Reproducibility of “The Bethesda System for Reporting Thyroid Cytopathology”: A Retrospective Analysis of 107 Patients

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Abstract

Objectives: Fine-needle aspiration cytology (FNAC) has emerged as an indispensable tool to discriminate thyroid lesions into benign or malignant for appropriate management. The need for simplicity of communication and standardization of terminology for thyroid FNAC reporting led to introduction of “The Bethesda system for reporting Thyroid Cytopathology” (TBSRTC) in a conference held at the National Cancer Institute in 2007. This study aims at establishing the reproducibility of TBSRTC for diagnosing thyroid lesions.

Materials and Methods: The present study comprised thyroid FNAC from 107 patients retrospectively over a period of 1.5 year (June 2013 to December 2014), which were reviewed by two trained cytopathologists and re-categorized according to TBSRTC. The interobserver variation and reproducibility of the reporting system was statistically assessed using Cohen’s kappa. Results: The cytopathologists were in agreement in 98 out of 107 cases (91.5%). Maximum concordance was noted in benign category (91 of 96 cases; 92.85%), followed by 2 cases each in nondiagnostic/unsatisfactory (ND/US) and follicular neoplasm/suspicious for follicular neoplasm (FN/SFN) category (2.04% each) and 1 case each in atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), suspicious for malignancy (SUS), and malignant category (1.02% each). The highest diagnostic disagreement was noted among ND/US and benign and benign and FN/SFN categories. Conclusion: The utilization of TBSRTC for reporting thyroid cytology should be promoted in our country because it provides a homogeneous, standardized, and unanimous terminology for cytological diagnosis of thyroid lesions. The present study could substantiate the diagnostic reproducibility of this system.

Keywords: Bethesda System, fine-needle aspiration cytology, reproducibility, thyroid

INTRODUCTION

Thyroid diseases are frequently encountered in India and approximately 42 million people in India suffer from thyroid diseases.[1] The prevalence of a palpable thyroid nodule in India is approximately 12.2%, however, the incidence of thyroid cancer is 8.7 cases per 100,000 population per year.[2] As a palpable thyroid nodule may not always be malignant, it is important for the clinician to distinguish between benign and malignant nodules for appropriate management. Consequently, fine needle aspiration cytology (FNAC) surfaced as an indispensable first-line diagnostic tool to classify palpable thyroid nodules into benign or malignant, thereby reducing unnecessary surgeries in benign thyroid nodules.[3]

In the pre-FNAC era, only 14% of surgically resected thyroid nodules were malignant. However, with the introduction of FNAC, the surgical resection of malignancy increased up to 50%.[4] Traditionally, the use of diverse nomenclature and diagnostic criteria by pathologists for reporting of thyroid nodules has limited the understanding of cytopathology reports by clinicians, thus hindering a definitive management.[5]

In 2007, The Bethesda system for reporting thyroid cytology (TBSRTC) was proposed at the National Cancer Institute Thyroid FNA State of Science Conference at Bethesda, Maryland. This reporting system includes suggestions regarding the layout of the report, adequacy of the sample, diagnostic category, risk of malignancy, and proposed...
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clinical management. TBSRTC standardized the cytology reporting for thyroid lesions, providing a uniform, explicit, and clinically pertinent reporting nomenclature.\(^6,7\)

The present study was undertaken to study and assess TBSRTC for ease of reproducibility and to note the rate of overall disagreement or in any particular category.

**Materials and Methods**

The retrospective study included smears from all thyroid FNACs performed over a period of 1.5 year (June 2013 to December 2014). Wright Giemsa and Papanicolaou-stained FNAC smears along with relevant clinical and radiological details of 107 patients having a non-TBSRTC diagnosis were retrieved from cytopathology records and analyzed by two trained cytopathologists in a double-blinded fashion. The FNAC smears were reclassified according to the 6 diagnostic categories of TBSRTC as nondiagnostic/unsatisfactory (ND/US); benign; atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS); follicular neoplasm/Suspicious for a follicular neoplasm (FN/SFN), suspicious for malignancy (SUS), and malignant.\(^6,7\)

The results of both the cytopathologists were evaluated for interobserver variability by calculating the percentage of agreement. Statistically, the degree of reproducibility was estimated using Cohen’s kappa to confirm an agreement beyond chance.

