

Clinico-Cytological Spectrum Of Thyroid Mass Lesions Using FNAC And Corellating Biopsy

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Abstracts: Background: Fine needle aspiration technique generally applied, involves firm attachment of the aspiration needle to a syringe usually held in a specially designed syringe holder ie franzen's handle, that enables single handed application of suction. The main aim of suction is to hold the cells against sharp cutting edge of the needle. It is the initial screening test for patients with thyroid lesions. Objective is 1) to find out diagnostic accuracy and role of fine needle aspiration cytology in the diagnosis of thyroid lesions, and to establish cyto-histopathological correlation. 2) to find out sensitivity, specificity, positive and negative predictive value, pitfalls and complications of fnac in the diagnosis of thyroid lesions. Methodology & Results: The present study was carried out on 110 patients presenting with thyroid lesions. FNA was conducted in cytology department of mmimsr mullana from July 2011 to Nov. 2013. In all cases, a thorough clinical examination including detailed history, general examination and local examination of thyroid gland was performed and findings recorded. FNA was performed in all cases without anesthesia keeping in view the clinical diagnosis. Equipments: included disposable syringe(10 ml), 2.5 cm long and 23-25 gauge disposable needles, Coplin jars, Cotton, and Clean glass slides. Chemicals and reagents included Spirit, Fixatives (alcohols) and Reagents for hematoxylin and eosin stain (H&E), Giemsa stain, and papanicolaou stain etc. Conclusion: FNAC is a well developed, cost effective and frequently used method carrying low morbidity. It is also widely accepted as most accurate procedure to differentiate benign and malignant thyroid nodules and helps preoperatively in selecting patients for surgery. FNAC used together with other diagnostic modalities such as thyroid scanning, ultrasonography, thyroid hormone profile and antibody level measurements enhances diagnostic accuracy of the technique. [Chand N NJIRM 2015; 6(2):84-89]

Key Words: FNAC, Cytological, Histological, Sensitivity, Specificity.

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Introduction: A clinician is always in search of an easy, harmless and accurate diagnostic modality, which will give him correct picture of a disease. Diagnostic methods for surgical lesions, that can't be diagnosed correctly by biochemical and occasionally by radiological methods also, have undergone a lot of modifications and improved a lot in the 20th century. For over 100 years, the discipline of anatomical pathology was centered on diagnostic histopathology, and now on surgical biopsy. The pathologist sitting on his microscope, analyzing the arrangement and pictorial patterns of cells, frequently provides the definitive diagnosis by which, therapy is determined.¹

Fine needle aspiration cytology (FNAC) is one of the most rapidly advancing fields of diagnostic cytopathology. In fact, cytopathology has already attained a status of independent specialization. Core needle biopsy is an extremely supplementary tool in selected cases, however FNAC remains the

first choice for the initial investigation and diagnosis of both superficial and deep lesions. FNAC made a remarkable comeback in a big way only in late twenties, although historical developments in cytopathology can be traced back to nineteenth century. Since then developments in these fields have been remarkable.

Aims And Objectives:

- 1) To find out diagnostic accuracy and role of fine needle aspiration cytology in the diagnosis of thyroid lesions. And to establish cyto-histological correlation.
- 2) To find out sensitivity, specificity, positive and negative predictive value, pitfalls and complications of FNAC.

Material and Methods: The present study was carried out on 110 patients presenting with thyroid lesions. FNA was taken without anesthesia, in cytology OPD of Pathology department of

MMIMS&R Mullana, Ambala (HR) from July 2011 to Nov. 2013. 104/110 cases were subjected to surgical biopsy. In all cases, a thorough clinical examination including detailed clinical history, general physical examination and local examination of thyroid gland was done and findings recorded. The presumptive clinical diagnosis was made.

Equipments: 10 ml disposable syringe, 2.5 cm long and 23-25 gauge disposable needles, Cotton swabs, Coplin jars for fixatives and Clean glass slides respectively. **Chemicals and reagents:** include **Spirit:** for local disinfection. **Fixatives:** Ether alcohol mixture, 50-50 v/v for wet smears and methanol for air dried smears. **Reagents** for hematoxylin and eosin stain (H&E) Giemsa stain, and papanicolaou stain etc.

