Original Article

Assessment of thyroid lesions using fine-needle aspiration cytology in accordance with the Bethesda System and its histopathological correlation

Himachal Mishra[1], Manika Alexander[1], Basavaraj P Bommanahalli [1]

[1]*Department of Pathology, Gadag Institute of Medical Sciences, Gadag (Karnataka), India*

ABSTRACT

Background: Fine Needle Aspiration Cytology is a first-line diagnostic technique that provides an accurate and precise diagnosis for assessing thyroid abnormalities. This study was conducted to analyze the cytology smears of thyroid lesions using The Bethesda system of reporting thyroid cytology and to correlate the cytological findings with histopathology diagnosis to determine the diagnostic accuracy of FNAC.

Materials and methods: A prospective cross-sectional study was carried out. FNAC of thyroid lesions of 203 patients were examined and reported as per the Bethesda system for reporting thyroid cytopathology. Of these, 33 patients underwent surgery, whose histopathological findings were compared and correlated with respective cytopathological diagnoses. The IBM SPSS (Statistical Package for the Social Sciences) software version 27 was used for data analysis.

Results: Among 203 cases evaluated, there were 11 Non-diagnostic (Category I) cases, 171 benign (Category II) cases, 4 cases of atypia of undetermined significance (Category III), 7 were suspicious for Follicular Neoplasm (Category IV), 2 were suspicious for malignancy (Category V) and 8 were malignant (Category VI). Out of 203 patients, only 33 patients underwent surgery, of whom 26 (78.79%) were benign and 7 (21.21%) were malignant on histopathology. The corresponding values for sensitivity, specificity, and diagnostic precision of FNAC were 71.42%, 100%, and 93.93% respectively, while positive and negative predictive values were determined as 100% and 92.85% respectively.

Conclusions: The study shows that thyroid tumors can be successfully categorized and reported cytologically as per The Bethesda system.

Correspondence:
Dr. Himachal Mishra, Resident,
Department of Pathology,
Gadag Institute of Medical Sciences, Gadag (Karnataka), India
ORCID: 0000-0001-9486-6822
Email: himcha252@gmail.com

INTRODUCTION

Thyroid lesions can present as diffuse, solitary, or multiple nodules which can be attributed to various etiological factors. Thyroid nodules are more common in females. Thyroid lesions are predominantly benign, presenting as solitary nodules. Thyroid lesions can be seen throughout the age spectrum, however, it is commonly seen in the adult age group.[1]

FNAC is a simple and minimally-invasive method for evaluating thyroid nodules and is effective in differentiating

benign from malignant tumors, reducing unnecessary surgical intervention in many cases.[3] It can be done as an OPD-based procedure and thus avoiding unnecessary hospital stays. USG-guided FNAC can significantly increase accuracy, especially in cystic and sub-centimetric thyroid lesions.[4] Apart from giving a direct morphological picture of thyroid lesions it also provides therapeutic benefits in cystic lesions filled with fluid and for relief of pressure symptoms.[2]

The Bethesda system for reporting thyroid cytopathology (TBSRTC) is widely accepted and categorizes thyroid lesions into six tiers each having a determined likelihood of malignancy in subsequent surgeries. TBSRTC is used across the world, allowing a uniform and reproducible approach to cytological interpretation and management of thyroid lesions.[5]

MATERIALS AND METHODS

Study design: A prospective cross-sectional study was conducted for the duration of 18 months, from January 2021 to June 2022, in the Department of Pathology at Gadag Institute of Medical Sciences, Gadag (Karnataka).

All patients undergoing FNAC of thyroid swelling and patients undergoing thyroid surgery after FNAC were included in the study. Patients who did not give consent were excluded from the study. Purposive sampling was done.

Patients referred for FNAC of thyroid lesions from various clinical departments underwent ultrasound (USG) of thyroid prior to FNAC. Written informed consent was taken from all patients for FNAC and the present study. In the case of illiterate patients, a left thumb impression was taken with the signature of a witness. In the case of patients belonging to the pediatric age group, the procedure was explained to both the child and the respective guardian.

FNAC was done in a supine position with an extended neck under all aseptic conditions using a 23 gauze needle. Aspirate was taken and spread on slides. After appropriate fixation, these smears were stained with Hematoxylin and eosin, Papanicolaou, Leishman stains, or Giemsa stains. Except for mild pain at the aspiration site, no major complication was noted and the procedure was well tolerated even in children.

