

A Comparative Study of Thyroid Cytology Reporting by Bethesda System and Routine Cytology in a Teaching Institute of Sub Himalayan Region

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ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) is an important preoperative diagnostic tool for thyroid lesions which are endemic in the Sub-Himalayan belt. But sometimes, the FNAC procedures are unable to guide clinicians for definite management. Bethesda System for Reporting Thyroid Cytology (BSRTC) has been formulated to be more sensitive and specific than routine cytological examination in diagnosis of thyroid swellings and act a better tool than the latter due to its objectivity. It may, thus, improve the clinical management of thyroid diseases and even may prevent unnecessary thyroidectomy.

Aims and Objective: The study is aimed to compare the interpretation of thyroid FNAC smears by conventional reporting and by BSRTC in patients of thyroid swellings in the Sub-Himalayan regions.

Material and Methods: This observational study was done at the Department of Pathology from July 2015 to June 2016. Total 145 cases of thyroid swellings were included for study and reported by both BSRTC and conventional (routine) reporting system. Each of the reporting system was correlated with the available histopathological findings and statistical assessments were performed.

Results: Among the total 145 cases, colloid nodules followed by thyroiditis were most common benign conditions in both the reporting systems and among the malignancies; papillary carcinoma was the most predominant. Statistical assessment showed that sensitivity, specificity as well as positive and negative predictive values was higher in BSRTC compared to the conventional reporting system.

Conclusion: BSRTC is more accurate than conventional reporting system for thyroid cytology and its management strategy can help to prevent unnecessary thyroidectomy.

Keywords: Thyroid Swelling, FNAC, Conventional Reporting System, BSRTC

Introduction

Thyroid swelling is an important worldwide problem and is more common among South Asian women.^[1] The Sub-Himalayan belt is an endemic zone of goitrous thyroid diseases.^[2] The area of the study is included in this belt. Fine Needle Aspiration Cytology (FNAC) was introduced for the same purpose and quickly it became widely accepted as an important diagnostic tool among clinicians due to its good patient compliance and cost effectiveness. Moreover, FNAC evaluation of thyroid swelling reduces load of unnecessary surgeries for benign lesion and opens the way to timely surgical intervention when there is significant risk of malignancy.^[3] However, some diagnosis cannot be reliably made on routine FNAC procedure as for example, differentiation between follicular adenoma and minimally invasive follicular carcinoma. As a result, certain number of misdiagnosis is unavoidable. Inter-observer variability and inadequate aspiration also limit the effectiveness of this procedure. Again, various institutes have their own system

of reporting of cytology smears. Hence, standardized categorical systems for FNAC reporting can make results easier to understand for clinicians and give clear indications for therapeutic action. BSRTC streamlines the assessment and reporting of thyroid aspirates and alleviates the inter-observer variability of this procedure.

This system categorizes the FNAC diagnosis into six groups with well defined cancer risk and clear indications for further clinical management.^[4] A few studies conducted in Western countries reported a good diagnostic concordance between BSRTC and available histologic diagnosis; however such type of data is scarcely available in this country^[5] as well as in this part of the country.

Hence, the study is aimed to evaluate the interpretation of diagnosis for thyroid swelling by both BSRTC and routine cytology and to assess superior correlation of BSRTC, if any, with available histopathology in the study population in the northern region of West Bengal.

Materials and Methods

It was an observational study conducted in the northern region of West Bengal for a period of one year after obtaining clearance from the Institutional ethics committee. The patients who presented with clinical or radiologically diagnosed cases of goiter were included in the study after obtaining informed written consent. Those with already diagnosed thyroid lesions or on cytotoxic drugs known to cause thyroid enlargement were excluded from the study. As per the above criteria, the total numbers of cases were 145. The thyroid FNA smears were classified into group A (for BSRTC) and group B (for routine cytology). The diagnostic accuracy of each reporting protocol was compared in relation to the gold standard i.e. histopathology. Total numbers of available histopathology reports were 58.

The cases were diagnosed and placed as per the conventional method of reporting,^[6] under the following categories:

- A) Nondiagnostic/Unsatisfactory:** Cases were categorized into this group when the aspirations were not fulfilling the adequacy criteria of thyroid cytology. The adequacy criteria for thyroid cytology^[7-9] are:
1. The sample should contain at least six group of well visualized (not obscured by blood, not a thick smear) thyroid follicular cells.
 2. Each group should contain at least 10 thyroid follicular cells, preferably on a single slide.
- Exceptions of these criteria were applied to the following special circumstances^[7]:
- a) Solid nodules with cytologic atypia
 - b) Solid nodules with inflammation
 - c) Colloid nodules
- B) Benign:** When the aspirates were obtained from multinodular goiters, benign microfollicular adenoma, colloid nodules and various thyroiditis.^[10]
- C) Indeterminate (Suspicious for Malignancy):** Conditions where there were presence of atypical cellular features but not fulfilling the definite diagnosis of malignancy.^[11]
- D) Malignant:** Conditions where there were presence of features suggesting definite diagnosis of following malignant conditions^[12] e.g. Papillary Carcinoma, Medullary carcinoma, Anaplastic Carcinoma, Lymphomas and Metastatic tumors.