Procedure of FNA sampling: Patient was explained about procedure and consent taken. Patient was asked to lie in supine position and by placing a pillow under the neck to maximize exposure of gland. Patient was instructed to keep still and to restrain from swallowing. Material was obtained by using a 2.5 cm long, 23-25 gauge needle attached to 10 ml disposable syringe by applying mild suction. Multiple smears prepared and equally divided into air dried and wet fixed smears. Wet fixed smears were immediately fixed in ether-alcohol mixture taking precaution that smears did not get air dried. These smears were stained with H & E stain/ Pap stain. Smears intended for Giemsa stain were quickly air dried, fixed with methanol and stained. Specimens were considered "unsuitable" for cytodiagnosis, if they consisted mainly of blood or absence of cellular material, making them inadequate for determination of benign or malignant change. Specimens were considered cellular/ adequate, where at least 5-6 clusters of cells with more than 10 cells per cluster in at least two slides prepared from different aspirates are present. So smears were divided into satisfactory and unsatisfactory smears. All lesions were diagnosed cytologically after clinical correlation and later compared Histologically with available biopsies.²

Results: 110 patients presenting with thyroid lesions were subjected to FNA. Only 104 biopsies were available for histological correlation.

Table 1: Age and Sex Wise Distribution Of Cytological Diagnoses

Cyto-logical diagnosis	No. of Case	Age in years						Sex		%
		0-10	11-20	21-30	31-40	41-50	51-60	M	F	
		-	-	-	-	-	-			
In-adequate	10	-	-	03	04	03	-	2	8	9.1
Goitre (BFL)	79	-	08	26	21	21	03	10	69	71
Follicular Neoplasms	02	-	-	-	01	01	-	0	2	1.8
Lymphocytic thyroiditis	01	-	-	01	02	-	01	0	1	0.9
Hashimoto's thyroiditis	02	-	02	-	01	-	01	0	2	1.8
Toxic goiter	04	-	-	01	01	01	-	0	4	3.6
Papillary Carcinoma	04	-	-	-	-	03	-	1	3	4.5
Medullary Carcinoma	03	-	-	01	01	-	-	1	2	2.7
Anaplastic Carcinoma	03	-	-	01	-	-	-	1	2	2.7
Others	02	-	-	-	-	01	01	2	0	1.8

The lowest age was 16 yrs and highest as 57 yrs. Maximum number of patients (85%) were in age group of 20-50 yrs. The mean age was 45 yrs. Sex wise distribution shows, 93/110 (84.5%) cases were females and 17 (15.5%) were males. Distribution of lesions according to quality of smears shows, 10/110 (9%) were inadequate (ie unsatisfactory for diagnosis) and 91% were cellular (diagnostic). Sex wise distribution of benign and malignant lesions shows that 87/110 lesions were benign, 11 malignant, 2 suspicious for malignancy and 10 were inadequate for diagnostic purposes, respectively. Out of 87 benign lesions, 76 were females and 11 as male patients. Similarly, out of 11 malignant cases, 7 were females and 4 as males. 2 cases were suspicious for malignancy (both females). While, 10 were inadequate for diagnosis. Out of total 85 female patients, 7 were malignant

(malignancy rate - 8.3%). Out of 15 cases in males, only 4 were malignant (26.3%).

Benign follicular lesions constituted largest category (71%) and mainly distributed between 21-50 yrs of age group. Follicular neoplasm made only 2% and equally distributed in 31-40, and 41-80 yrs of age groups(Both females). Toxic goiter constituted 4%(all females).Lymphocytic and Hashimoto’s thyroiditis constituted 1% and 2% respectively(mainly females) .Papillary carcinoma constituted 5% of total incidence (1 male and 3 females). 50% of papillary carcinoma occurred in less than 20 yrs of age group. Medullary carcinoma constituted 3% of total incidence and equally distributed in middle age groups (1 male and 2 females).Anaplastic carcinoma constituted 3% and all cases were found in, around 50 yrs of age group, (1 male and 2 females). Out of 11 malignant lesions diagnosed cytologically, 4 were papillary carcinoma (36%). Medullary and anaplastic carcinoma constituted 27% each and others included metastatic SCC of thyroid constituting 10% all cases. Rate of malignancy was 26 % in males and females as 8 %, respectively.

