RESEARCH

THE BETHESDA SYSTEM EVALUATION OF THYROID FINE-NEEDLE ASPIRATION FOR REPORTING CYTOPATHOLOGY AND ITS HISTOPATHOLOGIC FOLLOW-UP

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Abstract

Background: Reporting thyroid cytopathology by using the Bethesda system is a key pace towards Calibration which improved clinical implication, and greater analytical value of thyroid fine needle aspiration cytology (FNAC). Aims: To evaluate the malignancy risks in thyroid nodules using Bethesda system for reporting thyroid fine needle aspiration cytology with histopathological follow up. **Materials and Methods:** We prospectively did thyroid FNA between October 2016 to August 2018. Then used the Bethesda system to classify them into different category, and considered the malignancy risk for each category by follow-up histopathology. **Results:** Out of the 80 cases who underwent FNAC in our study, 2 cases (2.9%) turned out to be non-diagnostic, 54 (67.9%) benign, 4 (9%) AFLUS, 11 (18.7%) SFN,5(6.2%) SM, and 4 (9%) malignant as per Bethesda classification. Histopathology follow-up were available. In present study malignancy rate of category I is 0%, category II is 1.85%, category III is 0%, 36.36% for category IV,60% for category V, and 100% for category VI lesions. **Conclusions:** In the present research study, the case distribution as per the Bethesda classification, we have higher number of benign cases and the number of non-diagnostic and AFLUS cases being lower. The malignancy values reported in our research were constant and comparable with the results of other published data with respect to the risk of malignancy. The Bethesda system thus allows more precise cytological diagnosis, tuning in reporting, improves insights of diagnostic terminology between pathologists and clinicians, and leads to more reliable management approaches.

INTRODUCTION

Evaluation of thyroid lesion by Fine needle aspiration cytology (FNAC) is the most broadly usedinvestigative test as an initial procedure.[1] It is amodest, speedy, reasonably priced and safe OPD procedure that can excellently distinguish between benign and malignant lesions of the thyroid for proper treatmentof the patient.[2] The main goal of thyroid FNA is to differentiate nodules that need surgical treatment from those which need a follow-up, thus reducing the rate and need of unnecessary thyroid surgeries. At the same time, itincreases the percentage of resection of malignant cases.[3]
Nevertheless, due to the nonexistence of a consistent format, cytopathologists of different institution have been writingdiverseterms for thyroid cytopathology reporting, thus referring clinicians are confused in the interpretation which eventually impeding an ultimate clinical managing.[4]
Several organizations have proposed diagnostic strategies for reporting thyroid FNAC results, including the Papanicolaou Society of Cytopathology Task Force and the American Thyroid Association, even though none have been universally acknowledged.[5,6]
The National Cancer Institute (NCI), Bethesda, Maryland, United States, organized the NCI Thyroid Fine Needle Aspiration State-of-the-Science Conference in the year 2007, and an ingenuity was commenced to put out an plans and guiding principle for a uniform terminology for the explanation of FNAC of thyroid, acknowledged as the Bethesda system for reporting thyroid

cytopathology.[7]This defines six categories of lesions: non-diagnostic/unsatisfactory, benign, atypical follicular lesion of undetermined significance (AFLUS), "suspicious" for follicular neoplasm (SFN), suspicious for malignancy (SM), and malignant.[7] This categories of the Bethesda system have estimated malignant risk of each categories that impact management standards.[4,8]
This prospective study was commenced to explain the practicality of the Bethesda system in reporting FNAs of thyroid cytopathology and tries to stratify the malignancy risks in thyroid nodules.

