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Original Research Article

Validity Assessment of 'The Bethesda System for Reporting Thyroid Cytopathology'

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ABSTRACT

Background: To keep uniformity and to achieve standardization of thyroid Cytopathology reporting NCI proposed 6 tiered diagnostic classification system named The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)
Aims: To assess the reproducibility and validity of the Bethesda system for reporting thyroid FNA
Material and Methods: The present study was prospectively undertaken at SMS Medical College, Jaipur, India between May 2012 to Oct. 2013, on thyroid FNA classifying them according to TBSRTC. The distribution and malignancy risk was assessed in all six categories along with sensitivity, specificity, predictive values and diagnostic accuracy of TBSRTC.
Results: In the present study total 1287 FNAC cases were studied, out of them 21.98% were Non diagnostic, 73.9% were benign, 0.7% were AUS, 1.5% were SFN/FN, 0.38% were SM and 1.3% were malignant. A total of 62 cases here followed up for histopathological examination. Risk of malignancy was 18.18% in Non diagnostic category, 2.6% in benign category, 0% in AUS category, 50% in SFN/FN, 50% in suspicious for malignancy and 100% in malignant category. Sensitivity was 85.7%, specificity, 95.2% positive predictive value 75%, negative predictive value 97.5% and diagnostic accuracy of test was 93.87%.
Conclusion: TBSRTC is a standardized system for thyroid FNA reporting having well established uniformity, thereby improving communication between cytopathologists, radiologists and clinicians. In this study Non diagnostic rates and benign rates were comparable with other studies; While AUS rate was lower than most studies. Malignancy risk for each Bethesda category was almost similar to other studies except AUS. Specificity and negative predictive value and diagnostic accuracy was higher than other studies. TBSRTC provides a uniform reporting system having high specificity and diagnostic accuracy.

Key words: Bethesda system thyroid, validity, fine needle aspiration, standardization.

INTRODUCTION

Fine needle aspiration (FNA) plays an essential role in evaluating thyroid nodules because of it's rapidity, lower cost, simplicity and safety. Thyroid FNA is the first line diagnostics test for preoperative evaluation of thyroid nodules reducing unnecessary thyroid surgeries for patients with being lesions and facilitative better management of malignant nodules. [1]

In the past due to lack of uniformity and standardization different pathologists used different terminologies creating confusion and making interpretation of cytological reports different for clinicians. So, definite clinical management of patient was biased.

To provide uniformity and to achieve standardization of thyroid FNA reporting, a6 tiered diagnostic classification system was proposed by NCI Thyroid Fine Needle Aspiration State of the Science Conference hosted by National Cancer Institute (NCI) in 2007 at Bethesda, Maryland, limited states. [2-4]

Non diagnostic/US: A smear was labeled non diagnostic/US having obscuring blood, air dried thick smears, inadequate cellularity having less than six groups of benign follicular cells each composed of ten follicular cells or having cyst with or without macrophages. Smear having abundant thick colloid and smear containing exclusively macrophages are never considered non diagnostic. Smear having significant cytological atypia never considered ND regardless of cellularity.

Benign: Smear having adequate cellularity comprising of varying proportion of colloid and benign follicular cells arranged in macrofollicles and sheets are labelled as benign e.g. Colloid nodule, Hashimoto's thyroiditis, Graves disease, Granulomatous thyroiditis and benign follicular nodule.

Atypia of Undetermined significance (AUS): Smears containing cells (Follicular, lymphoid) having nuclear and architectural atypia but not so marked as to report as SFN/FN or suspicious for malignant, labeled as AUS category. Smears having virtually exclusive population of hurthle cells are also kept in AUS category with no colloid or lymphocytes in background.

SFN/FN: Moderate to Hypercellular smears having nuclear crowding, microfollicle formation with scant to no colloid, labelled as SFN/FN. Aspirates with Cytomorphological features of hurthle cell neoplasm are also placed in this category.

Suspicious for malignancy: Smears having Cytomorphological features suggestive of papillary carcinoma of thyroid, medullary carcinoma of thyroid or lymphoma but insufficient for conclusive diagnosis of malignancy are kept in this category.

