

# Cytohistologic Correlation Study of Thyroid Lesion: Insight into the Causes of Discordance

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#### Keywords: FNAC, Thyroid, Cytohistology Correlation

## ABSTRACT

**Background:** Fine needle aspiration cytology (FNAC) is a popular diagnostic as well as therapeutic test in thyroid pathology. Like any other diagnostic modality, FNAC also has its limitations and pitfalls. This study was aimed at finding the causes for cytohistologic discordance, thereby minimizing the false positive and negatives.

**Methods:** 1091 patients underwent thyroid FNA in a period of 2 years in our institute. Histopathological diagnosis was available in 313 cases. Data of these cases was collected and statistically analysed. Cases showing cytohistologic disparity were reevaluated to unmask the causes of discordance.

**Result:** Of 313 cases with histopathological diagnosis, 19.48%(n=61) were neoplastic out of which 73.77%(n=45) were malignant. Mean age of study population was 42.48 years. 86.58%(n=271) were females. We found that sensitivity and specificity of FNA was 54.83% and 98.40% respectively. Positive predictive value was 89.47% and negative predictive value was 89.81%. Cytohistologic concordance was achieved in 89.78% of the cases. Of the discordant cases, false positive accounted for 1.2%(n=4) and false negative for 8.94%(n=28). Too much emphasis on cellularity and amount of colloid, failure to appreciate subtle nuclear features and sampling error were the most common causes for failure.

**Conclusion:** Proper representative sampling, if needed guided by imaging modalities and meticulous examination of all the smears are the key points in reducing the number of discrepant cases.

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# Introduction

Fine needle aspiration cytology (FNAC) is a popular diagnostic as well as therapeutic test in thyroid pathology. Given the ease of technique and relatively minimal invasive nature of the procedure, it has become a popular diagnostic modality. It is being widely used to differentiate benign from malignant lesions. But there is some "gray zone" of thyroid FNAC where the diagnostic efficacy becomes low, making it less reliable in categorizing the nature of the lesion leading to discrepant cases.<sup>[1]</sup>

We conducted this study to determine the diagnostic efficacy of thyroid FNAC by comparing it with histopathology which is considered gold standard. We also reviewed the discordant cases and looked at causes for cytohistologic discordance. This may help in minimizing the false positive and false negative cases.

# **Materials and Methods**

This retrospective study was conducted in the Department of Pathology at Father Muller Medical College, Mangalore. A total of 1091 patients with thyroid swelling were aspirated during a period of two years from 2011 to 2013 using a 23-gauge needle and a 5-ml syringe. The slides were both air-dried and wet-fixed for May-Grünwald Giemsa and Papanicolaou stains, respectively. A concise clinical history, examination and details of relevant investigations were also obtained. Surgical follow-up was available for 313 aspirations. The concordance between cytological and histological diagnoses was determined. Cases with cytohistological discrepancy were selected and cytological smears of these cases were reevaluated for the detection of possible causes of failure.

The aims of the study were: 1) To find the sensitivity, specificity, positive and negative predictive values of thyroid FNAC. & 2) To critically evaluate the discordant cases and find out causes of discordance.

# Result

Among the 1091 patients, the cytological diagnoses were divided into 2 categories: non neoplastic (Table 1) and neoplastic (Table 2). Non neoplastic category included nodular goitre, adenomatous goiter and different cases of thyroiditis like hashimoto's thyroiditis, lymphocytic thyroiditis and de quervain's thyroiditis. Neoplastic category included indeterminate cases, papillary carcinoma, medullary carcinoma and anaplastic carcinoma. The lesions suspicious of malignancy, follicular and hurthle cell neoplasms were also included in the indeterminate category.