MATERIALS AND METHODS

The present study is a prospective, observational one that was undertaken in the Department of Pathology in a tertiary care hospital in western Odisha from October 2016 to August 2018. The study was approved by the institutional ethics committee. Written information consent was taken from the patient before considering for study.
Patient of either sex, aged between 18-80 yr. with thyroid sweeling attending to various clinical department were included in the study. The patient having Fine Needle Aspirations (FNA) of thyroid without further thyroidectomy and histopathology were excluded from the study.
A detailed history of swelling of thyroid, thyroid hormone profile and ultrasound scan of neck were recorded. The cytopathologist performs FNAC on patients with thyroid swellings with or without ultrasound guidance. On an average four to six smears were prepared. Two smears were allowed to dry and the air-dried smears were kept for Diff-Quik staining. Two to three wet slides were fixed in 95% alcohol for 30 minutes. These slides were used for Papanicolaou stain.
Malignancy risk of each category was calculated on the cytology according to The Bethesda System (TBS) of reporting and were followed up by biopsy. The FNAC and biopsy were compared to find the efficacy of The Bethesda System of reporting.
All the statistical calculations were performed using IBM SPSS statistics (IBM SPSS statistic for windows, version 21.0).

RESULTS

The study was undertaken in the department of pathology, VIMSAR, Burla from October 2016 to august 2018. In this study, common age group involved was 31-40 years, with 22 cases (27.5%) and least common age group involved was 71-80 years, with 2 cases (2.5%). Most of the patients are female comprising of 76.25% of our total cases. There is female preponderance with female: male ratio being nearly 3:1. The thyroid profile of majority of the patients are euthyroid (58.75%) followed by hypothyroid (31.25%) & hyperthyroid (10%). Out of the 80 cases who underwent FNAC in our study,
2 cases (2.9%) reported to be non-diagnostic, 54 (67.9%) benign, 4 (9%) AFLUS, 11 (18.7%) SFN,5(6.2%) SM, and 4 (9%) malignant as per Bethesda classification. Non-diagnostic category comprises the smear which did not accomplish the suitability criteria put forth by the Bethesda system. An adequate specimen for a solid nodule is which comprise of minimum six well-preserved and well-stained follicular groups, containing minimum ten cells.
Benign category smears show the clear cut benign cytological features which include colloid goitre/adenomatoid goitre, Hashimoto's thyroiditis, lymphocytic thyroiditis [Figure1] thyrotoxicosis, de Quervain's thyroiditis, and granulomatous thyroiditis. In our study, most common category is benign group constituting 54 cases (67.5%).
On histopathology, most common benign lesion is colloid goitre (26 cases).
Aspirates which were adequate, had few features of atypia but could not be considered absolutely into either of the benign, SFN, SM, or malignancy categories were considered under the Atypia of undetermined significance/atypical follicular lesion of undetermined significance category, as per Bethesda system guiding principle.
Aspirates with cytomorphologic features of moderate to high cellularity, scant or absent colloid, with predominantly microfollicular or trabecular configuration of follicular cells in repetitive pattern were grouped under the Follicular neoplasm/Suspicious for follicular neoplasm category. [Figure 2]
Smears that had cytopathological features indicative of, but not conclusive of, papillary carcinoma, medullary carcinoma, or lymphoma [Figure 5] were categorised under Suspicious for malignancy category.
Smears having features that were unambiguously malignant were placed in the malignant category. Most common malignant lesion is follicular variant of papillary carcinoma in our study (5 cases) [Figure4].
In neoplasm category of our study Benign category was considered negative; and the categories like Follicular neoplasm, Suspicious for Malignancy, and Malignant were considered positive. Comparison was done between Bethesda system as a screening test and biopsy as the confirmatory test.Our results were true positive 14,true negative 49,false positive 10,false negative 5.Most common lesions that contribute to false positive results probably were the nodular hyperplasias with dense micropapillary stuctures. Distinguishing hyperplastic nodules from Folicular neoplasm is difficult because they have similar cytomorphological features. False negative results were attributed to inadequate sampling due to cystic degeneration in large areas, few cases with sclerotic or calcified nodules, inaccessibility of the diffuse

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swellings. Multiple passes to cover all areas, USG guided aspiration and through clinical examination could have reduced these errors. But analysis of few USG reports and inability to do US guided FNAC remains as one of our limitations.

From the histopathological data malignancy rate of each category of Bethesda system was calculated. In present study malignancy rate of category II is 1.85%, 36.36% for category IV, 60% for category V, and 100% for category VI lesions.