E.g.: Smears having sparse to moderate cellularity comprising spindloid cells or plasmacytoid cells with matrix (amyloid) in background classified as suspicious for medullary carcinoma of thyroid and smear having monomorphic small to medium lymphoid cells or sparse atypical lymphoid cells are kept in suspicious for lymphoma.

Malignant: Smears having Cytomorphological features conclusive for malignancy were placed in this category.

MATERIALS AND METHODS

The present study was undertaken in our department from May 2012 to Oct, 2013 to assess the validity of TBSRTC, assuming histopathology as gold standard.

Bongiovanni et al in their study on the met analysis showed high overall accuracy indicating that TBSRTC represents a reliable and valid reporting system for thyroid cytology. [5]

In the present study we prospectively collected thyroid FNA smears from 1287 patients and stained by Haematoxylin and Eosin and May Grunwald Geimsa stain. Each case was categorized than as per the current recommended Bethesda nomenclature. Histological follow up was available in 62 cases.

Follow up histology: We followed up 62 cases with histopathological examination (HPE) and cytological diagnoses according to TBSRTC. Thereafter we calculated malignancy risk for each category, sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of TBSRTC.

RESULTS

Out of total 1287 FNAC cases283 (21.98%) were Non diagnostic, 952 (73.97%) were benign, 10 cases (0.7%) were AUS, 20 cases (1.5%) were SFN/FN, 5 cases (0.38%) were suspicious for

malignant and 17 cases (1.32%) were malignant.

Preoperative FNA diagnoses of 62 cases with histological follow up had 11 cases as ND/US, 38 cases as benign, 4 cases each of AUS and SFN/FN, 2 cases as SM and 3 cases as malignant.

An FNA diagnosis according to TBSRTC was compared with diagnoses on HPE and malignancy risk was calculated for each category.

Among 11 cases which had FNA diagnoses as ND/US, 2 turned out to be malignant in HPE. Malignancy risk came out to be 18.18% in this category.

There were 38 cases which were diagnosed as benign on FNA in which 1 turned out to be malignant on HPE. So malignancy risk was 2.6% in this category.

4 cases were diagnosed as AUS, none of which was reported malignant in HPE. So the malignancy risk was 0% in this category.

Out of 4 cases diagnosed as SFN/FN two turned out malignant on HPE. Hence malignancy risk for this category was 50%.

2 cases were diagnosed as SM of which one was confirmed as malignant on HPE. The malignancy risk in this category was 50%.

There were malignant cases in FNA, all of which turned out to be malignant on HPE, confirming the malignancy risk as 100% in this category.

The cases diagnosed as benign in both cytology and histology were taken as true negative, while those diagnosed as malignant both in cytology and histology were taken as true positive. Those cases which were benign in cytology and malignant on histology were taken as false negative and cases malignant on cytology and benign on HPE were labeled as false positive.

In this study sensitivity to diagnose malignancy was 85.71%, specificity to rule out malignance was 95.23%, positive predictive value was 75%, negative predictive value was 97.56% and diagnostic accuracy was 93.87%. False positive rate to this study was 4.08% while false negative rate was 2%. We excluded ND/US cases from this statistical analysis.

In our study 1.32% FNA cases were malignant, while 0.38% were suspicious for malignancy and majority of cases were benign (73.97%). A significant number of cases (21.98%) formed the non diagnostic category.

The above table depicts the malignancy risk associated with different categories of TBSRTC after histopathological examination.

