Research Article

Thyroid FNAC Reporting Post-Bethesda - Problems and Challenges Faced in Our Center - A Preliminary Study

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Abstract

Aims and Objectives: The Bethesda system for reporting thyroid cytopathology (TBSRTC) was proposed to standardize the reporting of thyroid cytopathology for more effective clinical communication and patient management. This study was undertaken to see the challenges, if any, faced in our center post the implementation of the new system.

Materials and Methods: Retrospective analysis of 250 thyroid aspirates was done wherein all slides were reviewed and reclassified as per TBSRTC.

Results: The mean age of patients was 40.2 years and females comprised 86.4% of the study group. Histological follow-up was available in 19.6% of cases. On reclassification, 6% of cases were put in the category of atypia of unknown significance/follicular lesion of unknown significance (AUS/FLUS). The benign category comprised 80.6% down from 87.6% reported earlier. The non-diagnostic group also increased marginally from 8% to 8.8%. No changes were observed in the following categories: Follicular/Hurthle cell neoplasm, suspicious for malignancy and malignant.

Conclusion: TBSRTC was useful in achieving the goal of improving thyroid cytopathology reporting by adopting a standardized format. However, due to the heterogeneity of the AUS/FLUS category, more cases than warranted were put in this category, which did not correlate with a higher risk of malignancy. More stringent criteria for inclusion of patients in the AUS/FLUS group and further stratification of these patients into high-risk and low-risk categories are suggested.

Keywords: Bethesda, Thyroid, Cytology

Introduction

Fine needle aspiration cytology (FNAC) is a simple, cost-effective and widely accepted primary method for the diagnosis of thyroid lesions. It helps to triage patients, i.e., to determine whether surgical intervention is indicated.

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However, the terminology for thyroid FNAC has varied significantly from one laboratory to another leading to wide inconsistencies in reporting with a lack of a standardized reproducible system of reporting of thyroid cytology aspirates.[1] The Bethesda system for reporting thyroid cytopathology (TBSRTC) was proposed in 2009 to standardize the diagnostic criteria and terminology utilized for thyroid cytopathology and improve clinical communication and management.[2]

TBSRTC comprises of 6 diagnostic categories (DC), each with a unique risk of malignancy and recommendation for clinical management.[2] The categories are: Non-diagnostic, benign, atypia of unknown significance/ follicular lesion of undetermined significance (AUS/FLUS), suspicious of follicular neoplasm (SFN), suspicious for malignancy (SM), and malignant.

Our Institute also uses a similar in-house classification (IC), which employs the categories similar to TBSRTC without the inclusion of the category of AUS/FLUS.

After the implementation of TBSRTC, various authors have described their experience with Bethesda. Most of these studies have been from the Western countries where epidemiology and demography of thyroid lesions is usually different.[3-6] Since there have not been many studies from India, this study was undertaken to compare our IC classification with TBSRTC, do a cytological and histological correlation and assess the feasibility of using Bethesda in our clinical setting.[7]

Materials and Methods

Approval for this study was taken from the Institute's Academic and Ethics committee to retrospectively review the slides and case histories of 250 consecutive thyroid aspirates performed in the hospital between January 2012 and February 2013. Cases which were submitted by outside laboratories for second opinion were not included. All the aspirates had been performed by a junior pathologist with an average of 2–3 passes per case. Rapid on-site evaluation of adequacy was routinely not performed, and liquid-based preparations for thyroid aspirates were not used. Air-dried smears stained by Leishman Giemsa and ethanol fixed smears stained by the Papanicolaou method were available in all cases and were reviewed and recategorized using TBSRTC by two independent cytopathologists, who were blinded to the original diagnosis. In case of any disputed cases, both the cytopathologists reviewed the case together on a multihead microscope and reached a consensus to assign it to a best fit-category. The FNA cases, which had a follow-up thyroid resection, were also retrieved. The corresponding surgical pathology slides were also reviewed and a cyto-histo correlation performed. (a) Smears were considered non-diagnostic, if they did not show the minimum number of 6 well-preserved follicular groups with a minimum of 10 cells each. Smears with sample preparation artefacts were included in this group. However, we did not consider smears with the presence of cyst macrophages only as non-diagnostic, if an ultrasonographic evidence of cyst was present. (b) Smears were considered benign if they showed features of colloid cyst or colloid goiter, adenomatous goiter, lymphocytic thyroiditis or hyperthyroidism. Smears with sparse follicular cells but with abundant pools of colloid in the setting of colloid goiter were also categorized as benign.

