Original Research Article

Categorisation of thyroid lesions according to bethesda system and their histopathology correlation in a tertiary care hospital

Sathyashree K V[1*], Mahesh H Karigoudar[2], Anil Reddy Konduru[3], Pyla Ramadevi[4], Disha B S[5], Ramyashree G[6]

[1]Assistant Professor, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (DU), Vijayapura, Karnataka, India

[2]Professor, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (DU), Vijayapura, Karnataka, India

[3]Assistant professor, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE(DU), Vijayapura, Karnataka, India

[4]Post graduate, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (DU), Vijayapura, Karnataka, India

[5]Post graduate, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (DU), Vijayapura, Karnataka, India

[6]Post graduate, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE (DU), Vijayapura, Karnataka, India

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Abstract

Introduction: Thyroid is affected by variety of conditions, whose preoperative diagnosis is of great significance in appropriate management. Fine needle aspiration cytology (FNAC) offers cellular level diagnosis with comparable sensitivity and specificity with respect to gold standard histopathological examination. **Aim:** To categories Fine Needle Aspiration Cytology of Thyroid lesions according to The Bethesda System of Reporting Thyroid Cytopathology and to correlate with histopathological findings wherever possible and to estimate diagnostic accuracy of FNAC. **Materials and methods:** A prospective study was carried out over a period of 2year, during which FNAC was done in 328 patients with thyroid swelling. Amongst whom 126 underwent surgery and histopathological correlation was done in those cases. **Results:** There was female preponderance with female to male ratio of 6.9:1, and mean age of 40.6 years. Out of 126 cases, 117 were non-neoplastic and 9 were neoplastic on histopathology. Among 117 non-neoplastic lesions, 106 cases showed cyto-histological concordance and 11 were discordant. Among the 9 neoplastic lesions, cyto-histological concordance was obtained in 4 cases and discordant in 5. Sensitivity and specificity of FNAC for non-neoplastic lesions were 93.8% and 69.2% respectively. Positive predictive value and negative predictive value were 96.3% and 56.2% respectively with a diagnostic accuracy of 91.2%. **Conclusion:** FNAC is simple, inexpensive and effective diagnostic modality with complications being minimal. Precise technique and rational use of USG guidance improves the adequacy and reduces the non-diagnostic rates. FNAC reporting according to TBSRTC aids clinicians and Pathologists in providing optimal management of patients.

Keywords: FNAC, Thyroid, Histopathology.

Introduction

Thyroid is an important endocrine organ with significant effects on the overall metabolism and functions of the human body in normal as well as diseased states[1]. Thyroid gland is associated with wide variety of conditions and their accurate diagnosis is of utmost importance in instituting an appropriate medical or surgical therapy[2,3]. Enlarged thyroid gland is investigated by biochemical, radiological and pathological evaluation[4,5].

*Correspondence

Dr. Sathyashree K V

Assistant Professor, Department of Pathology, Shri B M Patil Medical College, Hospital and Research Centre, BLDE(DU), Vijayapura, Karnataka, India.

E-mail: drsathyashree@gmail.com

Amongst the investigative modalities, cytological examination (FNAC) has a distinct advantage in offering cellular level diagnosis with comparable sensitivity and specificity of certain conditions with respect to histopathological examination. However, this is not universal and some conditions cannot be differentiated on FNAC alone. Hence, the histopathological correlation of FNAC is still a continuous area of interest.Histopathological examination and correlation of the findings of the FNAC has been done widely with regards to the benign v/s malignant lesions, whereas the non-neoplastic lesion correlation is having very scarce literature available. Hence, present study was conducted to better understand the nature of the type of diagnosis offered in a non-neoplastic lesion by FNAC and to correlate with the diagnosis on histopathological examination.

Aim of the study

To categories Fine Needle Aspiration Cytology of Thyroid lesions according to The Bethesda System of Reporting Thyroid Cytopathology and to correlate with histopathological findings of non-neoplastic and neoplastic lesions of thyroid wherever possible and to estimate diagnostic accuracy of FNAC.

