Original Article

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Reproducibility and Utility of Implementing the Bethesda System for Reporting Thyroid FNAC Smears

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Abstract

Introduction: Thyroid Fine Needle Aspiration (FNA) has been widely used as a first-line investigation to assess thyroid nodules, as it is rapid, cost effective, safe and reliable. To bring uniformity and standardization in thyroid cytology reporting, "The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC) was introduced and it is gaining acceptance. This study has been undertaken to evaluate the reproducibility using TBSRTC system while reporting thyroid FNACs and to find out the utility of Bethesda system after correlating with the histopathology. *Methods:* A retrospective study was conducted in which 506 cases of thyroid aspirates were reclassified according to TBSRTC in to six categories by two cytologists separately and reproducibility of the system was assessed. In 97 cases histopathological correlation was available and risk of malignancy in all these TBSRTC categories was calculated. *Results:* Category wise distribution of aspirates was non diagnostic (ND) 1.38%, Benign(BN) 88.15%, Follicular neoplasm (FN) 2.38%, follicular lesion of uncertain significance(FLUS) 2.96 %, suspicious of malignancy(SM) 1.38% and malignant category (3.75%). Overall Percentage of agreement between the two cytologists was 97.5% and rate of disagreement was more in follicular lesion of undetermined significance, follicular neoplasm and suspicious category. On cytohistological correlation, malignancy rate in different categories are ND 0%, BN 1.4%, FLUS 20%, FN 28.6%, SM 60% and MGT 100%. *Conclusions:* It was observed that standardized nomenclature of the Bethesda system has brought much needed clarity in thyroid FNAC reporting. Substantial interobserver agreement was found for thyroid cytological lesions using Bethesda reporting. Along with MGT category, the FLUS, FN and SM categories carry higher malignancy risk.

Keywords: Thyroid FNAC; Bethesda System; Reproducibility; Malignancy Risk.

Introduction

Thyroid nodule is a common clinical condition and nearly 85 to 90% of them are benign lesions[1,2]. Thyroid FNA has been widely used as a first-line investigation to assess thyroid nodules, as it is rapid, cost effective, safe and reliable [3]. It is important that cytology report is unambiguous and clinically useful. In reporting thyroid FNAC smears terminologies vary significantly from one laboratory to other, sometimes from one cytologist to other in the same institution. This is creating confusion in some cases and has become an obstacle in sharing information amongst different institutions [4,5]. To address this issue of terminology related to thyroid cytology, National Cancer Institute (NCI) hosted "NCI thyroid FNA state of the science conference" which led to the formation of "**T**he **B**ethesda **S**ystem for **R**eporting **T**hyroid **C**ytopathology" (TBSRTC) [6]. The TBSRTC system is presently being widely used in US and several European Countries, and in India also it is gaining acceptance.

This study has been undertaken to evaluate the reproducibility using TBSRTC system while reporting thyroid FNACs and to find out the utility of Bethesda system after correlating with the histopathology.

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Materials and Methods

Details of all the thyroid FNAC cases done from Jan 2011 to December 2015 in a tertiary care hospital of south India were retrieved from archives of cytology section. Two experienced cytologists who are having more than five years experience in cytology reporting and self learned the different aspects of TBRTC, reviewed the slides. All the clinical details and available radiological and thyroid function test results which were noted down in the original cytology request forms were provided to them. However, they were not aware of the original cytology diagnosis. The FNA smears were reclassified in a double blinded fashion into six categories as per TBSRTC. Study was conducted after getting clearance from institute ethics committee.

