

## An Analytical study of Fine Needle Aspiration Cytology in Various Thyroid Lesions and their Correlation with Histopathology

Anjana Sharma<sup>1</sup>, Avishesh Singh<sup>2</sup>, Ajay Sahu<sup>3\*</sup>

<sup>1</sup> Associate Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Bhilai (C,G) India

<sup>2</sup> Assistant Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Bhilai (C,G) India

<sup>3</sup> Assistant Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Bhilai (C,G) India

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### Abstract

**Introduction** :The efficacy and diagnostic accuracy of FNAC is quite reliable in the hands of well experienced cytopathologist and correlates well with histological diagnosis. The present study was undertaken with the aim of classifying the cytomorphology of palpable thyroid lesions by FNAC and correlate the results with histo- pathology wherever possible. **Methods**: This Retrospective & Analytical study involved 200 Subjects. The period of study was 6 months & all the Information about the patient's age, sex, ultrasonography findings, and cytological report was recorded. **Results**: Analysis of various thyroid lesions in relation to age and gender was done, cytohistological correlation was done in all cases, and diagnostic accuracy of FNAC was calculated. Data was filled in Microsoft Excel & analysed using a computer software Epi Info version 6.2 (Atlanta, Georgia, USA) & SPSS. Benign lesions comprised the maximum number of cases 83 % , followed by AUS in 4 % cases. The patients mean age in the malignancy and the suspicious for malignancy category was higher. The sensitivity for cytological diagnosis of neoplasia was 95.7%, specificity 100% and diagnostic accuracy of 96.0%, showing a good positive correlation with histopathology. Results were comparable with the previous published data. **Conclusion**: FNAC is an invaluable tool in the management of thyroid lesions with a high degree of accuracy. It is safe, simple, cost-effective procedure with absence of major complications and can be performed on out- patients with wide patient compliance. FNAC provides a more rapid and accurate diagnosis of thyroid lesions than any other combination of clinical laboratory tests.

**Keywords**: FNAC , TBSRTC , Thyroid Nodule , Bethesda Classification.

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### Introduction

Fine-needle aspiration cytology (FNAC) plays a vital role in the evaluating patients with thyroid nodules. Thyroid nodules are a common clinical finding with reports of a prevalence ranging from 4–7% of population available in the literature.[1,2] The vast majority of thyroid nodules are non-neoplastic lesions and only < 5% are malignant. Clinical features alone cannot distinguish between benign and malignant nodules.[3] Thyroid cytology not only provides a definite diagnosis of malignancy but also the tumour type, thus enabling appropriate therapeutic surgery. Benign lesions can be managed conventionally. However, the incidence of thyroid malignancy is quite low and only 1 in 20 clinically identified nodules turn out to be malignant, thyroid FNAC helps in reducing the rate of surgery for benign thyroid diseases.[1,4,5] Aspirations considered unsatisfactory or inadequate should be subjected to arepeat aspiration since malignancy has been reported in 4-15 % of such cases.[6] FNAC has allowed a dramatic decrease in the surgical treatment of the patients with thyroid nodular diseases enhancing the percentage of malignant operated nodules over 50%[3] . To assess terminology, description and interpretation of cytological appearances and transmit them to the clinicians in a clear and reproducible way,

several classifications for thyroid cytology report have been proposed [4-6]. Also The routine use of FNAC in the assessment of thyroid lesions has reduced the number of patients subjected to thyroidectomy for benign lesions. As a result, the incidence of malignancy at thyroidectomy has increased from 5-10% to 30-50% in the recent years. The efficacy and diagnostic accuracy of this modality is quite reliable in the hands of well experienced cytopathologist and correlates well with histological diagnosis. Different imaging techniques are now used for pre operative diagnosis of thyroid nodules, like radio nucleotide scanning, high resolution ultra sonography etc. However FNAC is still regarded as the single most accurate and cost effective OPD procedure, particularly if ultra sound is used as a guide for better sample collection especially for cystic lesions. However success of FNAC is dependent on several important contributing factors like Aspirate experience , Skilful cytological interpretation & Rational analysis based upon cytological and clinical information in the context of individual patient. The present study was undertaken with the aim of classifying the cytomorphology of palpable thyroid lesions by FNAC as per The Bethesda System for Reporting of Thyroid Cytopathology (TBSRTC) [7] and correlate the results with histo- pathology wherever possible[8-10]

\*Correspondence

Dr. Ajay Sahu

Assistant Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Bhilai (C,G) India .