Table 1: Details Of Distribution of the Fnac Cases in This Study (n=1287)

S.N.	Diagnostic Category	Number of cases of each category	%
1	**Non Diagnostic**	283	21.98
2	**Benign**		
	• Colloid nodule	237	18.41
	• Colloid Goitre	178	13.83
	• Benign follicular nodule	192	14.91
	• Adenomatoid Nodule	39	3.03
	• Hashimoto's Thyroiditis	266	20.66
	• Granulomatous Thyroidits	06	0.4
	• Grave's Disease	34	2.6
3	**Atypia of Undertermined Significance**	10	0.7
4	**SFN/FN**		
	• SFN	06	0.4
	• FN	14	1.08
5	**Suspicious for malignancy (Suspicious for PCT)**	05	0.38
6	**Malignant**		
	• Papillary carcinoma of thyroid	12	0.8
	• Medullary carcinoma of thyroid	02	0.1
	• Poorly differentiated carcinoma	01	0.05
	• Non Hodgkin's Lymphoma (NHL)	01	0.05
	• Anaplastic Carcinoma	01	0.05
	TOTAL	**1287**	

Table 2: Comparison of pre-operative FNAC diagnosis with the diagnosis of histopathological examination after surgical resection and calculation of malignancy risk for each Bethesda category (n=62)

S.N.	Preoperative FNAC as per TBSRTC	Actual Diagnosis on HPE after surgical resection	Number of cases turned out to be malignant	Malignancy Risk
1	Non Diagnostic/ Unsatisfactory (n=11)	Follicular adenoma – (n=6)*PCT – (n=1) Adenomatoid/ Colloid Goitre – (n=3) Follicular carcinoma – (n=1)	2	18.18%
2	Benign (n=38)	Adenomatoid/ Colloid goiter – (n=31) Hashimoto's thyroiditis – (n=1) Follicular adenoma – (n=4) *PCT – (n=1) *FNUMP – (n=1)	1	2%
3	Atypia of Undetermined Significance (n=4)	Hashimoto's Thyroiditis – (n=1) Adenomatoid goiter – (n=2) Follicular adenoma – (n=1)	0	0%
4	SFN/FN (n=4)	Medullary carcinoma – (n=1) Follicular adenoma – (n=1) Follicular carcinoma – (n=1) *PCTUMP – (n=1)	2	50%
5	Suspicious for malignancy (n=5)	*PCT – (n=1) Hashimoto's Thyroiditis – (n=1)	1	50%
6	Malignant (n=3)	*PCT – (n=3)	3	100%

*PCT – Papillary carcinoma of Thyroid, FNUMP – Follicular Neoplasm of uncertain malignant potential, PCTUMP – Papillary carcinoma of thyroid of uncertain malignant potential

Table 3: Comparison of % of Distribution of FNA Diagnoses of Present Study with Previous Studies

	ND/US	Benign	AUS	SFN/FN AFLUS	Suspicious for malignant	Malignant
Present Study	21.98	73.97	0.7	0.5	o.38	1.2
Yassa et al [6]	7	66	4	9	9	5
Yang et al [7]	10.4	64.6	3.2	11.6	2.6	7.6
Theoharis et al [8]	11.1	73.8	3	5.5	1.4	5.2
Jo et al [9]	18.6	59	3.7	9,7	2.3	7
Renshaw et al [10]	24	54	7.7	8.6	1.9	4.2
Juing Wu et al [11]	20	39	27.2	8.4	2.6	2.7
Santosh Kumar Mondel et al [12]	1.2	87.5	1	4.2	1.4	4.7
Mehra et al [13]	7.2	80	4.9	2.2	3.6	2.2
Naz et al [14]	4.7	76.3	12.7	2.1	3.4	0.8

Table 4: Comparision of the % of Malignancy Risk of Present Study with Previous Studies

	ND/US	Benign	AUS	SFN/FN AFLUS	Suspicious for malignant	Malignant
Present Study	18.1	2	0	50	50	100
Yassa et al [6]	10	0.3	24	28	60	97
Yang et al [7]	10.7	0.7	19.2	32.2	64.8	98.4
Theoharis et al [8]	9	2	6	14	53	97
Jo et al [9]	8.9	1.1	17	25.4	70	98.1
Renshaw et al [10]	20	2	25	30	97.3	100
Juing Wu et al [11]	14	9.5	22	27	67	100
Santosh Kumar Mondel et al [12]	0	4.5	20	30.6	75	97.8
Mehra et al [13]	0	1.66	9.09	20	37.5	80
Naz et al [14]	0	11.1	33.3	25	100	100

