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A Cytohistological Correlation in Thyroid Swelling with Special Reference to The Bethesda System: A Study of 192 Cases.

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Abstract:
Context and background: *Cytological grading of thyroid swelling, which is a simple, feasible and reproducible method, can be used as tool for selection of treatment modality. The National Cancer Institute, Bethesda introduced one guideline for reporting of thyroid cytology and thus helps in individualised treatment.*
Aims & Objectives: *1) To establish the validity and reliability of The Bethesda System of cytological grading in diagnosis of thyroid swelling, 2) To calculate malignancy risk.*
Materials & Methods*: After taking approval from the institutional ethical committee and informed consent, this study was conducted on 192 cases at Department of Pathology in collaboration with Department of Radiology and Endocrinology in a tertiary care centre. FNACs were performed with or without radiological assistance as per protocol and diagnoses were given as per the Bethesda classification. Histopathological correlations were done in each case following total or partial thyroidectomy.*
Results*: A total of 192 cases of thyroid lesions were included in the present study, of which were 41 males (21.35%) and the rest 151 were females (78.64%). Smears were reported as unsatisfactory in 4 cases (2.08%), benign in 105 cases (54.69%), AUS/FLUS in 8 cases (4.17%), FN/SFN in 25 cases (13.02%), suspicious of malignancy in 10 cases (5.21%) and malignant in 40 cases (20.83%). Malignancy risks were calculated for each category.*
Conclusions: *The six tier diagnostic categories of The Bethesda system helps in triaging patients with thyroid swelling and thus facilitate individualised management.*
Keywords: *Fine needle aspiration, thyroid, Bethesda.*

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I. Introduction

Terminology and reporting of thyroid fine needle aspiration report have been problematic due to significant variation within laboratories. Several classification schemes have been suggested by various authors including the Papanicolaou Society of Cytology, the American Thyroid Association in, the Royal College of Physician-British Thyroid Association and Italian Society of Anatomic Pathology and Cytopathology. To bring uniformity in reporting pattern, The Bethesda System for Reporting Thyroid Cytopathology was introduced in 2007[1]. In our study, we conducted FNAC of 192 cases of thyroid swelling and reported according to the guideline laid by The Bethesda System to note the prevalence of different thyroid lesion in our centre. Subsequently, histological correlations were done in all cases to calculate malignancy risk of each category mentioned in the system.

II. Materials And Method

This prospective study was carried out in the Department of Pathology in collaboration with Department of Radiology and Endocrinology in a tertiary care centre from October 2010 to September 2012. Institutional ethical committee approval was taken. 192 patients attended Endocrinology OPD & indoor and diagnosed as cases having thyroid swelling clinically & radiologically (USG) were selected. After taking valid consent from the patient, a detailed history and report of thyroid function test were taken and clinical examination was done. Inclusions criteria were 1) clinically suspected and radio logically diagnosed cases of thyroid swellings, 2) patients who gave the consent and fully co-operative during the study process.Fine needle aspiration was performed under ultrasound guidance in case of non-palpable and diffuse swellings and without ultrasound guidance in case of nodular swellings. The procedure was done with the patient in supine position and placing a pillow under the neck. 25 gauge needles were used and aspiration was avoided unless the lesion is

cystic. In case of multiple nodules, more than one aspirate was done from prominent nodules. In cystic nodules, the cyst contents were aspirated centrifuged and the slides were made from the sediment for microscopic examination. Four slides were prepared of passes 1 and 2 by a Cytopathology technologist for each case. Two slides were air dried and stained with May-Grunewald-Giemsa (M.G.G) stain. Two slides were fixed in 95% ethyl alcohol and stained with Papanicolaou stain. Stained slides were examined under light microscope and findings were recorded according The Bethesda System for Reporting Thyroid Cytopathology in the following categories: unsatisfactory/ non-diagnostic (UNS/ ND), benign, atypia of undetermined significance/ follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/ suspicious of follicular neoplasm (FN/SFN), suspicious of malignancy (SM) and malignant.

The resected masses following total or partial thyroidectomy were sent for histopathological examination in all the 192 cases. First a careful gross examination was done. After proper processing of the representative sections, slides were stained withHaematoxylin and Eosin stain. Histopathological categorization was done according to WHO classification after examining the slides under light microscope. Cytological and histological findings were evaluated by two separate pathologists. Results of cytology and histopathology were compared. Malignancy risk was calculated by following formula:

No of cases turned out to be malignant on HP in each category X100%
No of cases in each category on cytology

III. Results

A total of 192 cases of thyroid lesions were included in the present study, of which were 41 males (21.35%) and the rest 151 were females (78.64%). Male: Female ratio is 1:3.68.Cytological diagnoses were broadly classified according to The Bethesda System for Reporting Thyroid Cytopathology. Smears were reported as unsatisfactory in 4 cases (2.08%), benign in 105 cases (54.69%), AUS/FLUS in 8 cases (4.17%), FN/SFN in 25 cases (13.02%), suspicious of malignancy in 10 cases (5.21%) and malignant in 40 cases (20.83%).

