



## Role Of Fnac In Thyroid Lesions

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### ABSTRACT

*Background: Fine needle aspiration cytology (FNAC) is a simple, safe, minimally invasive and outpatient procedure that commonly used in diagnosis of thyroid swellings.*

*Objective: The aim of the present study was to determine the prevalence, sensitivity, specificity and diagnostic accuracy of various thyroid lesions in our institute.*

*Material and Method: This prospective study was conducted in pathology department of our institute for the duration of 1 year (March 2013- April 2014). Total 90 patients were included in study irrespective of age and sex. Aspiration was taken after a written consent, detailed clinical history, physical examination and thyroid function test. FNAC results were compared with final histopathological diagnosis wherever feasible.*

*Result: The most common age group of presentation was 31-40 years with M:F -6.5:1. Out of total 90 cases of thyroid, FNAC revealed 70 cases (77.8%) as benign (Bethesda category 2) which comprises of colloid/nodular goitre (53.3%) and lymphocytic thyroiditis (24.5%) and 11 (12.5%) as malignant (Bethesda category 6). 5 cases (5.6%) were reported as follicular neoplasm (Bethesda category 4), 2 (2.2%) as suspicious for malignancy- (Bethesda category 5) and 1 case (1.1%) each as follicular lesion of indeterminate significance (Bethesda category 3) and cystic lesion (non diagnostic – Bethesda category 1). The sensitivity of FNAC in this study was found 70% and specificity was 94.7%. The overall diagnostic accuracy found to be 86.2%.*

*Conclusion: FNAC can use as first line of investigation for diagnosis of thyroid nodule. It is safe, inexpensive, outpatient procedure with high sensitivity, specificity and diagnostic accuracy.*

### KEYWORDS : FNAC, Goitre, Histopathology ,Thyroid

#### Introduction:

Thyroid swellings are a common clinical problem. Thyroid nodules may cause hypothyroidism, hyperthyroidism, cosmetic issues, and problems in other organs such as compression, and they also have the potential for malignancy.<sup>1</sup> Therefore, the accurate evaluation of thyroid nodules is crucial.

Palpable thyroid nodules are more common in women, and male/female ratio ranged from 1.2- 4.3.<sup>2,3</sup> Fine needle aspiration cytology is considered the gold standard diagnostic test for the diagnosis of thyroid nodules. It is minimally invasive with low complication rate. Based on cytology findings, patients can be followed in cases of benign diagnosis and subjected to surgery in malignant cases thereby decreasing the rate of unnecessary surgery. More over when surgery is indicated, FNAC can provide important pre-operative information to determine the type and extent of the surgery. It helps in triaging patients with solitary thyroid nodules to operative and non-operative groups.

The aim of this study was to determine the prevalence of various types of thyroid diseases in our institute and to evaluate effectiveness of FNAC through the correlation between cytological diagnoses of thyroid FNA and the postoperative histopathologic diagnoses.

#### Material and method:

This prospective study was conducted in pathology department of JLN Hospital and Research centre Bhilai (C.G.) for the duration of 1 year (March 2013- Feb 2014). A total of 90 cases were included irrespective of age or sex. Out of 90 cases histopathological correlation was available only in 29 cases.

**Technical aspect:** Aspiration was performed using disposable 5/10 ml syringe with a 23G needle. To reduce contamination of specimen with blood not more than 2 – 3 passes were made and non-aspiration technique was used in some. All the FNACs done during the 1 year period are enumerated. Adequacy of cytological smear is judged by presence of 5 – 6 groups of well preserved follicular cells, with each group containing 10 or more cells, according to Bethesda system of classification of thyroid diseases. Minimum 3 smears are made for each case. Staining is done by H&E, Papanicolaou and Giemsa methods.

Cytology reporting is done according to Bethesda system of classification of thyroid diseases.

#### Data analysis

The data collected was compiled in MS EXCEL 2007 SPSS (17.0) software. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Fine needle aspiration cytology were calculated by correlating the results of cytology with histopathology (Gold Standard) on samples which have gone through both tests, using Galen and Gambino method with following formulas.

1. Sensitivity = TP /TP+FN x100
2. Specificity = TN /TN+FP x 100
3. Positive predictive value = TP /TP + FP x 100
4. Negative predictive value = TN /TN+FN x100
5. Accuracy = TP +TN /TP+TN+FP+FN x100

Where, TP (True Positive) = defined as malignant cytological diagnosis from a lesion found to be malignant on histopathology.