Atypia of Unknown Significance/ Follicular Lesion of Unknown Significance (AUS/FLUS)

In the category of atypia of unknown significance/ follicular lesion of unknown significance (AUS/ FLUS), TBSRTC guidelines suggest that all adequate samples having focal atypia not enough to be categorized as benign, suspicious for malignancy, or malignant were put in this group. As described earlier, aspirates with sample preparation artefacts were not included in this group.

Follicular Neoplasm/ Suspicious for Follicular Neoplasm/ Hurthle Cell Neoplasm

Smears having a high cellularity with a repetitive pattern of microfollicles and scant colloid were included in this category. Similar features seen in Hurthle cells were reported as a Hurthle cell neoplasm.

Suspicious for Malignancy

Smears which were suggestive of, but not diagnostic of malignancy, were categorized as suspicious.

Malignant

Aspirates having unequivocal features of malignancy were included in this category.

Results

There were 216 females (86.4%) and 34 males (13.6%). Mean age was 40.2 years (range 11–79 years). The percentage of repeat aspirations was 7.2 (n=18) and 16% of aspirates were USG guided (n=40). The benign category had the highest number of repeat aspirations (n=10).

On reclassification with TBSRTC, no changes were observed in the following categories: Follicular/Hurthle

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neoplasm, suspicious for malignancy, and malignant. Histological follow-up was available in 49 cases (19.6%)

The comparison of our current IC classification with TBSRTC was as shown in Table 1.

Table 1.Comparison of IC and TBSRTC

Category	Non-diagnostic	Benign	AUS	Follicular Neoplasm	Suspicious for Malignancy	Malignant
In house	20 (8)	219 (87.6)	NA	6 (2.4)	1 (0.4)	4 (1.6)
TBSRTC	22 (8.8)	202 (80.8)	15 (6.0)	6 (2.4)	1 (0.4)	4 (1.6)

The distribution of cases in the benign category post TBSRTC was as follows: Colloid goiter (n=76), colloid cyst (n=30), adenomatous goiter (n=72), and lymphocytic thyroiditis (n=24)

Of the 250 patients, who underwent FNAC initially, 20 cases were non-diagnostic. All of these showed inadequate number of follicular cells. On review, one patient originally labelled as benign, was put into the non-diagnostic category as she had less than 6 groups of follicular cells and also scant colloid.

Our five-tiered classification originally did not include the category of AUS/FLUS but on reclassification with Bethesda, 15 cases were put in this category, which had been categorized as benign earlier. Most of these cases (n=9) showed features of cytological atypia in the form of nuclear enlargement, nuclear crowding and elongated to spindled morphology. Three cases showed a prominent Hurthle cell change with anisonucleosis in a background of lymphocytic thyroiditis. One case had scant cellularity with architectural atypia in the form of tight clusters of follicular cells and scant colloid. One case showed an occasional group of follicular cells having nuclear grooves with prominent nucleoli. As described earlier, samples with a preparation artefact were not included.

Though the majority of cases were still benign, their number declined from 87.6% to 80.4% post TBSRTC as 15 cases were recategorized to AUS/FLUS and two cases were categorized as non-diagnostic.

The FNAC diagnosis and the corresponding histopathological diagnosis and the calculated malignancy risk are given in Table 2.

The discordant cases between IC and TBSRTC are given as per Table 3.