The study was carried out after due approval from the Human Ethics Committee of the institute. A waiver of consent was obtained for the same.

**Results**

A total of 107 patients were included in the present study, out of which 90 (84.1%) were females and 17 (15.8%) were males, with a female: male ratio of 5.3:1. The age of the patients ranged from 21 to 60 years, with a mean of 37.8 years. Majority of the cases (24.3%) belonged to the age group of 21–50 years.

In the present study, concurrence of diagnosis by two cytopathologists was observed in 98 cases (91.5%) whereas disparity was noted in 9 cases (8.5%). The highest number of cases were re-categorized in the benign category (96 cases; 89.7%), followed by the FN/SFN category (4 cases; 3.7%), 2 cases (1.87%) each in ND/US, SUS, and malignant categories, and 1 case in AUS/FLUS (0.93%). There was absolute agreement on the cases in the ND/US and AUS/FLUS category followed by a 94.8% concordance in the benign category. The FN/SFN, SUS, and malignant categories displayed agreement only in 50% of the cases.

The highest diagnostic disagreement was noted among ND/US and benign and benign and FN/SFN categories, i.e., the maximum number of discordant cases of ND/US category by one observer were put into benign category by the second observer. Similarly, the maximum number of discordant cases of benign category by one observer was put into FN/SFN category by the second observer followed by the ND/US or AUS/FLUS category. These cases of benign category were previously diagnosed either as hyperplastic nodule or colloid goiter. In the FN/SFN category, disagreement was noted in 2 out of 4 cases. Both the discordant cases were categorized in the benign category by one of the observers. Of the two discordant cases, 1 case was earlier diagnosed as hyperplastic nodule and the other as colloid goiter with cystic change. Out of the 2 cases in the SUS category, consensus was not reached in 1 case between the two observers and was kept in malignant category by one of the observers. In 1 out of 2 cases in the malignant category, complete agreement was recorded whereas the other case was kept in the SUS category [Table 1].

| Table 1: Evaluation of thyroid lesions recategorized according to TBSRTC by two observers |
|-----------------|--|--|--|--|--|--|
| Category according to experts | ND/US | Benign | AUS/FLUS | FN/SFN | SUS | Malignant | Total |
| According to observer 1 |   |   |   |   |   |   |   |
| ND/US | 02 | - | - | - | - | - | 02 |
| Benign | 04 | 91 | 01 | - | - | - | 96 |
| AUS/FLUS | - | - | 01 | - | - | - | 01 |
| FN/SFN | - | 02 | - | 02 | - | - | 04 |
| SUS | - | - | - | - | 01 | 01 | 02 |
| Malignant | - | - | - | - | - | 02 | 02 |
| Total | 06 | 93 | 02 | 02 | 02 | 02 | 107 |

Cohen’s kappa to confirm an agreement beyond chance revealed “good agreement” (61.30%; 0.613).

**Discussion**

FNA is a widely accepted diagnostic modality for the preliminary assessment of thyroid nodules. However, the deficiency of a consistent and homogenous reporting terminology for the diagnosis of thyroid FNA led to the introduction of TBSRTC in October 2007.\(^8-10\) The appropriate communication of FNA results in reporting thyroid cytology
is very crucial as the management of the thyroid nodule depends on the cytological diagnosis. Before the advent of TBSRTC, a variety of terminologies were used for thyroid FNA which were ambiguous and led to uncertainty, thus debilitating the suitable treatment and sharing of data among multiple institutions.[11] The TBSRTC system is a universal reporting system which helps cytologists and physicians in understanding and foreseeing the scenario by estimating the malignant potential of individual categories.[12]