Materials and methods

A prospective study was carried out on cases who presented with thyroid swellings in the cytology section and the surgically resected specimens received in the histopathology laboratory of Pathology department.Patients with both cytology and histopathology examination of thyroid were included in the study. Patients having either histopathology or cytology examination alone were excluded from the study.Study started after obtaining permission from the Institutional Ethical Committee. A detailed clinical history followed by thorough examination of 328 patients was done. Informed and written consent was obtained. FNAC procedure was performed by using 22gauge needle. In cases of inadequate sample (only bloody aspirate / less than six clusters of follicular cells with each cluster containing 10 well visualised follicular epithelial cells) on conventional FNAC and in patients with swelling <1cm, ultrasound guided FNAC was done. Direct smears were prepared from the aspirate of which minimum of 2 were fixed in 95% ethanol and stained with Haematoxylin - Eosin (H & E) and Papanicoloau (PAP) stains. Rest were air dried and stained with May-GrunwaldGiemsa (MGG) stain. Reporting was done according to The Bethesda System for Reporting Thyroid Cytopathology.One hundred twenty-six patients had undergone total/hemi thyroidectomy and the specimens were fixed in 10% formalin followed by gross examination. After overnight fixation tissues were processed, sectioned and stained with H & E stain. Stained sections were examined and statistical correlation of the findings with the cytology smear was done.

Results

A total of 328 patients had undergone FNAC, whose results were analysed according to Bethesda System of Thyroid Cytopathology was mentioned in detail in Table 1.

Table 1: Categorisation of total FNAC cases according to The Bethesda System of Reporting Thyroid Cytopathology

Category		FNAC diagnosis	No. of cases		%
I	Non diagnostic	Inadequate	10	10	3.1
II	Benign	Benign cystic lesion	04	298	90.3
		Benign thyroid lesion	25		
		Colloid cyst	06		
		Colloid goitre	68		
		Nodular goitre	119		
		Adenomatoid goitre	10		
		Hashimoto thyroiditis	64		
		Granulomatous thyroiditis	01		
III	AUS/FLUS	Atypia of undetermined significance	03	03	1.1
IV	FN	Follicular neoplasm	05	05	1.6
V	Suspicious	Suspicious for malignancy	05	05	1.6
VI	Malignant	Papillary carcinoma	05	07	2.3
		Poorly differentiated carcinoma	01		
		Non-Hodgkins lymphoma	01		
	Total			**328**	**100**

AUS*- Atypia of undetermined significance, FLUS*-Follicular lesions of undetermined significance, FN*-Follicular neoplasm

Most common presenting symptom was diffuse or nodular swelling in midline of neck which moved with deglutition and size ranged from 1x1cm to 12x9cm. Twenty patients presented with pain and difficulty in swallowing. USG guided FNAC was done for 10 patients with swelling <1cm in size and for 6 cases with inadequate samples on direct FNAC. Aspirate was blood mixed to frankly haemorrhagic in majority of cases (118 cases). Eight cases yielded brownish fluid ranging from 0.5 to 5ml.

Out of 328 cases, 126 cases were operated. Of these 126 cases, female to male ratio was 6.9:1 with 110 (87.3%) females and 16 (12.7%) males. Age group of the cases ranged from 15-80 years, with a mean age of 40.6 years. The predominant number of cases were included in the age group of 21-30 years (n=40) with nearly one third of the cases, followed by 31-40 years (n=27), 51-60 years (n=24), 41 – 50 years (n=22) and above 60 years (n=9).

Cytological diagnosis

FNAC diagnosis offered for the cases under the sub categorisation of TBSRTC were represented in the Table 2.