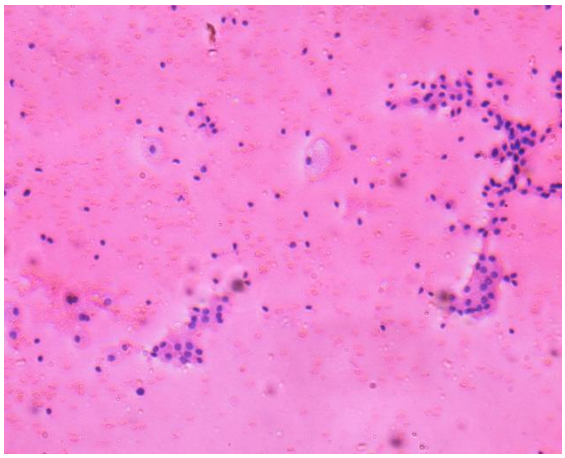


Fig.1: BENIGN. Benign follicular cells have delicate cytoplasm with ill-defined borders and evenly spaced uniform nuclei with abundant colloid in the background, and scattered cyst macrophages.

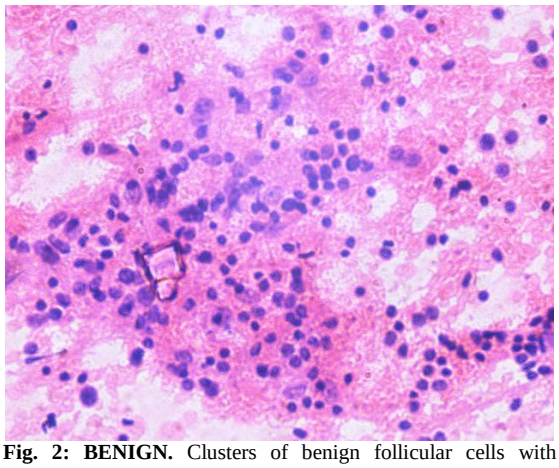


Fig. 2: BENIGN. Clusters of benign follicular cells with anisonucleosis and numerous dispersed lymphocytes in the background.

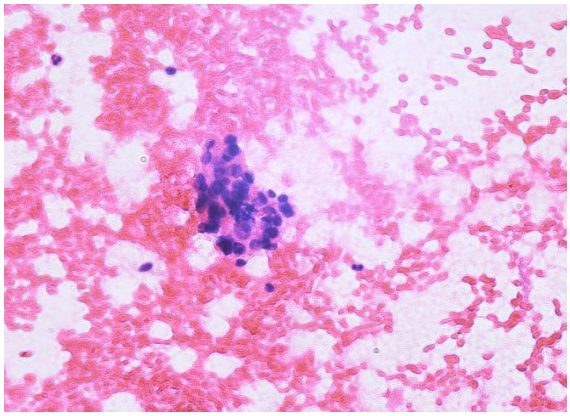
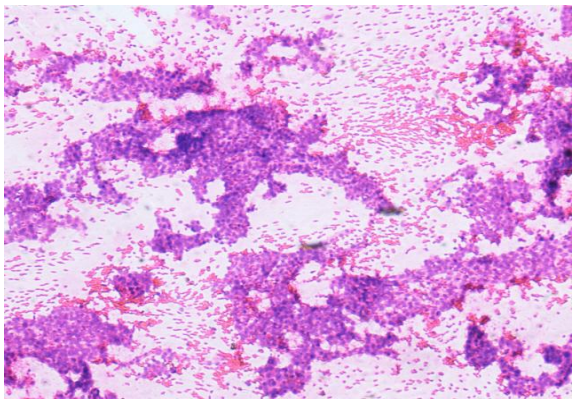
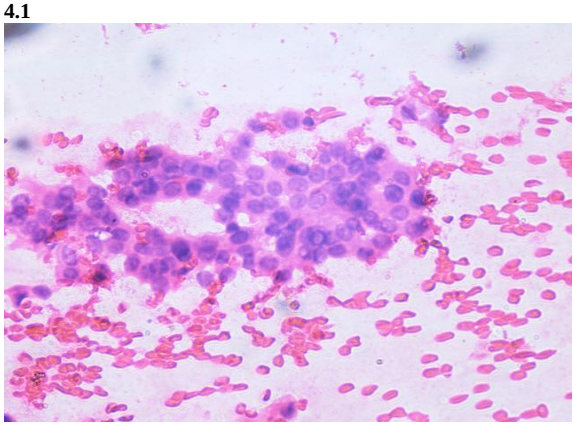