33 patients underwent surgery. Surgically resected specimens were collected and fixed in 10% formalin solution for 24 hours. Representative sections were submitted after a proper gross examination of the specimen. Light microscopy analysis of paraffin-embedded Hematoxylin and eosin-stained sections were performed.

Obtained data were entered into a Microsoft Excel spreadsheet and data analysis was done on the IBM SPSS version 27 software (Statistical Package for Social Sciences). A correlation between cytological and histopathological

diagnosis of these 33 surgically resected samples was done. Analysis was done to obtain true positive, false positive, true negative, and false negative results, along with positive predictive value, negative predictive value, specificity, sensitivity, and diagnostic accuracy of FNAC as compared to the final histopathological diagnosis.

RESULTS

Out of the 203 patients who underwent FNAC of thyroid lesions between January 2021 to June 2022, the majority of patients were in their 4th decade, forming 43.17% of total cases. The youngest patient was only 11 years old, while the oldest was 75 years. 86.7% were females, and 13.3% were males. (fig. 1)
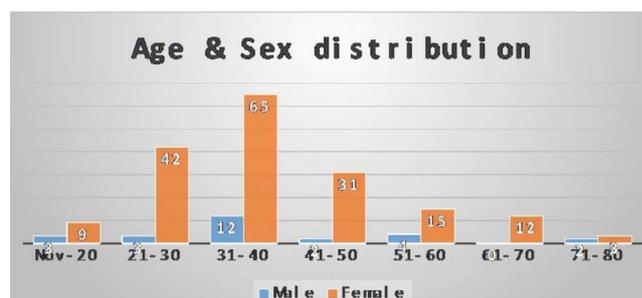
Figure 1: *Bar diagram showing age and sex distribution for patients undergoing FNAC.*
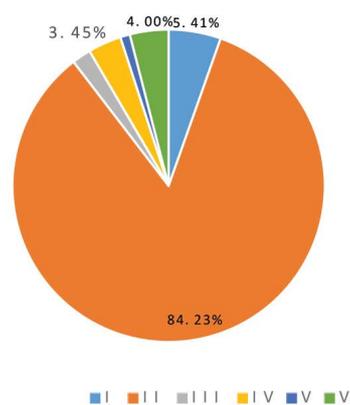
Figure 2: *Pie-chart showing categorization of thyroid lesions based on The Bethesda system for reporting thyroid cytopathology.*

203 cases of thyroid lesions were classified as per TBSRTC. 11 (5.4%) were of Category I, 171 (84.23%) cases were of Category II, 4 (2%) cases were of Category III, 7 (3.5%) cases were of category IV, 2 (1%) cases of category V and 8 (4%) cases of category VI. (fig. 2)

Table 1: Distribution of Non-neoplastic lesions on cytology

Categories	Number (%)
Colloid goitre	88 (54.85)
Hashimotos' Thyroiditis	40 (22.86)
Lymphocytic Thyroiditis	29 (16.6)
Hyperplastic nodule	9 (5.26
Granulomatous Thyroiditis	1 (0.5)
TOTAL	171(100)

Out of 171 non-neoplastic lesions evaluated, colloid nodular goiter was the commonest type comprising 54.85%, followed by Hashimoto's Thyroiditis, lymphocytic thyroiditis, hyperplastic nodule, and granulomatous Thyroiditis. (Table 1)

Out of 21 cases of Categories III-VI classified as per TBSRTC, follicular neoplasms were predominant comprising 7 (33%), followed by 5 (23.8%) cases of papillary thyroid carcinoma, 4 (20%) cases of atypia of undetermined significance (AUS), 2 (10%) cases of medullary thyroid carcinoma and 1 (5%) of anaplastic Thyroid carcinoma. Also 2 (10%) cases were reported as suspicious for malignancy.

Out of 203 patients evaluated, only 33 patients underwent surgery. Out of 33 patients, 26 (78.78%) were confirmed as benign, and 7 (21.12%) were found to be malignant on histopathology. Among the 26 benign lesions reported on histopathology, multinodular goiter was the commonest followed by follicular adenoma and Hashimoto thyroiditis. Papillary thyroid carcinoma was the most frequent type of malignancy noted in our study.