In histopathological correlation, among the four cases with unsatisfactory smears, three turned out to becolloid goitre and one came out as papillary carcinoma (malignancy risk 25%). Among 105 cases of benign category, 100 cases were true non-neoplastic benign cases and two were follicular adenoma(malignancy risk 2.8%); among 25 cases of FN/SFN category, follicular adenoma and follicular carcinoma were diagnosed in 14 cases and 3 cases respectively along with 2 cases of Hurthle Cell Carcinoma and one case of Follicular variant of Papillary Carcinoma with(malignancy risk 24%). In the AUS/FLUS category, cases were distributed as follows: follicular adenoma-4, adenomatoid goitre- 2, Hurthle cell adenoma-1 and follicular carcinoma-1(malignancy risk 12.5%). In SM category, true malignancy was present in 7cases(malignancy risk 70%). In the last malignant category, true malignancy was present in 38 cases(malignancy risk 95%) (Table 1)

IV. Discussion

Fine needle Aspiration cytology (FNAC) has aroused interest since 1949 and is the principal method of preoperative diagnosis in both children and adults[2]. The reported pitfalls are those related to specimen adequacy[3, 4] sampling techniques, the skill of the aspirator performing the aspirations, the experience of the cytopathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasms and inadequate, indeterminate FNA. One important drawback of thyroid cytology is its inability to distinguish between follicular adenoma and carcinoma as diagnosis of follicular carcinoma requires presence of vascular/or capsular invasion.The current study has been performed to assess the utility of this six tier grading system for cytological categorisation the thyroid lesions and also to assess risk of malignancy in each category when the lesions were examined histologically.The female to male ratio in our study was 1:3.68. Sinna et al. noted the ratio of1:5.2 and Verma et al. found the ratio to be 1:4.2[5, 6]. This clearly shows female preponderance of thyroid lesion in our study simulates with others studies.

Of 192 cases, we studied, smears were unsatisfactory in 2.08% cases. In study by Kaler et al. smears were unsatisfactory in 8.6% of the cases[7]. So in our study, number of unsatisfactory smears were significantly less. This is because of radiologically-assisted aspiration in diffuse and non-palpable swellings.Though unsatisfactory results usually occur in 2% to 20% of cases but ideally should be limited to no more than 10% of thyroid FNAs, excluding samples composed exclusively of macrophages.The risk of malignancy for ND/UNS (not including cyst fluid only) is 1% to 4%[8-10]. But in our study, it appears to be 25% which does not reflect the true incidence.This falsely high malignancy risk in this category in our study is due to relatively lownumber of cases, particularly in this subcategory.Benign category constituted 54.69% of our total cases and most of the cases were non-neoplastic benign entities (95.24%).According to Cibas et al. benignresult is obtained in 60% to 70% of thyroid FNAs[11]. Colloid goitre constituted maximum number of cases in benign category (64.76%). Handa et al. found similar result[12].In our study, malignancy risk was to be found to be 2.8%.According to Yassa et al. false negative rate or in other word, risk of malignancy is 0-3%which is consistent with our finding[13].

The category AUS/FLUS is reserved for specimens that contained cells (follicular, lymphoid, or other) with architectural and/or nuclear atypia that is not sufficient to be classified as suspicious for a follicular neoplasm or suspicious for malignancy[14]. An AUS result is obtained in 3% to 6% of thyroid FNAs. Higher rates likely represent overuse of this category when other interpretations are more appropriate. The recommended management is clinical correlation and a repeated FNA at an appropriate interval[13]. In our study, 4.17% of the cases belong to this category. Clinical correlation and repeat FNAC are recommended for management of these cases.The purpose of this diagnostic category is to identify a nodule that might be a follicular carcinoma (FC) and triage it for surgical lobectomy. FNA is diagnostic of many thyroid conditions (eg, papillary carcinoma, lymphocytic thyroiditis), but, with regard to follicular carcinoma, it is better considered a screening test[11]. The term SFN is favoured by some of the authors because approximately 35% of the cases in this category turn out to be hyperplastic nodules on histological examination[10]. In our study 13.02% cases were diagnosed in this category and 8% of cases in this category turned out to be adenomatoid goitre. Malignancy risk in this category, we calculated, was found to be 24%.

We observed 5.21% cases in suspicious of malignancy category with malignancy risk of 70%. Mondal SK et al. found 1.4% cases in this category in their study[15].