In the present study, a concurrence of diagnosis was observed in 91.5% of the cases, and the agreement beyond chance was ruled out by Cohen’s kappa (0.613). This was in corroboration with findings of other studies in literature.[6,13-15]

The interobserver disagreement in the present study was found to be in the benign category with five discrepant cases. Out of the 5 cases, 4 were classified in the ND/US category by one of the observer because of the presence of only cyst macrophages. However, the other observer found the presence of thin colloid in the background and categorized the cases in the benign category. According to TBSRTC, a sparsely cellular specimen with abundant colloid should be considered benign.[4]

The presence of thin colloid can be mistaken for tissue fluid, confusing the cytopathologist. In our case, the presence of predominantly cystic macrophages in a fluid background prompted one of the observers to diagnose the cases as cyst fluid only, and hence these cases were categorized into the ND/US category [Figure 1a]. One out of 5 discrepant cases in the benign category was categorized as AUS/FLUS by one of the observer as it showed focal follicular atypia. These focal changes were attributed to repair by the other observer and the presence of abundant colloid in the background prompted a benign category diagnosis [Figure 1b]. Similar findings have been observed in previous studies where a discrepancy in diagnosis has been attributed to low cellularity with focal nuclear atypia.[6]

Two cases in the FN/SFN category were discordant between two observers and were categorized as benign by one of the observers. The existence of high cellularity and predominance of microfollicular arrangement along with scant or absent colloid may call for a diagnostic deviation from benign to FN/SFN category [Figure 1c] as has also been noted in earlier studies.[6] The presence of fire flares may encourage a diagnosis of benign lesion but fire flares have also been noted in follicular adenoma [Figure 1d]. However, a clear distinction between hyperplastic nodule in multinodular goiter and follicular adenoma is not possible by FNA and does not have much clinical significance.[3,4,6]

The discordant cases among the SUS and malignant category were underdiagnosed by one of the observers due to low cellularity of FNA smears [Figure 2a] compared to the concordant case in malignant category [Figure 2b]. The thyroid lesion is categorized in the SUS category if there is low cellularity or there is focal atypia due to which a definite diagnosis of malignancy cannot be rendered. Though the risk of malignancy for SUS is lower as compared to malignant category, the preferred mode of treatment for both is near total thyroidectomy. Some authors have suggested a surgical lobectomy for the SUS category, however as the malignancy risk is as high as 60–75%, an eventual near total thyroidectomy has to be done for a majority of patients. Thus, the distinction between SUS and malignant category might not be of much clinical significance.[4]

TBSRTC has proven to be a very valuable, practical, and standardized system of reporting thyroid lesions. It has many advantages over other terminologies and classification systems used for reporting thyroid cytology. It not only provides uniform terminology which is better understood it also associates the risk of malignancy and recommends the clinical management for each category, thus avoiding unnecessary surgeries.

However, along with its many advantages a few pitfalls were noted in the present study. The AUS/FLUS category appears to
be a waste basket category, and the categorization of a lesion in this category is very subjective. The overlapping cytological features of hyperplastic nodule and follicular adenoma led a cytologist to mistake one for the other. Lastly, for the SUS and malignant category, the differentiation is not very clear and depends to some extent on the confidence and experience of a pathologist.

The limitation of the present study was a lack of histological correlation for the AUS/FLUS and FN/SFN cases. We only had a histological diagnosis of SUS and malignant category cases.

To conclude, TBSRTC is a distinctive, universal, and homogeneous terminology for reporting the thyroid cytology and its execution should be promoted in our country because of its virtual ease of reproducibility. The practicing cytopathologists as well as clinicians should be adequately trained for the diagnostic criteria, terminology, and guidelines of TBSRTC for a more efficient usage of this system.

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Conflicts of interest
There are no conflicts of interest.

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