

FNAC study of thyroid lesions using the Bethesda system

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Abstract

Background: The most reliable, safe, cost-effective and accurate way to evaluate thyroid nodule is cytology, which has become the standard of care. As there is a 10% lifetime risk of developing a thyroid nodule, screening thyroid nodules had turned out to become a common medical problem affecting the general population. According to the guidelines of American association of clinical endocrinologists, fine needle aspiration cytology [FNAC] is the gold standard method available for distinguishing between benign and malignant thyroid swelling and is the most commonly performed non-gynaecological cytological procedure. **Aims:** To study the cytomorphological features and to classify cytologically the thyroid lesions based on the Bethesda system. **Methods and Material:** The present descriptive study was undertaken in a tertiary care hospital for a period of 3 years to analyse the role of FNAC in the diagnosis of thyroid lesions and classify them cytologically according to the Bethesda system. **Results:** 40 cases were classified as unsatisfactory, 328 cases as benign, 5 cases as AUS, 23 cases as FN/ HCN, 1 case as SFM and 3 cases as malignant. Out of 328 cases in benign category, 281 cases belonged to BFN subcategory which was the most common non-neoplastic lesion of thyroid. The age range of patients presenting with the thyroid lesion was from 7-75 years. Maximum number of cases i.e. 116 were in the age group 31-40 years followed by 95 cases in the age group 21-30 years. Maximum cases in the benign category belonged to the age group of 31-40 years. Maximum cases [10 out of 23 cases] in the follicular neoplasm category were seen in the age group ranging 21-40 years. Out of 400 cases, females [359] cases outnumbered male [41] cases contributing 89.75% and 10.25% respectively with male to female ratio of 1:8.7. There was overall female preponderance seen in all diagnostic categories of TBSRTC. 5 cases diagnosed as AUS in our study were according to recommended criteria mentioned in Bethesda system i.e. less than 7%. One case each of PTC, MTC and UTC were seen in malignant category in our study. **Conclusions:** The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) helped to communicate interpretations of thyroid FNAC to referring physicians in terms that are short, concise and clinically helpful and it will also be a source of information for pathologists as well.

Keywords: Bethesda, Aspiration, Thyroid, Cytology.

Introduction

Thyroid gland is affected by a vast array of disorders like developmental, inflammatory, hyperplastic and neoplastic disorders. The incidence of palpable thyroid swelling is 4-7% [1]. A thyroid enlargement whether diffuse or in the form of a nodule has to be investigated to rule out neoplasm [2]. Only about 20% of patients undergoing thyroid surgery for suspicion of carcinoma actually show the histology of malignancy [3].

The FNAC [Fine Needle Aspiration Cytology] showed the importance of suspicious thyroid swellings in

cytology as an indication for surgery and decreased the overall incidence of thyroidectomy in patients with benign disease. The FNAC provide highly accurate cytologic information from which a definitive management plan could be arranged with high sensitivity and specificity approaching to 96%. [4].

Aims and objectives of the study were to classify cytologically the FNAC of thyroid lesions as per the Bethesda system, to study the cytomorphological features in thyroid lesions and to study the clinic cytopathological correlation in patients with thyroid lesions.

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Material & Methods

Place and duration of study: The present descriptive study was undertaken in a tertiary care hospital for a period of 3 years to analyse the role of FNAC in the diagnosis of thyroid lesions and classify them cytologically according to the Bethesda system.

Inclusion criteria: All the cases of palpable thyroid swelling who were referred for FNAC were included in the present study.

Exclusion criteria: Neck swellings other than thyroid are excluded from the study.

A detailed clinical history was obtained and a thorough clinical examination was done prior to procuring sample for the cytological study. Written informed consent was obtained and the proper information regarding the procedure was given to the patient. Thyroid FNAC was

done with patient lying comfortably in a supine position or sitting position and the neck was extended so as to make the swelling appear prominent. The fine needle aspiration was performed by either fixing the swelling by palpation or under ultrasound (US) guidance with a 23-24-gauge needle attached to 10 ml disposable syringe and under all aseptic precautions.

The obtained material was spread on glass slides of 75 x 25 x 1.35 mm. The slides were kept dry for Giemsa staining and those for PAP [Papanicolaou] staining was fixed in 95% ethanol. The patients were instructed to restrain from swallowing and speaking during the procedure. The FNAC smears were examined microscopically after staining and the results were categorized into 6 diagnostic categories according to the Bethesda System for reporting thyroid cytopathology.

Results

The present study included a total of 400 thyroid lesions.

Table-1: Distribution of thyroid lesions according to the Bethesda diagnostic categories.

