

## Usefulness of Preoperative FNAC of Thyroid Swelling Along with Application of Bethesda System of Reporting

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### ABSTRACT

**Introduction:** Fine needle aspiration cytology (FNAC) is the commonly used test for diagnosis of thyroid swellings. FNAC is a cost-effective procedure that provides specific diagnosis rapidly with minimal complications. Based on the cytology findings, patients can be subjected to surgery, thereby decreasing the rate of surgery and its consequent complications.

**Aims and Objective:** Study is aimed to accuracy of FNAC in thyroid as compare with histopathology and classify various cytomorphological lesions of thyroid according to The Bethesda System for Reporting of Thyroid Cytopathology (TBSRTC).

**Material and Methods:** This prospective study was done at our department from January 2013 to June 2015. Total 411 cases presented with thyroid swelling were subjected to thyroid fine needle aspiration cytology (FNAC) and the smears were made followed by routine staining and reporting. The categorization according to the Bethesda system of reporting thyroid cytology was done. The cytological diagnosis was correlated with the histological diagnosis wherever it was available. The accuracy of FNAC for the diagnosis of non-neoplastic and neoplastic lesions was determined using histopathology as the gold standard.

**Results:** Out of total 411 cases, 387 (94.16%) were benign, 15 (3.52%) were Follicular neoplasm, 7(1.70%) cases were malignant and 2 (0.48%) were inadequate. Most frequently encountered lesion was colloid goitre in 217 (52.79%) cases

followed by thyroiditis in 75 (18.24%) cases, 67 (16.30%) cases of nodular goitre, 26 (6.32%) cases of hyperplastic goitre and 2 (0.48%) cases of thyroglossal cysts. The cytological and histological concordance was determined in 97 cases. FNA revealed a sensitivity of 85.71%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 98.76%.

**Conclusion:** TBSRTC can help with a better patient's outcome due to proper clinical management of thyroid swellings and saves patients from unnecessary thyroid surgery.

**Key Words:** FNAC, Thyroid lesions, The Bethesda system.


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### INTRODUCTION

Thyroid diseases are frequently encountered endocrine disorders in clinical practice. Majority of these are benign, of which Goitre is the commonest. Only a few are malignant. The prevalence of goitre is more than 40 million in India with more than 2 billion globally.<sup>1</sup>

The prevalence of thyroid swelling ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children. The majority of clinically diagnosed thyroid swelling is non-neoplastic; only 5%–30% are malignant and require surgical intervention.<sup>2</sup>

Percentage of solitary thyroid nodule increases linearly with age along with increased prevalence of malignancy in third, fourth and fifth decades of life. Thyroid tumors are more prevalent in females and papillary carcinoma is the most common histological type of thyroid tumors followed by follicular carcinoma, medullary carcinoma, anaplastic carcinoma, non-Hodgkin's lymphoma and unclassified tumors in order of frequency.<sup>3</sup>

Fine needle aspiration technique was evolved first time by Martin and Ellis in 1934.<sup>4</sup> Subsequently Franzen et al (1968) described

the technique of aspiration cytology in detail.<sup>5</sup> FNAC is being reliable, minimally invasive and is considered the gold standard in evaluation of thyroid swelling. It is a simple, cost effective and having high sensitivity and specificity has been applied routinely as a useful and indispensable method to diagnose thyroid lesions. It can be readily repeated and quick to perform procedure in the outpatient department, with excellent patient compliance.<sup>6</sup> But like any other test FNAC also has its limitations. The reported pitfalls are those related to specimen adequacy, sampling techniques, the skill of the physician performing the aspiration, the experience of the pathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasm.<sup>7-9</sup>

This study aims correlating the cytological diagnosis with the final histopathological diagnosis to evaluate the sensitivity, specificity and predictive values of positive smears, thereby to assess its role in preoperative diagnosis and planning of proper management of Thyroid swellings.

