# Reliability of The Bethesda System for Reporting Thyroid Cytopathology

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**Abstract:**
**Introduction:** *Thyroid lesions comprise a wide group of diseases ranging from congenital, inflammatory, and benign to malignant lesions. The prevalence of palpable thyroid nodules in India is 12.2% and distinguishing benign from a malignant nodule is essential. For proper management "The Bethesda system for reporting Thyroid Cytopathology" (TBSRTC) was introduced in 2007 to standardize the terminology used to categorize various thyroid lesions.*
**Materials and Methods**: *A prospective study comprising of 49 cases for the duration of 10 months i.e.,from March 2019 to December 2019.*
**Results:** *Among 49 cases, 44 were females and 5 were males with a male to female ratio of 1:8.8. Incidence of thyroid lesions was most common in fourth decade (28.57%). Highest number of cases (71.43%) were reported under benign category.*
**Conclusion:** *TBSRTC is a universal, homogeneous and reproducible terminology for reporting the thyroid cytology. Efficient usage of this system can be achieved by adequate practice of TBSRTC by cytopathologists as well as clinicians. The overlapping features of hyperplastic nodule (TBSRTC-II) and follicular adenoma (TBSRTC-IV) still continuing to be the confusing entities for clinicians. Combined use of USG neck for thyroid and routine FNAC from thyroid nodules will yield highly reliable diagnosis which will guide the surgeon towards the appropriate patient management.*
**Key Words:** *FNAC, Reliability, TBSRTC, Thyroid cytopathology*

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## I.    Introduction

Thyroid neoplasms are one of the most common diseases encountered worldwide as well as in India. About 40 million people in India are estimated to have been suffering from thyroid diseases[1].  In a recent study, the prevalence of a palpable thyroid nodule in India was estimated as approximately 12.2%[2]. As a palpable thyroid nodule may not always be malignant, the clinician needs to distinguish between benign and malignant nodules for appropriate management.

FNAC is the cornerstone diagnostic tool in distinguishing between benign and malignant thyroid nodules, thereby reducing unwarranted surgeries[3]. However, sharing this information between clinicians and pathologists is hampered due to multiplicity in nomenclature and variation in surgical pathology terminologies[4].

In 2007, National Cancer Institute introduced "The Bethesda system for reporting Thyroid Cytopathology" which addresses the necessity of uniformity in reporting by the pathologists and its interpretation by the surgeons with a proposed six diagnostic categories. TBSRTC for thyroid FNA will facilitate effective communication among cytopathologists, clinicians, surgeons, radiologists and other health care providers and facilitate research in epidemiology, and molecular pathology[5].

This reporting system includes suggestions regarding the report format, adequacy of the sample, diagnostic category, risk of malignancy, and proposed the clinical management. For clarity of communication, TBSRTC recommends that each report begin with 1 of 6 general diagnostic categories. Each of the categories has an implied cancer risk ranging from 0% to 3% for the benign category to virtually 100% for the malignant category that helps in guiding a rationale clinical management[3].

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The current study concentrates validating utility, standardization and reliability of TBSRTC in reporting thyroid FNAs.

## II.      Materials and Methods

Study Design: Prospective study.

Study Location: This study was conducted in the Department of Pathology, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram.

Duration of study: Prospective study March 2019- December 2019.

Sample size: 49 cases

Inclusion criteria:

1. Routine FNAC of palpable thyroid nodules/ lesions

2. USG-guided FNAC of thyroid nodules/ lesions which are not obviously palpable.

Methodology: Permission from superintendent, MIMS hospital, and Department of pathology and from Ethics committee of MIMS, were obtained to conduct this study. Smears from all thyroid FNACs performed over a period of 10 months (March 2019 to December 2019). They were classified according to the 6 diagnostic categories of TBSRTC as follows. [6,7]

Category I- Nondiagnostic/unsatisfactory (ND/US)

Category II- Benign

Category III-Atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS)

Category IV- Follicular neoplasm/Suspicious for a follicular neoplasm (FN/SFN)

Category V- Suspicious for malignancy (SUS)

Category VI- Malignant

## III.      Results

The present study included 49 cases, which were reported using TBSRTC. Incidence of thyroid lesions was most common in fourth decade (28.57%). Among 49 cases, 44 were females and 5 were males, with male to female ratio of 1:8.8. The incidence of malignancy is high among males over females.

