Original Research Article

Evaluation of fine needle aspiration cytology of thyroid lesions by Bethesda system and its histopathological correlation

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A B S T R A C T

Introduction: The Bethesda system of thyroid cytopathology (TBSRTC) established a standardized, category –based reporting system for thyroid fine needle aspiration cytology.

Aim: The objective of this study was to analyse the thyroid cytology smears by TBSRTC, and to determine the distribution of diagnostic categories and subcategories, to analyse cytomophologic features and to correlate cytopathology with histopathology wherever surgery was done.

Materials and Methods: In this study FNA of 248 patients of clinically palpable thyroid and deep-seated lesions were evaluated and categorised according to bethesda system of reporting thyroid cytopathology. 66 patients underwent surgical management in our hospital. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNA reported under bethesda system were obtained by comparing the cytological and histopathological diagnosis where ever possible.

Results: The distribution of various categories from 248 evaluated thyroid nodules is as follows: 2.82% ND/UNS, 83.87% Benign, 4.03% AUS/FLUS, 2.41% FN, 0.8% SFM and 6.04% malignant. Sensitivity, specificity, positive predictive value, negative predictive value were calculated.

Conclusion: Simplicity, diagnostic accuracy and most of all cost effectiveness of FNA of thyroid has gained wide spread acceptance as first-line diagnostic test in the pre-operative evaluation of thyroid lesions. TBSRTC is an excellent reporting system for thyroid FNA. It also provides clear management guidelines to clinicians.

1. Introduction

Thyroid lesions are one of the common conditions encountered in clinical practice. With an annual incidence rate of 2-6%.[1] Palpable thyroid nodules are more common in females than in men.[2,3] Fine needle aspiration has been the safest and most accurate of diagnostic tools in thyroid lesions.[2] It plays an essential role in the evaluation of the euthyroid patient with a thyroid nodule. Ultrasound guided FNA of thyroid is useful, especially in cystic and multinodular lesions harboring malignancy. Recent guidelines recommending ultrasound examination in patients with palpable nodules have led to an emerging trend of US-guided FNA.[3]

The Bethesda system of reporting thyroid cytopathology was introduced in 2007.[4,5] It had established a standardized, category based reporting system. The 2017 rivision (Table 1) reaffirms that every thyroid FNA report should begin with one of the 6 diagnostic categories. It includes category Non diagnostic /Unsatisfactory(ND/US), category 2 -Benign(B), category 3 -Atypia of undetermined significance / Follicular lesion of undetermined significance(AUS/FLUS), category 4- Follicular neoplasm/ suspicious of follicular neoplasm (FN/SFN), category 5 -Suspicious of malignancy (SM)and category 6 - Malignant(M). Each category has an implied risk of malignancy. The usual management now incorporates the option of molecular testing. The purpose is to delineate patients who require surgical excision of thyroid lesions from patients who can be managed conservatively.

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Table 1: The Bethesda System for reporting thyroid cytopathology: recommended diagnostic categories, implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%)	Usual management[1]
(1) **Nondiagnostic or Unsatisfactory** Cyst fluid only Virtually acellular specimen Other(obscuring blood, clotting artefact, etc.)		Repeat FNA with ultrasound guidance
(2) **Benign** Consistent with benign follicular nodule (includes adenomatoid nodule,colloid nodule etc.) Consistent with lymphocytic thyroiditis (Hashimoto) thyroiditis in the proper clinical context. Consistent with granulomatous (sub acute) thyroiditis other	0-3	Clinical and sonographic follow-up
(3) **Atypia of undetermined significance or follicular lesion of undetermined significance(AUS/FLUS)**	5-15[2]	Repeat FNA,Molecular testing or lobectomy
(4) **Follicular neoplasm or suspicious for follicular neoplasm(FN/SFN)** -Specify if Hurthle cell (oncocytic) type	15-30	Molecular testing or Surgical lobectomy
(5) **Suspicious for malignancy (SFM)** Suspicious for papillary carcinoma Suspicious for medullary carcinoma Suspicious for metastatic carcinoma Suspicious for lymphoma Other	60-75	Near-total thyroidectomy or surgical lobectomy[3]
(6) **Malignant** Papillary thyroid carcinoma Poorly differentiated carcinoma Medullary thyroid carcinoma Undifferentiated(anaplastic)carcinoma Squamous cell carcinoma Carcinoma with mixed features(specify) Metastatic carcinoma Non-Hodgkin lymphoma Other	97-99	Near-total thyroidectomy[3]