Table 2: Distribution of cases according to FNAC impression

BETHESDA CATEGORY		FNAC IMPRESSION			N		%	
I	NON DIAGNOSTIC	Inadequate	F	02	2		1.6	1.6
			M	00				
II	BENIGN (NON NEOPLASTIC)	Adenomatoid nodule	F	6	7	116	5.5	92.0
			M	1				
		Benign thyroid lesion	F	04	5		4.0	
			M	01				
		Colloid cyst	F	02	2		1.6	
			M	00				
		Colloid goitre	F	20	23		18.2	
			M	03				
		Nodular goitre	F	59	69		54.8	
			M	10				
		Hashimoto thyroiditis	F	10	10		7.9	
			M	00				
IV	FOLLICULAR NEOPLASM	Follicular neoplasm	F	02	3		2.4	3.2
			M	01				
		Hurthle cell neoplasm	F	01	1		0.8	
			M	00				

V	SUSPICIOUS FOR MALIGNANCY	Suspicious	F	02	2	1.6	1.6
			M	00			
VI	MALIGNANT	Papillary carcinoma	F	02	2	1.6	1.6
			M	00			
		Total			126	100	100

The most common diagnosis being nodular goitre in 69 cases (54.8%), followed by colloid goitre in 23 cases (18.2%), Hashimoto thyroiditis in 10 cases (7.9%), adenomatoid nodule in 7 cases (5.5%), benign thyroid lesion in 5 cases (4%), colloid cyst in 2 cases (1.6%), follicular neoplasm in 3 cases(2.4%) and 2 cases (1.6%) each of suspicious for malignancy and papillary carcinoma. Two cases of inadequate for opinion were included as they were operated upon and the histopathology follow up was available for those cases.

Histopathological diagnosis

Out of 126 cases, 117 cases were non-neoplastic and 9 cases were neoplastic. The ratio of non-neoplastic to neoplastic lesions was 13:1. Out of 117 non-neoplastic cases, multinodular goitre was the most common diagnosis offered on histopathology examination in 58 cases(46%), followed by simple nodular goitre in 26 cases (20.6%), adenomatoid nodule in 15 cases (12.0%), colloid cyst in 9 cases (7.2%), Hashimoto thyroiditis in 7cases (5.5%) and colloid goitre in 2 cases (1.6%). Out of 9 neoplastic cases, 4 cases (3.1%) were benign which included follicular adenoma and 5 cases were malignant which included 3 (2.4%) cases of follicular variant of papillary carcinoma and 2 (1.6%) cases of papillary carcinoma. Amongst the group, multinodular goitre with cystic change was noted in 11 cases, MNG with secondary changes in 5 cases, MNG with adenomatoid nodule in 4 cases and MNG with Hurthle cell change in 2 cases, MNG with thyroiditis in 1 case and NG with papillary hyperplasia in 2 cases.MNG with FNAC induced changes comprised of calcification, hyalinisation, fibrosis, nucleomegaly, haemorrhage, hemosiderin laden macrophages and cholesterol clefts noted in three cases.

Comparision of cytology results with corresponding histopathological diagnosis

Out of 126 cases, 110 cases (87.3%) correlated well with histopathology and 16 cases showed discordance.

Out of 117non-neoplastic lesions, 106 cases (90.5%) showed cyto-histological concordance and 11 cases were discordant. Out of 9 neoplastic lesions, 4 (44.4%) cases were correlated histologically and 5 cases were discordant. (Table 3)

Table 3: Comparison of Histopathology and Cytology findings

	HISTOPATHOLOGY	No. of cases	CYTOLOGY	
			Concordant	Discordant
Non Neoplastic	Adenomatoid Nodule	15	11	4
	Colloid Cyst	9	9	0
	Colloid Goitre	2	2	0
	Simple Nodular Goitre	26	24	2
	Multinodular Goitre	58	54	4
Autoimmune	Hashimoto Thyroiditis	7	6	1
Neoplastic– Benign	Follicular Adenoma	4	1	3
Neoplastic– Malignant	Papillary Carcinoma	2	2	0
	FVPTC	3	1	2
	Total	126	110	16

List of discordant cases were represented in Table 4.