In our study the Bethesda system classification had sensitivity of 73.68%, specificity of 83.05% with positive predictive value 58.33% and negative predictive value 90.74% compared to histopathologic confirmation of malignant risk. ($p < 0.001$).

Table 1: Correlation of cytology with histologly.

Cat.	No. of case	CG	NG	AG	AT	ST	FW	FA	FC	FVPTC	PC	MC	AC	NHL
I	2	2	0	0	0	0	0	0	0	0	0	0	0	0
II	54	24	10	6	7	1	1	4	0	0	1	0	0	0
III	4	0	3	0	1	0	0	0	0	0	0	0	0	0
IV	11	0	2	1	1	0	0	3	1	3	0	0	0	0
V	5	0	1	0	1	0	0	0	0	2	0	0	0	1
VI	4	0	0	0	0	0	0	0	0	0	2	1	1	0

CG-Colloid Goitre NG-Nodular Goitre AG-Adenomatous -Autoimmune Thyroiditis
ST-Subacute Thyroiditis FW-Filarial Worm FA-Follicular Adenoma FC-Follicular Carcinoma FVPTC-Follicular Variant of Papillary Carcinima PC-Papillary Carcinoma MC-Medullary Carcinoma AC-Anaplastic Carcinoma NHL-Non Hodgekin Lymphoma

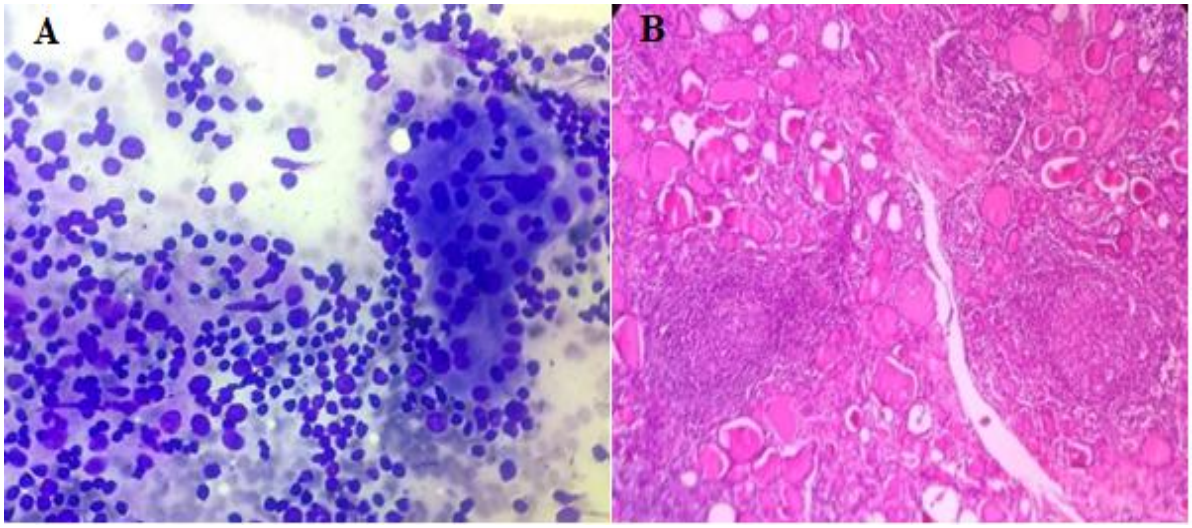

Figure 1: (A) Diff Quik (X400) Autoimmune Thyroiditis Showing Follicular Cells Admixed With Lymphoid Cells And Hurthle Cell Changes, (B): Lymphocytic Thyroiditis (Colloid Filled Follicles Along With Lymphoid Follicle And Germinal Center Formation).

