ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 11, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

DIAGNOSTIC EFFICACY OF FNAC IN THYROID LESIONS, CLASSIFIED ACCORDING TO BETHESDA SYSTEM WITH CYTOHISTOLOGICAL CORRELATION

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Received: 20 July 2024, Revised and Accepted: 9 September 2024

ABSTRACT

Objective: The objective of the study is to estimate the diagnostic accuracy (DA) of fine needle aspiration cytology (FNAC) in thyroid lesions with cytohistological correlation.

Methods: The study was a cross-sectional study which was conducted in the Department of Pathology, Rabindranath Tagore Medical College, M.B.G. Hospital, Udaipur, Rajasthan, from December 2022 to December 2023. A total of 201 thyroid aspirations were performed, and the smears were classified according to The Bethesda system. Cytological and histopathological findings were compared in 132 cases that proceeded to surgery. Sensitivity, specificity, negative predictive value (NPV), positive predictive value, and DA were calculated using standard statistical methods.

Results: The distribution of thyroid lesions on cytology was as follows: Non-diagnostic (1%), benign (92%), atypia of unknown significance (1%), follicular neoplasia (3%), suspicious for malignancy (2%), and malignant (1%). The sensitivity, specificity, positive predictive value, NPV, and DA in our study were 78.94%, 100%, 100%, 96%, and 96.9%, respectively.

Conclusion: FNAC's cost-effectiveness, patient-friendly nature, swift results, and high sensitivity, specificity, and accuracy render it a primary diagnostic tool for assessing patients with thyroid swelling preoperatively. The Bethesda system categorizes thyroid lesions cytologically, aiding in their diagnosis and subsequent management. Histopathological correlation facilitates the assessment of DA and ensures quality assurance.

Keywords: Thyroid, Bethesda, Fine Needle Aspiration Cytology, Cytohistological correlation, Accuracy.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i11.52112. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The thyroid gland is notable among endocrine organs as the largest in the body and the first to develop during fetal life. This butterfly-shaped gland is located at the front of the neck [1].

The frequency and incidence of thyroid lesions are steadily increasing. Thyroid cancer, the most common cancer of the endocrine system, is rapidly rising in both men and women. Its prevalence ranges from 3% to 7% by palpation and 17% to 19% by high-resolution ultrasound. Goiter affects over 40 million people in India and more than 2 billion people globally. If left untreated, these conditions pose significant morbidity and mortality risks [1].

Most clinically diagnosed cases are non-neoplastic, highlighting the importance of distinguishing between neoplastic and non-neoplastic lesions. While the majority of isolated swellings are benign, malignancy cannot be definitively excluded without excision and histological examination [1].

Various diagnostic modalities are employed to efficiently evaluate and diagnose thyroid nodules, including clinical examination, thyroid function tests, ultrasonography, fine needle aspiration cytology (FNAC), and histopathological examination (HPE) [2]. For a definitive diagnosis, morphological examination of the lesions is essential, making FNAC and HPE mandatory tests [1].

FNAC was first introduced by Leyden in 1883. The application of aspiration cytology for diagnosing thyroid lesions was initially reported by Martin and Ellis in 1930 [3].

Thus, FNAC serves as the initial diagnostic test for evaluating thyroid swellings. The primary purpose of FNAC is to distinguish benign lesions from malignant ones, thereby reducing unnecessary surgeries [2].

Thyroid lesions exhibit a wide range of variations, from simple inflammation to neoplasms. FNAC assists in categorizing these lesions, with estimates suggesting that only 5% are malignant and necessitate immediate intervention. Anaplastic and poorly differentiated lesions can be treated with palliative radiotherapy or chemotherapy. As a result, FNAC is widely accepted, facilitating earlier diagnosis of more thyroid cases [1].

The efficacy of FNAC depends on several factors, including specimen adequacy, sampling techniques, the skill of the person performing the aspiration, and the interpretation of the aspirate. In addition, overlapping cytomorphological features between benign and malignant follicular neoplasms (FN), as well as the detection of certain papillary carcinomas, can impact its accuracy [3].

Even if non-surgical and non-invasive techniques can offer a diagnosis, the definitive answer lies in the HPE of the excised thyroid tissue. This information is crucial in guiding appropriate treatment strategies, which significantly influence patient outcomes and prognosis [3].