The same cases were also categorized according to BSRTC (Table 1).^[13]

Histopathological diagnosis of the available biopsy specimens were taken as gold standard for correlation of the cytological reporting.

Results

Distribution of all cases according to conventional method of reporting was represented as in Table 2 and distributions of cases according to BSRTC were represented as in Table 3.

For statistical assessment among the total 145 cases only 58 cases who were undergone biopsy, were included and subcategorized according to their cytological diagnostic system into "Positive for neoplasia" and "Negative for neoplasia" in relation to gold standard histopathological findings. For conventional reporting system, total 26 cases that included the "Indeterminate (Suspicious for malignancy)" and "Malignant" lesions were grouped into "Positive for neoplasia" on the other hand, remaining 32 cases those who were subcategorized into the "Inadequate" and "Benign" lesions were grouped into "Negative for neoplasia" and statistical analysis was then performed. Similarly, according to BSRTC, the categories IV to VI were grouped into "Positive for neoplasia" (total 21 cases) and remaining category I to III lesion types (total 37 cases) were grouped into "Negative for neoplasia" for statistical assessment considering biopsy as gold standard. The comparative studies of statistical parameters were shown in Table 4. In our study the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of BSRTC were 95%, 94.74%, 90.47%, 97.29% and 94.83% respectively. Among them, specificity as well as PPV was significantly higher in BSRTC than conventional system.

Discussion

Thyroid nodules are one of the commonest clinical problems and FNAC of the thyroid is the first line preoperative investigation of thyroid lesions. The majority of nodules are benign, mostly non neoplastic. The present study was carried out with an aim to evaluate the role of FNAC in diagnosis of various neoplastic and non neoplastic lesions of thyroid and to assess the superior correlation of BSRTC compared to conventional cytology reporting. In their study, Raab et al.^[14] mentioned that "Unsatisfactory" specimens may be grouped into "Negative for neoplasia" as like benign categories. On the other hand, Papanicolaou Society of Cytopathology^[15] and the American Association of Clinical Endocrinologists^[16] told that "Indeterminate" cytologic category should be treated as like "Malignant" lesions for better management. According to Nadira Mamoon et al.^[17] the conventional reporting system of thyroid cytology were categorized into inadequate, benign, suspicious, and malignant where the follicular neoplasm

Table 1: Distribution of categories according to Bethesda system.

I. Nondiagnostic or Unsatisfactory (ND/UNS)
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, etc.)
II. Benign
Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
Consistent with granulomatous (subacute) thyroiditis
Other
III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance (AUS/FLUS)
IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm (FN/SFN)
specify if Hürthle cell (oncocyctic) type
V. Suspicious for Malignancy (SFM)
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other
VI. Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma
Carcinoma with mixed features (specify)
Metastatic carcinoma
Non-Hodgkin lymphoma Other

Table 2: Distribution of cases according to conventional reporting system.

Type of cases		Number of cases		Percentage
Inadequate		11		7.59
Benign	Colloid goitre & changes	52	Total 105	72.41(Total)
	Nodular goiter	7		
	Adenomatoid goiter	6		
	Thyroiditis & changes	40		
Indeterminate (suspicious to be malignant)		16		11.03
Malignant	Papillary carcinoma (PTC)	7	Total 13	8.97 (Total)
	Medullary carcinoma (MTC)	2		
	Anaplastic carcinoma (AC)	2		
	Metastasis	1		
	Poorly differentiated carcinoma	1		
Total		145		100

Table 3: Distribution of cases according to Bethesda system.