**MATERIALS & METHODS**

This prospective study was conducted at Department of Pathology J. L. N. Medical College and Hospitals, Ajmer (Rajasthan) over the period of Jan 2013 to June 2015. Appropriate permission had been taken from Institutional ethics committee. Patients who gave informed consent and referred to Pathology laboratory with a clinical diagnosis of Thyroid swelling were included in this study. Uncooperative patients were excluded. All the referred patients, who had undergone routine investigations, were clinically evaluated in detail and a cautious palpation of the thyroid swelling was done to judge in particular the location for aspiration. FNAC was done on the thyroid swelling using a 24-26 gauge needle attached to a 5 ml syringe under aseptic precautions.<sup>10</sup> Then several smears were prepared and promptly fixed in a fixative containing 95% ethyl alcohol. These were stained by Hematoxylin and Eosin (H&E) stain.<sup>11</sup> Air dried smears were also prepared and stained with May Grunwald's Giemsa stain. Whenever fluid was found, all the contents were made to empty by gentle pressure in the thyroid gland. The fluid was centrifuged for Microscopic examination and smears were made from the sediment and. If residual mass felt, Re-aspiration was done.

At every time the biopsy specimen came in the pathology department, paraffin sections were made and stained by H&E. Histo-pathological examination was done. A Cyto-histopathological correlation of results was done to estimate the efficacy of FNAC. Pre-operative FNAC results were compared with final histopathological diagnosis. Taking histopathology as gold standard criteria, sensitivity, specificity and accuracy were calculated.

**RESULTS**

FNAC was performed on thyroid swelling of 411 patients, which included 372 (90.51%) females and 39 (9.49%) males and with F: M ratio of 9.54:1. The average age of total cases was 39.30 years

with a range of 6 years to 70 years. The most common presenting symptom was diffuse and or nodular swelling of the thyroid gland. Other symptoms reported by patients were pain in the midline neck, difficulty in swallowing and hoarseness of voice. The maximum number of cases 159 (38.68%) were presented within the duration of 1-6 months.

The FNAC results revealed 387 (94.16%) cases as non-neoplastic and 15 (3.64%) cases of Follicular neoplasm and 7 (1.70%) cases as neoplastic. On cytological examination a diagnosis of thyroglossal cyst was made in 2 cases (0.48%), Colloid goitre was present in 217 (52.79%) cases, Nodular goitre in 67 (16.30%) cases, hyperplastic goitre in 26 (6.32%) cases, Hashimoto's thyroiditis in 46 (11.22%) cases, Lymphocytic thyroiditis in 24 (5.38%) cases, 2 cases of Grave's Disease, 3 cases of Granulomatous thyroiditis. Follicular Neoplasm in 15 (3.64%) cases, 3 cases of Medullary Carcinoma, 3 cases of papillary carcinoma and 1 case of metastatic deposits of Breast carcinoma. [Table 1]

According to Bethesda system of classification out of total 411 cases, maximum numbers of cases were in benign category 387 (94.40%) cases, 15 (3.64%) cases under the Suspicious for Follicular Neoplasm/Follicular Neoplasm, 7 (1.70%) cases under malignant category, 2 cases under unsatisfactory smears. There were no cases found under the Atypia with Undetermined Significance and Suspicious for malignancy. [Table 2]

Cytological diagnosis and histological diagnosis of thyroid gland lesions were correlated in 97 cases. Results are found to be consistent in 85 cases (87.62%) and inconsistent in 12 cases (12.37%). There was 1 false negative case (which was cytologically diagnosed as benign and on histopathology found to be malignant). [Table 3]

The sensitivity, specificity and diagnostic accuracy of FNAC for detection of malignant lesions was 85.71%, 100% and 88.65% respectively. [Table 4]

**Table 1: Routine cytological diagnosis of 411 cases**

Cytological diagnosis	Male	Female	Total	Percentage (%)	pValue
Inadequate smear	-	2	2	0.48	
Benign	33	354	387	94.16	
Thyroglossal cyst	1	1	2	0.48	
Colloid Goitre	27	190	217	52.79	
Nodular Goitre	2	65	67	16.30	
Hyperplastic Goitre	2	24	26	6.32	0.002
Grave's Disease	-	2	2	0.48	(S)
Granulomatous Thyroiditis	-	3	3	0.72	
Hashimoto' Thyroiditis	-	46	46	11.19	
Lymphocytic Thyroiditis	1	23	24	5.84	
Malignant	7	15	22	5.35	
Follicular neoplasm	5	10	15	3.64	
Papillary carcinoma	1	2	3	0.72	
Medullary carcinoma	1	2	3	0.72	
Metastatic breast Carcinoma	-	1	1	0.24	
<b>Total</b>	<b>39</b>	<b>372</b>	<b>411</b>	<b>100</b>	

Chi-Square=9.30; pValue=0.0022 (significant)

