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RESEARCH ARTICLE

THE BETHESDA SYSTEM FOR REPORTING THYROID FINE NEEDLE ASPIRATES IN TERTIARY CARE CENTRE

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ABSTRACT

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has put an effort to overcome personalized usage of descriptive terminologies in thyroid aspiration smears.

Aims: The objective of this study was to interpret thyroid cytology by TBSRTC, to look for distribution of diagnostic categories and subcategories and to correlate the cytopathology with histopathology.

Material and Method: This was 11 years retrospective study of 114 fine needle aspirations (FNA) of thyroid swelling.

Results: An overall sensitivity of 80%, specificity of 91.86%, positive predictive valve of 92.85%, negative predictive valve of 97.46%, and efficiency of the study was 91.22%.

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INTRODUCTION

Fine needle aspiration cytology (FNAC) is considered as the first line investigation part from other investigations like ultrasonography (USG), thyroid function test, thyroid scan, and antibody levels for the primary evaluation of the patients (Caruso and Mazzaferri, 1991). It effectively distinguish thyroid lesions suitable for surgical resection with those that can be managed conservatively (Ali and Cibas, 2011). FNAC being minimally invasive and cost effective is extremely useful in reducing unnecessary surgery for with benign disease. However, FNAC interpretation suffers from personalized usage of descriptive terminologies (Garg *et al*., 2015). In addition, there was never an effective linkage between the clinical management plans and thyroid FNA reporting, thus undermining the clinical utility of cytopathologic diagnosis. The Bethesda System for Reporting Thyroid Cytology (TBSRTC) has six distant diagnostic categories (Table 1) and is constructed on the concept of the probability of finding malignancy in each diagnostic category. Each category has an implied risk of malignancy which ranges from 0% to 3% for the benign category to virtually 100% for the malignant category (Table 2).

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Those aspirates that fall between benign and malignant were considered in AUS/FLUS, SFN/ H"urthle cell neoplasm, and SFM. As a function of these risk associations, individual category is linked to evidence based clinical management plans.

Aim and Objective

This was retrospective study, was to interpret thyroid cytology smears by TBSRTC into various diagnostic categories, to determine distribution of diagnostic categories and subcategories, conveying brief management plan to clinicians and its correlation with histopathology.

MATERIALS AND METHODS

The study has been conducted in department of pathology, Pt. J.N.M. Memorial medical College, Raipur (C.G.) from the duration of 2006 to 2016 (11 years). This study was approved by ethical commette. 1150 total number of fine needle aspiration performed from thyroid swelling during this period but 114 cases of thyroid swelling was review retrospectively reclassified thyroid fine-needle aspiration into the Bethesda System for Reporting Thyroid Cytopathology nomenclature. Clinical details, histological slides and blocks were retrieved and reviewed. Immunohistochemisty (IHC) done, whenever required.

Table 1. The Bethesda System for Reporting Cytopathology: Diagnostic categories

I	Non diagnostic or Unsatisfactory Cyst fluid only, Virtually acellular smear, Other (obscuring blood, clotting artefact ect.)
II	Benign Consistent with a benign follicular nodule (includes adenomatous nodule, colloid nodule ect.) Consistent with lymphocytic(Hashimoto) thyroiditis in proper clinical context. Consistent with granulomatous(sub acute) thyroiditis and Others
III	Atypic of Undetermined significance/ Follicular lesion of Undetermined significance(AUS/FLUS)
IV	Follicular neoplasm or suspicious for a follicular neoplasm(SFN) Specify if Hurtle cell (oncocytic) type
V	Suspicious for malignancy (SFM) Suspicious for papillary carcinoma Suspicious for medullary carcinoma Suspicious for metastatic carcinoma Suspicious for lymphoma
VI	Malignant Papillary thyroid carcinoma Poorly differentiated carcinoma Medullary thyroid carcinoma Undifferentiated(anaplastic) carcinoma Squamous cell carcinoma Metastatic carcinoma Non Hodgkin lymphoma and Others

Table 2. TBSRTC: Implied risk of malignancy and recommended management

Diagnostic Category	Risk of malignancy in(%)	Management plana
I	1 - 4	Repeat FNA with ultrasound guidance
II	0 - 3	Clinical follow up
III	5 - 15b	Repeat FNA
IV	15 - 30	Surgical lobectomy
V	60 - 75	Surgical lobectomy Or Near total thyroidectomy c
VI	97 - 99	Near total thyroidectomy c

a) Actual management may depend on other factors (e.g. clinical and sonographic) besides the FNA interpretation.
b) Estimate extrapolated from histopathologic data from patients with " repeated atypicals".
c) In case of " suspicious for metastatic tumour" or a " malignant" interpretation indicating metastatic tumour rather than a primary thyroid malignancy, surgery may not be indicated.

Table 3. Cytological/histopathological diagnosis correlation.