The Six Categories are

a. Non diagnostic(ND); Smears were considered as nondiagnostic when a thyroid FNA sample failed to fulfill the recommended criteria for adequacy which are presence of a minimum of six groups of well-visualized follicular cells, with at least ten cells per group, preferably on a single slide, absence of colloid or only blood.

b. Benign (BN); Lesions were classified into this category if the smears showed features suggestive of colloid nodule, multinodular goiter, ,thyroiditis, as well as if the aspirate showed benign follicular cells only.

c. Follicular lesion of undetermined significance (FLUS); smears that contain cells with architectural and/or nuclear atypia that is not sufficient to be classified as suspicious for a follicular neoplasm or suspicious for a malignancy.

d. Follicular neoplasm(FN)/Suspicious for follicular neoplasm(SFN); Lesions were classified into this category if they were having high follicular cellularity with predominant microfollicle formations, scant colloid.Lesions exhibiting Hurthle cells predominantly were also included.

e. Suspicious for malignancy(SM); Smears in this category were mainly cellular with crowded cell groups exhibiting nuclear and cytoplasmic pleomorphism with some occasional single atypical cells. In the context of suspicious papillary carcinoma rare presence of nuclear enlargement, grooves, overlapping and/or pseudoinclusions along with thick colloid were considered suspicious.

f. Malignant (MGT); Lesions were classified into this category if they were frankly malignant with type specification [8].

The reproducibility of the system in implementing was evaluated. This was checked by percentage agreement. The cases in which disagreement was seen were reviewed again by both the cytologists, discussed and consensus was reached.

Out of 506 FNAC cases, 97 patients undergone thyroidectomy in our institute and histopathological correlation was available. We compared the diagnoses offered in FNAC as per the Bethesda system with the final histopathologic examination (HPE).We have calculated the risk of malignancy in each Bethesda category.

Results

Of the 506 cases which were reclassified according to TBSRC, 7 (1.38%) were non diagnostic. Most of the cases in this study were reclassified as benign lesions 446 (88.15%), along with 12 (2.38%) FLUS, 15 (2.96%) SFN, 7 (1.38 %) SM, and 19 (3.75%) malignant (Table 1).

On initial work up, an agreement was observed in 493 cases (97.5%) between two cytologists. The experts disagreed in 13 (2.6%) cases.(where 1 cytologist did not agree with the other) [Table 2]. There was a complete agreement on seven ND cases .Similarly all malignant cases were placed in malignant category by both the cytologists. Most of the cases of benign lesions were categorized as benign only. Disagreement was noted more in FLUS, FN or suspicious of malignant categories.

All these discordant cases were originally diagnosed as hyperplastic nodular goitre, multi-nodular goiter, follicular neoplasm or as adenomatous goitre. After discussion and review of slides, consensus was reached on these cases.

Surgical resection of thyroid was done in 97 cases and histopathological correlation was available. There were 12 cases of malignancy (rate of malignancy in resected specimens being 12.4%), 11 follicular adenomas,2 hurthle cell adenomas and 72 benign lesions.

Discussion

Lack of uniformity is a big hindrance in interpreting the reports of thyroid FNA. Institutional, personalized

Table 1: Category wise classification of thyroid aspirates.

Sl. No	Bethesda Category	No. of cases	Percentage
1	Non-doagnostic	7	1.38
2	Benign	446	88.15
	a. Colloid goitre / Nodular goitre	288	
	b. Hashimoto's/ lymphotic Thyroiditis	151	
	c. Granulomatous Thyroiditis	1	
	d. Suppurative thyroiditis	4	
	e. Graves disease	2	
3	FLUS	12	2.38
4	FN	15	2.96
	a. Follicular Neoplasm	13	
	b. Hurthle cell Neoplasm	2	
5	SM	7	1.38
	a. Suspicious of papillary carcinoma	6	
	b. Suspicious Medullary carcinoma	1	
6	Malignant	19	3.75
	a. Papillary carcinoma	16	
	b. Medullary carcinoma	2	
	c. Anaplastic carcinoma	1	
	Total	506	100

Table 2: Comparison of reclassified lesions according to TBSRTC between two cytologists

Category	ND	B	FLUS	FN	SM	M	Total
Cytologist 1	7	443	14	18	5	19	506
Cytologist 2	7	450	11	13	6	19	506
agreement	100%	98.45%	83.3%	86.7%	86.6%	100%	