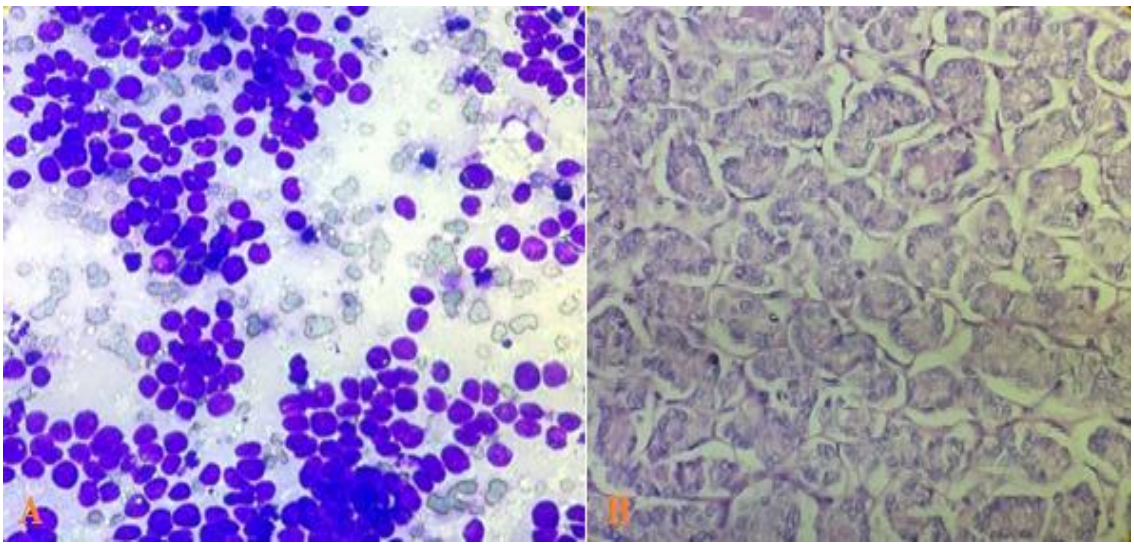

Figure 2: (A) Diff Quik (X400) Follicular Neoplasm Showing Nuclear Overcrowding, Overlapping, Micofollicle Formation, (B) H & E (X400) Follicular Adenoma

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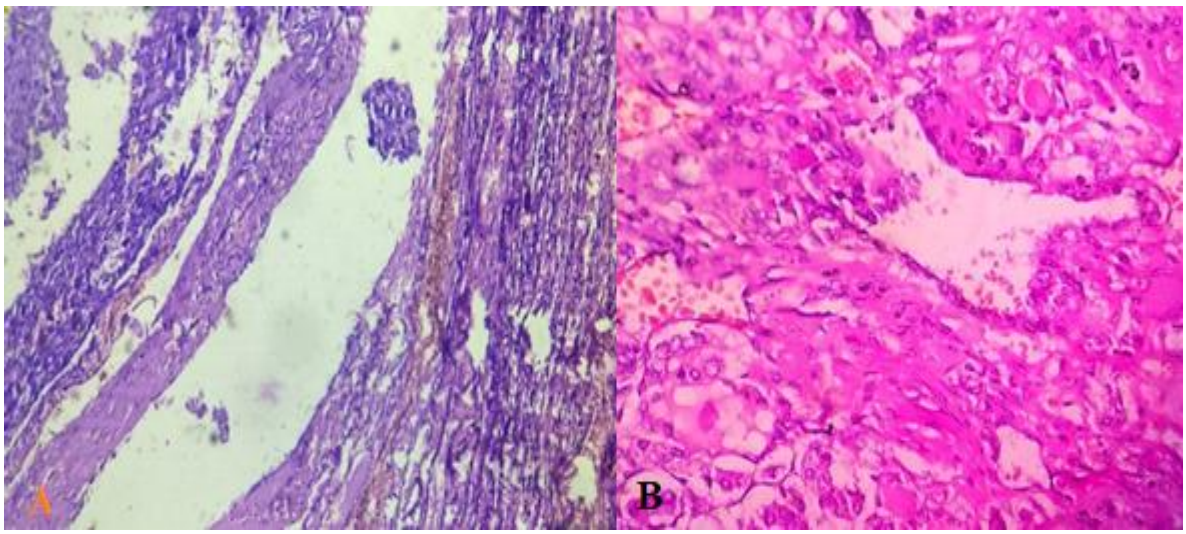