E-mail: [ajay\\_ajay781@yahoo.com](mailto:ajay_ajay781@yahoo.com)

### Methodology

This Retrospective & Analytical study involved Prior Consent from Hospital Authorities / Medical Superintendents of the Randomly

selected Pathology Department of the Local Private Tertiary care hospitals in an area of within 50 kms to see the records of the patients from Medical Records Department (MRD) with the disclosure that we will use the data for study purpose only. Medical record numbers were used to generate the data for analysis. The study was conducted within ethical standards & doesn't involved any direct Intervention to any mentioned subjects nor any physical Examination was performed. Randomization was done using computer tables in selecting data. All Patients data had details of standard clinical examinations, routine biochemical and haematological investigations. The study duration was 6 months. Information on each patient selected were carefully obtained by an in-depth study of the patients' case notes (folder), which contain the house officer's detailed clerking at patient's presentation to clinic, casualty or referral before FNAC / Admission to hospital. This was a Retrospective study of 200 diagnosed cases of thyroid lesions referred to the Cytopathology section for FNAC [11-14].

All patients had clinically palpable thyroid swellings, irrespective of their age and sex, were included in the study. Exclusion criteria were (1) patients not willing for FNAC of thyroid lesions even after explaining the purpose, utility, and consequences of the procedure, (2) lesions of parathyroid, lymph nodes, and other surrounding structures. All patients with thyroid swellings, irrespective of the age who have undergone Fine needle aspiration cytology of the swelling, followed by its subsequent Histopathological examination were included in the study. Patients in whom either of one (HPE/FNAC) was not available were excluded. The period of study was 6 months & all the Information about the patient's age, sex, ultrasonography findings, and cytological report was recorded. Those patients who underwent surgery for lobectomy or partial or total thyroidectomy were subjected to histopathological examination and then their diagnoses were recorded. To maintain Uniformity & to reduce the bias in our study Only those cases / patients / case sheets were selected whose aspiration was done with full aseptic precautions using 23 gauge needle using a 10 ml syringe. Multiple smears were prepared from the aspirate and those immediately fixed in 95% ethanol were stained using Haematoxylin and Eosin (H&E) and Papanicolaou (Pap) stains and air dried smears were restained with May Grunwald Giemsa (MGG). Whenever the aspirate yielded fluid, it was cyto-centrifuged and the smears were prepared from the sediment and stained using the above mentioned stains. TBSRTC was followed for reporting and cytological classification of the lesions. Cytological diagnosis was correlated with the histopathology report in all the cases that underwent surgery. Patients with other neck swellings were excluded from the present study. SPSS software was used for statistical analysis. All patients had clinically palpable thyroid swellings, irrespective of their age and sex, were included in the study. Exclusion criteria were (1) patients not willing for FNAC of thyroid lesions even after explaining the purpose, utility, and consequences of the procedure, (2) lesions of parathyroid, lymph nodes, and other surrounding structures. For retrospective study, the records of the patients who have undergone FNAC of thyroid were collected from the files. Written informed consent was obtained from all the patients. It was noted that FNAC was done under aseptic conditions using 23G needles with 10 cc or 20 cc disposable syringes. Two to three passes were made. If the swelling was cystic, fluid was aspirated. The material aspirated was immediately transferred onto glass slides, half of which were air dried and half

alcohol fixed for Giemsa stain and Papanicolaou stain, respectively. Stained smears were evaluated according to Bethesda system of reporting thyroid lesions [15-18]. Smears were considered adequate for evaluation if it contained at least six well-preserved and well-stained follicular groups, each containing at least ten cells. In cases of colloid cysts, abundant thick colloid obtained was considered as adequate for diagnosis, irrespective of a minimum number of follicular cells. Smears showing atypical cells were never considered inadequate, regardless of cellularity. For retrospective cases, paraffin blocks and slides were retrieved from Surgical Pathology and reviewed. The findings of gross examination of surgical specimens were noted [19-22]. Tissues were processed; sections were cut by microtome and evaluated after staining by Hematoxylin and Eosin method. Analysis of various thyroid lesions in relation to age and gender was done, cytohistological correlation was done in all cases, and diagnostic accuracy of FNAC was calculated. Data was filled in Microsoft Excel & analysed using a computer software Epi Info version 6.2 (Atlanta, Georgia, USA) & SPSS. Chi-square test was used to analyze nonparametric or categorical data. For analysis of ordinal scale data, Student's t-test was used. Karl-Pearson correlation coefficient was calculated to observe correlation between variables.  $P < 0.05$  was taken as significant and  $< 0.01$  as highly significant.  $P$  value of 0.05 and less was considered as statistically significant [23-24].