**Table 1: Age Distribution**

| Age | Number of cases | Percentage |
|---|---|---|
| 0-10 | 0 | 0 |
| 11--20 | 6 | 12.25% |
| 21-30 | 10 | 20.41% |
| **31-40** | **14** | **28.57%** |
| 41-50 | 12 | 24.48% |
| 51-60 | 6 | 12.25% |
| 61-70 | 1 | 2.04% |
| 71-80 | 0 | 0 |
| Total | **49** | 100% |

**Table 2: Sex Distribution of thyroid lesions**

| SEX | NUMBER OF CASES | PERCENTAGE |
|---|---|---|
| MALES | 5 | 10.21% |
| **FEMALES** | **44** | **89.79%** |
| TOTAL | 49 | 100% |

**Table 3:** Results according to 2017 Bethesda System for Reporting Thyroid Cytopathology

| | BETHESDA CATOGERY | NUMBER | PERCENTAGE |
|---|---|---|---|
| I | Nondiagnostic or Unsatisfactory | 10 | 20.41% |
| II | Benign | **35** | **71.43%** |
| III | Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance | 0 | 0 |
| IV | Follicular Neoplasm or Suspicious for a Follicular Neoplasm | 0 | 0 |
| V | Suspicious for Malignancy | 1 | 2.04% |
| VI | Malignant | 3 | 6.12% |
| | TOTAL | 49 | 100% |

Highest number of cases 35 (71.43%) were reported under benign (TBSRTC-II) lesions followed by 10 cases (20.41%) of non-diagnostic/ unsatisfactory (TBSRTC-I).

Among 10 cases of thyroid lesions under non diagnostic category 6 (60%) were 'cyst fluid only' and 4 (40%) case was reported under 'virtually acellular specimen'. Among35 cases of benign lesions, subcategories reported 25 cases (71.43%) were benign follicular nodule and 10 cases (28.57%) were lymphocytic thyroiditis.

One case was reported under 'suspicious of malignancy' and three cases under 'malignant', of which all were included in the sub-category papillary thyroid carcinoma.

**Table 4: Distribution of cases according to the Bethesda System**

| Nondiagnostic or Unsatisfactory | Number | Percentage |
|---|---|---|
| Cyst fluid only | 6 | 12.24% |
| Virtually acellular specimen | 4 | 8.17% |
| Other (obscuring blood, clotting artifact, etc.) | - | - |
| **II. Benign** | | |
| Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.) | 25 | 51.02% |
| Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context | 10 | 20.04% |
| Consistent with granulomatous (subacute) thyroiditis | - | - |
| Other | - | - |
| **III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance** | **-** | **-** |
| **IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm** | **-** | **-** |
| specify if Hürthle cell (oncocytic) type | - | - |
| **V. Suspicious for Malignancy** | | |
| Suspicious for papillary carcinoma | 1 | 2.05% |
| Suspicious for medullary carcinoma | - | - |
| Suspicious for metastatic carcinoma | - | - |
| Suspicious for lymphoma | - | - |
| Other | - | - |
| **VI. Malignant** | | |
| Papillary thyroid carcinoma | 3 | 6.12% |
| Poorly differentiated carcinoma | - | - |
| Medullary thyroid carcinoma | - | - |
| Undifferentiated (anaplastic) carcinoma | - | - |
| Squamous cell carcinoma | - | - |
| Carcinoma with mixed features (specify) | - | - |
| Metastatic carcinoma | - | - |
| Non-Hodgkin lymphoma | - | - |
| Other | - | - |
| Total | 49 | 100% |

## IV. Discussion

The usage of "personalized", local, institutional and descriptive terminologies leads to confusion in reporting thyroid lesions as there are a wide range of entities[8]. This is due to deficiency of a consistent and universalised reporting terminology for the diagnosis of thyroid FNA which led to the introduction of TBSRTC in October 2007, which was revised in 2017[9]. The diagnoses as per the criteria laid down in the standardized nomenclature of the Bethesda system, seemed more simplified, systematic, with more clarity especially it would prove to be more useful in guiding clinicians towards the management of thyroid nodules[10].