TN (True Negative) = defined as benign cytological results from a lesion proved to be benign on histopathology.

FP (False Positive) = defined as a malignant FNA diagnosis which turned out to be benign on histopathology.

FN (False Negative) = defined as benign cytological results from a lesion which turned out to be malignant on histopathology.

p- Value of cytohistological association was calculated by using chi-square test.

#### Observation and results:

The youngest patient of our study was 20 years old and oldest was 70 years old. Most of the cases were from 21-50 years. The commonest age group of presentation was 31- 40 years (table- 01). Females were conspicuously outnumbered the males with M: F -6.5:1.

**Table-1: Age wise distribution of thyroid lesions**

Age Group	Number of patient
10-20	02
21-30	13
31-40	32
41-50	23
51-60	11
61-70	09
Total	90

Lesions of thyroid were reported according to Bethesda system of thyroid reporting. Out of total 90 cases of thyroid, FNAC revealed 70 cases (77.8%) as benign (Bethesda category 2 ) which comprises of colloid/nodular goitre (53.3%) and lymphocytic thyroiditis (24.5%) and 11 (12.5%) as malignant (Bethesda category 6). 5 cases (5.6%) were reported as follicular neoplasm (Bethesda category 4), 2 (2.2%) as suspicious for malignancy- (Bethesda category 5) and 1 case (1.1%) each as follicular lesion of indeterminate significance (Bethesda category 3) and cystic lesion (non diagnostic – Bethesda category 1) (table-02).

**Table -02 Distribution of various thyroid lesions according to Bethesda system**

Cytological Diagnosis		NO. OF CASES	%
1.Bethesda Category 1 Nondiagnostic/Unsatisfactory		01	1.1
2.Bethesda category 2 Benign lesions	Colloid Goitre	48	53.3
	Thyroiditis	22	24.5
3. Bethesda Category 3 Atypia Of Undetermined Significance/ Follicular Lesion Of Undetermined Significance		01	1.1
4. Bethesda category 4 follicular neoplasm		05	5.6
5. Bethesda category 5 suspicious for malignancy		02	2.2
6.Bethesda Category 6 Malignant (Papillary Carcinoma)		11	12.2
TOTAL		90	100.0

Histopathological correlation was available in 29 cases, which was in concordance with cytology in 25 cases, while 4 cases showed discordance which comprises of 3 false negative and 1 false positive case (Table -03)

**Table -03 Cytohistopathological correlation of thyroid lesions**

Sr no.	FNAC Diagnosis	No. of cases (90)	No. of cases with surgical biopsy (29)	Concordance (25)	Discordance (04)	Histopathological Diagnosis
1.	Cystic lesion(non diagnostic)	01	-	-	-	-
2.	Colloid goitre/Nodular Goitre	48	20	17	03	Colloid Goitre-17 Papillary Carcinoma-03
3.	Lymphocytic Thyroiditis	22	-	-	-	-
4.	Follicular lesion of undetermined significance	01	-	-	-	-
5.	Follicular Neoplasm	05	02	02	-	Follicular Carcinoma-01 Follicular Adenoma-01

6.	Suspicious for malignancy	02	01	-	01	Nodular goitre with papillary hyperplasia-01
7.	Malignant	11	06	06	-	Papillary Carcinoma-06
TOTAL		90	29	25	04	

**TABLE - 04 Analysis of cyto- histological co-relation of thyroid lesions (n= 29)**

		HISTOLOGY		TOTAL	COMMENT
		Benign	Malignant		
CYTOLOGY	Benign	18(TN)	3 (FN)	21	03 (FN)
	Malignant	01 (FP)	07(TP)	08	01 (FP)
Total		19	10	29	

Of these 29 cases, 21 were diagnosed as benign and 8 as malignant on cytology, whereas 19 cases were diagnosed as benign and 10 as malignant on histopathology. There were 3 false negative and 1 false positive cases (table-04). It showed strong association between cytological and histological diagnosis (p value <0.005).

The sensitivity, specificity, and accuracy of FNAC were calculated using Galen and Gambino method. The sensitivity of FNAC in this study was found 70% and specificity was 94.7%. The overall diagnostic accuracy found to be 86.2%.

**Discussion**

In present study total 90 (36%) aspirates were from thyroid gland, cytological diagnosis was classified into 6 groups based on standard 'BETHESDA SYSTEM'<sup>4</sup>of reporting thyroid lesions.