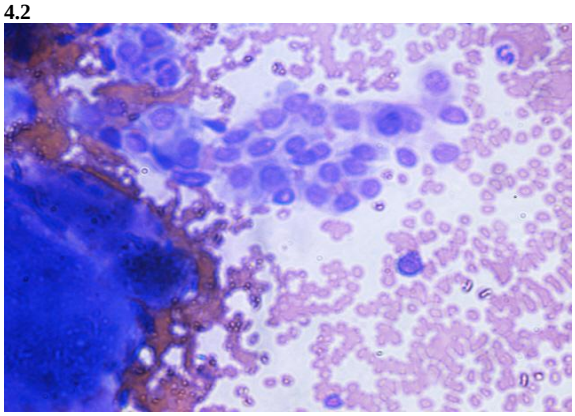
Fig. 3: AUS. Minor population of follicular cells showing nuclear enlargement and prominent nucleoli at places.



4.1



4.2



4.3

Fig. 4.1, 4.2, 4.3: MALIGNANT .cellular smears in flat sheets and papillary fragments, with a syncytial like appearance. Higher magnification shows frequent INCIs, nuclear grooves and powdery chromatin. Papillary thyroid carcinoma.

DISCUSSION

We compared the results of our study with studies done earlier. [6-14] Table 3 shows comparison of distribution of cases among various categories in present study with previous studies. It was seen that ND/US and benign rate were higher and AUS rate was lower in our institution when compared with most other studies. FNAC is performed as a blind procedure and were not US guided leading to ND/US smears. Despite being a tertiary level referral institution patients also came directly, so a large number of general population was encountered in our study having benign lesions while most other studies dealt with only referred cases which were not exactly representative of general population. FNA diagnoses according to TBSRTC were compared with diagnoses on HPE and malignancy risk was calculated for each category. Table 4 shows comparison of risk of malignancy for various bethesda categories in present study with other studies.

Malignancy risk in Non diagnostic category was high (18.18%) in our study because in our sample non diagnostic rate was also high. It was similar to the study of Renshaw et al. In benign category, malignancy risk was 2.6% which was similar to TBSRTC guidelines and all other studies.

We had no case of AUS in our study. TBSRTC guidelines recommend this entity to be kept between 5-15%. In a very recent study it was concluded the rates of AUS category should not exceed the recommended target of 7% as the AUS rates and the malignant outcomes are inversely related. The higher a cytopathologists AUS rates, the lower is the rate of malignancy for that AUS group. [15] In our study the number of AUS cases was much lower than most studies.

In SFN/FN category malignancy risk was higher in our study (50%) than TBSRTC guidelines (15-30%).

In Suspicious for malignant category the malignancy risk was 50%. It was almost similar to other studies and TBSRTC guidelines (60-75%).

In malignant category-malignancy risk was 100% which was similar to all other studies and TBSRTC guidelines (97-99%)

In this study following statistical values were obtained:

Sensitivity (85.71%), Specificity (95.23%), Positive predictive value (75%), negative predictive value (97.56%) and diagnostic accuracy was (93.87%). False positive rate was (4.08%) and false negative rate was (2%).

These statistical values were comparable and similar to all other studies.

CONCLUSION

TBSRTC provides uniform reporting system for thyroid FNA and has high specificity. The easy reproducibility with a universal terminology can help in establishing a better communication among cytopathologists, endocrinologists, surgeons, radiologists and other health care providers who work at the same centre. The inter laboratory consensus leads to more consistent management approach. [16]

This system directly confers the risk of malignancy in each category which in turn prompts the recommended clinical management of that category; thus establishing an excellent clinico-pathological correlation.