Table 3: Distribution of lesions in resected thyroids and rate of malignancy in different Bethesda categories

Bethesda Category	HPE correlation available (n=97)	HPE Diagnosis	rate of Malignancy
ND	4	Nodular Goitre : 3 Hashimotos thyroiditis : 1	0%
Benign	71	Nodular Goitre 50 Hashimotos thyroiditis : 15 Follicular adenoma : 5 Papillary Ca: 1	1.4%
FLUS	5	Nodular Goitre : 1 Hashimotos thyroiditis : 1 Follicular adenoma : 1 Hurthle cell adenoma : 1 Papillary Ca: 1	20%
FN	7	Follicular adenoma : 4 Hurthle cell adenoma : 1 Papillary Ca: 1 Follicular Ca : 1	28.6%
SM	5	Hashimotos thyroiditis : 1 Follicular adenoma : 1 Papillary Ca: 2 Follicular variant of papillaryCa : 1	60%
Malignant	5	Papillary Ca : 4 Medullary Ca : 1	100%

and descriptive terminologies without proper categorization is leading to confusion in the minds of treating physicians. TBSRTC system was introduced after the Bethesda meeting of cytopathologists, surgical pathologists, endocrinologists, radiologists and surgeons to put in place, a universal reporting system through which cytologists and physicians could understand each other and could help in predicting the prognosis by estimating the malignant potential of the individual category [8, 9,10].

In the present study, an attempt was made to reclassify the 506 cases according to the new proposed six tier diagnostic classification system in reporting thyroid FNA results. Unsatisfactory/ND was 1.38 % cases, malignancy was 3.75%, 88.5% BN, 1.38% FLUS, FN, 2.96% and 3.75 % positive for malignancy. Benign category was maximum in our study similar to the other studies (Table 4). However, percentage of BN is much higher accounting for 88% in our study may be because of the fact that along with the referral cases, our hospital caters to the needs of many direct hospital visitors without reference. Like in general population, benign lesions were maximum in our set up. Percentage of FLUS category was less as per TBSRT recommendations. Inter observer disagreement was only 2.5% overall and most of these cases belonged to FLUS, FN or SM categories (more than 10-15%). Similar observation was made by Bhasin et al [15] and Kocjan et al [16]. The malignancy risk for the different categories in our study, as seen by follow up HPE, has corroborated well with the implied risks mentioned in the Bethesda System and also with the studies of Jo *et al*., Yang *et al*., Mondal et al., and Pratheema et al. The malignancy risk for the non diagnostic category is 0%, probably because of low percentage of cases in this category. Similar observation was made by Mondal et al. The malignancy risk for the FLUS category was 20% and risk of malignancy was much higher for SM and MGT categories, similar to the observations of various other studies [Table 5]. The main drawback of present study is that histopathological correlation was available in only 97 cases.

Table 4: Distribution of various thyroid Bethesda categories in different studies(in percentage)

Diagnostic category	Yassa et al[11]	Yang et al[12]	Mondal et al[13]	Nayer and Ivanovic[14]	Present study
ND	7	10.4	1.2	5	1.38
BN	66	64.6	87.5	64	88.15
FLUS	4	3.2	1	18	2.38
FN	9	11.6	4.2	6	2.96
SM	9	2.6	1.4	2	1.38
MGT	5	7.6	4.7	5	3.75

Table 5: Comparison of malignancy rate (percentage) in follow up histopathological study in different published studies

Diagnostic category	Jo et a[17]]	Yang et al	Mondal et al	Pratheema et al[18]	Present Study
ND	8.9	10.7	0	33.3	0
BN	1.1	0.7	4.5	2.1	1.4
FLUS	17	19.2	20	50	20
FN	25.4	32.2	30.6	25	28.6
SM	70	64.8	75	67	60
MGT	98.1	98.4	97.8	100	100