In the present study, benign lesions outnumbered malignant lesions with a ratio of 15:1. The incidence of malignancy is high among males over females i.e., out of 3 malignant lesions two were diagnosed in females(2/44) and one in male(1/5).

**Table 5**. The 2017 Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

| | BETHESDA CATOGERY | Risk of malignancy if NIFTP s CA (%) | Risk of malignancy if NIFTP = CA (%) | Usual Management |
|---|---|---|---|---|
| I | Nondiagnostic or Unsatisfactory | 5-10 | 5-10 | Repeat FNA with ultrasound guidance |
| II | Benign | 0-3 | 0-3 | Clinical and sonography follow up |
| III | Atypia of Undetermined Significance -of Follicular Lesion -of Undetermined Significance | 6-18 | ≈10-30 | Repeat FNA, molecular testing, or lobectomy |
| IV | Follicular Neoplasm or Suspicious for a Follicular Neoplasm | 10-40 | 25-40 | Molecular testing, lobectomy |
| V | Suspicious for Malignancy | 45-60 | 50-75 | Near-total thyroidectomy or lobectomy |
| VI | Malignant | 94-96 | 97-99 | Near-total thyroidectomy or lobectomy |

*NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features; CA, carcinoma; FNA, fine-needle aspiration.*

In the present study, out of 49 cases 10 cases were classified under ND/US category. Six cases were reported as cyst fluid only as there were only cyst macrophages in a fluid background and hence categorised under ND/US (TBSRTC-I). Four cases were reported as no opinion possible because of lack of cellularity.

One case was reported as colloid nodule though the smears showed occasional follicular epithelial cells and mostly cyst macrophages in a background of thin colloid and therefore classified under benign category (TBSRTC-II). According to TBSRTC a sparsely cellular specimen with abundant colloid should be considered benign[9].

Twenty four cases reported as colloid nodular goitre and adenomatoid nodule were included under benign category (TBRTC- II)

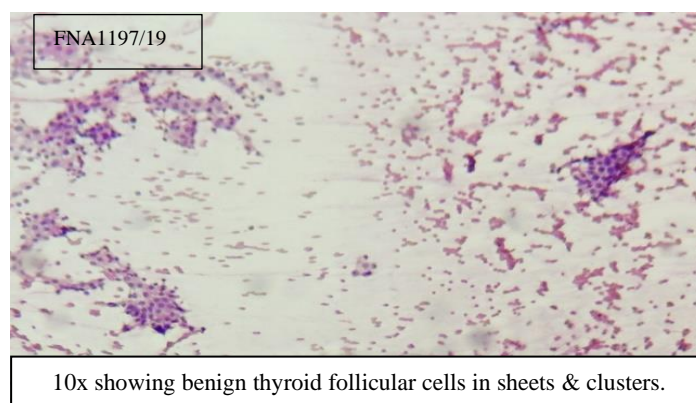Ten cases of Hashimoto's thyroiditis were classified under benign category (TBRTC- II).

One case was reported as suspicious for malignancy and hence included in TBSRTC-V