	Bethesda diagnostic categories	Number of cases	Percentage (%)
1	Unsatisfactory [UNS]/ Non-diagnostic.	40	10
2	Benign.	328	82
3	Atypia of undetermined significance [AUS]	5	1.25
4	Follicular neoplasm [FN]/ Hürthle cell neoplasm [HCN]	23	5.75
5	Suspicious for malignancy[SFM]	1	0.25
6	Malignant	3	0.75
	Total	400	100

In the present study of 400 cases, 328 [82%] cases were benign followed by 23 [5.75%] cases of FN/ HCN, 5 [1.25%] cases of AUS, 3 [0.75%] cases of malignant neoplasms and only 1 [0.25%] case of SFM. 40 [10%] cases were unsatisfactory or non-diagnostic.

Table-2: Distribution of cases according to age and Bethesda diagnostic categories:

Age (years)	Bethesda diagnostic categories						Total
	UNS	Benign	AUS/FLUS	FN/HCN	SFM	Malignant	
1-10	0	3	0	0	0	0	03
11-20	5	36	1	3	0	1	46
21-30	10	77	3	5	0	0	95
31-40	17	91	1	5	1	1	116
41-50	6	48	0	4	0	0	58
51-60	1	39	0	3	0	1	44
61-70	0	34	0	3	0	0	37
71-80	1	0	0	0	0	0	01
Total	40	328	5	23	1	3	400

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In the present study, 116 [29%] patients were in the age range of 31- 40 years, followed by 95 [23.75%] patients in the age range of 21-30 years. Minimum number of patients belonged to the age group of 71- 80 years i.e. 1 patient [0.25%]. The mean age of the patients was 38.53 years, ranging between 7-75 years. The maximum 91 [27.74%] cases in 328 benign lesions category belonged to the age group of 31- 40 years followed by 77 [23.47%] cases in age group 21- 30 years. Out of 23 cases in the FN category, maximum 10 cases were seen in the age group ranging 21- 40 years. 1 case diagnosed as SFM was seen in age group 31- 40 years.

The 3 diagnosed malignant cases were in the age group 11- 30, 31- 40, 51- 60 years each.

Table-3: Distribution of cases as per gender and Bethesda diagnostic categories:

Sex	UNS	Benign	AUS	FN/ HCN	SFM	Malignant	Total [%]
Male	3	35	1	1	0	1	41 [10.25]
Female	37	293	4	22	1	2	359 [89.75]
Total	40	328	5	23	1	3	400

In the present study, out of total 400 cases 359 [89.75%] were females and 41 [10.25%] were males with male to female ratio of 1:8.7.

Table-4: Distribution of cases in the sub categories of the Bethesda diagnostic categories:

Bethesda categories	Number of cases	Percentage (%)
1. Unsatisfactory	40	10
2. Benign	[328]	[82]
Benign follicular nodule (BFN)	281	85.68
Hashimoto's/ Lymphocytic thyroiditis	41	12.5
Granulomatous thyroiditis	6	1.82
3. AUS	5	1.25
4. FN/ HCN	[23]	[5.75]
Follicular neoplasm	15	65.3
Hürthle cell neoplasm	8	34.7
5. SFM	1	0.25
6. Malignant	[3]	[0.75]
Papillary thyroid carcinoma [PTC]	1	33.33
Medullary thyroid carcinoma [MTC]	1	33.33
Undifferentiated [anaplastic] thyroid carcinoma [UTC]	1	33.34
Total	400	100

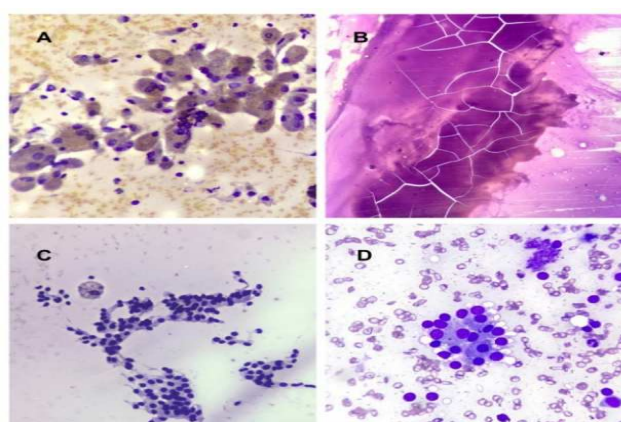


Fig 1:A: Cyst fluid only: Hemosiderin laden cyst macrophages.[PAP:40X], B: Thick colloid: Demonstrating“stained glass cracking appearance”. [PAP:40X], C: BFN: Monolayer sheets of follicular cells with hemosiderin laden macrophage in the background of thin colloid. [PAP:10X], D: Graves' disease: Clusters of hyperplastic epithelial cells with 'fire flares'. [Giemsa:10X]