[1]Actual management may depend on other factors (e.g., clinical and sonographic) besides the FNA interpretation.
[2]Some studies have recommended molecular analysis to assess the type of surgical procedure (lobectomy versus total thyroidectomy)
[3]In the case of "suspicious for metastatic tumor" or a malignant interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated.

The objective of this study is to categorise thyroid cytology smears into various diagnostic categories, to analyze their cytopathological features and to correlate with histopathological diagnosis of surgical specimens received.

2. Materials and Methods

Our study includes 248 cases of clinically diagnosed thyroid nodules since august 2017 to July 2019 referred for FNA to our department. Relevant clinical history was taken, examination done. With the patient sitting upright or supine with pillow behind, the neck with hyperextension a fine needle capillary sampling was done using needle (gauge 25-27). The needle was passed quickly and gently with different directions at the point of entry. Needling was concluded before or as soon as material appeared in the hub. The smears were prepared using conventional methods and stained with MGG, routine H&E and papanicolaou (pap) stain. US-guided FNA was done in some multinodular goiters and some

radiologically suspicious lesions. The cytological features evaluated and reporting was done categorised according to TBSRTC. Histopathological specimens wherever available were processed as per standard operating procedures. Sensitivity, specificity, positive predictive value, negative predictive values were calculated using histopathology diagnosis as gold standard.

After exclusion of nondiagnostic results cytological diagnoses was classified as positive \negative. Benign lesions were taken as negative where as SFM, and Malignant cytological diagnosis were considered as positive.

3. Results

The age distribution of cases were shown in Table 2. Ranges from 16-90 years of age. Majority of cases were presented in between 4th and 5th decades of life. Of which 216 were female and 32 were male. With female to male ratio of 7.7:1.

The cytomorphologic distribution of cases were given in Table 3. Benign category was the largest and constitutes

83.87% followed by the malignant category about 6.04%. AUS/FLUS constituted 4.03% cases while FN/SFN had 2.41% cases.

The ND/UNS category includes a total of 7 cases all cases were of cyst fluid only. In benign category a total of 208 cases were consistent with benign follicular nodule. The subcategory lymphocytic thyroditis included 38 cases in the benign category. In our study category AUS/FLUS constituted 4.03% .80% of the cases showed moderately cellular smears with predominantly microfollicles and scant colloid. Two cases showed predominantly benign appearing smear with focal features of papillary thyroid carcinoma including intranuclear inclusion, enlarged nuclei with irregular nuclear margin.

There were 2.41% of cases in FN/SFN category and there were no case of FN, Hurthle cell type. In the category SFM two cases of suspicious of malignancy NOS were reported. In the malignant category constitutes 6.04%.All cases were of papillary thyroid carcinoma.

A total of 66 patients underwent surgery in our hospital for which the histopathological diagnosis was available. Among these 48 cases were benign and 18 cases were malignant. 34 of 66 cases in this study with subsequent tissue diagnosis had a definitive cytologic diagnosis of being benign or malignant.

The cyto-histomorphologic correlation were summarized in Table 4.

Sensitivity, specificity, positive predictive value, negative predictive value were found to be of 60%, 96.43%, 75%, 93.10% respectively. The diagnostic accuracy was found to be 90.91% Table 2.