Cytodiagnosis	no of cases	Benign Histodiagnosis	no of cases	Malignant Histodiagnosis	no of cases
ND/UNS	2	Colloid goitre	1	Papillary carcinoma	1
Benign	54	Goitre	10	Papillary carcinoma	1
		Colloid goitre	22	Medullary carcinoma	1
		colloid goitre with cystic degenerative changes	9		
		Multinodular goitre	7		
			2		
		Colloid cyst	2		
		Lymphocytic thyroiditis Hashimoto thyroiditis	2		
AUS/FLUS	10	Colloid goitre	3	Papillary carcinoma	1
		Multinodular goitre	5		
		Follicular adenoma	1		
FN/SFN	20	Goitre	2	Follicular carcinoma	3
		Colloid goitre with cystic degenerative changes	2	Papillary carcinoma	3
		Follicular adenoma	10		
SFM	6		1	Papillary carcinoma	3
		Multinodular goitre		Follicular carcinoma	1
		Follicular adenoma	1		
Malignant	22		0	Papillary carcinoma	18
				Follicular carcinoma	1
				Medullary carcinoma	2
				Anaplastic carcinoma	1
Total no of cases	114		79		35

ND/UNS = non diagnostic/ unsatisfactory; AUS/FLUS = atypic of undetermined significance/Follicular lesion of undetermined significance; FN/SFN =follicular neoplasm/suspected for a follicular neoplasm; and SFM= suspected for malignancy.

RESULTS

FNA was performed for 1150 thyroid swelling mean age, of 34.48 years with range of 15 to 73 years. Most of the patients was outnumbers female, female to male ratio was 3:1.

All 114 cases were processed with conventional preparation. The cytological diagnoses were classified according to the diagnostic categories of TBSRTC 02 (1.75%) cases, 54 (47.36%) cases, 10 (8.77%) cases, 20 (17.54%) cases 06 (5.26%) cases and 22 (19.29%) were reclassified under

category I, category II, category III, category IV, category V and category VI respectively. [Table 3].

Category I: The totals of 2 (1.75%) cases were diagnosed under non diagnostic or unsatisfactory category in which colloid goitre and papillary carcinoma was reported each on histological finding respectively.

Category II: It included most of the study cases with 54(47.36%) cases. It consists of cases consistent with 52(45.61%) cases were benign lesions in which colloid goitre, goitre, colloid goitre with cystic degeneration, multinodular goitre and lymphocytic thyroiditis were diagnosed 22, 10, 9, 7, 3 respectively. Colloid cyst, hashimoto thyroiditis was reported 2 case each. The total of 2 cases was diagnosed as malignant lesions, papillary carcinoma, medullary carcinoma each.

Category III: It includes lesions which were indefinite for benign or malignant. The totals of 10 cases were reported, it consist of the cases consistent with 9 cases were benign lesion such as multi nodular goitre, colloid goitre, follicular adenoma, 5, 3, 1, respectively. Single case was reported papillary carcinoma on histology.

Category VI: The totals of 20 cases were reported, 14 were benign lesions and 6 were malignant lesions on histology. Out of benign lesions, follicular adenoma was 10 cases, and goitre, colloid goitre with cystic degeneration was reported 2 cases each. Malignant lesions were diagnosed as follicular carcinoma, papillary carcinoma 3 each.

Category V: It includes 6 lesions, 2 were reported benign lesions under with multi nodular goitre and follicular adenoma each case.

The total of 4 cases turned out to be malignant lesions, in which papillary carcinoma, follicular carcinoma were diagnosed 3, 1, respectively on histology.

Category VI: It includes second most common diagnosis 22 cases, underwhich papillary carcinoma, medullary carcinoma, 18, 4 and follicular carcinoma and anaplastic carcinoma 1each on histology. Cyto-Histological correlation was 100%.

Of 114 cases, follicular variant of papillary carcinoma was most common malignant tumor that constitutes 24 cases. Youngest patient was 15 years and oldest patient was 73 years in male. Youngest patient was 16 years and oldest patient was 71 years in female. Incidence of malignancy was observed in female: male 1.4:1. Medullary carcinoma was second most common tumor followed by follicular carcinoma and anaplastic carcinoma, with nodal metastasis observed in 4 cases. Medullary carcinoma of thyroid was confirmed IHC stain, showed strong positivity for calcitonin and thyroglobin. Of the 114 cases, cytological and histological diagnosis correlation was done. [Table 4]. 79 cases were diagnosed as benign, 35 cases were diagnosed malignant on histology. Category VII of the total 22 cases, cyto-histological diagnosis correlation was 100%. An overall sensitivity of 80%, specificity of 91.86%, positive predictive value 92.85%, negative predictive 97.46% of study, and efficiency of study was 91.22%.