Table 2: Cytological-histopathological correlation

Cytological diagnosis	Histopathological diagnosis	Case (n)
Nodular colloid goiter	Multinodular goiter	16
	Follicular variant of papillary thyroid carcinoma	1
	Hashimoto thyroiditis	2
	Follicular adenoma	1
	Papillary microcarcinoma	1
Hyperplastic Nodule	Follicular adenoma	5
Lymphocytic Thyroiditis	Hashimoto thyroiditis	1
Hyperplastic nodule	Multinodular goitre	1
Hurthle cell neoplasm	Hurthle cell carcinoma	1
Follicular neoplasm	Hurthle cell carcinoma	1
Papillary thyroid carcinoma	Papillary thyroid carcinoma	3
TOTAL		33

Table 3: Statistical analysis

CYTOLOGICAL DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS		
	Malignant	Benign	Total
Malignant	TP-5	FP-00	5
Benign	FN-2	TN-26	28
TOTAL	7	26	33

Cyto-histopathological correlation based on 33 cases of surgically resected specimens was carried out. Sensitivity, specificity, and diagnostic accuracy of FNAC as per TBSRTC in identifying malignancy were found to be 71.42%, 100%, and 93.93% respectively, while negative predictive value and positive predictive value were calculated as 92.85% and 100% respectively. 26 were found to be true negative, 5 were true positive, and 2 cases were found to be false negative, but none were reported as false positive. (Table 3)
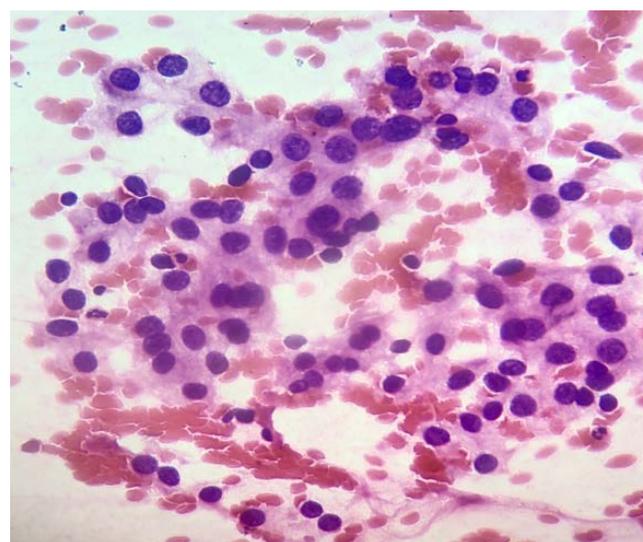
Figure 3: *Thyroid follicles cells in clusters showing pleomorphism. Follicular Neoplasm (HE stain, X100)*

Figure 4: *Gross image showing encapsulated solid, tan areas of tumor*
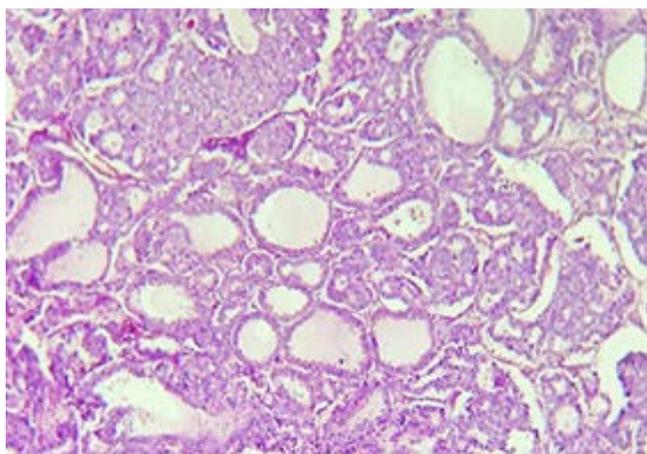
Figure 5: *Solid and papillary pattern of growth in Hurthle cell carcinoma (HE stain, X100)*
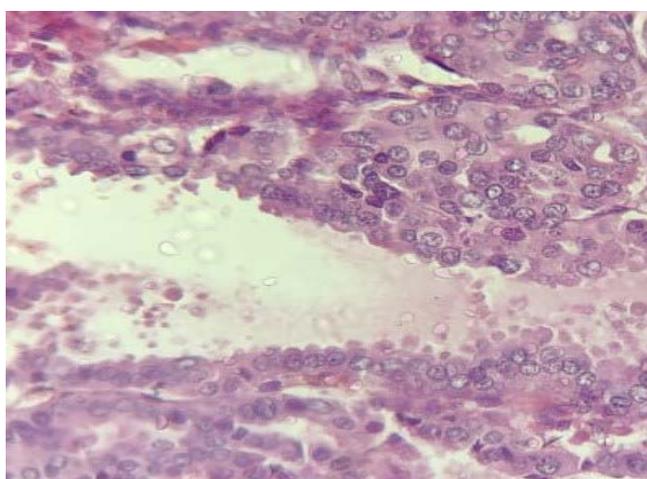
Figure 6: *Hurthle cells displaying eosinophilic granular cytoplasm. Hurthle cell carcinoma (HE stain X400)*