Table 2: Age distribution of cases

Age group	Number of cases	Percentage
0-10	00	00
11-20	03	1.20%
21-30	42	16.93%
31-40	74	29.83%
41-50	56	22.58%
51-60	45	18.14%
61-70	22	8.874%
714-80	05	2.01%
81-90	01	0.40%

4. Discussion

Thyroid malignancies constitute 1% of all cancers and are responsible for 0.5% of all cancer related deaths. Thyroid cancers are nearly three times more common in women than in men. FNA plays an essential role in evaluation of euthyroid patients with thyroid nodule. FNA combined with ultrasound is the initial approach to obtain cells for pathologic review.FNA is usually performed in patients with nodules >1cm with no associated risk factors. In patients
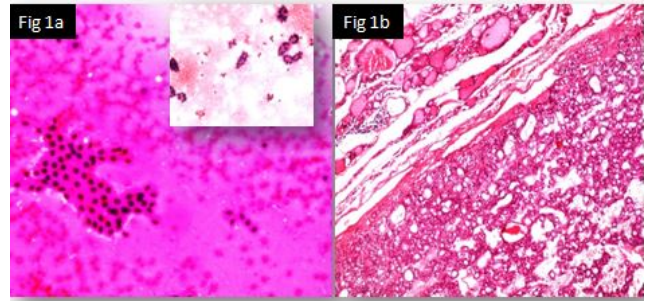

Fig. 1: a): Benign follicular nodule pictomicrograph showing monolayer sheets of evernlyspaced follicular cells (inbox image show microfollicles); **b):** Benign follicular nodule: Pictomicrograph showing nodulargoiter
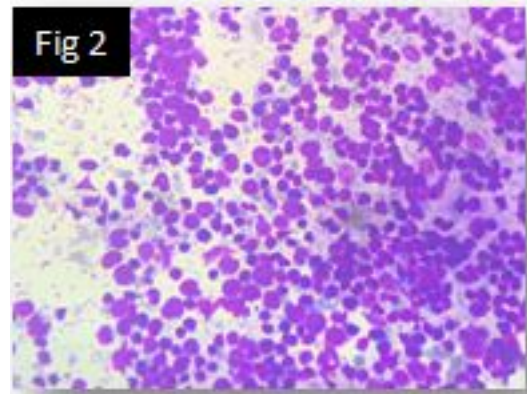

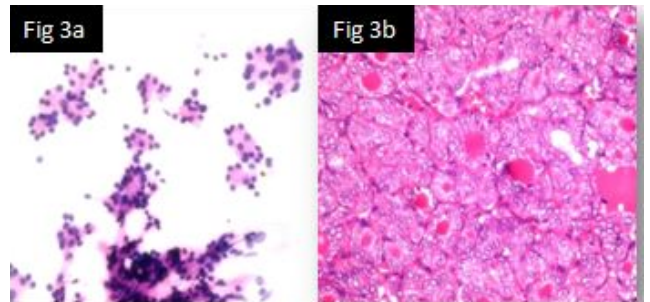**Fig. 2:** Pictomicrograph showing Hashimoto thyroiditis

Fig. 3: a): Follicular neoplasm: Pictomicrograph showing micro-follicular pattern; b) Papillary thyroid neoplasm: Pictomicrograph showingpapillary pattern; b: Papillary thyroid neoplasm: Pictomicrograph showingnuclear crowding, overlapping and intranuclear inclusions; **c):** Papillary thyroidneoplasm: Pictomicrograph showing nuclear crowding, overlapping andintranuclear inclusion; **d):** Papillary thyroid neoplasm: Pictomicrograph showingpapillary thyroid neoplasm: Benignfollicular nodule: Pictomicrograph showing follicular neoplasm