According to different studies, malignant thyroid FNAC diagnosis is expected to account for 4–8% of all thyroid FNACs but much higher and lower results have been reported in the literature. However, the 'malignant' category consists mostly of papillary thyroid carcinoma (PTC) cases[16]. These observations go hand in hand with our findings as malignant category comprised 20.83% of total cases in our study with malignancy risk of 95%. Most of the malignant neoplasm also was papillary carcinoma (85%).So to conclude, it may be assumed that the Bethesda System for reporting thyroid FNA is a sensitive, minimally invasive tool for interpreting different thyroid lesions and radiological assistance during aspiration increases its diagnostic yields.

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Table 1. Details of distribution of FNA cases according to the Bethesda category and their histopathological correlation. (Total Case = 192)

Cytology Category	**No Of Cases**	**Histopathology Diagnosis**		**Malignancy Risk %**
		Benign	Malignant	
Unsatisfactory	4 (2.08%)	Colloid Nodule- 03	Papillary Thyroid Carcinoma-01	25%
Benign	105 (54.69%)	Colloid Nodule-68	Follicular Carcinoma-02	2.8%
		Adenomatoid Nodule-10		
		Hashimoto Thyroiditis- 20	Papillary Thyroid Carcinoma-01	
		Granulomatous Thyroiditis-02		
		Follicular Adenoma-02		
AFLUS	8 (4.17)	Follicular Adenoma- 04	Follicular Carcinoma-01	12.5%
		Adenomatoid Goitre- 02		
		Hurthle Cell Adenoma-01		
FN/ SFN	25 (13.02)	Follicular Adenoma-14	Follicular Carcinoma- 03	24%
		Adenomatoid Goitre- 02	Hurthle Cell Carcinoma-02	
		Hurthle Cell Adenoma- 02	Follicular Variant Of Papillary Carcinoma- 01	
		Hashimoto Thyroiditis- 01		
SM	10 (5.21%)	Hashimoto Thyroiditis- 02	Papillary Thyroid Carcinoma-05	70%
		Hyalinising Trabecular Adenoma -01	Medullary Carcinoma-01	
			Lymphoma-01	
Malignant	40 (20.83%)	Hyalinising Trabecular Adenoma -01	Papillary Thyroid Carcinoma-34	95%
			Medullary Carcinoma-02	
		Hashimoto Thyroiditis- 01	Lymphoma-01	
			Anaplastic Carcinoma-01	

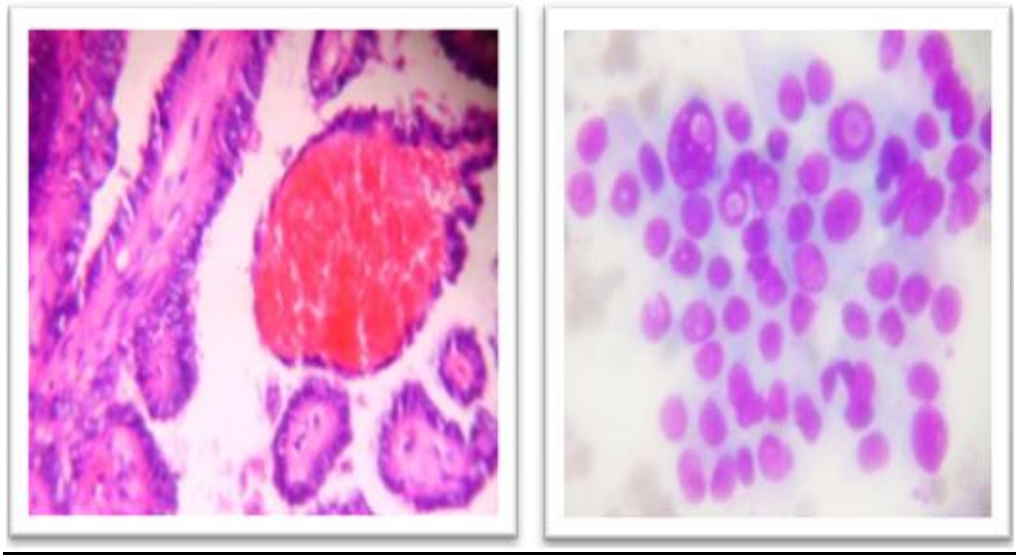

Fig 1. &Fig 2. Histology (X100) & cytology of papillary carcinoma (X400)