Table 4: List of discordant cases

Sl. No	Case no.	Histopathology Impression	Cytology Impression
1	1	Nodular goitre	Hashimoto thyroiditis
2	7	Follicular adenoma	MNG
3	27	Follicular adenoma	Colloid cystic nodular goitre
4	38	MNG	Lymphocytic/Hashimoto thyroiditis
5	41	MNG	Lymphocytic/Hashimoto thyroiditis
6	55	Adenomatoid nodule (MNG)	Follicular neoplasm. D/D: Follicular adenoma/ Carcinoma, Adenomatoid nodule
7	65	Hashimoto thyroiditis	Colloid cyst/ nodular goitre
8	68	FVPTC with MNG (Encapsulated variant)	Adenomatoid nodule
9	73	Follicular adenoma	MNG with colloid nodule
10	82	MNG	Hashimoto thyroiditis
11	87	MNG with extensive Hurthle cell change with FNAC induced secondary changes	Suspicious for malignancy
12	88	Adenomatoid goitre with Hurthle cell change	Hurthle cell neoplasm
13	107	Adenomatoid MNG	Follicular neoplasm. D/D: Follicular adenoma/ Carcinoma
14	126	FVPTC	Colloid goitre
15	111	Nodular goitre	Inadequate
16	108	Adenomatoid goitre	Inadequate

Statistical analysis

Present study showed sensitivity of 93.8%, specificity of 69.2%, positive predictive value of 96.3%, negative predictive value of 56.2% and diagnostic accuracy of 91.2% for FNAC in detecting non-neoplastic lesions.

In the present study, FNAC showed sensitivity, specificity, PPV, NPV and diagnostic accuracy of 44.4%, 100%, 100%, 95.9% and 96% respectively for neoplastic lesions.Overall sensitivity, PPV and diagnostic accuracy were 90.2%, 96.4% and 87.3% respectively.

Discussion

As found in various published studies world over, the sex distribution in the present study also had a female preponderance. Out of 126 cases, 87.3% (110 cases) were females and 12.7% (16 cases) were males with Female to Male ratio of 6.9:1, which was comparable with the studies done by Patel S *et al* [6] and Sharma R *et al* [7] with F:M ratio of 6.6:1 and 7:1 respectively.

In the present study, age group of cases ranged from 15-80years, with a mean age of 40.6years, which was comparable with the studies done by Patel S *et al*, [6] Sharma R *et al*, [7] Arul P *et al*, [8] Gupta M *et al* [9] and Nandedkar SS *et al* [10] which showed mean age of 40.5 years, 43 years, 38.2 years, 38.7 years and 37.6 years respectively.

In the present study, on FNAC satisfactory cell sample was obtained in 124 cases and unsatisfactory in 2 cases with satisfactory to unsatisfactory ratio of 62:1, which was better than the studies conducted by Patel S *et al* [6] and Nandedkar SS *et al* [10] with satisfactory to unsatisfactory ratio of 43.3:1 and 22.3:1 respectively.

Most common diagnosis offered on cytology was colloid / nodular goitre in 73% (92 cases). Studies conducted by Nandedkar SS *et al*, [10] Handa U *et al*, [11] Sharma C *et al* [12] and Hathila R *et al* [13] also experienced the same result.

Non-neoplastic lesions accounted for 92.8% (117 cases) of the cases and neoplastic cases for 7.2% (9 cases) on histopathology with non-neoplastic to neoplastic lesions ratio of 13:1.

Out of 117 non-neoplastic lesions, cyto-histological concordance was obtained in 90.1% (106 cases) and discordant in 9.9% (11 cases) which was comparable with other studies conducted by Arul P *et al*, [8] Handa U *et al* [11] and Bamanikar*et al* [14].

False positive rate was 3.2% (4 cases) in our study. Three cases of adenomatoid goitre were reported on histopathology. Among these 3 cases, 2 cases were reported as follicular neoplasms on cytology (Figure 1).