Table 2.Calculation of Malignancy Risk for Each Category

FNAC Diagnosis	No. of Cases HP Follow up	Malignant (n)	Malignancy risk
Non-diagnostic	2	0	0
Benign	39	1	2.5%
AUS/FLUS	4	0	0
Follicular neoplasm	2	2	100%
Suspicious for malignancy	1	1	100%
Malignant	2	2	100%

Table 3.Description of Discordant Cases between IC and TBSRTC

No. of Cases	Earlier Category	Post TBSRTC	Cytological Features
2	Benign	Non-diagnostic	Less than 6 groups of follicular cells with scant colloid
9	Benign	AUS	Cytological atypia in the form of nuclear enlargement, nuclear crowding and elongated to spindled morphology (Fig. 1)
3	Benign	AUS	Prominent Hurthle cell change with anisonucleosis. Background showed lymphocytic thyroiditis (Fig. 2)
1	Benign	AUS	Scant cellularity with architectural atypia tight clusters of follicular cells with scant colloid
2	Benign	AUS	Occasional group of follicular cells with prominent nucleoli and nuclear grooving

Discussion

The percentage of non-diagnostic aspirates both pre- and post-TBSRTC remained low at 8.0% versus 8.8% as recommended by Bethesda (<10%), as in our center FNACs are performed by the cytopathologist leading to

better adequacy of samples. Also, smears comprising only cyst macrophages were not considered as unsatisfactory if a sonological evidence of cyst was present.[8] However, if repeat aspirations and radiological correlation were not considered then the rate of unsatisfactory smears in our study was 31.2%. Studies have shown that it can range from 1.8% to 23.6%, suggesting that in spite of established criteria, there is a variability among institutions in classifying thyroid FNA as non-diagnostic.[5] Laboratories which had included "cyst macrophages" only in the non-diagnostic category, had unsatisfactory rates, which ranged from 15% to 30%.[9]

We had 30 cases of colloid cyst which showed presence of cyst macrophages only. On recategorization, the AUS/FLUS category in our study was within the recommended rate of usage, but showed a lower than expected rate of malignancy (0%).

Authors have demonstrated wide variations for the use of this category (0.7%–17.8%) and the malignancy rate associated with the same (6%–48%).[10] In our analysis, the AUS/FLUS: Malignant ratio was 3.75 which is higher than the recommended ratio of 1:3, as proposed by Krane et al.,[11] suggesting a possible overuse due to unfamiliarity with the new classification. Since none of the cases available for surgical follow up had malignancy and the cytological atypia seen in most of our cases could occur due to reparative changes in epithelial lining cells of benign thyroid cysts, so the utility of this category is questionable. It has been shown that adjunct molecular tests could be of benefit in further triaging these cases.[12,13]

We compared our results with other studies (Table 4). The higher number of benign cases (80.4%) was comparable to another Indian study by Mondol[7] and was reflective of the general population which our center catered to.

Table 4.Comparision of Present Study with Other Studies

Study	No.of cases	ND	Benign	AUS/ FLUS	FN/SFN	SM	Malignant
Jo[3]	2987	509 (17.0)	1792 (60)	101 (3.4)	298 (10)	71 (2.4)	216 (7.2)
Kim[14]	865	16 (1.8)	504 (58.3)	141 (16.3)	10 (1.2)	54 (6.2)	140 (16.2)
Bongiovanni[4]	250	40 (16)	166 (66.4)	28 (11.2)	6 (2.4)	5 (2)	5 (2)
Mondol[7]	1020	12 (1.2)	893 (87.5)	10 (1)	43 (4.2)	14 (1.4)	48 (4.7)
Present study	250	22 (8.8)	202 (80.8)	15 (6.0)	6 (2.4)	1 (0.4)	4 (1.6)

The number of cases in the AUS/FLUS category was 6% post Bethesda, lower than that reported by Kim and Bongiovanni,[4,14] but higher than Mondol.[7] This was basically due to the fact that any case showing even focal nuclear atypia was put in this category. A review done by Ohori NP[15] revealed a marked variability in the incidence (0.7%–18%) of use of this category.

The percentage of cases in our study that had a histological follow up was 19.6%. Surgical follow up rates have varied ranging from 11.8%[6] to 45.1%[16] with an average of 25% in different studies. The variable rates quoted in different studies could be explained by the different follow up times used. Patients' reporting to our center for FNAC have a choice of undergoing surgery in any of the service hospitals in the country, thus explaining the slightly lower than average histological follow up at our centers.

