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RESEARCH ARTICLE

THYROID CYTOPATHOLOGY REPORTING BY BETHESDA SYSTEM

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ARTICLE INFO	ABSTRACT	
Article History: Received 11 th September, 2017 Received in revised form 15 th October, 2017 Accepted 14 th November, 2017 Published online 27 th December, 2017 Key words: Thyromegaly, Fine Needle Aspiration Cytology (FNAC), The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).	 Background: Thyroid nodules are common in the general population, with a clinical prevalence between 5.3% to 6.4% for women and between 0.8% to 1.6% for men in normally "iodine countries". Thyroid FNAC represents a simple, fast, reliable and minimally invasive technique to explore nodules. The Bethesda System for reporting thyroid cytology is standardized, reproducible and clinically significant system. Aim: The present study was aimed at evaluation of FNAC smears of thyroid swelling as per guidelines of 'The Bethesda System of Reporting Thyroid Cytopathology', its categorization into six different categories and its correlation with histopathology wherever possible. Methods: The prospective observational study was conducted at tertiary care center in which 120 cases of thyromegaly were subjected to FNAC. Smears were prepared by conventional method and stained with H&E and Giemsa stain. Thorough microscopic examination of all smears was done. Cytological features were evaluated and reporting was done by 'The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)' to categorize the smears into six different categories. The cytohistopathological co-relation was done wherever possible. Result: Present study showed female predominance. The mean age of presentation of thyromegaly was 38.18 years. Out of the 120 FNACs 93.33 % of cases were benign. However 4.16% of cases and 2.5% of cases were Category I (ND/UNS) and Category IV (FN/SFN) respectively. Cytohistological correlation was possible in 20.83% of cases. Conclusion: Reporting by Bethesda System is an accurate and precise tool for the diagnosis of thyroid lesion on cytology, which triages the patients for clinical management. This can be used as a primary modality in the evaluation of thyroid lesions as the accuracy rate is fairly good. 	

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INTRODUCTION

Thyroid nodule is a common problem with high clinical prevalence in women ranging from 5.3 to 6.4 % (Ratour *et al*, 2013). Benign nodules outnumber the malignant one, but the risk of malignancy is to be evaluated preoperatively for management. (Gita Jayaram, 2012) Fine needle aspiration cytology (FNAC) is a simple, rapid, minimally invasive, cost effective procedure which plays an important role in evaluation of patients with thyroid pathology. FNAC is the most appropriate diagnostic modality to separate benign nodules from malignant nodules which triages the patients of malignant nodule for timely clinical intervention (Syed Z. Ali and Edmund S. Cibas, 2010). Thyroid cytology reporting needs the communication between pathologist, treating physician or surgeon and radiologist. Previously pathologists were using

**Corresponding author:* Dr. Khiste, J. A. Department of Pathology, Dr. V.M.G.M.C, Solapur, Maharashtra. different terminologies for the same lesion, creating confusion amongst treating clinicians (Syed Z. Ali and Edmund S. Cibas, 2010) (Santosh Kumar Mondal *et al*, 2013) (Payal Mehra *et al*, 2015). To avoid this confusion and ambiguity in terminology, "The Bethesda System of Reporting Thyroid Cytopathology" came into existence (Syed Z. Ali and Edmund S. Cibas, 2010) (Santosh Kumar Mondal *et al*, 2013). The National Cancer Institute hosted 'NCI- Thyroid Fine Needle Aspiration State of the Science Conference' at Bethesda, Maryland, USA where subsequently a monograph titled as 'The Bethesda System for Reporting Thyroid Cytopathology' was published (Syed Z. Ali and Edmund S. Cibas, 2010) (Santosh Kumar Mondal *et al.*, 2013) (Payal Mehra *et al.*, 2015). The monograph includes six tier system of reporting thyroid cytopathology which takes into consideration the management protocol.