Table 3: Distribution of cytologic diagnosis

S. No.	Category	Sub category	Number of cases	Total number of cases (%)
1.	Nondiagnostic / unsatisfactory (ND/UNS)	Cyst fluid only	07	07(2.82)
		Acellular smears	0	
		Other (obscuring blood, clotting, artifacts)	0	
2.	Benign	Consistent with benign follicular nodule (includes adenomatoid nodule, colloid nodule)	170	208(83.87)
		Consistent with lymphocytic thyroiditis (hashimoto) thyroiditis in the proper clinical context	38	
		Consistent with granulomatous thyroiditis	00	
		Other	00	
3.	Atypia of undetermined significance (AUS\FLUS)			10(4.03)
4.	Follicular neoplasm (FN\SFN)			06(2.41)
5.	Suspicious of malignancy(SFM)			02(0.8)
6	Malignant			15(6.04)
	Total			248

Table 4: Cytological/Histopathological correlation

Cytologic category	No of cases surgical specimens received	Percent of category	Histopathological diagnosis	No. of cases
Non diagnostic/unsatisfactory	01		Papillary thyroid carcinoma	01
Benign	28(50)		Nodular goiter	20
			Follicular adenoma	05
			Papillary thyroid carcinoma	02
			Non invasive follicular neoplasm with papillary like features	01
AUS/FLUS	01		Nodular hyperplasia	01
Suspicious of malignancy	01		Lymphocytic thyroiditis	01
Malignancy	03		Papillary thyroid carcinoma	03

Table 5: Comparision with other studies

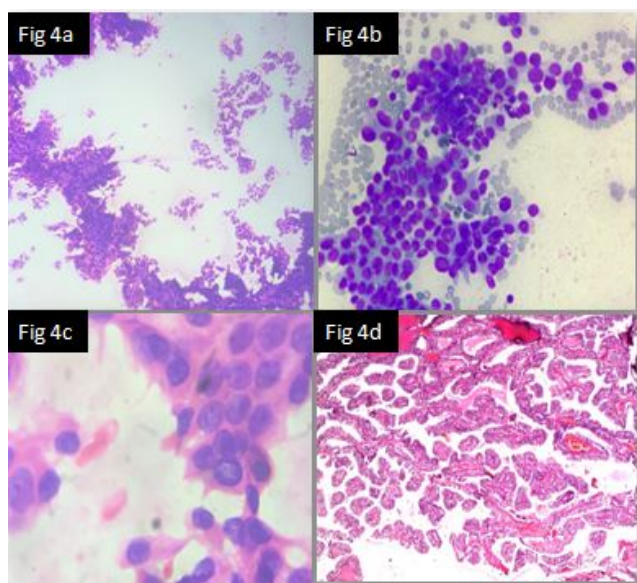| Study	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Goswami et al[6]	85.71%	96%	85.71%	96%	93.33%
Roy PK et al.[7]	81.48%	95.29%	84.61%	94.18%	91.16%
Muratli et al.[8]	87.1%	64.6%	76.1%	79.5%	77.3%
Sheikh et al.[9]	83.2%	63.3%	74.3%	76.4%	74.4%
Sreemani et al.[10]	67.4%	99.2%	93.9%	94.2%	94.1%
Present study	60%	96.43%	75%	92.10%	90.91%

Fig. 4: a): Papillary thyroid neoplasm: Pictomicrograph showing papillary pattern; **b):** Papillary thyroid neoplasm: Pictomicrograph showing nuclear crowding, overlapping and intranuclear inclusions; **c):** Papillary thyroidneoplasm: Pictomicrograph showing nuclear crowding, overlapping and intranuclear inclusion; **d):** Papillary thyroid neoplasm: Pictomicrograph showing papillary thyroid neoplasm

with risk factors FNA of all nodules more than or equal to 5 mm is performed. If malignancy cannot be excluded by FNA, a lobectomy is usually performed to obtain adequate tissue for correct diagnosis.

Current study deals with 248 cases of thyroid swellings where FNA was performed in our department. Majority of the cases were presented between 3rd to 5th decades of life. Most common presenting complaint was swelling in front of neck. Majority of patients were euthyroid and most common clinical diagnosis was solitary thyroid nodule. US–guided FNA was performed wherever necessary.