DISCUSSION

FNAC is a simple, quick, and affordable procedure that is highly valuable in guiding the management of different thyroid lesions.[2] FNAC is a blind procedure so the clinician and the pathologist should be aware of the limitations of FNAC. The ability of FNAC to categorize thyroid lesions into various categories including malignant from benign ones has led to reduced surgery rates for thyroid lesions.[2] For cases of neoplastic thyroid lesions with cystic changes such as papillary thyroid carcinoma and follicular neoplasm, aspiration cytology may not be accurate.

Five to six groups of well-preserved follicular cells, each having ten or more cells, should be present in an acceptable thyroid cytological smear.[2] This study showed an adequacy rate of 94.5%, which is found to be comparable with the studies done by Choden et al[6] and Nandedkar et al.[2,6] In the present study, 87.57 % were female and 12.43% were male patients with a male-to-female ratio of 1:7. These results were comparable with Handa et al.[8]

Table 4: Comparison of parameters observed in various studies

Studies	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	DA (%)
Present Study	71.42	100	92.85	100	93.93
Kapila et al [10]	91	61.9	84.2	75	---
Abdullah et al [11]	95.6	54.8	89.5	75.4	78.9
Hajmanoochehri et al [12]	95.2	68.4	89.6	83.3	85.14
Leonard & Melcher [13]	88	78	97	46	80
Burch et al [14]	80	73	90	55.8	75.2

The cyto-histopathological correlation done on 33 patients showed high specificity in identifying malignant lesions, high negative predictive value, positive predictive value, and diagnostic accuracy, and a relatively low sensitivity as compared to previous studies. Two reasons can be attributed to the high value of specificity, negative predictive value, and diagnostic accuracy. First, all the cases underwent a pre-procedure USG scan of thyroid, helping in determining the location of any suspicious area if present in the thyroid swelling. Thus improving our diagnostic accuracy. Secondly, non-aspiration technique was utilized for FNAC which yielded better cellularity and also reduced the blood particles on the smear.

Table 5: Distribution of cytological diagnoses based on The Bethesda system in various studies

Diagnostic Category	Present study	Nandedkar et al [2]	Swati et al [3]	Yang et al [9]	Choden et al [6]
I	5.41%	4.29%	3.09 %	10.4%	6%
II	84.23%	82.67%	82.47%	64.6%	82%
III	1.97%	0.82%	2.06%	3.2%	1.4%
IV	3.45%	9.07%	2.06%	11.6%	3.8%
V	1%	1.15%	1.03%	2.6%	2.4%
VI	4%	1.98%	9.29%	7.6%	4.4%

In our study, benign lesions (category II) were predominant.

The Findings were comparable to the study done by Choden et al. [6]   In the present study, categorization of thyroid lesions based on the Bethesda system showed category 1 lesions-5.5%, category II lesions-85%, category III – 2.5%, category III-3.5%, category IV-1%, Category V-4% and category VI- 6%. These findings are comparable to the information gathered from earlier investigations done by Kanukuntla et al[15] and Swati et al.[3]

Table 6: Discordant cases observed in the present study

Cytological diagnosis	Histological diagnosis
Nodular colloid goitre	Follicular variant of papillary thyroid carcinoma
Follicular neoplasm	Hurthle cell carcinoma
Nodular colloid goitre	Papillary microcarcinoma

There were three discordant cases in the present study. (Table 6) In the 1st case, aspiration yielded colloid with sparse cellularity and absence of nuclear features of papillary thyroid carcinoma. This might have been due to aspiration of the cystic component of the tumor. This can be corrected by aspirating the cystic fluid and then doing syringing from the residual solid area which could have yielded the tumor. In the 2nd case, follicular cells were seen in clusters showing nuclear pleomorphism with no cluster of Hurthle cells with eosinophilic cytoplasm. We suggest carrying out more passes from different directions to get an accurate diagnosis. In the 3rd case, aspiration yielded brown colloids and showed few thyroid follicular cells in clusters with thick colloids and could not hit the microfocus of less than 1cm in size. Ultrasound-guided FNAC could have helped out in the detection and aspirating of the tumor foci.