METHODS

The study was a cross-sectional study that was conducted in the Department of Pathology, Rabindranath Tagore Medical College, M.B.G. Hospital, Udaipur, Rajasthan, from December 2022 to December 2023.

Inclusion criteria

All cases presented with palpable thyroid swellings and those ill-defined/deep-seated swellings (taken by USG-guided FNAC) at cytology section irrespective of age and sex. Moreover, all cases of excised thyroid tissue were received at the histopathology section whose FNAC has been done.

Exclusion criteria

Patients who refused FNAC and those with other neck lesions were excluded from the study. In addition, inadequate or poorly preserved histopathology samples were also excluded.

Procedure

Informed consent and detailed clinical history including clinical examination of all patients, radiological, and relevant investigations were also obtained, if available. Then, FNAC was performed using a syringe with a 22–23-gauge needle, and the aspirate obtained was smeared on glass slides, fixed by 95% ethyl alcohol, and then, stained with May-Grunwald Giemsa (MGG) and then studied under the microscope. "FNAC slides were reported as per the Bethesda system for reporting thyroid cytopathology (TBSRTC) as follows:

- Non-diagnostic
- Benign
- Atypia of undetermined significance (AUS)
- FN
- Suspicious of malignancy
- Malignant lesion.

The cases that underwent surgery were received at the histopathology section, which were fixed, tissue processed, stained with H and E (hematoxylin and eosin), and then, examined under microscope. Then, correlation between FNAC and histopathology was done using available cases.

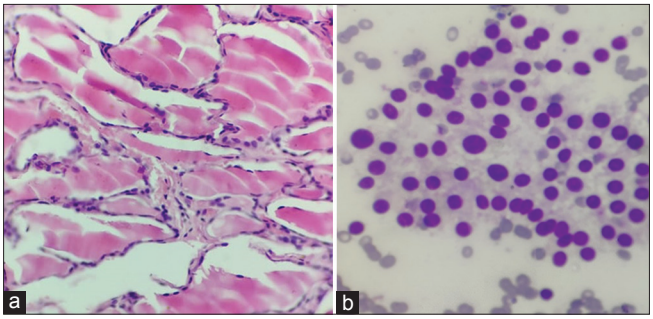

Fig. 1: Photomicrograph showing (a) colloid goiter on histology (H and E ×40). (b) hyperplastic goiter on cytology (May-Grunwald Giemsa, ×40)

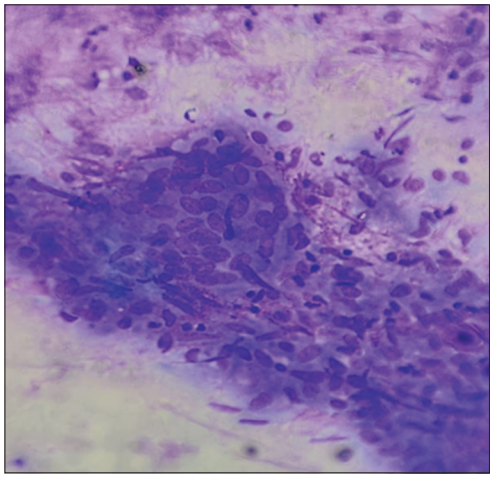

Fig. 2: Photomicrograph showing granulomatous thyroiditis on cytology (May-Grunwald Giemsa, ×40)

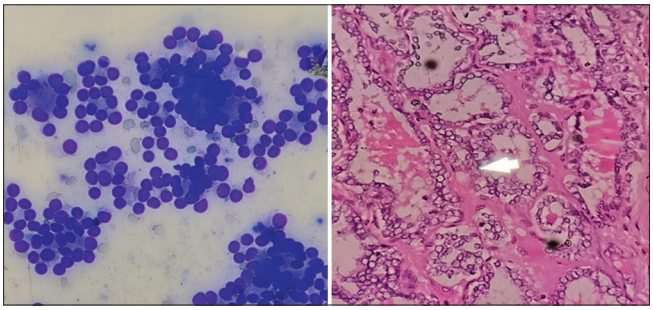

Fig. 3: Photomicrograph showing (a) follicular neoplasm on cytology (May-Grunwald Giemsa, ×40). (b) non-invasive follicular thyroid neoplasm with papillary-like nuclear features on histology (H and E ×40)