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In the present study, out of 328 benign cases, 281 [85.68%] cases were BFN followed by 41 [12.5%] cases of Hashimoto's/ Lymphocytic thyroiditis and 6 [1.82%] cases of granulomatous thyroiditis. Amongst 23 cases of FN/ HCN, there were 15 [65.3%] cases of FN and 8 [34.7%] cases of HCN. Only 1 [0.25%] case was diagnosed in the SFM. 3 [0.75%] cases in the malignant category were PTC, MTC and UTC each.

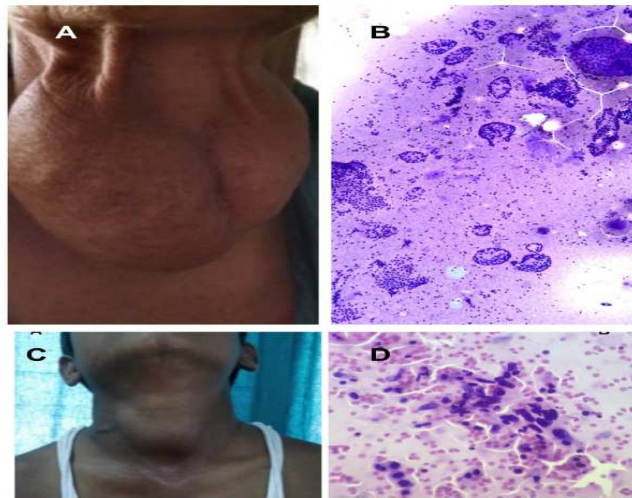


Fig. 2: A: BFN: 65 years female with nodular thyroid swelling [both lobes], B: BFN: Three dimensional variably sized balls/spheres with monolayer sheets and macro follicular arrangement of follicular cells in the background of abundant colloid. [PAP: 4X], C: Granulomatous thyroiditis: 14 years male with diffuse thyroid swelling, D: Granulomatous thyroiditis: Mixture of epithelioid cells, histiocytes, inflammatory cells and the follicular epithelial cells [PAP:10X]

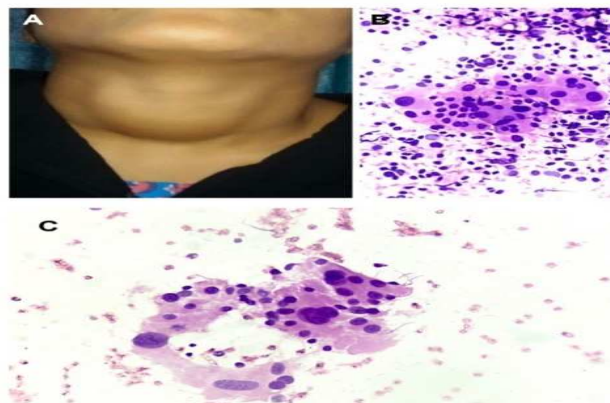


Fig-3:A: Lymphocytic/ Hashimoto thyroiditis: 28 years female with diffuse thyroid swelling, B: Lymphocytic/ Hashimoto thyroiditis: Syncytial cluster of oxyphilic cells with abundant lymphoid cells in the background [PAP:10X], C: AUS: Follicular cells admixed with atypical cells showing anisonucleosis. [PAP:10X]

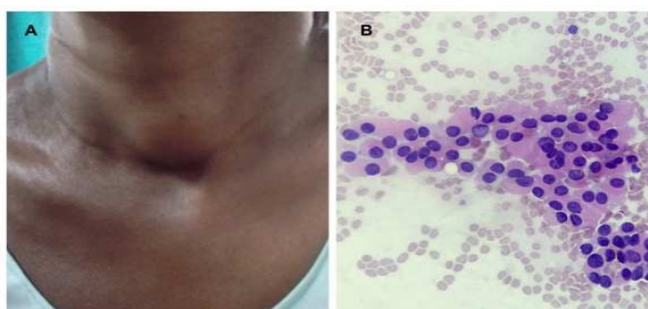


Fig-4: A: SFNHCT: 50 years old female patient with solitary thyroid swelling, B: SFNHCT: Exclusively Hurthle cells with no colloid [PAP: 10X]