### Results

The present study included a total of 200 patients having thyroid lesions. The age range of patients was from 7 years to 81 years with a mean age of 36.58 years. Females were 157 and males were 43 with a F:M ratio of 3.6:1. The results were categorized as per the 2007 Bethesda classification into –

I-Non-diagnostic or unsatisfactory; ( Fig 1)

II-Benign; ( Fig 2 )

III – Atypia of undetermined significance (AUS) or follicular lesion of undetermined significance; ( Fig 3 & 4 )

IV-Follicular neoplasm or suspicious for a follicular neoplasm; ( Fig 5 )

V- Suspicious for malignancy and, ( Fig 6)

VI- Malignant categories ( Fig -6)

Aspirates yielding insufficient or low cellularity or those that were of poor quality were considered “unsatisfactory”. For thyroid FNAC specimens to be labelled as satisfactory for evaluation at least 6 groups of benign follicular cells are required and each group should be composed of at least 10 cells. This group also comprised of aspirates consisting of cyst fluid only aspirates. Aspirates classified as benign included colloid goitre, colloid or adenomatous nodule, hashimoto's thyroiditis, sub-acute thyroiditis, and cysts of thyroglossal duct. Suspicious smears included follicular neoplasms, cellular adenomatoid nodules, hurthle cell proliferations and lesions suspicious for malignancy. Benign lesions comprised the maximum number of cases 83% , followed by AUS in 4% cases. The patients mean age in the malignancy and the suspicious for malignancy category was higher as compared to that in the benign category. Cases that underwent lobectomy, partial or complete thyroidectomy were subjected to histopathological examination. The biopsy reports were correlated with the pre-operative cytology reports. Comparison of the outcome of the present study with other previous studies available in the literature.

Table 1:Cytological diagnostic category

Age Group (Years)	I		II		III		IV		V		VI	
	M	F	M	F	M	F	M	F	M	F	M	F
< 10	-	-	-	3	-	-	-	-	-	-	-	-
11-20	-	1	2	23	-	2	-	-	-	-	-	-
21-30	-	1	17	30	-	3	-	-	-	1	-	1
31-40	-		12	33	1	1	-	1	-	1	-	-
41-50	-	2	8	31	1	2	-	2	1	1	-	2
51-60	1	2	1	5	-	1	-	1	-	1	-	-
> 60	-	1	1	0	-	-	-	2	-	-	1	-
<b>Total</b>	1	7	41	125	2	9	0	6	1	4	1	3
<b>% Cases</b>	4.0 %		83.00%		5.50%		3.0 %		2.50%		2.0%	
<b>Average Age (Years)</b>	48.36		35.19		32.74		49.27		41.59		48.7	

Table 2: Cytological and histopathological diagnosis

Cytological Diagnosis	Histopathological Diagnosis											
	N	Thyroglossal cyst	Colloid Goitre	Thyroiditis	Tubercular	Adenomatous Goitre	Follicular Adenoma	Follicular carcinoma	Hurthle Cell Adenoma	Papillary Carcinoma	Medullary Carcinoma	Anaplastic Carcinoma
Non-Diagnostic	3	1	1	-	-	-	-	-	-	-	-	-
Thyroglossal Cyst	2	2	-	-	-	-	-	-	-	-	-	-
Colloid Goitre	84	2	48	1	-	2	2	-	-	1	-	-
Adenomatous Goitre	9	-	1	-	-	5	1	1	-	-	-	-
Hashimoto's Thyroiditis	14	-	1	10	-	-	-	-	-	-	-	-
Granulomatous Thyroiditis	2	-	-	-	2	-	-	-	-	-	-	-
Suspicious of Malignancy	5	-	-	-	-	-	-	-	-	1	-	1
Follicular Neoplasm	7	-	-	-	-	1	3	2	-	-	-	-
Hurthle Cell Neoplasm	4	-	1	-	-	1	-	-	2	-	-	-
Papillary Carcinoma	1	-	-	-	-	-	-	-	-	1	-	-
Medullary Carcinoma	1	-	-	-	-	-	-	-	-	-	1	-
Anaplastic Carcinoma	2	-	-	-	-	-	-	-	-	-	-	1
<b>Total</b>	104	5	52	11	2	09	6	3	2	3	1	2