Table 2: Sex Wise Distribution Of Malignant Thyroid Lesions

	M	F	Total	Percentage
Papillary	1	3	4	36 %
Medullary	1	2	3	27 %
Anaplastic	1	2	3	27 %
Others	1	0	1	10 %
Total	4	7	11	

Out of 10 inadequate smears, 5 were diagnosed as multinodular goitre, 2 as colloid goitre and 3 as follicular adenoma on HPE. Similarly, out of 79 BFL diagnosed cytologically, 14 were colloid goitre,22 MNG, 40 as follicular adenoma and 1 case each of lymphocytic thyroiditis, Hashimoto thyroiditis and follicular variant of papillary carcinoma on HPE, respectively. 2 cases suspicious for malignancy later proved to be follicular adenoma and 4 cases of papillary carcinoma on HPE. Out of 3 cases of medullary carcinoma,1 proved to be poorly differentiated carcinoma on HPE. 1 case of lymphocytic thyroiditis later proved to be lymphocytic thyroiditis, Out of 4 cases of toxic goiters , 2 were multinodular goiter, 1 follicular

adenoma and 1 toxic goitre on HPE, respectively. Histopathological correlation was not available for 3 cases of anaplastic carcinoma & 1 case of metastatic SCC that underwent radiotherapy. Also, correlation was not available in 2 cases of Hashimoto thyroiditis that underwent medical / conservative management. 1 case diagnosed as non-specific as it contained lymphocytes and eosinophils only, later turned out to be undifferentiated carcinoma, histopathologically.

Table 3: Cyto-Histological Correlation Between Benign, Malignant And Suspicious Lesions.

Cytological.diagnosis	Benign	Malignant
Benign (87)	85	2
Malignant (7)	0	7
Suspicious (2)	2	0

Out of 87 benign lesions cytologically, 2 turned out to be malignant on HPE. Out of 11 malignant cases cytologically, histological correlation was available only in 7 cases, and later confirmed. 2 suspicious cases (follicular neoplasm), both turned out to be follicular adenoma. Out of 10 inadequate smears, 3 were FA, 5 MNG and 2 colloid goiters on HPE (sampling error). Out of 3 Toxic goiters on cytologic smears, 2 were multinodular goiters and 1 as follicular adenoma on HPE (diagnostic error). Similarly, Out of 3 BFL diagnosed, 1 lymphocytic thyroiditis, 1 Hashimoto’s Thyroiditis and 1 proved to be follicular variant of papillary carcinoma indicating diagnostic error respectively. One case of medullary carcinoma proved to be poorly differentiated carcinoma on HPE indicating diagnostic error, although significant, but not false negative. One case diagnosed as non-specific, showing lymphocytes and eosinophils on cytology smears, later turned out to be undifferentiated carcinoma on HPE (significant diagnostic error) constituting false negativity. Out of discrepant cases, 3 were significant and 2 constituted as false negatives respectively.

Cytological results were divided into following categories:

1. Positive results: Cytological results, in correlation with HPE reports were considered as positive results.
2. Non-Diagnostic: cytologically indicates no or very few thyroid cells in the aspirate and/or consisted mainly of blood, ie non diagnostic.

3. False positive results: Results, which are malignant cytologically and benign on HPE.
4. False negative results: Result that are benign cytologically and malignant histologically are false negative results.

Table 4: Interpretation Of Cytological Results.

Results	No's	%age
Positive results	92	97.87 %
Non diagnostic	10	9 %
False negative	02	2.12 %
False positive	00	-

Above table indicates that, Out of 110 patients, 10 were non-diagnostic, 92 positive, 2 false negative and no false positive case.