Figure 3: (A) H&E (X100) Follicular Carcinoma Showing Capsular Invasion, (B) H&E (X400) Follicular Carcinoma Showing Vascular Invasion

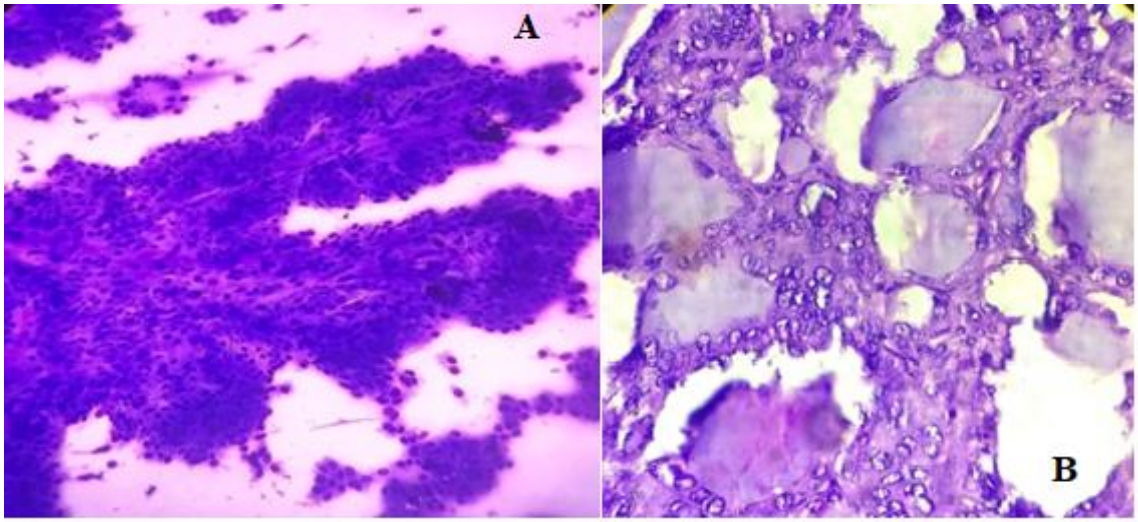

Figure 4: (A) Diff Quik (X100) Cells in Papillary Clusters with Fibrovascular Core, (B) H& E (X400) Follicular Variant of Papillary Thyroid Carcinoma