**Discussion**

Thyroid FNAC was initially started by Martin and Ellis in 1930. The terminology used for reporting thyroid FNAC has shown significant inter-laboratory variations, creating confusions and also interfering with the data exchange among different centres. Keeping this in view, in 2007 TBSRTC was evolved with the aim of forming a uniformity

in the reporting of FNAC findings of thyroid that would facilitate effective discussion among cytopathologists and clinicians; facilitate correlation between cytopathology and histopathology, epidemiological studies, molecular genetics, and, diagnostic interpretation of thyroid diseases in particular neoplasia[. 25,26]It also ensured that the data between various laboratories and institutions could be shared without any specific interpretive mistakes.[7] Palpable thyroid

nodules are present in approximately 4–7% of adults[1,2] and are more common in females.[4-6] In the present study also there was a female predominance.[8,9] Thyroid nodules may lead to either hypo or hyperthyroidism, cosmetic and compression problems, besides having the potential for malignancy. Accurate evaluation of thyroid

nodules is thus crucial. In recent years, the role of FNAC is increasing regarding detection of thyroid nodules which are malignant. Thyroid gland carcinoma accounts for less than 1% of all cancers and is responsible for 0.5% of all cancer-related deaths.[10]

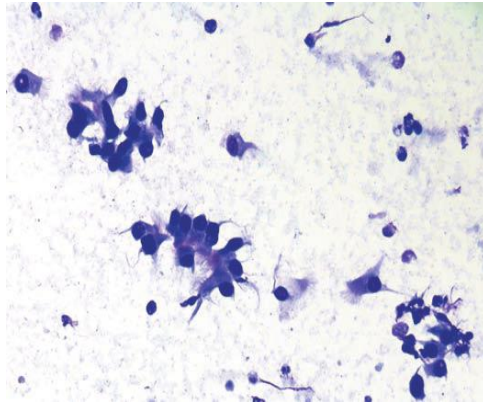


Fig 1: showing Non Diagnostic lesion

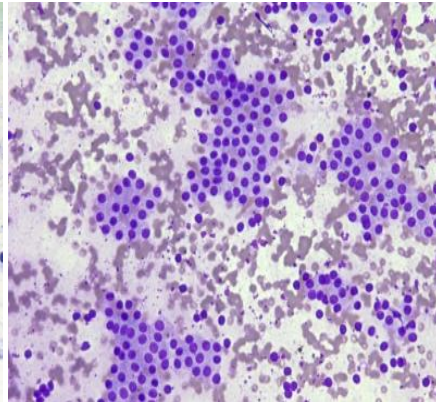


Fig 2 : Sheets of Benign Follicular cells

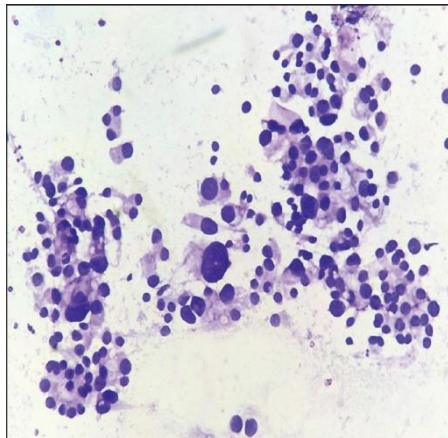


Fig 3 : Atypia

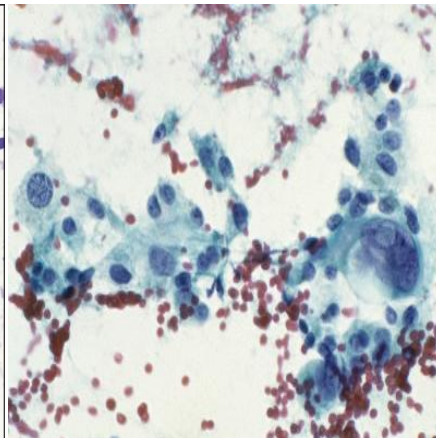


Fig 4: Atypia Cells

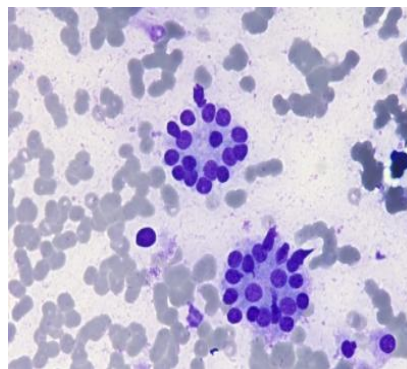
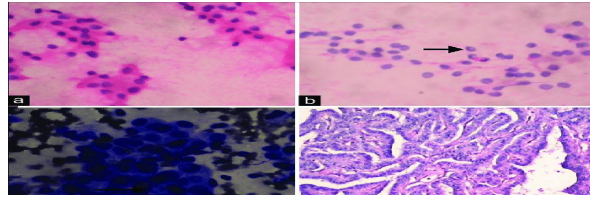