Our study had 7(2.82%) cases in ND/UNS category. Other recent studies had 1.2% to 16% cases in this group.[6–9,11–14] Guidelines for this category are very clear in TBSRTC. The number of cases in this category is depends not only on the aspirator but also on the inherent nature of the lesion (e.g., solid vs cystic). TBSRTC provides 5-10% an implied risk of malignancy for this category.[4] Also recommends nodules with an initial ND result should be re-aspirated unless the nodule is purely cystic. Ultrasound guidance with an immediate on-site adequacy evaluation is preferred for repeat aspiration especially for solid nodules in the absence of on-site evaluation for adequacy obtaining a minimum of three separate samples of the nodules can reduce the rate of unsatisfactory specimens. After two successive ND/UNS specimens, close clinical and sonographic follow-up or surgery should be considered,

depending on clinical findings. In this category we had a case were the initial diagnosis was cyst fluid only. For this case an intraoperative consultation was taken, on frozen section examination it was reported as papillary thyroid carcinoma and later on histopathological examination it was consistent with papillary thyroid carcinoma

The benign category had 208 (83.87%) cases. Nodular goiter was most common thyroid lesion diagnosed on cytological examination followed by lymphocytic thyroiditis. The benign category is associated with very low risk of malignancy, and patients are usually followed conservatively with periodic clinical and radiologic examinations.

The diagnostic criteria of all the subcategories are well characterized in TBSRTC. By definition the sample is adequate for evaluation and consists of colloid and benign appearing follicular cells in varying proportions. In the subclassification a more specific benign diagnosis was given, depending on the cytomorphologic findings and associated clinical presentation.

A total of 50 cases surgical specimens were received. Clinical diagnosis was predominantly multinodular goiter followed by solitary thyroid nodule. All of them were operated for cosmetic reasons or pressure symptoms. Cyto-histo correlation was available for 28 cases, of which 20cases were nodular goiter, 05 cases were follicular adenoma and 02 cases were reported as papillary thyroid carcinoma of which one case showed a tiny focus i.e., papillary microcarcinoma

A case of noninvasive follicular thyroid neoplasm with focal papillary like nuclear features (NIFTP)[15] which showed an encapsulated, follicular patterned lesion with focal nuclear features of papillary thyroid carcinoma. Cytological diagnosis for this case was nodular goiter.

Chetna J mistry et al[15] and Neiki et al[16] stated that presence of degenerarative changes in the monolayer sheets with abundant colloid in the background would suggest a possibility of non-neoplastic lesion. In a study of Das DK et al,[17] colloid goiter, cellular adenomatoid goiter(hyperplastic goiter), hyperplastic nodule and follicular neoplasm form a continous spectrum in terms of cellularity, microfollicles in increasing order and background colloid in decreasing order. Study done by Basavaraj P Bommanahali et al[18] Radhika puri et al[11] showed similar findings.

Baloch ZW et al.[19] stated that differential diagnosis of smears with predominanlty macro\normo follicular pattern often included nodular goiter and follicular neoplasm. The cyto and histomorphologic characteristics were also described.

Our study also included 4 cases where initial cyto-morphologic diagnosis was nodular goiter but later was diagnosed as follicular adenoma on histopathological examination.

FN/SFN category had 6 (2.41%) cases. TBSRTC provides a clear guidelines for this category. Aspirates

were cellular with predominantly microfollicular pattern. Cellularity, nuclear size, pleomorphism of cells and amount of colloid are helpful in distinguishing neoplastic from non-neoplastic follicular lesion. A cyto-histo correlation was available for one case in this category. Patients presented with solitary thyroid nodule

The category malignant had a range of 2.9%-11% in all the recent studies.[6–9,11–14] The present study had 6.04% cases in malignant category. We received 3 specimens from this category diagnosed as "malignant" on cytology. All of them were diagnosed as papillary thyroid carcinoma both histopathological examination.

The total accuracy of throid FNA was reported in our study is 90.91% was comparable with other studies (Table 5).