**Table 2: Diagnostic categorization of 411 thyroid FNACs based on Bethesda classification**

Categories	Total no. of cases	Percentage (%)
Group 1: Inadequate smear	2	0.48
Group 2: Benign	387	94.16
Group 3: Atypia with Undetermined Significance	0	0
Group 4: Suspicious for FN/FN	15	3.64
Group 5: Suspicious for malignancy	0	0
Group 6: Malignant	7	1.70
<b>Total</b>	<b>411</b>	<b>100</b>

**Table 3: Comparison of routine Cytological diagnosis with 97 Histo-pathological Diagnosis**

Sr. No	Histopathological Diagnosis	Concordance with Cytological diagnosis	Dis-concordance	False Negative	False Positive	Accuracy (%)
1.	Thyroglossal cyst (1)	1	0	-	-	100
2.	Goitre (72)	69	3-Thyroglossal Cyst (1) Hashimoto's thyroiditis (2)			95.83
3.	Thyroiditis (5)	3	2- Colloid Goitre			60
4.	Hurthle cell Adenoma (1)	1	0			100
5.	Follicular Adenoma(12)	6	6- Colloid Goitre (4) Nodular Goitre (2)			50
6.	Follicular Carcinoma (3)	2	1-Hyperplastic nodular Goitre	1		66.67
7.	Papillary Carcinoma (3)	3	0			100
	<b>Total (97)</b>	<b>85</b>	<b>12</b>	<b>1</b>		
	<b>Percentage</b>	<b>87.62%</b>	<b>12.37%</b>			

**Table 4: Statistical values for thyroid malignant lesions**

True Positive	6
True Negative	80
False Positive	0
False Negative	1
Sensitivity	85.71
Specificity	100%
PPV	100%
NPV	98.76%
False positive error rate	0
False negative error rate	1.03%
Diagnostic Accuracy	88.65%

Sensitivity =  $(TP/TP+FN) \times 100$ ; Specificity =  $(TN/TN+FP) \times 100$   
 Positive predictive value =  $(TP/TP+FP) \times 100$ ; Negative predictive value =  $(TN/TN+FN) \times 100$   
 Diagnostic Accuracy =  $(TP+TN/FP+FN+TP+TN) \times 100$   
 False positive error rate =  $(FP/Total \text{ no. of cases}) \times 100$   
 False negative error rate =  $(FN/Total \text{ no. of cases}) \times 100$

**DISCUSSION**

FNAC is usually the first line of investigation and other investigations like ultrasound (US) examination, thyroid function tests, thyroid scan, and antibody levels are done subsequently with an aim to select the patients who require surgery and those that can be managed conservatively.

The present study was carried out with an aim to evaluate the role of aspiration cytology in diagnosis of various benign and malignant lesions of thyroid.

Aspiration biopsy is an extension of morphological diagnosis within both cytology and histopathology. It is also a useful tool for the oncologist, who deals with undiagnosed palpable and non-palpable masses and lesion. It is a short cut to direct diagnosis and can be carried out at the clinic or bed side. It will obviate the need for radiologist and surgical procedure, save time and expenses, and allay anxiety.

In the present study, cytological features of thyroid lesions were studied and correlated with histopathological diagnosis wherever available to determine its diagnostic accuracy.

The age group which was studied ranged from 6 years to 80 years and the mean age of patients with thyroid in our study was 39.3 years. In present study a female preponderance was noted with Male to Female ratio of 1: 9.54. Similar observations were noted by Sekhsar A et al.<sup>12</sup>

Neoplastic lesions were 7 (1.70%) cases, 15 (3.64%) cases of Follicular neoplasm and non-neoplastic lesions were 387 (94.16%) cases. Among the non-neoplastic lesion Colloid Goitre 217 (52.79 %) cases, Nodular goiter in 67 (16.30 %) cases,

hyperplastic goiter in 26 (6.32%) cases, Hashimoto's thyroiditis in 46 (11.22%) cases, Lymphocytic thyroiditis in 24 (5.38%) cases, 2 cases of Grave's Disease, 3 cases of Granulomatous thyroiditis and 2 (0.48%) cases were unsatisfactory, similar observations were also made by Handa U et al.<sup>13</sup>

For the purpose of study, the result of various lesion are classified according to the Bethesda System reporting terminology which includes six categories:<sup>14</sup>

In this study Category I or non-diagnostic had 2 cases or 0.48% in which sufficient material was not available, only cyst fluid, obscuring blood, only macrophage or preparation artifact.

