells show round to oval enlarged nuclei with uniformly dispersed granular chromatin (MGG, 400x)



DISCUSSION

FNAC of the thyroid gland has radically changed the management of patients with thyroid disease. FNAC is widely accepted as the most accurate, sensitive, specific and cost effective diagnostic procedure in the preoperative assessment of thyroid nodules.⁵ In the present study, 221 (88.4%) patients were found to have benign thyroid lesions and of these, nodular/ colloid goiter (NG/CG) were found more commonly (64%). A similar observation was made by Bagga PK, et al where 228 out of 252 patients had benign thyroid lesions and 78.07% cases showed CG and CG with hyperplastic foci.⁵ Of the 161 cases of CG/NG, histopathology was available in 38 cases. The cytodiagnosis was confirmed in 30 cases. It differed in 8 cases, of which 5 were papillary carcinoma and one each of the FC, FVPC and FA. Out of 5 cases of PC whose diagnosis was missed on FNAC, two were associated with cystic change. Das et al have suggested that cystic papillary carcinoma is a common cause for false negative reports in cytology.¹² In the study by Afroze et al, PC was missed in two cases which were diagnosed as thyroid cysts.¹⁰ It is accepted that upto 5-10% of cancers,

excluding the occult types, cannot be diagnosed by FNA. This could be due to sampling error or cytodiagnostic error.¹⁰ In two other cases of PC which were misdiagnosed as CG/NG, there were tiny foci of PC in a multinodular goiter. Amrikachi et al have reported that such sampling errors leading to false negative results were due to not using USG guidance.¹³ One of the cases was misdiagnosed as CG with papillary hyperplasia. Smears in this case were cellular, arranged in papillary pattern with indistinct nuclear features. Mandrekar et al attributed their false negative results to geographical misses and cytodiagnostic error. They reported that such geographical misses can be avoided by thyroid imaging prior to FNAC so that cold nodules can be localized.¹⁴ This indicates that every case of NG should be sampled from multiple sites to avoid missing of associated neoplastic lesion. USG guidance improves the efficacy. One case of FA was misdiagnosed as CG/NG. The cytology smears showed moderate cellularity with many small clumps of thyroid follicular cells arranged in poorly cohesive groups with moderate amount of colloid. Aspiration in this

case probably done over colloid rich areas of the neoplasm. Possible remedial measures include careful observation of cytological features like nuclear overcrowding and overlapping, microfollicles, uniform cell patterns on repeat aspirates and scant colloid which may help in distinguishing between the two although none of them is conclusive.¹ In the present study, 60 cases of Hashimoto's thyroiditis (HT) were diagnosed. Oxyphil cells, abundant polymorphous population of lymphocytes, scant or no colloid were found on aspirates. In 10 cases, small multinucleated giant cells and epithelioid cells were seen. Gharib et al have reported in their study that multinucleated giant cells were not infrequent in HT.¹⁵ Histopathological examination was done in 8 cases and was consistent with the cytology report in 7 cases. One case turned out to be FA. In burnt out case of HT, only oxyphil cells are seen and distinction from FN/HN may then be impossible. Multiple sampling offers the best chance of finding evidence of lymphoid infiltration.¹⁶ In this study, 6 cases (2.4%) were reported as inadequate. Repeated aspirations from these patients yielded abundant colloid with few follicular cells and abundant macrophages and in one case, only cyst macrophages were seen against abundant colloid. Of these patients, 3 underwent surgery, 2 were diagnosed as multinodular goiter (MNG) and one as MNG with cystic degeneration. The frequency of inadequate cases was 2.35% in a study by Afroze et al which is comparable with our study.¹⁰ An inadequate sample is encountered when there are large areas of cystic degeneration or necrosis or due to aspiration of sclerotic or calcified nodules. The application of USG guided FNA improved specimen acquisition and reduced the rate of inadequate specimens, especially in patients with small thyroid nodules.¹⁷ Neoplastic lesions constituted 11 (4.4%) of the total number of cases. The incidence is comparable with Raveto et al (3.3%).¹⁸ PC was the most common malignant lesion seen in 7 cases (2.8%). Anaplastic carcinoma accounted for 2 (0.8%) cases and FC for 2 cases (0.8%). Handa et al diagnosed PC in 2.53% cases and anaplastic carcinoma in 0.002%.⁶ Paterson et al have reported that at least 2/3rd of thyroid carcinomas are

papillary in origin.¹⁹ This is comparable with our study where PC was seen in 7 out of 11 cases (63.63%). In the present study, all the 7 PCs which underwent surgery were true positive. Ko et al have reported a predictive value of a cytologic diagnosis as 100% for PC.²⁰ Two cases of PC showed lymph node metastasis. Tseng et al have reported the occurrence of PC in the thyroid gland in 67.2%, in the thyroid and cervical nodes in 13% and cervical lymph nodes only in 19.7%.²¹ Two cases of anaplastic carcinoma were diagnosed on FNAC. Highly pleomorphic cells, which were spindle like along with giant cells were seen against a necrotic background. Gharib et al in their study have stressed for a careful search for malignancy when necrosis and purulent inflammation are seen in the smears.¹⁵ Two cases of FC were diagnosed on cytology of which one was a case of recurrence and the other patient had metastatic deposits. The value of thyroid FNAC is however limited by its inability to distinguish follicular lesions reliably. This is probably due to overlapping cytologic criteria between hyperplastic nodule in a nodular goiter, FA, well differentiated FC and FVPC.^{22,5} Two cases were diagnosed as hyperplastic or adenomatoid nodules in a NG. Afroze et al have reported that marked cellularity of the smear is a problem inherent in thyroid FNAC.¹⁰ Seven FNs were reported in the present study. Histopathological examination of these cases showed 3 cases of FA, 3 cases of FVPC and one DG. On reviewing the FNA slides of FVPC cases, the smears showed numerous follicular cells in clusters with nuclear crowding and overlapping without colloid. The presence of follicular structure led to misinterpretation as has been encountered by others.³ Focal nuclear features like grooving were ignored in view of predominant follicular pattern. A possible remedy is multiple aspirations from different sites and many feel that nuclear features in more than 20 cells have a greater risk of PC and typical nuclear features are always helpful.²³ Three cases were diagnosed FA which correlated with the FNAC diagnosis. It is difficult to differentiate between follicular/ Hurthle cell adenoma from carcinoma on cytological assessment, because cytology cannot evaluate the criteria for vascular or capsular invasion or of intra thyroidal spread.¹⁰ One case of FN was

diagnosed as DG. Karak K, Sahoo M and Bhatnagar D in their study have made a diagnosis of follicular neoplasm. They concluded that albeit rare, dysmorphogenesis should also be included as a possible rare differential diagnosis for the typical cytological findings of follicular neoplasm.²⁴ The histopathology of DG showed hyperplastic nodules consisting of follicles with minimal colloid, cystic spaces lined by flattened cells and contained debris along with areas of fibrosis consistent with DG.

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CONCLUSION

FNAC is a safe, simple, cost effective and accurate method for management of palpable thyroid lesions. FNAC can be used as an initial modality in the evaluation of palpable thyroid nodules and helps in differentiating lesions that require surgery from those that can be managed otherwise. Surgery can be avoided in cases of CG and thyroiditis.

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