DISCUSSION

This study shows the experience of 11 years in reporting thyroid aspirations by TBSRTC. TBSRTC recommend avoiding surgery and go for conservative management for ND/UNS, benign and AUS/FLUS categories and excision of

Table 4. Cytological/histopathological correlation with benign and malignant cases

Cytodiagnosis	No. of cases	Benign Histodiagnosis no. of cases	(%)	Malignant Histodiagnosis no. of cases	(%)
I	2	1	50	1	50
II	54	52	96.29	2	3.7
III	10	9	90	1	10
IV	20	14	70	6	30
V	6	2	33.33	4	66.66
VI	22	0		22	100
Total no. of cases	114	79	69.29	35	30.70

Table 5. Comparison of the percentage of follow-up malignancy of present study with other studies

Diagnostic category	Present study	Mondal *et al*	Jo *et al*	Yassa *et al*	Yang *et al*	Nayar and Ivanovic	Kapia K *et al*
Undiagnostic	50	0	8.9	10	10.7	9	33.3
Benign	3.7	4.5	11	0.3	0.7	2	11.4
AFLUS	10	20	17	24	19.2	6	18.6
SFN	30	30.6	25.4	28	32.2	14	35.3
SM	66.66	75	70	60	64.8	53	61.3
Malignant	100	97.8	98.1	97	98.4	97	96.5

AFLUS: Atypical follicular lesion of undetermined significance, SFN: Suspicious for follicular neoplasm, SM: Suspicious for malignancy

Table 6. Comparison of the percentage of distribution of fine needle aspiration diagnoses of present study with other studies

Diagnostic category	Present study	Mondal *et al*	Jo *et al*	Yassa *et al*	Yang *et al*	Nayar and Ivanovic *et al*	Kapila K *et al*
Non diagnostic	1.75	1.2	18.6	7	10.4	5	4.8
Benign	47.36	87.5	59.0	66	64.6	64	30.5
AFLUS	8.77	1	3.4	4	3.2	18	15.8
SFN	17.54	4.2	9.7	9	11.6	6	4.5
SM	5.26	1.4	2.3	9	2.6	2	21.4
Malignant	19.29	4.7	7.0	5	7.6	5	23.0

nodules or partial/complete thyroidectomy in FN/SFN, SFM and malignant categories. The predictive value of a test is often used to evaluate its clinical accuracy 5. The gold standard for thyroid fine- needle aspiration diagnosis is histologic follow-up.6 .The clinical sensitivity of thyroid fine-needle aspiration would indicate the frequency of test results that were positive for patients with thyroid disease and clinical specificity would likewise indicate the frequency of test results that were negative for patients without thyroid disease. Cytologically all benign thyroid nodules need not be subjected to histopathological evaluation. Follicular variant of papillary carcinoma (FVPTC) was observed most common malignant tumor on histology, but on cytological diagnosis was variable in 9 cases such as unsatisfactory due to blood aspiration, colloid goitre with cystic degeneration due to cystic papillary carcinoma, follicular neoplasm due to paucity of nuclear changes of papillary carcinoma and overlapping features with benign and malignant follicular lesion. FVPTC can pose a diagnostic challenge due to abundance of mono layered sheets and /or micro follicles with subtle nuclear features mimicking a follicular neoplasm. Constraining hyper chromatic chromatin of follicular neoplasm, FVPTC exhibits oval/ round monomorphic nuclei, pale, powdery chromatin with scarce nuclear grooves and intranuclear pseudo inclusions in addition to dense globular colloid in the background and lack of papillary pattern. Follicular adenoma and follicular carcinoma was difficult to differentiate on cytological basis, to label it was as follicular carcinoma, histopathology must show evidence of vascular and/ or capsular invasion.

Medullary carcinoma was reported as lymphocytic thyroiditis on cytology due to poor cellularity, and amyloid material very close to inspissated colloid in background. It was confirmed by IHC, showed strong positivity for marker such as calcitotonine, and thyroglobin. We compared the results obtained in our study with other studies.[Table 5] It was seen that the distribution of cases as per the six-tier Bethesda system in our study different from that in other studies as (Kapila *et al*., 2015; Jo *et al*., 2010; Yassa *et al*., 2007; Yang *et al*., 2007; Nayar and Ivanovic, 2009). In the present study the sensitivity for cytological diagnosis of neoplasia was 80%, specificity 91.86%, and diagnostic accuracy of 91.22%, thus showing a good positive correlation with histopathology. Our results were comparable with the previous published data where FNAC of thyroid is reported to have sensitivity ranging from 40% to 100%, and a specificity of 45% to 100%.7 Higher frequency of sensitivity and specificity accuracy were reported by various authors such as (Sengupta *et al*., 2011; Esmaili *et al*., 2012; Agarwal *et al*., 2015; Gupta *et al*., 2010; Power *et al*., 2003). 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 with Benign, AFLUS, SFN, SM, but slightly higher in Malignant category and much higher with Nondiagnostic category and also compared with the studies of others (Kapila *et al*., 2015; Jo *et al*., 2010; Yassa *et al*., 2007; Yang *et al*., 2007; Nayar and Ivanovic, 2009) though few differences have been noted. [Table 5]

Conclusion

The six diagnostic categories are well defined, morphologically distinct and ensure a uniform reporting system for thyroid FNA. This facilities effective communication among cytopathologists, endocrinologists, surgeons, radiologists, and other health care providers. It also facilitates cytological- histological correlation for thyroid diseases and allows easy and reliable sharing of data from different laboratories for national and international collaborative studies.

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