In 313 cases surgical follow up with histopathological diagnosis was available. Mean age of these cases was 42.48 years. 86.58% (n=271) were females. 19.48% (n=61) of the total cases were neoplastic out of which 73.77%(n=45) were malignant. Cytological diagnoses were then compared with histopathological diagnoses. Among the non neoplastic lesions, histopathology was available in 252 cases. Cyto-histo concordance was obtained in 244 cases, whereas remaining 4 showed malignant histology. Conversely, among the neoplastic category, histopathology was available for 61 cases(Table 3). Papillary carcinoma was the most common neoplasm(n=25). Complete cytohisto concordance was obtained in 33 cases. Of the 28 discordant cases, 22 were diagnosed as goiter, 2 as hashimoto's thyroiditis, 2 as cystic colloid nodules and 2 as follicular neoplasms. Evaluation of 32 discordant cases identified, 4 false positive and 28 false negative cases, which were missed on cytological examination.

A false negative diagnosis of goitre was made in 22 cases of which 8 turned out to be follicular adenoma, 7 were follicular variant of papillary carcinoma, 4 cases were papillary carcinoma and 3 turned out to be papillary micro carcinoma. The possible causes for misdiagnosis of these cases which were found on reviewing the cytology smears and histopathology sections are tabulated below (Table 4). Overall, we found that cytohistologic concordance was achieved in 89.78% of the cases. Positive predictive value was 89.81%. Of the discordant cases, false positive accounted for 1.28%(n=4) and false negative for 8.94%(n=28).

## Discussion

FNAC has become a primary diagnostic tool for evaluating thyroid nodules. A correct cytologic diagnosis obviates

Non neoplastic lesions (Cytology)	Number of cases
Goitre	739
Thyroiditis	290
Total	1029

#### Table 2

Neoplastic lesions (Cytology)	Number of cases
Papillary carcinoma	29
Anaplastic carcinoma	6
Medullary carcinoma	3
Indeterminate	24
total	62

Table 3

Type of neoplasm (Histopathology)	Number of cases
Follicular adenoma	12
Hurthle cell adenoma	03
Follicular carcinoma	02
Papillary micro carcinoma	03
Papillary carcinoma	25
Follicular variant of papillary carcinoma	16
Total	61

## Table 4: False negative diagnosis of goiter and possible reasons.

Cytology diagnosis	Histopathology diagnosis	Possible reasons for discordance
Goitre (n=22)	Colloid rich follicular adenoma (n=4)	Abundance of colloid in the background
	Follicular adenoma (n=4)	Small lesion in a thyroid with multiple nodules leading to sampling error, misinterpretation as hyperplastic goiter.
	Follicular variant of papillary carcinoma (n=7)	Subtle nuclear features, background hemorrhage, focal nuclear features
	Papillary carcinoma (n=4)	Focal and subtle nuclear features, grooves thought to be a part of adenomatous hyperplasia
	Papillary microcarcinoma (n=3)	Sampling error



Fig 1: Focal nuclear features of papillary carcinoma can be easily missed. Note the elongated, grooved nuclei with pale chromatin. (PAP 400X).

unnecessary thyroid surgeries. The percentage of patients undergoing thyroidectomy has decreased by 25%, and the yield of carcinoma in patients who undergo surgery has increased from 15% to at least 30%. Fine-needle aspiration has decreased the cost of care by 25%.<sup>[2]</sup> However, FNA has few inherent limitations which are related to inadequate sampling and its inability to distinguish between benign and malignant follicular lesions in the absence of nuclear features of papillary carcinoma.<sup>[3]</sup> Another limitation of FNAC is its inefficiency in diagnosing group of lesions which have overlapping benign and malignant features. For instance, the distinction between a cellular colloid goiter and a follicular neoplasm may be impossible.<sup>[4]</sup>

The important steps in FNAC thyroid are careful sample procurement, appropriate sample preparation and accurate interpretation. Meticulous and carefully scrutinization for various cytologic features may reduce the number of discrepant cases. In the present study, we have studied the efficacy and diagnostic ability of FNAC and made an attempt to ascertain the possible reasons for discrepancies and ways to minimize them. The value of a diagnostic test lies in its ability to detect the presence of disease when it is present (sensitivity) and reliably verify the absence of disease when it is not present (specificity). The reported sensitivity and specificity of the thyroid FNAC ranges from 43 to 99% and 72 to 100% respectively. Our findings are similar to those reported in other series.<sup>[5,6]</sup>