After the publication of TBSRTC in 2009 the American Thyroid Association revised its clinical guidelines for the management of thyroid lesions. [17] Hence, the implementation of TBSRTC in Thyroid FNA can play a pivotal role in the management of patients with thyroid nodules by providing clinicians with a clear and comprehensible cytopathology reports.

REFERENCES

1. Cibas ES. Fine needle aspiration in the work up of thyroid nodules. Otolarynagol clin North Am 2010; 43: 257-71.
2. Zubair W. Baloch, Virginia A. Livolsi, Sye L. Asa, Juan Rasai, Maria J Merino, Gregory Randolph, Philippe Vielh, Richard M. Demay, Mary K. Sidawy and William J. Frable. Diagnostic Terminology and Morphologic Criteria for cytologic Diagnosis of Thyroid lesions: A synopsis of the NCI Thyroid FNA State of the Science Conference. Diag. Cytopathol. 2008; 6: 425-457
3. Ali SZ, Libas E5. The Bethesda System for reporting thyroid Cytopathology. Thyroid 2009; 19: 1159-1165.
4. Cibas E5, Ali SZ, The Bethesda system for reporting Thyroid Cytopathology. Am. J. Clin Pathol 2009; 132: 658-665
5. Bongiovanni M, Spitale A, Faquin William C, Mazzuchelli L, Baloch Zuber W: The Bethesda system for reporting Thyroid Cytopathology: A Meta analysis.Acta Cytologica 2012; 56: 333-339.
6. Yassa L, Cibas ES, Benson CB, Et al. Long term assessment of multidisciplinary approach to thyroid nodule diagnostic evaluation cancer 2007; 111; 508-516
7. Yang J. Schnadig V, Logrono R, Wasserman PG Fine-Needle aspiration of thyroid nodles; a study of 4703 patients with histologic and clinical correlation. Cancer 2007; 111; 305-15.
8. Theohasis CG, Schofield KM, Hammers L, Udelsman R, Chhieng DC, The Bethesda thyroid fine needle aspiration classification system; year 1 at an academic institution. Thyroid 2009; 19: 1215-1223
9. Jo VY, Stelow EB, Dustin SM, Hanley KZ: Malignancy risk for fine needle aspiration of Thyroid lesions according to the Bethesda system for reporting thyroid cythopathology. Am J clin pathol 2010; 134-: 450-456.
10. Renshaw A A: Non diagnostic rates for the thyroid fine needle aspiration

are negatively correlated with positive for malignancy rates.Act a cytol 2011; 55 38-41.
11. Her –Juing wu H, Rose C, Elsheikh TM: The Bethesda system for reporting thyroid cytpathology: an experience of 1382 cases in a community practice setting with the implication for risk of neoplasm and risk of malignancy. Diag Cytopathol 2012; 40: 399-403
12. Santosh Kumar Mondel. The Bethesda system of reporting thyroid Fine-needle aspirates: a cytologic study with histologic follow up.Journal of cytology 2013; Vol 30, issue 2.
13. Payal Mehara, Anand Kumar Verma: Thyroid Cytopathology Reporting by the Bethesda System; A Two – Year Prospective Study in an Academic Institution. Pathology Research international Volume 2015, Article ID 240505.
14. Samreen Naz, Atif Ali Hashmi, Amna Khurshid, Naveen Faridi, Muhammad Muzzammi Edhi, Anwar Kamal and Mehmood Khan. Diagnostic accuracy of Bethesda system for reporting thyroid Cytopathology: an institutional perspective. International Archives of Medicine 2014, 7:46.
15. Van der Laan PA, Krane JF, Cibas ES. The frequency of "atypia of undetermined significance" interpretations for thyroid fine needle aspirations is negatively correlated with histlogically proven malignant outcomes. Act a cytol 2011; 55: 512-17
16. Tejinder Singh Bhasin: Reproducibility of the Bethesda system for Reporting Thyroid cytopathology: A multi centre study with review of literature. Journal of clinical and diagnostic Research. 2013; Vol 7 (6): 1051 -54.
17. Syed Z Ali. Thyroid cyst pathology: Bethesda and Beyond. Acta Cytologica. 2011; 55: 4-12.

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