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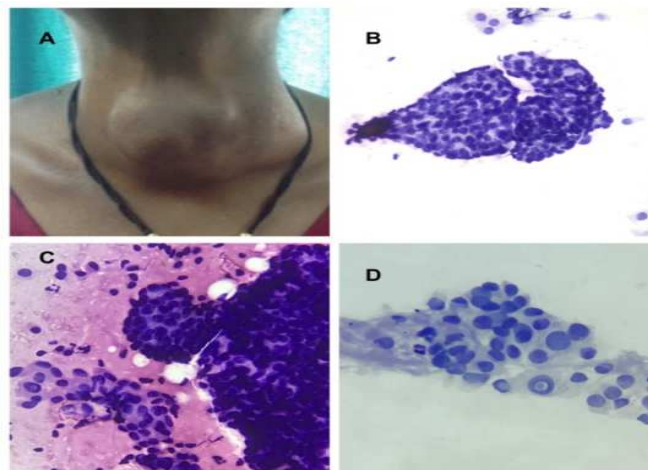


Fig-5: A: PTC: 19 years female with nodular thyroid swelling and supraclavicular lymph node enlargement. B: PTC: Syncytial sheet of cells with nuclear crowding, overlapping and distinct border forming 'finger like papilla'. [PAP:10X], C: PTC: Cell aggregates showing finger like papilla with distinct border, nuclear overlapping, crowding and intranuclear cytoplasmic inclusions. [PAP:10X], D: PTC: Cells with intranuclear cytoplasmic inclusion in a nuclei. [PAP:10X]

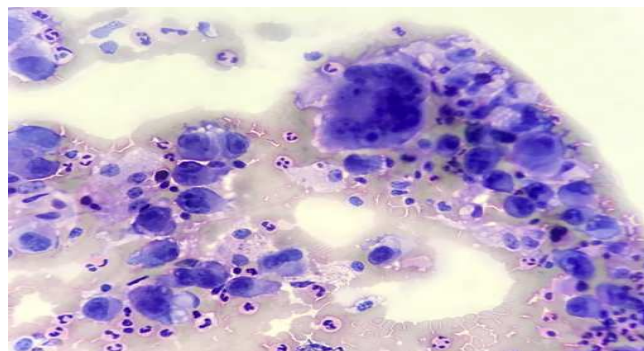


Fig-6: UTC showing highly pleomorphic cells and tumor giant cell in the background of inflammatory cells. [PAP:40X]

Discussion

The FNAC study of 400 patients with thyroid lesions was undertaken at a tertiary care hospital for a period of 3 years with the aims of studying the cytomorphological features, classifying the thyroid lesions according to the Bethesda system and to study the clinicocytopathological correlation in the patients with the thyroid lesions.

Table-5: Comparative study of FNAC diagnosis based on the Bethesda classification:

Authors	Year	Bethesda diagnostic categories [%]					
		UNS	Benign	AUS	FN/HCN	SFM	Malignant
Theoharis et al [5]	2009	11.1	73.8	3	5.5	1.3	5.2
Jo et al [6]	2010	18.6	59	3.4	9.7	2.3	7
Mufti et al [7]	2012	11.6	77.6	0.8	4	2.4	3.6
Basak et al [8]	2013	1.2	87.5	1.0	4.2	1.4	4.7
Bhagat et al [9]	2014	5.63	87.5	0	3.12	0.63	3.12
Kantola et al [10]	2015	15.8	69.2	7.4	2.2	0.7	4.9
Yasmin et al [11]	2016	0.68	88	3.4	4.5	1.4	2.06
Salma et al [12]	2016	6.6	82	2	2.5	1.6	5.1
Present Study		10	82	1.25	5.75	0.25	0.75

In the present study, the percentage of cases in each category of TBSRTC was in accordance with Mufti et al, [7] Salma et al, [12] Theoharis et al [5] and Yasmin et al [11].

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Smears with predominantly blood or absence of colloid or an insufficient number of follicular cells or fixation artifacts were categorized as non-diagnostic [Category I]. Aspirates diagnosed as cyst fluid only [Fig.1: A] were recorded and categorized as unsatisfactory.

40 [10%] cases were unsatisfactory in our study which correlates with the findings of Theoharis et al [5] and Mufti et al[7].

Smears classified as benign [Category II] accounted for the majority i.e. 328 [82%]. This was in agreement with the findings of all the studies mentioned in table 5 especially with the findings of Salma et al[12].

281 [85.68%] of the 328 cases were subcategorized as BFN, while 41 cases [12.5%] as chronic lymphocytic/ Hashimoto's thyroiditis [Fig.3: A, B] and 6 cases [1.82%] as granulomatous thyroiditis [Fig.2: C, D]. Thus, BFN/ colloid nodule [Fig.1: B, C, D] was the commonest lesion accounting for 281 cases (85.68%) in the benign category. This finding was in accordance with the finding of RajjaVojjala [13] who reported BFN in 82.35% of cases.