CONCLUSIONS

FNAC can be used as a technique for screening individuals presenting with thyroid swellings. The Bethesda technique for reporting thyroid cytopathology has proven to be accurate in classifying thyroid lesions. Hence it represents a trustworthy system for reporting thyroid cytology.

Conflict of Interest: None

References

1.   Erkinuresin T, Demirci H. Diagnostic accuracy of fine needle aspiration cytology of thyroid nodules. Diagnosis (Berl). Diagnosis. 2020; 7(1): 61-6. Crossref

2.   Nandedkar SS, Dixit M, Malukani K, Varma AV, Gambhir S. Evaluation of Thyroid Lesions by Fine-needle Aspiration Cytology According to Bethesda System and its Histopathological Correlation. Int J Appl Basic Med Res. 2018; 8(2):76-82. Crossref

3.   Patel S, Soni H, Sharma S, Purohit MR. A prospective study on cytology of thyroid lesions, its correlation with histopathology and evaluate diagnostic accuracy of FNAC in thyroid pathologies. IP Journal of Diagnostic Pathology and Oncology. 2018; 3(2): 81-8. Crossref

4.   Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: how useful and accurate is it? Indian J Cancer. 2010 Oct-Dec; 47(4): 437-42. Crossref

5.   Cibas ES, Ali SZ; NCI Thyroid FNA State of the Science Conference. The Bethesda System For Reporting Thyroid Cytopathology. Am J Clin Pathol. 2009 Nov;132(5):658-65. Crossref

6.   Choden S, Wangmo C, Maharjan S. Application of the Bethesda system for reporting thyroid cytopathology for classification of thyroid nodules: A clinical and cytopathological characteristics in Bhutanese population. Diagn Cytopathol. 2021 Nov; 49(11):1179-1187. Crossref

7.   Al Dawish MA, Robert AA, Muna A, et al. Bethesda System for Reporting Thyroid Cytopathology: A three-year study at a tertiary care referral center in Saudi Arabia. World J Clin Oncol. 2017 Apr 10;8(2):151-157. Crossref

8.   Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A Study on 434 patients. J Cytol. 2008, 25:13-7. Crossref

9.   Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. Cancer. 2007 Oct 25;111(5):306-15. Crossref DOI: 10.1002/cncr.22955.

10.   Kapila K, Qadan L, Ali RH, Jaragh M, George SS, Haji BE. The Bethesda System for Reporting Thyroid Fine-Needle Aspiration Cytology: A Kuwaiti Experience-A Cytohistopathological Study of 374 Cases. Acta Cytol. 2015; 59(2):133-8. Crossref

11.   Abdullah N, Hajeer M, Abudalu L, Sughayer M. Correlation study of thyroid nodule Cytopathology and histopathology at two institution in Jordan. Cyto Journal. 2018; 15(24): 1-12. Crossref

12.   Hajmanoochehri F, Rabiee E. FNAC accuracy in diagnosis of thyroid neoplasms considering all diagnostic categories of the Bethesda reporting system: A single-institute experience. J Cytol. 2015; 32(4): 238-43. Crossref

13.   Leonard N, Melcher DH. To operate or not to operate? The value of fine needle aspiration cytology in the assessment of thyroid swellings. J Clin Pathol. 1997; 50(11):941-3. Crossref

14.   Burch HB, Burman KD, Reed HL, Buckner L, Raber T, Ownbey JL: Fine Needle Aspiration of Thyroid Nodules. Acta Cytologica 1996; 40:1176-1183. Crossref

15.   Kanukuntla S, Pavani M, Deshpawde AK, Chaitanya. Evaluation of fine needle aspiration cytology of thyroid lesions by Bethesda system and its histopathological correlation. Indian J Pathol Oncol 2020; 7(2):273-278. Crossref