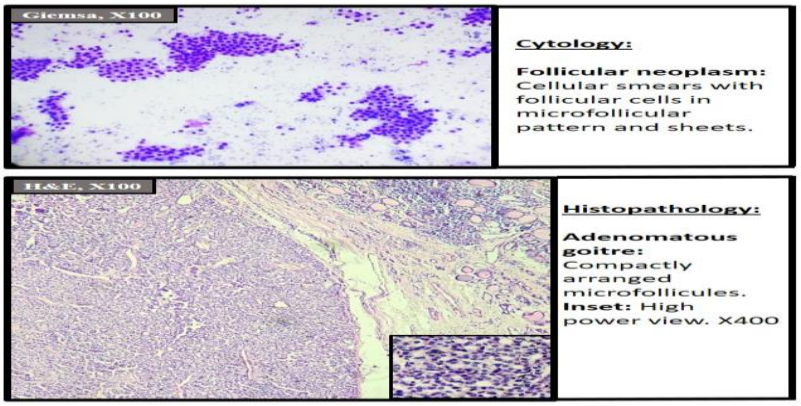

Fig 1: Microphotographs of discordant case of follicular neoplasm v/s adenomatoid goitre

The probable reason for this could be the overlapping cytology features of adenomatoid nodule with macro and normo follicular neoplasm. Arul P *et al*, [8] Nandedkar SS *et al* [10] and Sharma C *et al* [12] also experienced similar situation in their studies.

The other case with a discordant diagnosis was adenomatoid goitre with Hurthle cell change on histopathology. This case was diagnosed as Hurthle cell neoplasm on cytology (Figure 2).

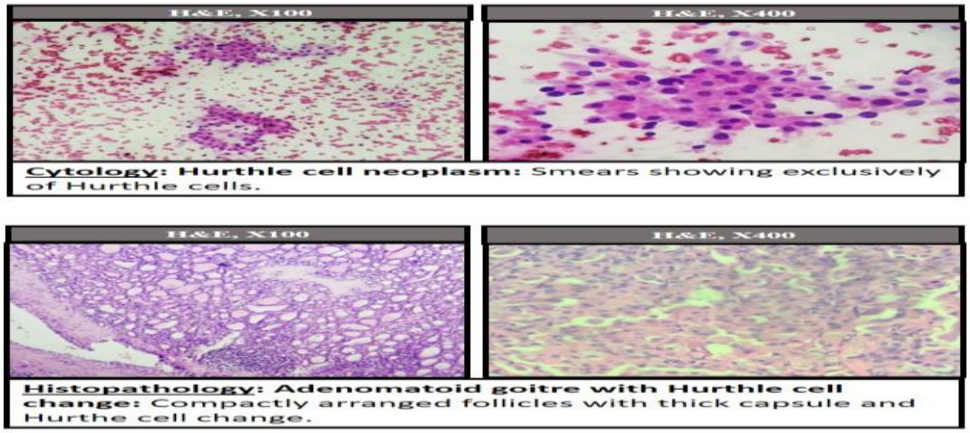

Fig 2: Microphotographs of discordant case of Hurthle cell neoplasm v/s adenomatoid goitre with Hurthle cell change

FNAC being the blind procedure, has its own limitations where in the Pathologist does not have control over the sampling. At times this leads to a situation where in the sample obtained may not truly represent the disease process when pathologic process is too small. This explains the probable reason for discordance in this case. Adding image guidance into the diagnostic algorithm may reduce such instances and might improve the quality of sample obtained making it more representative.

In the present study, one case of MNG with extensive Hurthle cell change with FNAC induced changes was diagnosed as suspicious for malignancy on cytology as the aspirate showed nuclear atypia in few follicular cell clusters. After certain duration of time, tissue surrounding the needle track show changes like hemosiderin laden macrophages, fibroblastic proliferation, fibrosis, aggregates of cholesterol clefts, calcification, epithelial changes and vascular changes. Vascular changes include thrombosis, recanalization of vessels and papillary endothelial hyperplasia. Epithelial changes include nuclear atypia, characterised by nuclear enlargement, chromatin clearing and prominent nucleoli[15]. In this case the patient had underwent thyroid FNAC six months prior to presenting to our

hospital. Patient had FNAC induced secondary changes like hemosiderin laden macrophages, fibrosis, nuclear atypia and vascular endothelial proliferation which have led to the suspicion of malignancy on FNAC and also findings were worrisome on histopathology. (Figure 3)