Fig 5:Follicular adenoma showing microfollicles



**Fig 6(a) FNAC thyroid showing follicular cells arranged in sheets with few showing Hurthle cell and degenerative change (H and E stain  $\times 200$ ); (b and c) Smears show few nuclei showing intra nuclear inclusions (black arrow) but features not sufficient enough to be diagnosed as papillary carcinoma. Case was diagnosed as category AUS/FLUS of BSRTC (b: H and E stain  $\times 200$ , c: May–Grunwald–Giemsa;  $\times 400$ ); (d) Histopathological examination of same case showed papillary carcinoma (H and E stain  $\times 200$ ) d c**

Early diagnosis of such cases is thus important for aiming at higher life expectancy especially since thyroid gland cancers have a low malignant potential and also have a slow progressive property. Majority of the clinically diagnosed palpable thyroid nodules are non-neoplastic.[4,5,7,11,12] Multiple aspirations avoid missing a neoplastic focus. Every thyroid FNAC should be evaluated for adequacy of the smears. Smears that are inadequate for reporting are categorized as “non-diagnostic” (ND) or “unsatisfactory” (UNS) and include smears that show obscuring blood, are overly thick, those alcohol-fixed slides subjected to air drying, or those having an inadequate or less number of follicular cells in the slides. Specimens containing large amount of colloid is considered adequate and benign, even if 6 groups of follicular cells are not identified in the smears. Cyst-fluid-only (CFO) cases are considered to be a subset of ND/UNS. The risk of malignancy reported in the ND/UNS (not including CFO) category ranges from 1% to 5.5%.[13-16] A repeat aspiration under high ultrasound guidance is recommended in such cases. However, some nodules remain persistently ND/UNS even on repeat aspirations and should be subjected to surgical excision. [14,17,18] Non-diagnostic or insufficient samples are common in nodules that are calcified, sclerotic or in those that have undergone major cystic degeneration. As per the review of literature the rate of ND/UNS ranges between 16 to upto 20%.[11, 12,16,18] Non Diagnostic test in our study was kept low. Authors suggest that the rate of non-diagnostic tests should be kept below 10%. [19] Some thyroid FNAC reports cannot be classified with ease into the benign, suspicious, or malignant categories and are reported as “atypia of undetermined significance” (AUS) or “follicular lesion of undetermined significance (FLUS).” This category includes a number of lesions that show morphological abnormalities of the follicular cells with or without presence of nuclear atypia. Benign cellular changes including lining cyst cells, focal Hürthle cell changes and, cellular changes following therapy with radioiodine should not be included in the category of AUS. As per the literature AUS constitutes about 3 to 6% of thyroid FNAC reports. [17] AUS accounted for 5.50% of all the cases in our study. The recommended management of such lesions includes clinical correlation and repeat FNAC after an appropriate interval. Only about 20% of such nodules repeated for FNAC still remain as AUS. These cases are subjected to excision biopsy. FNAC has a good diagnostic role in many thyroid lesions especially for papillary carcinoma (PTC) and lymphocytic thyroiditis. For thyroid follicular carcinoma, FNAC is considered as a “screening test” and these smears are reported as “follicular neoplasm” (FN) or “suspicious for a follicular neoplasm” (SFN). This category of Follicular neoplasm forms a gray zone with various differentials such as follicular carcinoma, follicular variant of papillary carcinoma, follicular adenoma and adenomatoid nodule. To label it as Follicular carcinoma, histopathology must show evidence of vascular and/or capsular invasion. In general, smears from adenomatous nodules show less number of cells, have presence of dispersed rather than tightly cohesive follicular cells and more colloid than those from follicular neoplasms. About 35% cases do not show any evidence of neoplasia but rather show hyperplastic proliferations of follicular cells, as in multinodular goitre.[15,20] 15