5. Conclusion

In our study we analysed thyroid cytology smears and classified according to the bethesda system. The bethesda system for reporting thyroid cytopathology is an excellent system of reporting thyroid cytopathology. It facilitates easy sharing of data. Each category also provides clear management guidelines to clinicians and also extent of surgery.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Siegel RL, Miller KD, Jemal A. Jemal A. cancer statistcian 2015. *CA Cancer J Clin*. 2015;65(1):5–29.
2. Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? *Indian J Cancer*. 2010;47(4):437–42.
3. Orell SR, Sterrett GF. Fine needle aspiration cytology, 5th ed. London, Churchill Livingstone: Elsevier; 2012.
4. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2017;27(1):1341–6.
5. Bongiovanni M, Spitale A, Faquin WC, Mazzucchelli L, Baloch ZW. The bethesda system for reporting thyroid cytopathology: A meta-analysis. *Acta Cytol*. 2012;56(4):333–9.
6. Goswami D, Agrawal P, Shinde P. Accuracy of fine needle aspiration cytology in comparision to histopathological examination for the diagnosis of thyroid swellings. *Int J Med Sci Public Health*. 2017;6:6–11.
7. Roy PK, Bandyopadhyay S, Dubey AB, Sengupta A. A comparative study on aspiration cytology and histopathology in diagnosis of thyroid nodule and its correlation. *Indian J Otolaryngol Head Neck Surg*. 2019;71(1):992–1001.
8. Muratli A, Erdogan N, Sevim S, Unal I, Akyuz S. Diagnostic efficacy and importance of fine-needle aspiration cytology of thyroid nodules. *J Cytol*. 2014;31(2):73–8.
9. Sheikh SA, Ganguly S, Ganguly S, Das SS, Phukan A, Das J. Evaluation of Bethesda system in cytopathological diagnosis of thyroid nodule and its histopathological correlation. *Indian J Pathol Oncol*. 2016;3(2):231–6.
10. Kumari NS, Parigi M, Afroze S. Accuracy of fine needle aspiration cytology with histopathology of thyroid lesions - 1.5 years study at Government ENT hospital, Hyderabad, Telangana. *IAIM*. 2017;4(8):49–63.
11. Puri R. Measuring and modifying consumer impulsiveness: A cost-benefit accessibility framework. *J Consumer Psychol*. 1996;5:87–113.
12. Agrawal R, Saxena M, Kumar P. A study of fine needle aspiration cytology of thyroid Lesions with histopathological correlation. *Indian J Pathol Oncol*. 2015;2(4):277–83.
13. Chuang CP, Chen YJ. ChemInform Abstract: Manganese(III) Acetate Mediated Oxidative Radical Cyclizations of α-Substituted N-[2-(Phenylethynyl)phenyl]acetamides. *ChemInform*. 2016;47:727–59.
14. Jo VY, Stelow EB, Dustin SM, Hanley KZ. Malignancy risk for fine-needle aspiration of thyroid lesions according to the Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol*. 2010;134(3):450–6.
15. Mistry CJ, Vijapura TY, Pande RK. Cytohistopathological correlation of thyroid swelling. *Int J Sci Res*. 2012;1:75–6.
16. Neiki NS, Kazal HL. Solitary thyroid nodule – An insight. *J, Indian Acad Clin Med*. 2006;7:328–33.
17. Bhartiya R, Mallik M, Kumari N, Prasad B. Evaluation of thyroid lesions by fine-needle aspiration cytology based on Bethesda system for reporting thyroid cytopathology classification among the population of South Bihar. *Indian J Med Oncol*. 2016;37:265–70.
18. Bommanahalli BP, Bhat RV, Rupanarayan R. A cell pattern approach to interpretation of fine needle aspiration cytology of thyroid lesions: A cyto-histomorphological study. *J Cytol*. 2010;27(4):127–32.
19. Baloch ZW, Livolsi VA. Follicular- patterned lesions of the thyroid: the bane of the pathologist. *Am J Clin Pathol*. 2002;117(1):143–150.

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