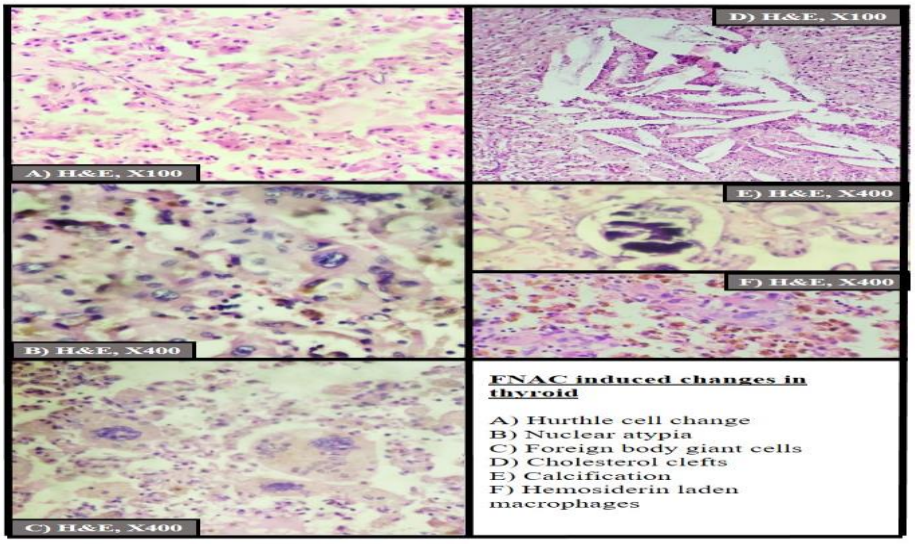

Fig 3: Microphotographs of common FNAC induced changes in thyroid

So, previous history of FNAC has to be given due consideration in reporting a case of thyroid cytology as the changes induced by previous FNAC can be over interpreted as malignancy both on cytology and histopathology.

False negative rate among non-neoplastic lesions was 5.5% (7 cases). A case of adenomatoid goitre and a case of nodular goitre were reported as inadequate on cytology, which is one of the plaguing issues in case of thyroid cytopathology. The range of this inadequate for opinion is documented anywhere from 5-30% getting affected by parameters like thyroid vascularity, disease process, operator experience and inherent limitations of FNAC. Our institutional protocol was to perform a minimum of two passes with rapid onsite evaluation and promptly repeating the procedure based on the assessment of cellularity. Even after repeating the procedure if the cellularity is inadequate as per the criteria, in select cases guided FNAC was performed. This protocol has yielded a comparatively lower inadequate rates of 1.6% where as other authors Patel S *et al*, [6] Sharma R *et al* [7] and Nandedkar SS *et al* [10] have reported inadequate rates of 2.3%, 5.5% and 4.3% respectively in their studies.

In the present study, four cases of nodular goitre on histopathology were diagnosed as Hashimoto / lymphocytic thyroiditis on cytology. Study conducted by Hathila R *et al* [13] also documented a similar experience. A case of Hashimoto thyroiditis was diagnosed as nodular goitre on cytology. In the present study, out of 9 neoplastic cases, cyto-histological concordance was obtained in 4 cases and discordant in five cases. False negative rate for neoplastic lesions was 3.2%. Two cases of follicular variant of papillary thyroid carcinoma (FVPTC) were reported as colloid goitre in one (Figure 4) and adenomatoid nodule in other on cytology.