The Bethesda System for Reporting Thyroid Cytopathology. (Syed Z. Ali and Edmund S. Cibas, 2010)

- (I). Non diagnostic / Unsatisfactory (ND/UNS)
 - Cystic fluid only, acellular, blood, artifact

(II). Benign

- Consistent with benign follicular nodule (adenomatoid, colloid nodule)
- Consistent with lymphocytic / Hashimotos thyroiditis in proper clinical context
- Consistent with granulomatous / subacute thyroiditis
- Other

(III). Atypia of undetermined significance or follicular lesion of undetermined significance (AUS /FLUS)

(IV). Follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN) specify if Hurthle cell (oncocytic type)

(V).Suspicious for malignancy (SFM)

- Suspicious for papillary carcinoma
- Suspicious for medullary carcinoma
- Suspicious for metastatic carcinoma
- Suspicious for lymphoma
- Other

(VI). Malignant

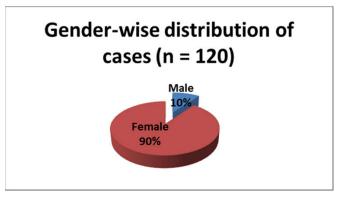
- Papillary carcinoma thyroid
- Poorly differentiated carcinoma
- Medullary carcinoma thyroid
- Undifferentiated carcinoma / anaplastic carcinoma
- Squamous cell carcinoma
- Carcinoma with mixed features (specify)
- Metastatic carcinoma
- Non Hodgkin's lymphoma
- Others

MATERIALS AND METHODS

This was a prospective study of consecutive 120 cases of thyroid enlargement referred to Department of Pathology for FNAC during a period from July 2015 to September 2016. Before subjecting the patient for FNAC pertinent clinical data were recorded from case records. Under all aseptic precautions FNAC of thyroid with 23 gauge needle and 10 ml disposable syringe was carried out with stereotactic technique. Ultrasound guided FNAC was done as per the merit of the case. Smears were prepared by conventional method and fixed in ether alcohol. Smears were stained with H&E and Giemsa stain. Thorough microscopic examination of all smears was done jointly by two pathologists. Cytological features were evaluated and reporting was done by 'The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)' to categorize smears into six different categories. the The cytohistopathological co-relation was done wherever possible.

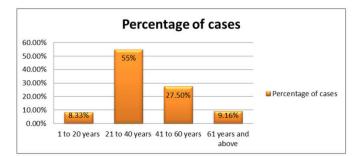
RESULTS

In the present prospective study 120 cases of thyromegaly were subjected for FNAC.



The females outnumbered the males consisting 90% of the cases.

Age-wise distribution of cases (n = 120)



Maximum number of cases were found in 21 to 40 years of age group forming main bulk of 55% of cases followed by 41 to 60 years of age group comprising 27.5% of cases. The mean age of presentation of thyromegaly was 38.18 years.



Photograph showing 38 year old female, with thyromegaly

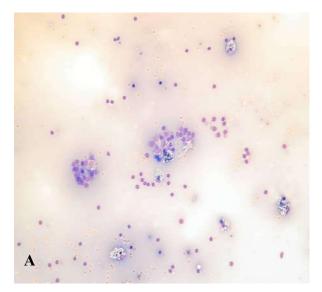
Table 1. Bethesda system - Distribution of cases (n=120)

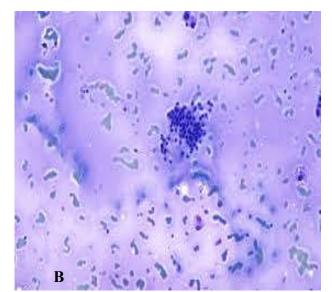
S. No.	Category	Number of cases	Percentage
1	I.(ND/UNS)	5	4.16
2	II. Benign	112	93.33
3	III. (AUS/FLUS)	-	-
4	IV. (FN/SFN)	3	2.5
5	V. (SFM)	-	-
6	VI. Malignant	-	-

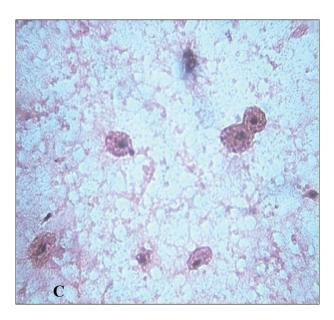
ND/UNS- Non diagnostic / Unsatisfactory; AUS /FLUS- Atypia of undetermined significance or follicular lesion of undetermined significance; FN/SFN- Follicular neoplasm or suspicious for a follicular neoplasm; SFM-Suspicious for malignancy.

