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 cytopathy. 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).
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>
<thead>
<tr>
<th>Age</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11-20</td>
<td>6</td>
<td>12.5%</td>
</tr>
<tr>
<td>21-30</td>
<td>10</td>
<td>20.41%</td>
</tr>
<tr>
<td>31-40</td>
<td>14</td>
<td>28.57%</td>
</tr>
<tr>
<td>41-50</td>
<td>12</td>
<td>24.48%</td>
</tr>
<tr>
<td>51-60</td>
<td>6</td>
<td>12.25%</td>
</tr>
<tr>
<td>61-70</td>
<td>1</td>
<td>2.04%</td>
</tr>
<tr>
<td>71-80</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 2: Sex Distribution of thyroid lesions

<table>
<thead>
<tr>
<th>SEX</th>
<th>NUMBER OF CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALES</td>
<td>5</td>
<td>10.21%</td>
</tr>
<tr>
<td>FEMALES</td>
<td>44</td>
<td>89.79%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>49</td>
<td>100%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>BETHESDA CATEGORY</th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>10</td>
<td>20.41%</td>
</tr>
<tr>
<td>II</td>
<td>35</td>
<td>71.43%</td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>V</td>
<td>1</td>
<td>2.04%</td>
</tr>
<tr>
<td>VI</td>
<td>3</td>
<td>6.12%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>49</td>
<td>100%</td>
</tr>
</tbody>
</table>

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’. Among 35 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

<table>
<thead>
<tr>
<th>Non diagnostic or Unsatisfactory</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst fluid only</td>
<td>6</td>
<td>12.24%</td>
</tr>
<tr>
<td>Virtually acellular specimen</td>
<td>4</td>
<td>8.17%</td>
</tr>
<tr>
<td>Other (obscuring blood, clotting artifact, etc.)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

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

- Suspicious for papillary carcinoma 1 2.05%
- Suspicious for medullary carcinoma - -
- Suspicious for metastatic carcinoma - -
- Suspicious for lymphoma - -
- Other - -

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

<table>
<thead>
<tr>
<th>BETHESDA CATEOGERY</th>
<th>Risk of malignancy if NIFTP = CA (%)</th>
<th>Risk of malignancy if NIFTP = CA (%)</th>
<th>Usual Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Nondiagnostic or Unsatisfactory</td>
<td>5-10</td>
<td>5-10</td>
</tr>
<tr>
<td>II</td>
<td>Benign</td>
<td>0-3</td>
<td>0-3</td>
</tr>
<tr>
<td>III</td>
<td>Atypia of Undetermined Significance</td>
<td>6-18</td>
<td>6-18</td>
</tr>
<tr>
<td>IV</td>
<td>Follicular Neoplasm or Suspicious</td>
<td>10-40</td>
<td>10-40</td>
</tr>
<tr>
<td>V</td>
<td>Suspicious for Malignancy</td>
<td>45-60</td>
<td>45-60</td>
</tr>
<tr>
<td>VI</td>
<td>Malignant</td>
<td>94-96</td>
<td>94-96</td>
</tr>
</tbody>
</table>

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**

![Image 1](https://example.com/image1)

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

**Image 2: Hashimoto’s Thyroiditis**

![Image 2](https://example.com/image2)

10x showing Hurthle cell change & lymphocytes.
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Image 3: Papillary carcinoma thyroid

Image 4: Papillary carcinoma thyroid

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**

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Mondal SK et al(^{(11)})</th>
<th>Jo et al(^{(12)})</th>
<th>Yassa et al(^{(13)})</th>
<th>Yang et al(^{(14)})</th>
<th>Nayar and Ivanovic et al(^{(15)})</th>
<th>Present study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Diagnostic</td>
<td>12%</td>
<td>18.6%</td>
<td>7%</td>
<td>10.4%</td>
<td>5%</td>
<td>20.41%</td>
</tr>
<tr>
<td>Benign</td>
<td>87.5%</td>
<td>59%</td>
<td>66%</td>
<td>64.6%</td>
<td>64%</td>
<td>71.43%</td>
</tr>
<tr>
<td>AUS/FLUS</td>
<td>1%</td>
<td>3.4%</td>
<td>4%</td>
<td>3.2%</td>
<td>18%</td>
<td>0</td>
</tr>
<tr>
<td>SFN</td>
<td>4.2%</td>
<td>9.7%</td>
<td>9%</td>
<td>11.6%</td>
<td>6%</td>
<td>0</td>
</tr>
<tr>
<td>Suspicious of malignancy</td>
<td>1.4%</td>
<td>2.3%</td>
<td>9%</td>
<td>2.6%</td>
<td>2%</td>
<td>2.04%</td>
</tr>
<tr>
<td>Malignant</td>
<td>4.7%</td>
<td>7%</td>
<td>5%</td>
<td>7.6%</td>
<td>5%</td>
<td>6.12%</td>
</tr>
</tbody>
</table>

**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