Three cases were reported as (suggestive of) papillary carcinoma thyroid and therefore included in TBSRTC VI.
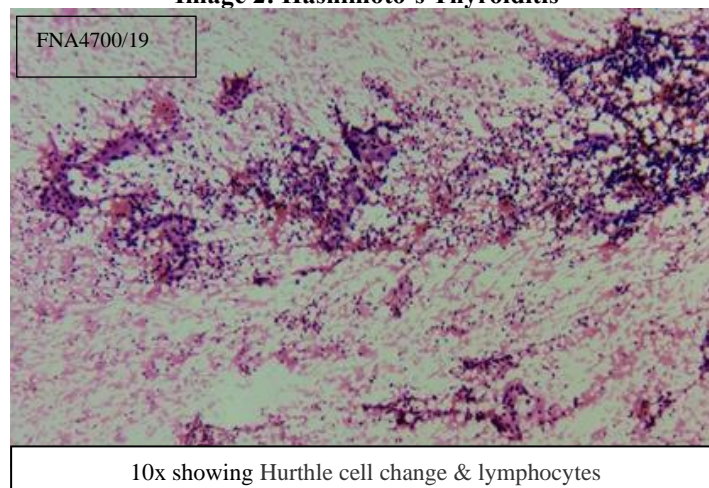
Cases included under ND/US category were advised to have repeat aspirations. If immediate repeated aspirations yielded only haemorrhage patients were advised to undergo repeat FNAC, in next visit after a week. Among benign cases, almost all the cases have good histological correlation except two cases which were turned out to be malignant on histopathology. The reason this could be, categorisation of TBSRTC is based on the material obtained from the aspirations i.e., either routine or USG-guided aspirations. As routine FNAC is a blind procedure the suspicious focus may be missed in adenomatoid nodules and non-palpable lesions e.g., papillary microcarcinoma, occult thyroid carcinoma with lymph node metastasis. Hence either USG-neck for thyroid followed by routine FNAC of palpable thyroid lesions or USG-guided aspirations from thyroid lesions which are not obviously palpable, will minimise the errors in diagnosing malignancy.

Three cases reported as papillary carcinoma thyroid on cytology were proved to be the same on histopathology, having 100% correlation.
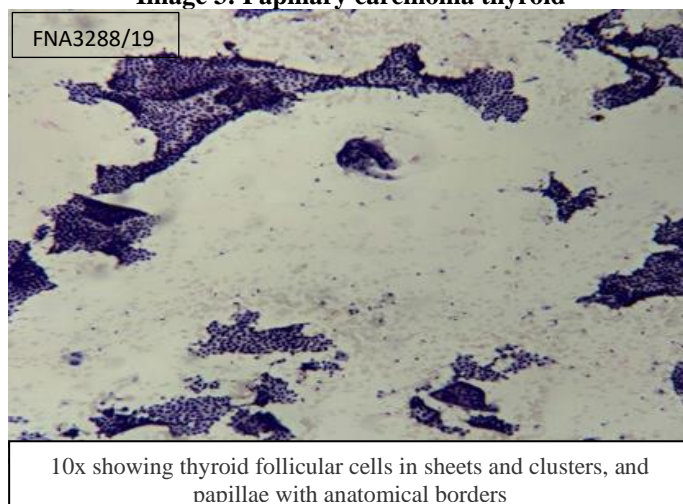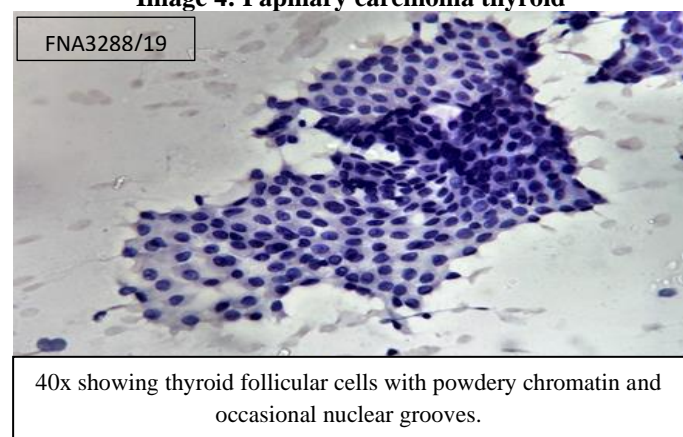
**Image 1: Nodular goitre**



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10x showing benign thyroid follicular cells in sheets & clusters.

**Image 2: Hashimoto's Thyroiditis**



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10x showing Hurthle cell change & lymphocytes

**Image 3: Papillary carcinoma thyroid**



10x showing thyroid follicular cells in sheets and clusters, and papillae with anatomical borders

**Image 4: Papillary carcinoma thyroid**



40x showing thyroid follicular cells with powdery chromatin and occasional nuclear grooves.