Table depicts the distribution of 120 cases. The dominant contributor was benign category (Grade II) consisting of 93.33 %(112) of cases in which 93.75% (105) of cases had cytomorphological features of benign follicular nodule, while

6.25% (7) of cases had the subcategory of Lymphocytic/ Hashimoto's thyroiditis.

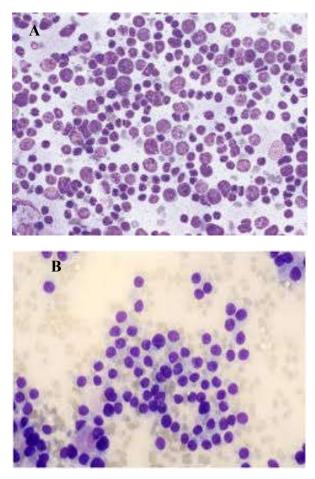






A, B and C- H & E stained 100X-Grade II Benign-Colloid Goiter:, Reporting by- The Bethesda System of Thyroid Cytopathology.

A and B- Photomicrograph of cellular smears showing clusters of benign follicular epithelial cells and background shows blood mixed colloid material. C- Photomicrograph of smear showing cyst macrophages.



A and B - H & E stained 400X : Grade II Benign - Hashimoto thyroiditis- Reporting by- The Bethesda System of Thyroid Cytopathology.

A – Photomicrograph of cellular smear showing thyroid follicles destructed by reactive lymphocytes. B-Photomicrograph of cellular smear showing Hurthle cell change.

Category I (ND/UNS) smears were found in 4.16% of cases. All the patients were advised for repeat FNAC but no patient turned up. Grade IV smears were diagnosed in 2.5% of cases. All were reported as suspicious of follicular neoplasia. Present study did not encounter any case in Grade III, V and VI category.

Out of 120 cases only 25 underwent surgical excision and hence were available for histopathological examination.

 Table 2. Cytohistological co-relation (n=25)

S. No.	Cytological diagnosis	No. of cases	Histological diagnosis	Correlation
1.	Benign Follicular Nodule	25	Benign Follicular Nodule (Goiter)- 23 Hashimoto's thyroiditis-1 Malignancy (Medullary Carcinoma)- 1	92% 4% 4%

Cytohistological correlation was possible in only 25 (20.83%) of cases. Out of 25 cases, 24 were reported as Grade II smear (Benign Follicular Nodule) which were confirmed as benign on histopathology. Out of 24 cases, 23 cases had follicular nodule and a case had Hashimoto's thyroiditis as a sub-category on histopathology. A single case with discordant result was found. It was confirmed as medullary carcinoma on histopathology, which was underdiagnosed as benign category on cytology.

DISCUSSION

The present study was conducted at tertiary care center which is a border district between Maharashtra and Karnataka. The influx of the patients is from both the states. Thyroid enlargement, whether solitary nodule, multinodular or diffuse swelling needs an array of investigations to rule out the possibility of malignancy. FNAC followed by Bethesda system of reporting has become a primary tool as it provides the risk of malignancy in individual group with management protocol (Syed Z. Ali and Edmund S. Cibas, 2010) (Payal Mehra et al, 2015). The present study had 4.16% of non diagnostic/ unsatisfactory smears. All the patients were advised reaspiration within 3 months period as per the recommendations of committee but no patient turned up. Nazma Afroze quoted that inadequate or unsatisfactory samples in various studies ranged from 0-25%. Inadequate samples are usually due to improper FNAC technique, cystic lesions, sampling error, inexperienced aspirator and small lesion aspirated by stereotactic technique. This all can be overcome by adopting a proper technique, giving multiple passes, taking help of imaging modalities as guide, search for mural nodule in cystic lesion and training of aspirator. Accurate diagnosis will depend upon proper technique of FNAC, procurement of sample, optimum sample processing and careful observation of slides. Maximum number of smears in present study were from benign category, comprising of 93.33% of the smears. Massimo Bongiovanni in his study of meta-analysis of all publications on TBSRTC during 2008-2011 at Philadelphia found benign lesions ranging from 39% to 73.8% with a malignancy rate of 3.7%, which was slightly higher than the recommendations of TBSRTC guidelines (0-3%). However the American Thyroid Association guidelines state it in the range of 0-5% (Payal Mehra et al., 2015). Jack Yana et al found 64.6% of smears in benign category in his study conducted in New York. A study of 528 cases conducted by Samreen Naz et al at Dhaka observed 76.3% of smears in benign diagnostic category with a 11.1% frequency of malignancy. She found four cases of Papillary carcinoma and a case of Medullary carcinoma on histopathological examination. Ji Hye Park et al in his study of 1730 cases found little lower percentage of benign lesions (40.6%), which was attributed to referral of high percentage of many diagnosed thyroid cancer cases from periphery. Payal Mehra et al, Santosh Kumar Mandal et al and V. Palaniappan et al from India observed benign category smears in 80%, 87.54% and 97.35% of cases respectively. Observations in the present study are in concordance with above studies.