Category II or Benign: majority of cases in our study were benign included in this category, maximum number of cases were colloid goitre 217 (52.79%), followed by thyroiditis 75 (18.24%), nodular goitre 67 (16.3%) and hyperplastic goitre 26 (6.32%), similar observations were made by Dr Vasudha M et al.<sup>15</sup>

Category III or AUS: It is reserved for specimens that contain cells with architectural and/or nuclear atypia that is not sufficient to be classified as suspicious for a follicular neoplasm. In our study we did not find any case in this category.

Category IV or FN/SFN: The goal of this category is to identify all potential follicular carcinomas and refer them for a diagnostic lobectomy. These cytomorphologic features do not permit distinction from follicular adenoma (FA), they are reportable as Follicular Neoplasm (FN) or suspicious of Follicular Neoplasm (SFN). The majority of FN/SFN cases turn out to be FAs or adenomatoid nodules of multi nodular goitre. Total 15 (3.64%) cases were found under this category.

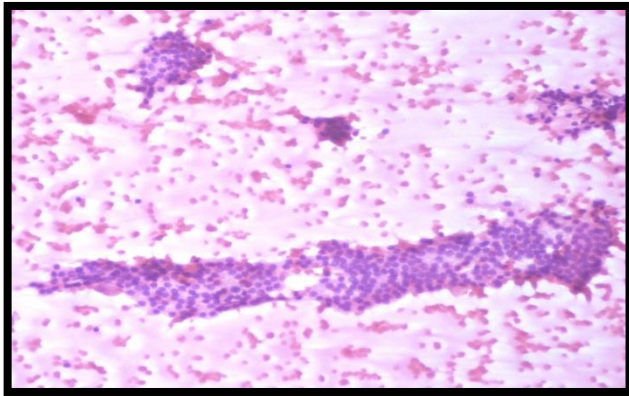


Fig 1: NODULAR GOITER: cytosmear shows monolayered sheet of thyroid follicular cells and clusters of follicular cells against the blood mixed thin colloid. (H & E; 400X)

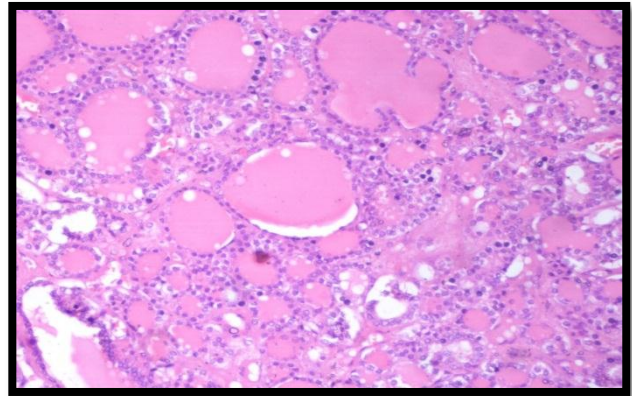


Fig 2: NODULAR GOITER: stained tissue sections shows thyroid filled follicles with flattening of lining epithelium. (H & E; 100x)

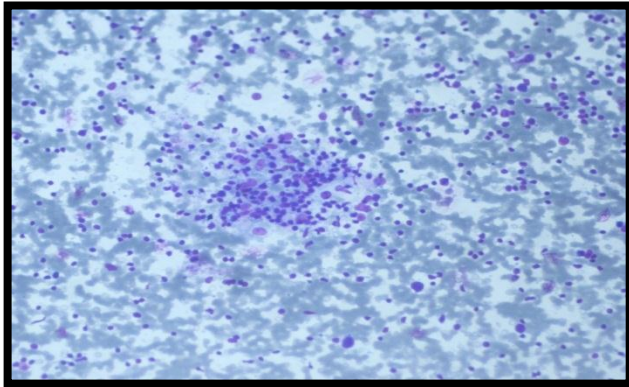


Fig 3: HASHIMOTO'S THYROIDITIS: cytosmear shows few thyroid follicular cells with askanazy change against the background of abundant lymphoid cells mixed with blood. (Giemsa; 100x)