Discussion: Fine needle aspiration cytology (FNAC) is widely accepted as the most accurate, sensitive, specific and cost effective diagnostic procedure in the assessment of patients with thyroid lesions

particularly thyroid nodules. FNAC has the single best predictive value of any test available currently and maximum benefit can be gained by using FNA as the initial diagnostic procedure in the management of thyroid lesions. All the patients were examined cytologically and the results compared histopathologically. Purpose of study was to evaluate the usefulness of FNAC as a complement to clinical, hormonal and ultrasonographic studies in both diffuse and nodular goiters. In De vos RJ study³, age range was 16-57 years with a mean age of 45 years and involved 79% female and 21% male patients. In Hsu C et al study⁴, mean age was 43.8 years (range 10-88 years) and female patient constituted 81% and males 19% of all patients. In present study, mean age was 45 years (range 16-57 years). Out of 110 patients, 93 (84%) were females and 17 (16%) as males.

Table 5 : Comparative Distribution Of Results In Different Series.

Series	Colacchio et al	Van Herle et al	GharibH, Goellner et al ⁷	Ramacciotti et al	Cusick et al	Rosa La et al	Present study
No. of Pts	300	12000	1097%	126	307	827	110
Benign	92.3 %	80 %	69 %	69 %	71 %	63.1 %	79 %
Malignant	7.7 %	10 %	4 %	13.5 %	20 %	22.1 %	10 %
Suspicious	NA	5 %	10 %	19.9 %	NA	12 %	2 %
Inadequate	0 %	NA	17 %	5.5 %	7.9 %	2.7 %	9 %

In the present study, 110 patients were studied cytologically by FNA technique. Histopathological correlation was available in 104 patients only. The material was inadequate in 9% of cases. Inadequate material in various series ranged from 0% (Colacchio et al)⁵ to 10% (Gharib / Goellner et al)⁷. Out of 110 satisfactory smears, benign lesions were 87 (79%) and Malignant lesions as 11 (10%). Benign and malignant lesions in various series ranged from 69 to 92.3% and 4 to 20.1%

respectively. Cases suspicious for malignancy were 2% and various other series varied from none to 19%(Ramacciott et al)⁸. Results of our study are in close correlation with Van Herle et al⁶ study group. In Afrose et al¹³ and Morgan JB et al,¹⁴ study groups, the overall malignancy rate in females was 11% and in males as (23%). In present study, malignancy rate among male patients was 26% and in females as 8% respectively.

Table 6: Distribution Of Cytological Lesions In Different Series

Diagnosis	Hawkin's et al	Hall et al	Present study
	1399	795	110
Inadequate	9 %	16 %	9 %
Goitre (BFL)	71 %	71 %	71 %
Toxic goiter	2.8 %	4 %	4 %
Inflammatory(Hashimoto & Lympho, Thyroiditis)	4 %	7 %	3 %
Follicular neoplasm	3 %	7 %	2 %
Malignant lesions	8 %	11 %	10 %
Papillary	5 %	8 %	4 %
Medullary	2 %	1 %	3 %
Anaplastic	1 %	2%	3%

In the study, benign follicular lesions constituted 71%, toxic goiter 4%, Hashimoto's thyroiditis 3% and malignant lesions as 10% respectively. Papillary carcinoma constituted, commonest malignant lesion. Medullary and anaplastic lesions were equally distributed in our series, while in Hawkins et al¹¹ study group, medullary carcinoma was more prevalent than anaplastic and in Hall et al¹² study group, anaplastic carcinoma was more common. Papillary carcinoma occurs in adult patients with female predominance slightly at younger age group as compared to other malignant lesions. In our study also, 2/3 patients were females and 50% of them were younger than 20 yrs of age. Medullary carcinoma occurs in middle age group with female predominance, in present study also 2 out of 3 patients with medullary carcinoma were females and all the patients were adults of middle age group. Among all malignant lesions, anaplastic

carcinoma occur in elderly patients, mainly females around 50 years of age. In our study also, out of 3 patients with anaplastic carcinomas, 2 were females of around 50 yrs of age.