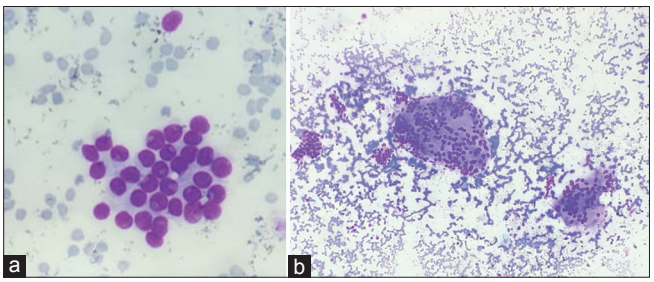

Fig. 4: Photomicrograph showing (a) intranuclear inclusions are seen. (b) multiple multinucleated giant cells are seen in papillary thyroid carcinoma on cytology (May-Grunwald Giemsa ×40)

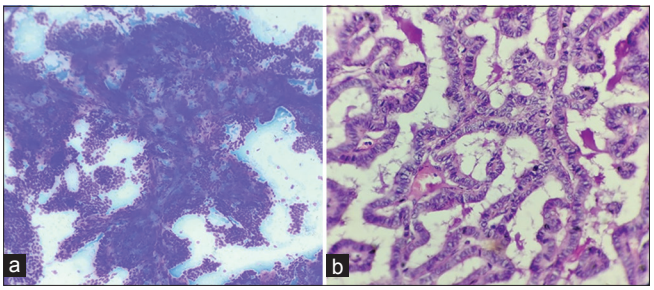

Fig. 5: Photomicrograph showing (a) papillae formation in papillary thyroid carcinoma on cytology (May-Grunwald Giemsa ×40). (b) papillary thyroid carcinoma on histology (H and E, ×40)

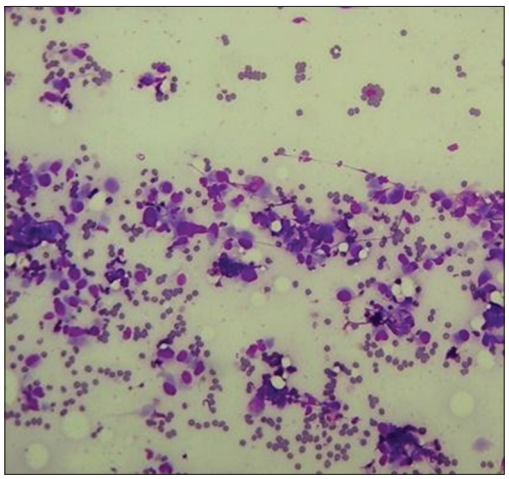

Fig. 6: Photomicrograph showing anaplastic thyroid carcinoma on cytology (May-Grunwald Giemsa, ×10)

RESULTS

A cytological study of thyroid lesions was conducted in 201 patients over 1-year period to examine the range of pathological findings, and these were compared with histopathological findings in 132 patients.

Age and gender

Thyroid swellings are more common in females (i.e., 85.1%) compared to males (i.e., 14.9%). The incidence of thyroid lesions was most commonly seen in the age group of 31–40 years (i.e.,) 52 cases and least common at the age group of 10–20 years (i.e.,) seven cases Table 1.

Clinically, most of the patients presented with diffuse (48%), right (32%), and left lobe (20%) thyroid swellings.

Cytological diagnosis

According to the classification of cytological findings using the Bethesda system, there was one non-diagnostic (ND) case. Among the 185 benign lesions, the categories included multinodular goiter, colloid cyst (CC), colloid goiter (CG), colloid nodule, hyperplastic goiter (HG), Hashimoto's thyroiditis, lymphocytic thyroiditis, and granulomatous thyroiditis (GT). There was one case categorized as AUS. In the neoplastic category, there were seven cases of FN, four cases of suspicious for malignancy (SM), and three cases of malignant lesions.

HISTOPATHOLOGY

Out of the 201 cases, 132 were received in the histopathology section. Of these, 90 cases were reported as CG on cytology, with 81 correctly correlated. The other six were benign, including Hashimoto's thyroiditis (2), lymphocytic thyroiditis (2), GT (1), and HG (1). The remaining three cases were diagnosed as papillary thyroid carcinoma (PTC), non-invasive follicular thyroid neoplasm with papillary-like nuclear features, and follicular adenoma (FA).