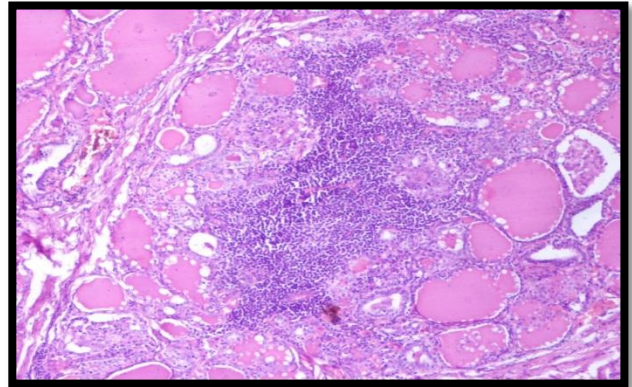


Fig 4: Hashimoto's Thyroiditis: Tissue section showing variable sized colloid filled follicles with dense lymphocytic infiltration and a prominent lymphoid follicle towards right side.(H & E; 100x)

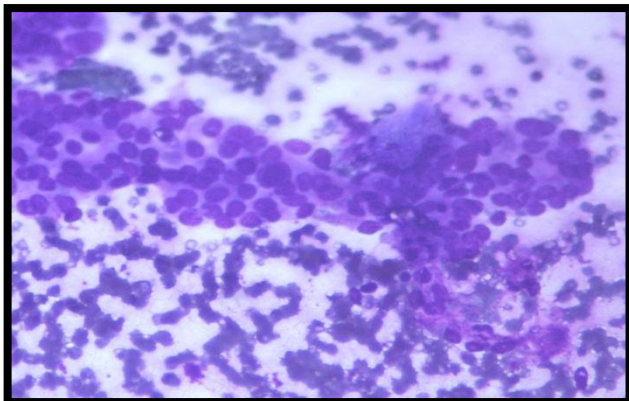


Fig 5: FOLLICULAR NEOPLASM: Cytosmear showing compact microfollicular clusters of follicular epithelial cells with scanty colloid. (Giemsa; 200X)

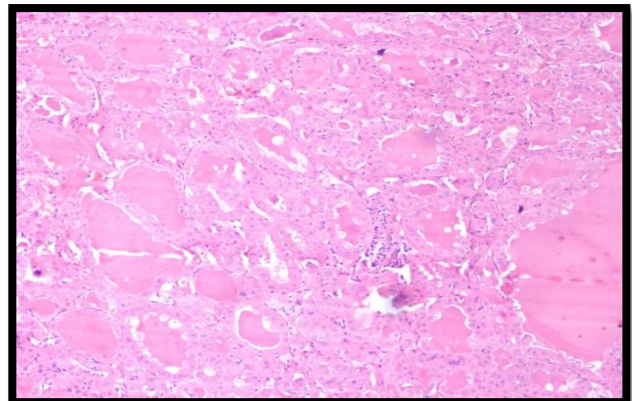


Fig 6: HURTHLE CELL ADENOMA: Tissue section shows follicles lined by cells having abundant eosinophilic granular cytoplasm and vesicular nuclei and colloid. (H & E; 200x)

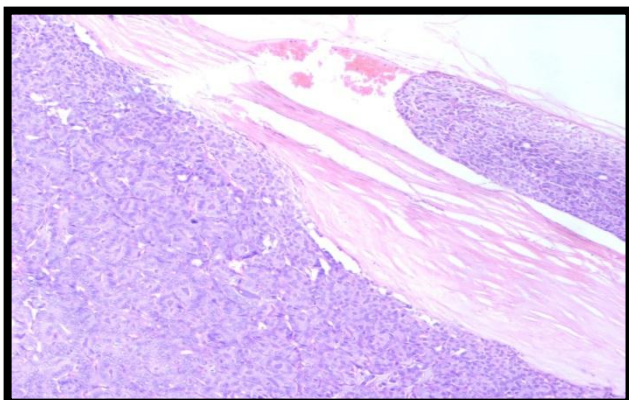


Fig 7: FOLLICULAR CARCINOMA: Tissue sections showing tumor mass and capsular and vascular invasion. (H & E; 200X)