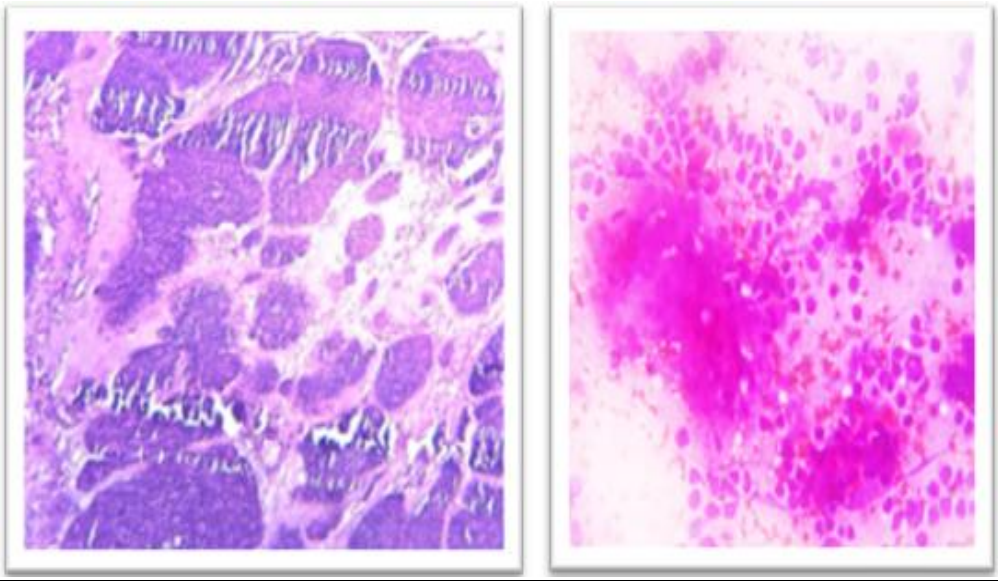

Fig 3. & Fig 4. Histology (X100) & cytology of medullary carcinoma (X100)

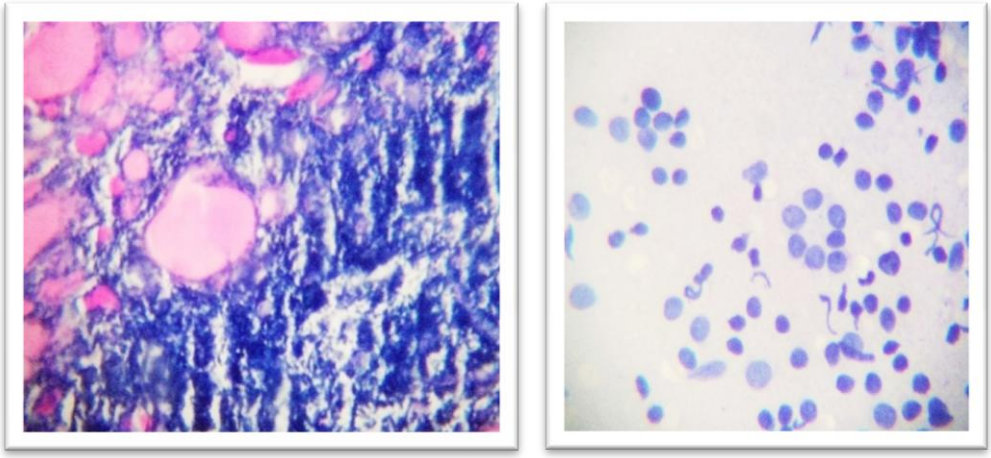

Fig 5. & Fig 6. Histology (X100) & cytology of lymphocytic thyroiditis (X400)

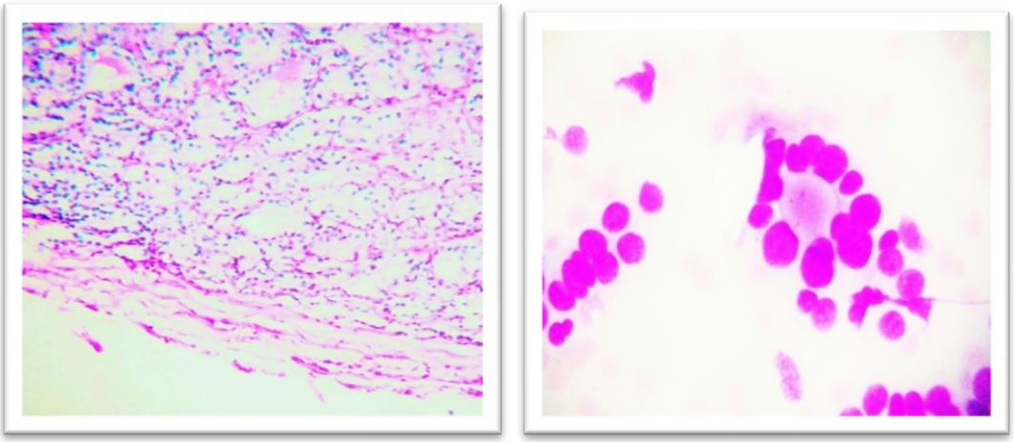

Fig 7. &Fig 8. Histology (X100)& cytology of follicular adenoma (X400)

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