Data above, show cyto-histological correlation, as there were 10 inadequate smears showing blood and colloid only, so excluded from the correlation study. There were two false negative results, one diagnosed cytologically as BFL and later turned out to be follicular variant of papillary carcinoma on HPE. Slides were reviewed again and concluded that, there were focal clusters showing nuclear features of papillary carcinoma (diagnostic error). Another false negative, diagnosed as non-specific, later proved to be undifferentiated carcinoma on HPE. So it may be due to sampling error or focal change. Needle may not have sampled the representative area.

Table 7: Distribution Of Results In Different Series

Results	Colacchio et al	Van Herle et al	Rosa La et al	Cusick et al	Gharib H et al	Ramacciotti et al	Present study
Positive	97.7 %	97.5%	94 %	92.1 %	79.3 %	86.8 %	88 %
Inadequate	0%	NA	2.7 %	7.9 %	17 %	55 %	9 %
False +ve	1.3%	0.9 %	1.1 %	0 %	0.7 %	12.7 %	-
False -ve	1%	1.6 %	2.3 %	NA	2 %	6.35 %	2 %

In present study, positive results were 88% and false negatives as 2%. In above mentioned series, positive results ranged from 86.8% to 97.7%, inadequate smears as 9% and in other studies, they ranged from 0% to 17%. The results of present study are in correlation with above mentioned studies.

positive while excluding suspicious and unsatisfactory smears, the cumulative data can be represented as follows: True Positive- 7. Sensitivity = 78%, False Negative- 2, True Negative-83. Specificity = 100%, Positive predictive value: = 100 % , Negative predictive Value: =97.6%, Diagnostic Accuracy = 97.8 %

Statistical Evaluation: To assess sensitivity, specificity and predictive value of FNA in diagnosis of thyroid lesions, the results of those patients, who had both cytologic and histological diagnosis were utilized. Taking cytologically benign lesions as negative for malignancy, malignant lesions as

Thus, a sensitivity of 78%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.6% and diagnostic accuracy of 97.8% achieved. False positive rate was 0% and False Negative rate as 2%. Thus a final Diagnostic accuracy of nearly 98% achieved.

Table 8: Distribution Of Results In Various Series

Series	Colacchio et al	Van Herle et al	Rosa La et al	Cusick et al	Gharib et al	Afroze et al	Morgan JB et al	Ramacciotti et al	Present Study
Sensitivity	85.7%	97.5%	97.8%	76%	98%	61.9%	55.0%	52%	78%
Specificity	98.4 %	70%	97.7%	58%	99%	99.3%	73.7%	78%	100%
Diagnostic accuracy	NA	NA	97.7%	69%	NA	94.5%	67.2%	72%	98%

Thus, overall diagnostic accuracy ranged from 67% - 97%, sensitivity ranged from 52%- 97.8% and specificity from 58% - 98.4% in different series. In our study, sensitivity was 78% specificity 100% and diagnostic accuracy index as 98%, which is in close correlation with other studies¹⁵.

Conclusion: FNAC is a simple and inexpensive procedure, which can be repeated in, within inadequacy. It has the best predictive value of all currently available diagnostic procedures. The simplicity, rapidity, lack of morbidity, a high sensitivity, specificity and diagnostic accuracy along with cost effectiveness of FNAC, makes it most valuable tool in the evaluation of thyroid lesions prior to surgery. Needle biopsy of thyroid lesion offers another opportunity to improve greatly the accuracy of diagnosis, that may follow surgical biopsy, if need arises. A false negativity seen in a few cases indicated that, all clinically malignant or suspicious lesions must undergo surgical excision biopsy. The only limitation of FNAC is its insensitivity in diagnosing malignant follicular neoplasms. In addition, a small proportion of cases can't be completely evaluated, because of paucity of material. Despite its apparent limitation, however, routine aspiration cytology is the most valuable and appropriate investigation in patients with thyroid lesions. FNAC used together with other diagnostic modalities such as thyroid scanning, ultrasonography, thyroid hormone and antibody levels enhance diagnostic accuracy of this technique. So, it is widely accepted as the most accurate procedure to differentiate benign and malignant thyroid nodules and helps preoperatively in selecting patients for surgery.

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