to 33% of FN/SFN cases prove to be malignant of which a significant proportion is constituted by follicular variant of papillary carcinoma.[2,13,15,17,18] Many a times the nuclear and architectural changes of some PTCs are patchy and not well discerned especially as seen in follicular variant of PTC, thus mimicking a benign follicular nodule on cytology. Nodules are resected by lobectomy or semi/total thyroidectomy. [2,15,17] Follicular lesions are categorized histopathologically as benign by some authors, while others categorize them as malignant.[11,12,16] Inclusion of such cases in the benign or malignant category imparts a significant difference in the sensitivity and specificity rates. As in the available literatures, the benign lesions represented the majority of cases. In our study benign lesions constituted 166 (83%) cases. This is in accordance to the previous other studies. The lesions included in the benign category were thyroglossal cyst, colloid goitre, adenomatous goitre, hashimoto’s thyroiditis, and granulomatous lesions. Cytologically all benign thyroid nodules need not be subjected to histopathological evaluation. In the present study the sensitivity for cytological diagnosis of neoplasia was 95.7%, specificity 100% and diagnostic accuracy of 96.0%, thus showing a good positive correlation with histopathology. Our results were comparable with the previous published data where FNAC of thyroid is reported to have sensitivity ranging from 40% to 100%, and a specificity of 45% to 100%. [2, 19-26] Various Factors contribute to this wide range of sensitivity and specificity. It depends on the adequacy of samples, technique of sample collection, the experience of the pathologist interpreting the smears, presence of overlapping cytological findings between some benign and malignant thyroid lesions and, duration of follow-up of the patient. FNAC has an overall accuracy rate of around 90-100% in the detection of thyroid malignancy.[6,23] the present study showed a rate of 100%. Every diagnostic procedure has its own limitations and diagnostic fallacies. It includes the presence of false negative (FNR) and false positive results (FPR) particularly with small tumours and when there is simultaneous inflammatory or degenerative changes in the surrounding tissue. Some of the lesions showing overlapping features cannot be distinguished cytologically with full confidence such as cellular colloid goitre and follicular neoplasm. It is so especially when there are presence of microfollicular arrangement of the cells in the former.[25,26] FNR usually occur following sampling errors, co-existence of benign and malignant lesions, or due to presence of cytomorphologic overlap between benign and low grade malignant tumours. These cases are of great importance more so since they indicate the potential of missing an underlying malignant pathology. It is very difficult to estimate the true FNR because only a handful of patients with benign cytological findings proceed further for surgery. FNR ranged from 1% to 16% in different series of publications and has been estimated to be usually less than 5%. [21, 23] FNR can be minimised by clinical follow-up and repeat aspiration to obtain adequate aspirates. FPR are less common and were not found in any patient in our study. This finding is consistent with the other reports that cited variable rates ranging from 0–9%. [23, 25] FPR are usually seen in cases of colloid nodule and nodular hyperplasia with numerous macropapillary structures, hashimoto’s thyroiditis, follicular or parathyroid or adenomas with

atypia. The sensitivity and specificity rate of thyroid FNAC as compared to histopathology may vary depending on the FNR, FPR and also on whether the suspicious cases are included in the negative or positive category. No single diagnostic method helps in providing a definitive diagnosis of cancer thyroid. However, FNAC is still the procedure of choice, particularly if ultrasound is used as an ancillary technique for better sample collection. [18] This holds true in cystic lesions. The interpretation errors can be reduced by obtaining aspirates from different portions of the lesion, using ultrasound-guided FNA procedure, advanced imaging techniques, immunologic analysis, electron microscopy and reviewing of slides by more than one cytopathologist. Both the cytopathologists should not be aware of each other's diagnosis thus making it a blinded method of quality control. The less palpable or ill-defined nodules may best be aspirated using ultrasound guidance, lest the palpable nodules are aspirated using standard methods. Thyroid scintigram shows neoplastic nodules as cold nodules. The cytological findings at times in Medullary carcinoma showing presence of giant cells may mimic the cytological findings seen in anaplastic carcinoma. In such cases application of Calcitonin Immunohisto-chemical marker, or electronmicroscopy usually helps in solving the problem. [22]

#### Conclusion

FNAC exhibits an adequate diagnostic correlation with the final histopathological examination and enables a comparison of results between different institutions. Our results are consistent with those available in the literature. If the cytology report is malignant, surgery is the recommended procedure; for suspicious lesions, repeat aspiration is required and for benign lesions no further immediate diagnostic studies are required. FNAC is an invaluable tool in the management of thyroid lesions with a high degree of accuracy. It is safe, simple, cost-effective procedure with absence of major complications and can be performed on out-patients with wide patient compliance. FNAC provides a more rapid and accurate diagnosis of thyroid lesions than any other combination of clinical laboratory tests.

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