False negative rates in our study are in accordance with other studies which report a range from 1 to 11%.<sup>[2,7]</sup> This high rate of failure to diagnose neoplasm could be attributed to the failure of aspiration from the representative site. This is of special concern since false negative diagnosis results in a delay in treatment and thereby adversely affecting the outcome in patients with thyroid cancer.<sup>[8]</sup> Most of the discordant cases in our study were those of follicular lesions of thyroid namely follicular adenoma and follicular variant of papillary carcinoma. These cases belong to the gray area of cytology due to the overlapping features. Greaves, et al studied 92 cases of follicular lesions of which in 63 cases there were no distinguishing features predictive of the histologic outcome.<sup>[9]</sup>

We reviewed these cases to find out the potential clues that can help us in differentiating benign from malignant lesions and also at the same time we attempted to delineate the features which can be potentially misleading. Syncytial pattern, papillary pattern and microfollicular pattern are more common in neoplasms and thyroiditis. The predominant cell pattern gives us a clue as to what we are dealing with and aids in diagnosis in combination with cell morphology and background details in the cytological diagnosis of thyroid lesions.<sup>[10]</sup> In a study conducted by Pandey, et al on 112 cases, they got 6 false negative cases which were reported as colloid goiter 4 of which turned out to be follicular adenoma and 2 were cystic papillary carcinoma. The cytological smears of all the 4 cases showed small groups of thyroid follicular cells and moderate amount of colloid which was misleading towards the diagnosis of nodular colloid goiter.<sup>[11]</sup>

In our study too, we misdiagnosed few cases due to overemphasis on the amount of colloid. Also cytologically it is difficult to distinguish nodular goiter and colloid rich follicular adenoma.<sup>[12]</sup> Occurrence of cystic change is another known pitfall in thyroid cytology. In our study, 2 cases of papillary carcinoma were misdiagnosed as cystic colloid nodule. This type of misinterpretation can be minimized by selective sampling from solid areas under the guidance of imaging modalities and also by strict adherence to adequacy criteria.

We missed 7 cases of follicular variant of papillary carcinoma (FVPTC). This is also a known pitfall due to failure to recognize the nuclear features of FVPCT (Figure 1). Cytological diagnosis is difficult again due to overlapping features with follicular lesions and masked or absent nuclear features in the sampled cells. A finding of 2 different population of follicular cells or cells with 2 different types of nuclear chromatin should raise a strong suspicion of neoplastic lesion. Also another pointer towards neoplastic lesion is the different looking or altered nature of the colloid.

False positive cases constituted 1.28% of the total cases in our study. 3 of the false positive cases reported as follicular neoplasms were goiter with adenomatous hyperplasia which is a known pitfall as described earlier. The feature of hypercellularity outshadowed the uniform cytomorphology of the follicular cells and paved the way for misdiagnosis of follicular neoplasm. Presence of few number of bare nuclei is another indicator towards neoplastic lesion. Too much emphasis on cellularity and amount of colloid, less emphasis on subtle nuclear features, nature of colloid and bare nuclei together with sampling error were the most common causes for failure.

## Conclusion

FNAC is a very important diagnostic method in thyroid pathology and helps in picking up neoplastic lesions and avoiding unnecessary thyroidectomies. The sensitivity and specificity of this method can be increased by strict adherence to adequacy criteria and relying on combination of various cytological features rather than emphasizing on only one feature. Proper representative sampling, if needed guided by imaging modalities and meticulous examination of all the smears are the key points in reducing the number of discrepant cases.

## Acknowledgements

None

## **Funding**

None

## **Competing Interests**

None Declared

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