Incidence of benign lesions is much higher in India as compared to Western countries. India has the world's largest goiter belt in Sub-Himalayan region (Uma Handa *et al.*, 2008). Many pockets of goitrous area in other parts of the country are also found. In these Iodine deficient areas the incidence of goiter in thyroid nodule is very high as observed in our study. In the present study goiter is forming the main bulk of benign diagnostic category. Though the hospital is a tertiary care center, the patients coming directly to the hospital are more than the referrals. The present study observed 2.5% of smears in SFN diagnostic category. Samreen Naz et al found 6.56% of smears in this category. In her study, histopathologically none of the cases showed benign follicular neoplasm, instead it showed Papillary carcinoma in a single case. Massimo Bongiovanni et al in his metanalysis of 9 different series found a wide range of 1.2% to 25.3% with a mean of 10.1% smears in SFN diagnostic category having 26.1% risk of malignancy. Payal Mehra and Anand Kumar Verma in their study of 225 cases found 2.2% of smears in this category. A single case underwent lobectomy which revealed papillary carcinoma on histopathology. Santosh Kumar Mandal et al reported 4.2% of smears suspicious of follicular neoplasm with a malignancy risk of 30.6%. In the present study out of 120 cases only 25 cases had histopathological follow-up in which 24 (96%) cases were confirmed as benign nodule, while a single case was under-diagnosed as follicular neoplasm (Grade IV). Histopathological examination revealed it as medullary carcinoma of thyroid and hence the overall discrepancy rate between cytological and histopathological diagnosis was 4% giving overall accuracy of 96%. Various studies have shown various cytohistological concordance rates ranging from 80% to 100%. Pinki Pandey et al found cytohistological concordance in 80.28% of cases in which false positive cases accounted for 11.60%. Author was of the opinion that too much emphasis on cellularity and architectural pattern led to erroneous false positive diagnosis. Samreen Naz et al quoted that various workers in various hospitals evaluated the diagnostic accuracy of thyroid cytopathology. She further quoted that Bagga et al, Gupta et al, Himakhm et al found diagnostic accuracy in 96.2%, 56% and 93% respectively. Jack Yang et al in his study of 4703 patients reported the cytohistological correlation in 84.7% of cases. The overall causes for false negative diagnosis relate to sample inadequacy, cystic papillary thyroid carcinoma. This could be overcome by on site sample adequacy evaluation and search for mural nodule in any cystic swelling followed by aspiration through nodule. Source for false positive diagnosis is misinterpretation in highly cellular smear. This could be avoided by meticulous microscopic examination in the light of clinical features, laboratory findings and findings of imaging studies. It is highly difficult to differentiate between follicular adenoma and hyperplastic nodule. Three dimensional groups, syncitial clusters, loosely cohesive micro-follicles, scanty colloid and clean background favor follicular neoplasm.

Conclusion

The thyroid FNAC and reporting by Bethesda System is an accurate and precise tool for the diagnosis of thyroid lesion which triages the patients for clinical management. This can be used as a primary modality in the evaluation of thyroid lesions as the accuracy rate is fairly good. The limitation of the present study was cytohistological co-relation as very few patients underwent surgical excision.

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