Type of cases		Number of cases		Percentage
Inadequate (Category I)		11		7.59
Benign (Category II)	Colloid goitre & changes	52	Total 103	71.03(Total)
	Nodular goiter	7		
	Adenomatoid goiter	4		
	Thyroiditis & changes	40		

Type of cases		Number of cases		Percentage
AUS/FLUS (Category III)		8		5.51
FN/ SFN (Category IV)	Suggestive of follicular neoplasm	6	Total 7	4.83 (Total)
	Suggestive of Hurthle cell neoplasm	1		
SFM (Category V)	Suspicious for Papillary Carcinoma	3	Total 7	4.83 (Total)
	Suspicious for lymphoma	1		
	Suspicious for Poorly differentiated carcinoma	1		
	Suspicious for Medullary Carcinoma	1		
	Metastasis	1		
Malignant (Category VI)	Papillary carcinoma (PTC)	6	Total 9	6.21 (Total)
	Medullary carcinoma (MTC)	1		
	Anaplastic carcinoma (AC)	2		
Total		145		100

AUS/FLUS: Atypia of Undetermined Significance / Follicular Lesion of Undetermined Significance

FN/ SFN: Follicular Neoplasm / Suspicious for a Follicular Neoplasm

SFM: Suspicious for Malignancy

Table 4: Statistical assessment of conventional reporting system and BSRTC.

		Biopsy	
		Neoplastic	Non-neoplastic
Conventional reporting system	Positive (26)	18 (TP)	08 (FP)
	Negative (32)	02 (FN)	30 (TN)
	Total (n=58)	20 (TP+FN)	38 (FP+TN)
BSRTC	Positive (21)	19 (TP)	02 (FP)
	Negative (37)	01 (FN)	36 (TN)
	Total (n=58)	20 (TP+FN)	38 (FP+TN)

TP: True Positive, TN: True Negative, FP: False Positive, FN: False Positive

Table 5: Comparative studies.

	Statistical analysis (%)	Present study (n=58)	Mamatha et al. ^[19] 2015 (n=240)	Bukhari et al. ^[20] 2012 (n=120)
Routine reporting system	Sensitivity	90	77	85
	Specificity	78.95	69	65
	PPV	69.23	37	32
	NPV	93.75	93	95.5
BSRTC	Sensitivity	95	100	100
	Specificity	94.74	82.5	82.5
	PPV	90.47	45	45
	NPV	97.29	100	100

PPV: Positive Predictive Value, NPV: Negative Predictive Value

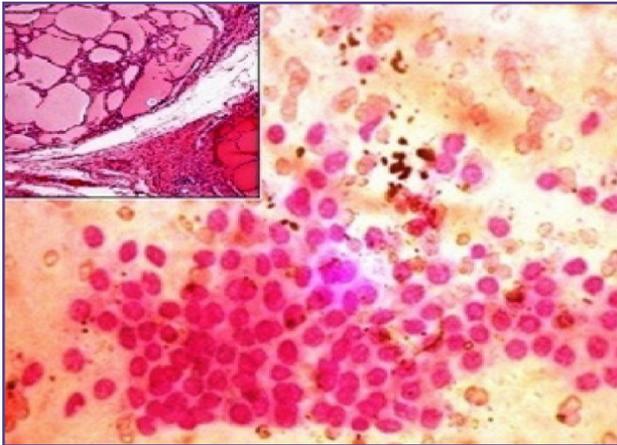


Fig. 1- FNA diagnosis- Nodular goitre (BSRTC Category II) [H/E 100X] along with Histopathology image on inset (H/E 10X).

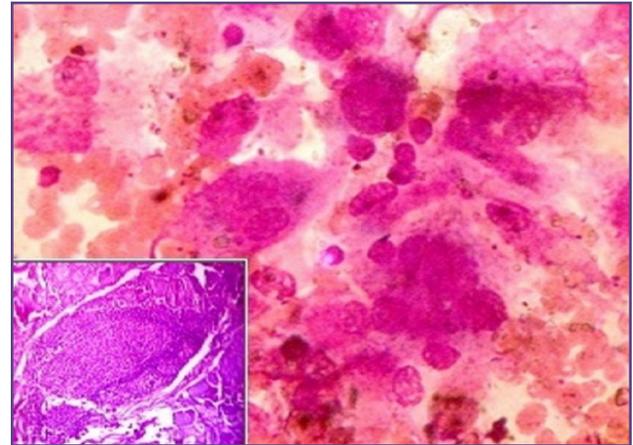


Fig. 2: FNA diagnosis- "Indeterminate" lesion in routine cytology & Category III in BSRTC (Leishman 400X) along with on follow-up Histopathology image [Inset] diagnosed as Hashimoto thyroiditis (H/E 100X).