Out of seven cases of HG on cytology, four were correctly correlated, while the other three were CG (2) and papillary carcinoma (1). All 17 cases of Hashimoto's thyroiditis were correctly correlated. Among the three cases of CC, two were CG, and one was Hashimoto's thyroiditis on histopathology.

The one case of AUS on cytology turned out to be FA on histopathology. Of the seven cases of FN on cytology, five were FA, one was follicular variant of papillary carcinoma, and one was follicular carcinoma on histopathology. Out of four cases SM on cytology, two were FA and the other two were papillary carcinoma and follicular carcinoma on histopathology. Finally, the three cases of malignant lesions on cytology were correctly correlated, with two being PTC and one anaplastic thyroid carcinoma (Table 2). Photomicrographs of few of the following cases are shown in figures 1-6.

Based on the provided information:

- True positives (TP): 15 cases
- True negatives (TN): 113 cases
- False negatives (FN): 4 cases
- False positives (FP): 0 cases.

To summarize the correlation between cytology and histopathology based on the Bethesda categories and the histological diagnosis:

Bethesda category I (ND) and AUS cases were excluded from the analysis as they did not undergo any surgery. Bethesda categories II and III (non-neoplastic) were grouped together for evaluation. Bethesda categories IV, V, and VI (neoplastic) were also analyzed collectively.

Hence, the study identified 15 true positive cases where both cytology and histopathology results confirmed neoplastic conditions and 113 true negative cases where both tests agreed on the absence of neoplastic conditions. There were four false negative cases where cytology failed to diagnose neoplastic conditions that were later confirmed by histopathology. Notably, no false positive cases were recorded where cytology incorrectly suggested a neoplastic condition that histopathology did not confirm.

Statistical analysis

Sensitivity(S) TP/TP+FN×100=78.94%

"True positives are patients with a positive neoplastic lesion in both cytology and histopathology. False negatives were patients who were diagnosed as having a benign lesion on FNAC but neoplastic on histology."

Specificity (SP): TN/TN+FP×100=100%

"True negatives were patients with benign non-neoplastic lesions both on cytology and histology. False positives were patients who were diagnosed as having a malignant lesion on cytology, but it was benign on histology."

Diagnostic accuracy (DA): TP +TN/FP+FN+TP+TN=96.9%

Positive predictive value (PPV): TP/TP+FP = 100%

Negative predictive value (NPV): TN/TN+FN=96%

In our study, the sensitivity, specificity, positive predictive value, NPV, and DA were 78.94%, 100%, 100%, 96%, and 96.9% respectively.

Table 1: Age distribution in all of the cases

Age range (in years)	No of cases	%
10–20	0	5
21–30	37	18
31–40	52	26
41–50	45	22
51–60	19	10
61–70	27	13
71–80	12	6

Table 2: Cytohistological correlation

S. no.	Cytological diagnosis	No of cases	Bethesda grade	Histopathological diagnosis
1.	Colloid goiter (CG)	90	Benign	CG-81, LT-2, HG-1, HT-2, GT-1, FA-1, NIFTP-1, PTC-1
2.	Hyperplastic goiter (HG)	7	Benign	HG-4, CG-2, PTC-1
3.	Hashimoto thyroiditis (HT)	17	Benign	HT-17
4.	Colloid cyst (CC)	3	Benign	CG-1, HT-1
5.	Atypia of undetermined significance (AUS)	1	AUS	FA-1
6.	Follicular neoplasm (FN)	7	FN	FA-5, FC-1, FVPC-1
7.	Suspicious for malignancy (SM)	4	SM	FA-2, PTC-1, FC-1
8.	Papillary thyroid carcinoma (PTC)	2	M	PTC-2
9.	Anaplastic thyroid carcinoma (ATC)	1	M	ATC-1

LT: Lymphocytic thyroiditis, FA: Follicular adenoma, FC: Follicular carcinoma, NIFTP: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features, GT: Granulomatous thyroiditis, FVPTC: Follicular variant of papillary carcinoma

DISCUSSION

Thyroid FNAC is widely practiced throughout India in academic institutions, private hospitals, and laboratories. Pathologists commonly obtain aspiration samples through manual palpation. These centers typically prepare both alcohol-fixed and air-dried smears, which are stained with Papanicolaou/H and E and MGG stains, respectively. TBSRTC is the predominant reporting system, demonstrating effective efficacy and interobserver concordance in numerous studies [4]. This study was conducted to assess its accuracy in diagnosing thyroid neoplasms. We compared the results obtained in our study with the other similar studies shown in the following Tables 3 and 4.