The classification of lesions according to the standardized nomenclature correlated with other studies like Mondal SK et al[11], Jo et al[12], Yassa et al[13], Yang et al[14], Nayar and Ivanovic et al[15]. Also it has corroborated well with the implied risks mentioned in the Bethesda System and also with the above studies.

**Table 6: Comparison of the percentages of distribution of the diagnoses with other studies**

| Diagnostic Catogery | Mondal SK et al[11] | Jo et al[12] | Yassa et al[13] | Yang et al[14] | Nayar and Ivanovic et al[15] | Present study |
|---|---|---|---|---|---|---|
| Non- Diagnostic | 12% | 18.6% | 7% | 10.4% | 5% | 20.41% |
| Benign | **87.5%** | **59%** | **66%** | **64.6%** | **64%** | **71.43%** |
| AUS/FLUS | 1% | 3.4% | 4% | 3.2% | 18% | 0 |
| SFN | 4.2% | 9.7% | 9% | 11.6% | 6% | 0 |
| Suspicious of malignancy | 1.4% | 2.3% | 9% | 2.6% | 2% | 2.04% |
| Malignant | 4.7% | 7% | 5% | 7.6% | 5% | 6.12% |

**AUS/FLUS-** Atypia of Undetermined Significance/ Follicular lesion of undetermined significance, SFN-Suspicious for follicular neoplasm.

## V.    Conclusion

1. Usage of TBSRTC is simplified, systematic and standardised system in guiding clinicians towards the management of thyroid nodules.

2. Though TBSRTC has proven to be a standardised system of reporting thyroid lesions, it has few drawbacks.

3. The overlapping features of hyperplastic nodule (TBSRTC-II) and follicular adenoma (TBSRTC-IV) still continuing to be the confusing entities for clinicians/ surgeons.

4. Combined use of USG neck for thyroid and routine FNAC from thyroid nodules will yield highly reliable diagnosis which will guide the surgeon towards the appropriate patient management.

Limitations:

a. Small sample size
b. Short duration of study.

# References

[1]. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J EndocrinolMetab 2011;15:78‑81.

[2]. UshaMenon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009;107:72–7.

[3]. Cibas ES, Ali SZ, NCI Thyroid FNA State of the Science Conference. The Bethesda System for reporting thyroid cytopathology. Am J ClinPathol 2009;132:658‑65.

[4]. Layfield LJ, Cibas ES, Baloch Z. Thyroid fine needle aspiration cytology: A review of the National Cancer Institute state of the science symposium. Cytopathology 2010;21:75‑85.

[5]. Ali SZ, Cibas ES. The Bethesda System for Reporting Thyroid Cytopathology. New York: Springer; 2009.

[6]. Bhasin TS, Mannan R, Manjari M, Mehra M, Sekhon AK, Chandey M, *et al*. Reproducibility of'The Bethesda System for reporting Thyroid Cytopathology': A multicenter study with review of the literature. J ClinDiagn Res 2013;7:1051‑4.

**[7].** Baloch ZW, Alexander E K, Gharib H, and Raab SS. Chapter 1; Overview of Diagnostic Terminology and Reporting I*n:* Ali SZ and Cibas ES Edi, *The Bethesda System forReporting Thyroid Cytopathology*. New York, NY: Springer; 2010:1-4**.**

[8]. Auger M, Nayar R, Khalbuss WE, Barkan GA, Benedict CC, Tambouret R, *et al*. Implementation of the Bethesda System for reporting thyroid cytopathology: Observations from the 2011 thyroid supplemental questionnaire of the College of American Pathologists. Arch Pathol Lab Med 2013;137:1555‑9.

[9]. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *J Am SocCytopathol* (2017) 6(6):217–22.

[10]. 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.

[11]. 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.

[12]. 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 ClinPathol. 2010;134:450–6.

[13]. 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.

[14]. 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.

[15]. 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.