The proportion of malignant FNAs was the lowest in comparison to other studies.[3,4,7,14] The risk of malignancy for the different categories post TBSRTC as seen by histopathological correlation showed a lower rate of malignancy. Singh and Wang[10] suggest that atypia in a thyroid FNAC, other than having features suggestive of papillary carcinoma, is of unknown clinical significance and should be avoided because it causes confusion and provokes unnecessary anxiety for both patients and clinicians.

The advantage of TBSRTC is that it is systematic, and has achieved the goal of standardization and improving thyroid cytopathology reporting. However, the category of AUS/FLUS is the most controversial, due to its heterogeneity, leading to confusion among clinicians regarding management.[5]

Our study is limited by a small sample size, and that not all thyroid nodules had histologic correlation. A larger population sample with a rigorous cytopathology to histopathology correlation needs to be studied to accurately categorize the risk of malignancy for each Bethesda category in our population. Since the AUS/FLUS category did not correlate with higher risk of malignancy in our patients, stratification of these cases into low-risk and high-risk groups could help in better patient management.

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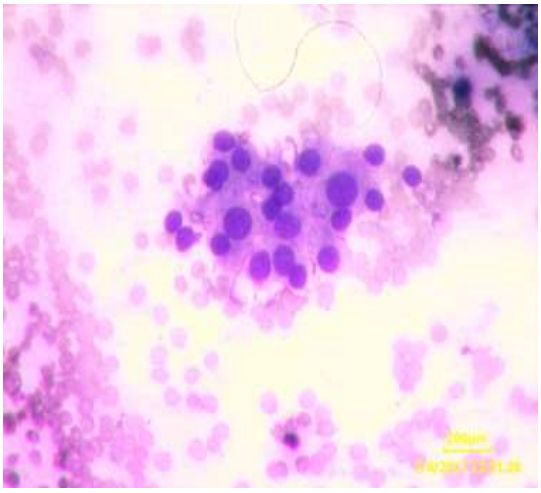


Figure 1.Follicular cell crowding and anisonucleosis (H&E 400x)

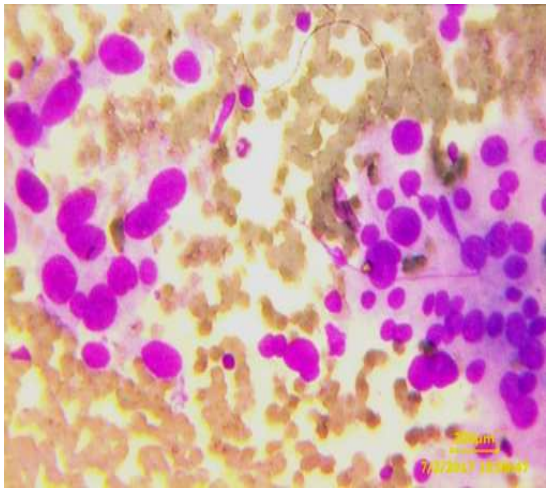
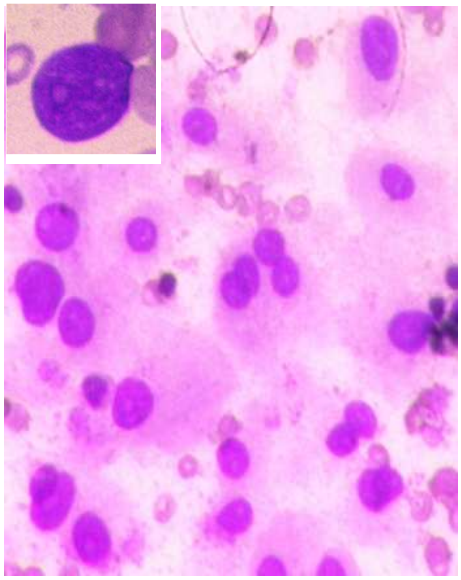


Figure 2.Prominent Hurthle Cell Change with Anisonucleosis (H&E 400x)



Inset: Single follicular cell with conspicuous nucleoli (H&E 1000x)

Figure 3.Group of Follicular Cells Showing Prominent Nucleoli (H&E 400x)

Conflict of Interest: None

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