The AUS [Category III] accounted for 5 [1.25%] cases. This finding was in accordance with Basak et al [8] Salma et al[12]. The less number of cases diagnosed as AUS in the present study could be explained by the strict adherence to diagnostic criteria mentioned in the Bethesda system.

The cases diagnosed as AUS on cytology were sparsely cellular and showed monomorphic population of small non-cohesive cells resembling follicular cells with high nuclear cytoplasmic ratio having scant colloid [Fig. 3: C]. The degree of cellular or architectural atypia was not sufficient to render an interpretation of FN/ SFN/ SFM. However, because the category is heterogeneous and some what subjective, differences between observers in using this diagnosis still exist.

Because of the inability of FNAC to distinguish Follicular and Hürthle cell adenomas from their malignant counterparts, the role of thyroid FNAC shifts from being a diagnostic test to a screening test for this category of FN/ FNHCT [Category IV]. In the present study, 23 [5.75%] cases were classified in this category which included 15 cases of FN and 8 cases of HCN. These findings were in accordance with that of Theoharis et al[5].

We categorized 15 cases as FN based on predominant arrangement of follicular cells as micro follicles or significant cell crowding having little or scant colloid in the background. The 8 cases of Hürthle cell were diagnosed as aspirate exclusively consisted of a population of loosely cohesive Hürthle cells showing marked anisonucleosis with scanty colloid in the background [Fig.4: A, B].

The SFM [Category V] was applied to the aspirates that demonstrated features of malignant neoplasm but were quantitatively or qualitatively insufficient to make a definitive diagnosis of malignancy. In our study, 1 [0.25%] case had a cytological diagnosis of SFM. This finding was comparable with that of Kantola et al [10]and Bhagat et al[9].

The present case showed scanty cellularity with atypical follicular cells having hyper chromatic nuclei, binucleation and absent colloid in the background.

The malignant[Category VI] was applied to cellular aspirates with definite evidence of a malignant neoplasm. 3 [0.75%] cases were classified as positive for malignancy. This finding was nearly similar with the finding of Yasmin et al[11] Of the 3 cases, 1 case was PTC, 1 was MTC and 1 case was UTC.

The PTC [Fig. 5: A, B, C, D] diagnosed, was characterized by the presence of follicular cells arranged in papillae and also in flat sheets. Follicular cells showed characteristics nuclear features of nuclear crowding and overlapping, irregular nuclear contours and intranuclear cytoplasmic inclusions.

The MTC demonstrated plasmacytoid cells with pleomorphic nuclei having stippled chromatin and binucleation. Intranuclear cytoplasmic d inclusions were seen in many nuclei. The UTC [Undifferentiated Thyroid Carcinoma][Fig.6] showed highly pleomorphic malignant cells with tumor giant cell formation and polymorphonuclear leukocytes in the background.

Table-6: Comparison of age distribution in various studies:

Authors	Year	Age range (years)	Mean age (years)	Age group [years] [Maximum cases]
Garg et al [14]	2008	5-80	37.69	-
Chandanwale et al [15]	2012	18-65	-	21-40
Kukkar et al [16]	2013	11-80	41.48	31-50
Park et al [17]	2014	14-86	50	-
Yasmin et al [11]	2016	6-85	40.7	21-49
Salma et al [12]	2016	11-73	36	-
Present study		7-75	38.53	31-40

In the present study, age range of the patients affected was from 7-75 years. This finding was in accordance with the finding of all the studies mentioned above but it was closest to Yasmin et al[11].

The mean age of the patients with the thyroid lesions in our study was 38.53 years. Our findings were comparable to Garg et al [14] and Salma et al. [12]. In the present study, maximum numbers of patients were in the age group of 31- 40 years which was similar to the finding of Chandanwale et al[15].

In the present study, thyroid lesions were more common in females with 359 [89.75%] cases as compared to males with 41 [10.25%] cases. Individual categories also showed a female predominance. Male: Female ratio in our study was 1:8.75 which was in accordance with the studies mentioned by Yasmin et al [11]and Kukkar et al. [16]

Conclusion

A FNAC study of 400 patients with the thyroid lesions was done in a tertiary care hospital for a period of 3 years. The cytomorphology was studied and the lesions were categorized according to The Bethesda System for Reporting Thyroid Cytopathology.

We concluded that the six-tiered diagnostic approach of TBSRTC for reporting thyroid FNAC was easy to use and an excellent reporting system.

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Permission from IRB: Yes

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