The commonest lesion encountered in this group was Colloid/Nodular Goitre (53.3%). Similar results were also observed by other authors which are shown below-

Studies	Colloid /nodular Goitre %
Tilak et al <sup>5</sup> (2002)	50%
Naila Tariq et al <sup>6</sup> ( 2007)	56.9%
G.G. Swamy et al <sup>7</sup> (2010)	52%
Gunvanti et al <sup>8</sup> (2012)	55.7%
Richa Sharma <sup>9</sup> (2012)	43.3%
Present study	53.3%

Out of 48 cases of Colloid/Nodular goitre, Histological correlation was available in 20 cases, which showed concordance with cytology in 17 cases (True Negative) and discordance in 3 cases.

**DISCREPANT RESULTS**

3 cases of cytologically diagnosed nodular goitre turned out to be papillary carcinoma on histopathology (False Negative -10.3%). Amatya B B et al<sup>10</sup>, Richa Sharma et al<sup>9</sup> and J Ayub et al<sup>11</sup>, found incidence of false negative cases 5.4% 13.6% and 4.7% respectively. Ashcraft and van Herle noted that false negative results varied in reported series from 2-50%<sup>12</sup>.

**Discrepant results can be due to following reasons**

1. Inadequate smear- Poorly cellular smear as encountered in large cystic papillary carcinoma; in marked desmoplasia, and in cases of thick fibrous or calcified capsule. We did not miss malignancy due to poor cellularity in our study. However, to avoid the false negative results, in cases of poorly cellular and excessive haemorrhagic smear, one can use liquid based cytology which enriches cell yield.<sup>13</sup>

2. Sampling error (geographic misses) – One of the three cytologically false negative cases was due to the aspiration needle failing to hit the exact pathological site. Histopathology demonstrated the presence of Papillary microcarcinoma. In cases of Papillary microcarcinoma, needle may not hit the target area<sup>10</sup>. "Papillary microcarcinoma" defined as papillary carcinoma measuring ≤ 1 cm in diameter. At high power, appearance of papillary microcarcinoma is not different from its larger counterpart. It is extremely common incidental finding seen in more than 25% of thyroid removed for other lesions<sup>10</sup>. Yang et al<sup>14</sup> emphasized on the importance of USG guided FNAC in sampling

micro carcinomas.

3. Dual pathology- In our study, two of the three cytologically false negative cases were due to dual pathology (Papillary carcinoma co-existing with nodular goitre). Gagnetten<sup>15</sup> stressed the importance of doing multiple aspirations in a large thyroid swelling in order to obtain representative material from different areas since the thyroid can be affected by more than one disease process simultaneously.

4. Interpretative error- It could be due to absence of clear cut features of benign/malignant lesion. We did not miss any malignant lesion due to wrong interpretation. All the 3 false negative cases were due to non-representative material obtained, as described above. To avoid interpretative error, one should ideally use all the stains (H & E, PAP, and MGG) on cytology smears which we did in all thyroid lesions. In PAP stain, thin colloid stains from pale green to orange with cracking artefacts and thick colloid forms clumps of variably dark green or orange material. The blue/ violet staining and hyaline texture makes colloid easier to identify in MGG stain than PAP stain. Colloid fire flares and amyloid are well depicted in MGG stain while oncocytes, psammoma body and nuclear characters are well seen in PAP stain. PAP stain also highlights the watery clear nuclei of papillary carcinoma.<sup>14</sup>

Though we had no false negative result attributed to interpretative error, one case diagnosed as suspicious for papillary carcinoma on cytology turned out to be nodular goitre with papillary hyperplasia (False Positive -3.4%) on histopathology. Other studies show False positive rates ranged from 0-8%<sup>16,17</sup>.

In our case, based on high cellularity and presence of papillaroid configuration along with occasional nuclear clearing and grooving, it was suspected for papillary carcinoma on cytology, however histopathological examination showed nodular goitre with papillary hyperplasia. Classical nuclear features of papillary carcinoma were absent in most parts of lesions. Overdiagnosis of neoplasia in case of adenomatous hyperplasia is well known on FNA smear<sup>18</sup> and only implies that unless classical nuclear features of papillary carcinoma are appreciated in the smear, the diagnosis of papillary carcinoma should not be considered on FNA.

Heimann A et al<sup>19</sup> suggests multiple criteria must be observed before making a confident diagnosis of papillary carcinoma. Logistic regression analysis of various criteria suggested that a combination of an intranuclear cytoplasmic inclusion, papillary structure with or without adherent vessel and dense metaplastic cytoplasm, were the three most common variants.<sup>20</sup>

11 cases (12.2%) were diagnosed as malignant (papillary carcinoma) on cytology, out of them histopathological correlation were available in 6 cases. It is to be stressed that all 6 cases were in concordance with cytological finding and showed accuracy of 100%. This is comparable with other studies<sup>7,9</sup>.