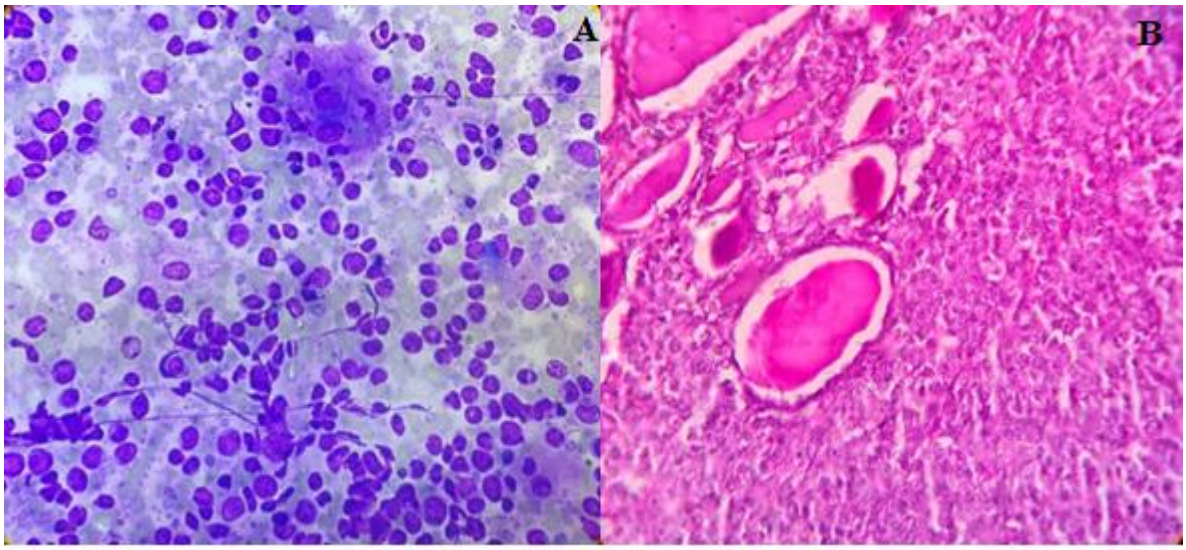

Figure 5: (A) Diffquik (X400) Highly Cellular Smear Showing Noncohesive Large Lymphoid Cells With Open Chromatin In A Background Containing Lymphoglandular Bodies, Raising Suspicion Of Lymphoma, (B) H&E(X400) Nonhodgkin Lymphoma Thyroid

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DISCUSSION

The descriptions and diagnoses that were used previously seems to be ambiguous and intricate waffle of cytological terms, which is unclear and of not any medical implication to the physicians.[9] Nevertheless, after Bethesda system classification, the reporting of cytopathology of thyroid lesions has become more standardised, organized, efficient with greater precision; therefore, would be more valuable inmanaging of thyroid lesion.[10]

Demographic data related to age and sex in the present study showed female preponderance with ratio being nearly 3:1 which was similar to other reported studies by Vickie Y. Jo et al,[11] Yassa et al,[12] Yang et al.[13]

The age group of 31-40 years showed the maximum number of FNA cases(22cases) which accounted for 27.5%, followed by 21-30years (20 cases) constituting 25% of total cases. Sirish Chandewale et al,[14] also showed major age group involved to be 21-40 years.

By using "The Bethesda System for Reporting Thyroid Cytopathology" criterion, thyroid cases were classified into 6 categories and the results were comparable with other studies by Reddy p. et al,[15]Ailiguo et al,[16] Reuters et al,[18] P. Mehra et al,[17] Yassa et al.[12]

Most of the cases in our study were benign and seen in the age group between 31-50years and maximum number of malignant cases in age group of 51-70years. Our results were similar to studies conducted by Sirish Chandewale et al.[14]

The Non-diagnostic/Unsatisfactory (ND/UNS) category constituted of 2 cases (2.5%). Ideally the non-diagnostic cases should be below 10%.The most common lesions in FNAC belonged to the benign category comprising of 54 cases (67.5%).

Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS) is a heterogenous category whose abnormalities or atypia must not be enough to place them in other categories.[19] The percentage of ND/UNS and AUS/FLUS of our study was quite lower and near about similar with studies by Ali et al.[19] In present study, the cytopathologist herself performed FNAC in our institute ensuring adequacy and better quality of aspirate, many under Ultrasound guidance. This significantly reduces ND/UNS and AUS/FLUS cases.

In present study, the cases under the category Follicular neoplasm/Suspicious for Follicular neoplasm (FN/SFN), Suspicious for malignancy(SM), Malignant (M) are higher and comparable to the study by Reuters et al.[18]

The results of our study substantiated well with the disguised malignant risks of each category stated in the Bethesda System and also with the studies by Reuters et al,[18] Yassa et al,[12] Vickie Y.Jo et al,[11] Arul p. et al.[21]In the present study the risk of malignancy for AFLUS/AUS category is 0% which is comparable to study by Arul p. et al.[21] The malignancy rate for SFN/FN category is 36.36% which is comparable to studies by Reuters et al.[18]

Sensitivity and Specificity of our study were 73.68% and 83.05% respectively. Moreover, Positive Predictive Value (PPV) and Negative Predictive Value(NPV) were 58.33% and 90.74%. The Accuracy of our study was 80.76%. This result was agreeable with other studies of other authors like Reddy p. et al.[15]

CONCLUSION

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is a uniform and standardized reporting system with a good accuracy. Its application helps in early and precise diagnosis of various thyroid lesions. Our study clearly establishes and emphasizes its applicability to avoid confusion and misinterpretation of results.

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