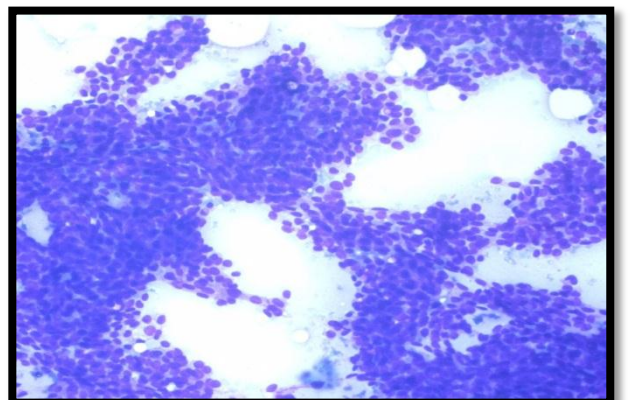
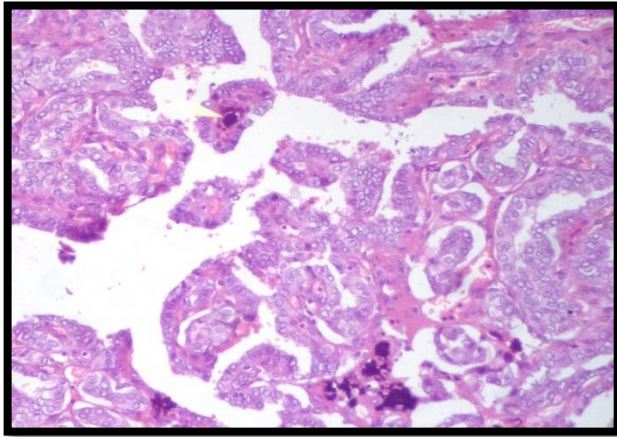


Fig 8: PAPILLARY CARCINOMA: Cells arranged in sheets and in clusters forming papillae with fibrovascular core. (Giemsa; 200X)



**Fig 9: Papillary Carcinoma: Tissue section showing papillae with fibrovascular core and overlapping of nuclei and optically clear nucleus, nuclear grooving and at places showing calcifications. (H & E; 200X)**

Category V or suspicious for malignancy: If there is 1 or 2 characteristic of malignancy present and they are only focal and not widespread throughout the follicular cell population, or if sample is sparsely cellular, a diagnosis cannot be made with certainty. In our study we did not find any case in this category.

Category VI or Malignant: The malignant category is used whenever the cytomorphic features are indicative of malignancy. Approximately 3% to 7% of thyroid FNAs have conclusive features of malignancy, and most are papillary carcinomas. Malignant lesions are usually treated by thyroidectomy. In this study 7 cases under this category.

In present study FNAC was done on total 411 cases, pre-operative FNAC results were compared with final histopathological diagnosis in 97 patients, out of 97 cases, 85 cases showed concordance with FNAC diagnosis, 12 cases not correlated with FNAC diagnosis.

The sensitivity of thyroid FNAC ranges from 65% to 99% and its specificity from 72% to 100%.<sup>16-18</sup> In our study, the sensitivity for cytological diagnosis of neoplasia was 85.71%, specificity of 100%, and diagnostic accuracy was 88.65%. This shows that FNAC is more specific than sensitive in detecting thyroid malignancy. Similar observations were also made by, Sumit Giri et al<sup>19</sup>, Bagga PK et al<sup>20</sup>, Prakash H et al<sup>21</sup>, Mahesh Kumar et al<sup>22</sup> and Naresh pahuja et al.<sup>23</sup>

There was one false negative case in our study which was diagnosed as adenomatous goitre in FNAC. On histopathological examination it was diagnosed as follicular carcinoma. The false negative FNAC results may occur because of sampling error or misinterpretation of cytology, and are of great concern because they indicate the potential to miss malignant lesion.<sup>24</sup>

## CONCLUSION

Management of patients with thyroid swellings has been radically changed by the routine use of FNAC. It has reduced the number of patients subjected to thyroidectomy for benign diseases of the thyroid. This relatively simple procedure has assumed a key role in determining of patients with thyroid swellings. However, equivocal FNAC results and diagnostic errors could not be avoided due to overlapping cytological features particularly in hyperplastic adenomatoid nodules, follicular neoplasms and follicular variants of papillary carcinomas.

TBSRTC (The Bethesda System for Reporting of Thyroid Cytology) is a vital guide for accurate management of thyroid lesions. Classifying the lesions in six categories and following the guidelines given by The Bethesda USA meetings solves all problems regarding the management of thyroid lesions and leaves no confusion. It plays a big role in establishing the uniform communications between the managing medical personnel. Marked cellularity of the smear is the problem inherent in thyroid FNAC. Increased cellularity of the smear and loss of cohesion may be present in hyperplastic/adenomatous goitre and follicular neoplasm which causes difficulty in differentiating them. This can be solved by using The Bethesda System of Reporting thyroid lesions.

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