Conclusion

It was observed that standardized nomenclature of the Bethesda system is more systematic and brought much needed clarity in thyroid FNAC reporting. Substantial interobserver agreement was found for thyroid cytological lesions using Bethesda reporting criteria in this study which is an indication that it can be easily introduced and cytology reports can be standardized. Along with MGT category, the FLUS, FN and SM categories carry higher malignancy risk. Close follow up of the patients and surgical intervention option has to be considered in FLUS, FN and SM categories. However, a prospective study with large number of cases for cytohistopathological correlation may be needed to improve our understanding of these TBSRTC categories.

References

1. Sakorafas GH. Thyroid nodules; interpretation and importance of fine needle aspiration (FNA) for the clinician – Practical considerations. Surg Oncol 2010; 19:130 9.
2. Redman R, Yoder BJ, Massoll NA. Perceptions of diagnostic terminology and cytopathologic reporting of fine-needle aspiration biopsies of thyroid nodules: a survey of clinicians and pathologists. Thyroid. 2006; 16:1003-8.
3. Baqqa PK, Mahajan NC. Fine needle aspiration cytology of thyroid swelling: how useful and accurate is it? Indian J Cancer 2010; 47:437-42.
4. Cibas ES. Fine-needle aspiration in the workup of thyroid nodules.Otolaryngol Clin North Am 2010; 43:257-71.
5. Park JH, Kim HK, Kang SW, Jeong JJ, Nam KH,

Chung WY, et-al. Second opinion in thyroid fine-needle aspiration biopsy by the Bethesda System. Endocr J 2012; 59:205-12.

6. Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, *et al*. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A synopsis of the national cancer institute thyroid fine needle aspiration state of the science conference. Diagn Cytopathol 2008; 36: 425-37.
8. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Am J Clin Pathol 2009; 132: 658-65.
9. Richmond BK, O'Brien BA, Mangano W, Thompson S, Kemper S. The impact of implementation of the bethesda system for reporting thyroid cytopathology on the surgical treatment of thyroid nodules. Am Surg 2012; 78:706-10.
10. Layfield LJ, Morton MJ, Cramer HM, Hirschowitz S. Implications of the proposed thyroid fine needle aspiration category of "follicular lesion of undetermined significance": A five year multi institutional analysis. Diagn Cytopathol 2009; 37:710-4.
11. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA,*et al*. Long term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer 2007; 111:508-16.
12. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine needle aspiration of thyroid nodules: A study of 4703 patients with histologic and clinical correlations. Cancer 2007; 111:306-15.
13. Mondal SK, Sinha S, Basak B, Roy DN,Sinha SK. The Bethesda system for reporting thyroid fine needle aspirates:A cytologic study with histologic follow-up. J Cytol 2013; 30:94-9.
14. Nayar R, Ivanovic M. The indeterminate thyroid fine needle aspiration: Experience from an academic center using terminology similar to that proposed in the 2007 national cancer institute thyroid fine needle aspiration state of the science conference. Cancer 2009; 117:195 202.
15. Bhasin TS,Mannan R,Manjari M,Mehra M,Sekhon AKG,Chandey M et al.Reproducibility of 'The Bethesda System for reporting Thyroid Cytopathology':A MultiCenter Study with Review of the Literature.JCDR 2013; 7:1051-4.
16. Kocjan G, Chandra A, Cross PA, Giles T, Johnson SJ, Stephenson TJ, et-al. The interobserver reproducibility of thyroid fine-needle aspiration using the UK Royal College of Pathologists' classification system. Am J Clin Pathol 2011; 135:852-9.
17. 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 cytopathology. Am J Clin Pathol 2010; 134:450 6.
18. Prathima S, Suresh TN, Harendra Kumar ML, Bhaskaran A. Impact of the Bethesda System in Reporting Thyroid Cytopathology. Thyroid Res Pract 2016; 13:9-14.