In our study, we observed a different distribution of cases according to the six-tier Bethesda system compared to other studies. Specifically, we found a higher percentage of cases categorized as benign and lower percentages in the non-diagnostic and AUS categories.

The higher proportion of cases classified as benign can be explained by several factors. First, our institute serves both referred patients and those who come directly, providing a broader representation of the general population. In addition, the accessibility of FNAC and its provision free of charge for economically disadvantaged patients' likely increases the number of benign cases included in our study.

Regarding the lower percentages in the non-diagnostic and AUS categories at our institute, this can be attributed to our practice of performing ultrasound-guided FNAC. This method allows for precise targeting of pathological areas, enhancing the quality and adequacy of aspirates obtained. As a result, cytopathologists are better able to make specific diagnoses, reducing the likelihood of non-diagnostic or indeterminate results and thereby minimizing cases falling into the non-diagnostic or AUS categories [6].

In FNAC, diagnosing follicular patterned lesions poses a challenge due to overlapping features between benign and malignant conditions, creating a gray area. This spectrum encompasses FA, carcinoma, and variant of PTC. Diagnosis of follicular carcinoma relies on demonstrating capsular or vascular invasion, necessitating complete embedding for accurate histopathological diagnosis. Distinguishing benign from malignant follicular nodules is difficult in FNAC, as criteria rely on histological evidence inaccessible through cytology [12].

The results of our present study and previous studies conducted by various authors indicate that FNAC exhibits high sensitivity and specificity for thyroid lesion diagnosis. This enables effective ruling out of malignancies in suspected cases, leading to improved patient management and quality of life by avoiding unnecessary surgeries. Early neoplastic diagnosis through FNAC facilitates timely and appropriate surgical decisions, reducing tumor burden and enhancing prognosis, thereby further improving patient quality of life [2].

Table 3: Distribution of lesions as per Bethesda classification in our study in comparison with other studies

Studies (in %)	I	II	III	IV	V	VI	Total cases
Nandedkar *et al*. [5]	4.25	82.6	0.82	9.48	1.15	1.98	606
Shri Lakshmi *et al.* [6]	3.4	81.89	1.72	7.7	0.86	4.3	232
Upadhyay *et al*. [7]	2.8	61.5	-	11.9	4.6	19.3	109
Anand *et al*. [8]	13.8	75.9	1.2	3.7	2.6	2.8	646
Zhu *et al*. [9]	14.8	17.1	15.8	2.3	11.6	38.5	232
Jain *et al*. [10]	2.73	83.03	0	9.70	0.61	3.94	330
Mondal *et al*. [11]	1.2	87.5	1	4.2	1.4	4.7	1020
Present study	1	92	1	3	2	1	201

Table 4: Comparison of sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy (DA) with other studies

Studies (in %)	SN	SP	PPV	NPV	DA
Nandedkar *et al*. [5]	85.7	98.6	97.1	90	98
Shri Lakshmi *et al.* [6]	78	87	78	87	84
Upadhyay *et al*. [7]	75	100	93.57	100	92
Anand *et al*. [8]	72.4	94.3	87.9	84	89.2
Zhu *et al*. [9]	98.35	30.9	94.9	58.3	93.55
Jain *et al*. [10]	100	60	94.29	100	94.73
Present study	78.94	100	100	96	96.9

CONCLUSION

FNAC is recognized for its rapidity, efficiency, cost-effectiveness, and relatively low discomfort, coupled with a high DA. It demonstrates a high sensitivity and positive predictive value in identifying thyroid neoplastic lesions, thereby serving as a valuable tool in patient diagnosis and management [13]. Cases with false-negative results can be mitigated by ensuring adequate sampling. Enhanced sampling techniques include obtaining aspirates from multiple sites within the nodule rather than repeatedly aspirating from a single spot [2].

The sensitivity and specificity of this method can be increased by strict adherence to adequacy criteria and reliance on a combination of various cytological features rather than emphasizing on only one. Proper representative sampling, if needed, along with improvement of technique and staying updated with knowledge for better interpretation, contributes to greater accuracy and quality [6].

AUTHORS OF INTEREST

All authors have contributed equally in the preparation of this manuscript.

CONFLICT OF INTERESTS

None.

AUTHORS FUNDING

None.

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