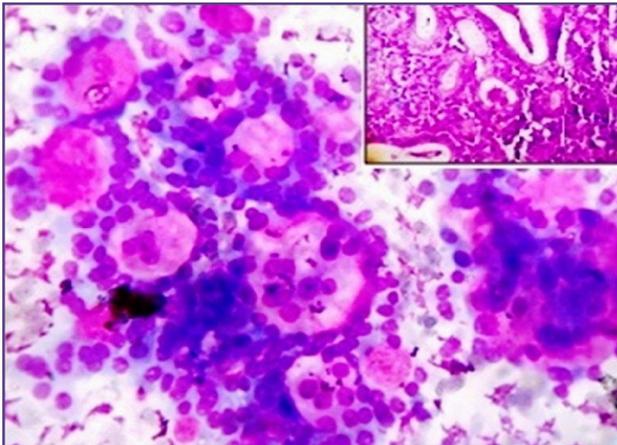


Fig. 3: FNA diagnosis- "Suspicious for follicular malignancy" in routine cytology & Category IV in BSRTC (Leishman 400X) that was diagnosed as Follicular carcinoma on biopsy (H/E 400X) [Inset].

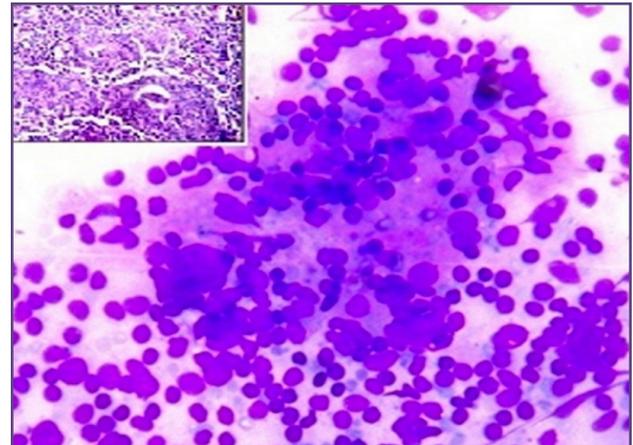


Fig. 4: FNA diagnosis- Suspicious for Lymphoma in (BSRTC Category V) [Leishman stain 400X] which was confirmed on biopsy as MALT lymphoma of thyroid [H/E 400X] [Inset]

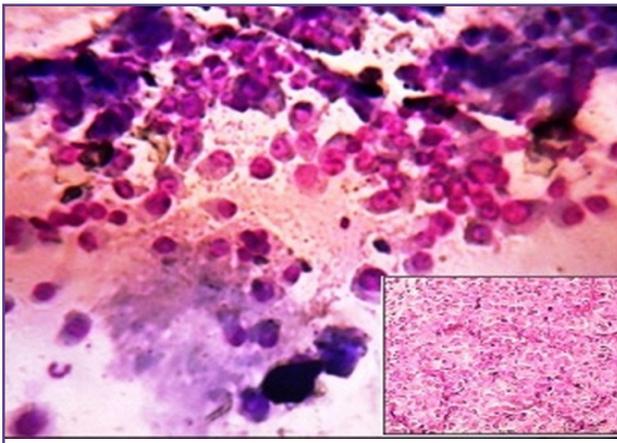


Fig. 5: FNA diagnosis- Suspicious for Medullary carcinoma in BSRTC (Category V) [Leishman stain 400X] which was confirmed on biopsy [H/E 400X] [Inset].

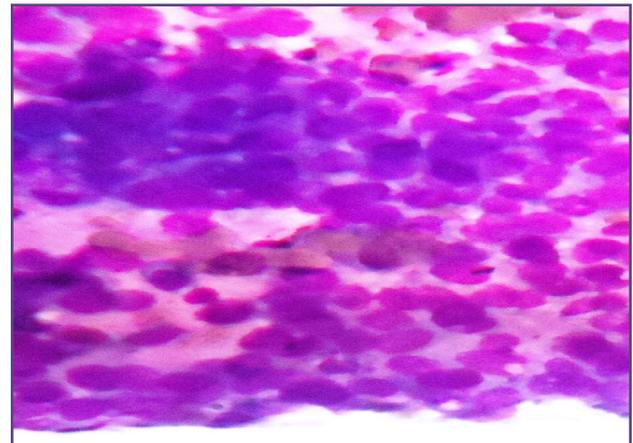


Fig. 6: FNA diagnosis- Suspicious for Poorly differentiated carcinoma in BSRTC (Category V) [Leishman stain 400X].