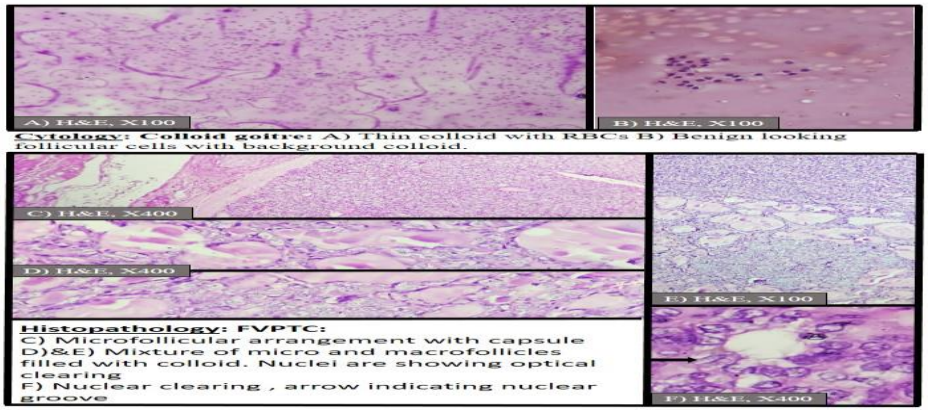

Figure 4: Microphotographs of a discordant case of colloid goitre v/s FVPTC

Follicular variant of PTC poses a diagnostic challenge which requires high level of suspicion in identifying the nuclear features which are not so frequent as in a case of classic variant of PTC. Interpretation of thyroid cytopathology in patients with high index of clinical suspicion are the candidates for guided FNAC to avoid missing out on the doubtful areas. Even in the studies done by Arul P *et al* [8] and Sharma C *et al* [12] FVPTC was among the cases with discordance on cyto-histological correlation. This was explained by the fact that nuclear features required for diagnosis of FVPTC were infrequent on cytology, thereby leading to low sensitivity of FNAC in diagnosing FVPTC[12].

Papillary carcinoma may also present with cystic change. So, in cases of cystic lesions after initial aspiration of cyst contents, thyroid should be palpated again to note the presence of any residual swelling and if

present should be sampled. In patients with heterogenous nodules, aspiration from multiple sites and from solid area is advisable. In such cases, ultrasound guided FNAC yields better sample with high accuracy. Three cases of macro follicular adenoma were diagnosed as nodular goitre on cytology. As these cases have shown colloid on smears along with follicular cells in clusters might have led to the misinterpretation. Similar observation was mentioned by Arul P *et al* [8] and Handa U *et al* [11] in their study.

Present study showed sensitivity, specificity, PPV, NPV and accuracy of FNAC in correctly detsecting non-neoplastic lesions as 93.8%, 69.2%, 96.3%, 56.2% and 91.2% respectively.

Overall sensitivity, PPV and diagnostic accuracy of FNAC in detecting thyroid lesions were 90.2%, 96.4% and 87.3% respectively.

Based on the observations in the present study, following recommendations are made

- In cases with unsatisfactory diagnosis on cytology, FNAC has to be repeated from different site by skilled Cytopathologist and preferably with USG guidance to obtain adequate aspirate.
- Benign lesions on cytology should be carefully interpreted as there are chances of getting false negative diagnosis. To avoid false negative diagnosis, smears should be properly and meticulously stained. These should be screened for the presence of neoplastic features like overlapping and overcrowding of follicular cells to rule out follicular neoplasms; and presence of nuclear grooves and intranuclear inclusions to rule out PTC.
- Previous history of FNAC has to be given due consideration in reporting as the changes induced by prior FNAC can be over interpreted as malignancy both on cytology and histopathology.
- Heterogenous lesions of thyroid many a times harbour a small focus of neoplastic component masked by the cystic component, which might be frequently missed out on direct FNAC. In such cases, fluid should be completely aspirated and FNAC should be repeated from the residual mass. If there is no palpable mass, patient should be followed up with USG examination and guided FNAC. If USG guided FNAC is not available, patient has to undergo surgical excision when there is a high clinical suspicion of malignancy.
- Reporting of cytology according to TBSRTC guide the clinician in having a better assessment of Risk of Malignancy, thereby optimising the management and offering better care for the patients.

Conclusion

Thyroid cytopathology as an initial diagnostic modality is expanding its reach over the spectrum of lesions with improved accuracy and predictive value. The ability of FNAC in offering a specific diagnosis when compared to the histopathology yielded a sensitivity, specificity and accuracy of 93.8%, 69.2% and 91.2% respectively. Thereby making it more reliable in the diagnostic workup algorithm and aiding in the precise management of the case. Proper technique and rational use of USG guidance for select cases improved the adequacy and reduced the non-diagnostic rates in the present study.

Conflict of Interest:Nil
Source of support:None

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