5 cases (5.6%) diagnosed as follicular neoplasm and 1 case (1.1%) as follicular lesion of undetermined significance. Histopathological examination was done in two out of five cases of follicular neoplasm, which showed follicular adenoma in one and follicular carcinoma in the other case. Histopathological examination was not available in the one case of follicular lesion of undetermined significance.

The differentiation of follicular adenoma from follicular carcinoma based on cytological criteria is difficult and challenging as cytological appearance of both is very similar. This requires capsular/ vascular invasion to be demonstrated, which cannot be seen in the smears.

Lowhagen et al<sup>21</sup> advocated that a cytological report should only state that a follicular neoplasm is present with no implication of its benign or malignant nature. Friedman et al<sup>22</sup> as early as in 1979 advised histopathological examination in such cases for final diagnosis based on capsular and vascular invasion. Bethesda system (2007) also mentions about Follicular Neoplasm (category- 4) with no differentiation between adenoma and carcinoma on cytology.

In our study, one case (1.1%) was diagnosed as cystic lesion (Bethesda Category-1). This case could not be further worked-up as patient was lost to follow-up. Cystic thyroid lesion often poses diagnostic difficulty. It is important that in such case reasonable evidence of a benign

lesion is established and malignancy ruled out, since in one series cystic changes and/haemorrhage in neoplasm was present up to 25% of primary papillary carcinoma and in 20% of follicular neoplasm. Occasionally aspiration itself can prove therapeutic in case of cystic thyroid lesion.<sup>5</sup>

In this study the sensitivity, specificity, and diagnostic accuracy of FNAC for thyroid lesions were 70%, 94.7%, and 86.2% respectively. Results of other studies shown below:

Study	Sensitivity	Specificity	Accuracy
G.G swamy et al <sup>7</sup>	80%	86.6%	84%
J Ayub et al <sup>23</sup>	61.5%	98.9%	-
Kessler et al <sup>24</sup>	79%	98.5%	87%
Present study	70%	94.7%	86.2%

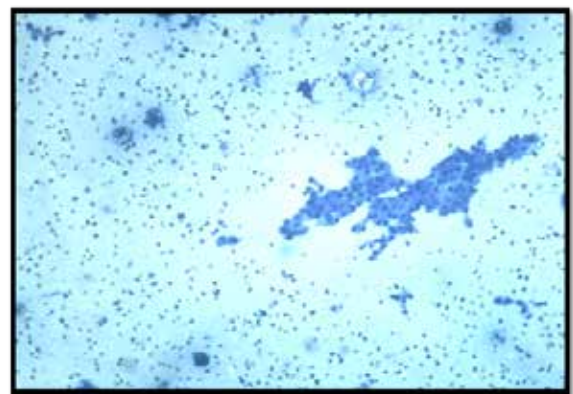
**Conclusion:**

Statistical analysis of various benign and malignant thyroid lesions, show strong co-relation between cytological and histological diagnosis. Hence, FNAC can be considered highly efficacious in distinguishing between benign and malignant thyroid lesions. FNAC can be used as an alternative tool to tedious surgical biopsy in these lesions (especially useful in debilitated patients who are not fit for surgery). A team work between a cytopathologist, radiologist and clinician maximises the diagnostic utility of FNAC.

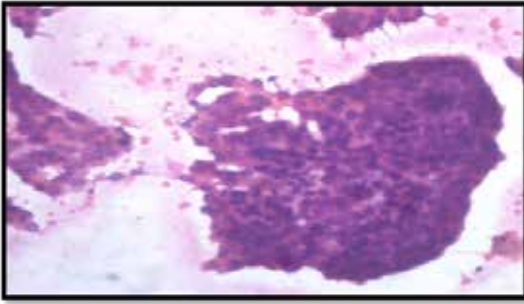
**PHOTO MICROGRAPH.**



**Clinical Photograph of a patient with midline neck swelling (thyroid region).**



**COLLOID GOITRE WITH CYSTIC DEGERATION- Thyroid follicular cells in sheet in a background of colloid and macrophages (MGG 10X4).**



**PAPILLARY CARCINOMA THYROID- tip of papillae with nuclear overlapping and clearing.(H&E, 10X10)**  
 clinician maximises the diagnostic utility of FNAC.

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