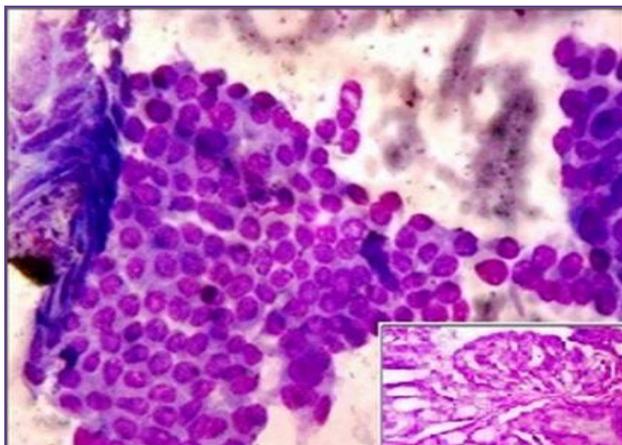


Fig. 7: FNA diagnosis- Papillary carcinoma in BSRTC (Category VI) [Leishman stain 400X] which was confirmed on biopsy [H/E 400X] [Inset].

were included into the suspicious category. They also mentioned that suspicious, and malignant categories should be counted as “Positive” and rest were counted as “Negative” for statistical assessment. In our study we also grouped “Indeterminate” and “Malignant” lesions into “Positive for neoplasia” and remaining “Unsatisfactory” along with “Benign” category were grouped into “Negative for neoplasia” for statistical assessment. In this study, some of the thyroid lesions which were diagnosed on biopsy as “Nodular Hyperplasia” and “Adenomatoid goitre” were cytologically categorized as “Indeterminate” in routine reporting system as like Nadira Mamoon et al.^[17] and caused false positivity. BSRTC is also a useful tool for the oncologist to manage those thyroid lesions. Bethesda system for thyroid reporting has six categories that increases the reproducibility of diagnosis of thyroid lesions and were logically relates to the prognosis of thyroid diseases. For example in our study, some thyroid lesions which were diagnosed on biopsy as “Nodular Hyperplasia”, “Adenomatoid goitre” and “Hashimoto’s thyroiditis with Hurthle cell changes”, were preoperatively categorized as “Indeterminate” in routine reporting system and included under the “Positive for neoplasia” group for statistical analysis but, those lesions were categorized as “Category III” in BSRTC and grouped for “Negative for neoplasia” Henceforth, the sensitivity, specificity, PPV, NPV and Diagnostic accuracy were higher in BSRTC in relation to conventional reporting system of thyroid cytology that were also correlated with other previous studies Mamatha et al.^[12] and Bukhari et al.^[18] (Table 5). Though BSRTC were better in relation to conventional reporting system for thyroid cytodagnosis, it also had some grey zone- mostly related to “Category III” and

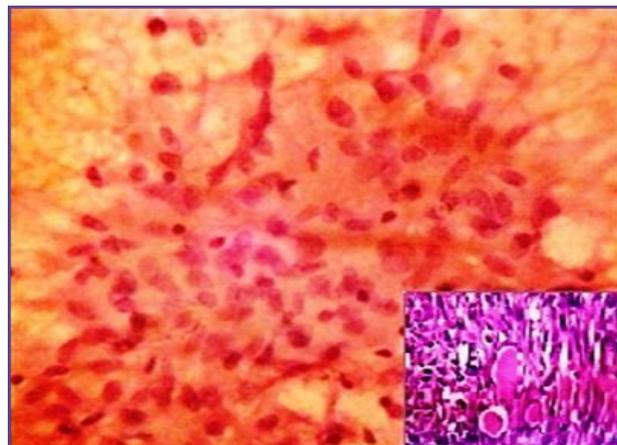


Fig. 8: FNA diagnosis- Anaplastic carcinoma in BSRTC (Category VI) [H&E 400X] which was confirmed on biopsy [H/E 400X] [Inset].

“Category IV” BSRTC lesions. Similar to Kasliwal et al.^[19] and Cibas et al.^[20] in our study, some false positive cases in BSRTC were also related with “Category IV” lesions e.g two cases of biopsy confirmed “Adenomatoid goitre” were categorized into “Category IV” lesions preoperatively and grouped into “Positive for neoplasia”. Similarly, one case of the “Thyroglossal cyst with coexistence of Papillary carcinoma thyroid” which was diagnosed on biopsy, was preoperatively categorized under “Category III” and treated as “Negative for neoplasia” for statistical assessment which caused one false negative case.

The study might have been more statistically significant if the study period was of longer duration, study population was large and all the cases were available for follow-up and/ or biopsy, which were the major drawbacks of our study.

Conclusion

The Bethesda system of reporting thyroid cytology has lead to a better sensitivity, specificity, PPV, NPV and Diagnostic accuracy than routine cytology. BSRTC reduces Inter observer variability of thyroid lesions and hence reduces unnecessary surgical procedures for thyroid swellings. This system has standardized management protocol that may help the clinician to treat the patient well which might not be possible if reported by routine cytology system.

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