

## Comparative Study of Reporting Fine Needle Aspiration Cytology of Thyroid Lesions by Conventional and Bethesda System

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### Abstract

**Background:** Thyroid lesions are common, presenting mostly as enlargement of thyroid gland. Fine needle aspiration cytology (FNAC) of the thyroid is an easy procedure providing rapid and accurate diagnosis. Terminology for reporting has varied amongst pathologists. Bethesda system provides guidelines for cytological reporting category and management. **Aim:** To classify the thyroid lesions according to Bethesda system for reporting thyroid cytology, compare with conventional system and correlate cytological diagnosis. **Material and Methods:** A prospective study was conducted over a period of 2 years on 202 consecutive patients. FNAC of thyroid gland was done and smears prepared. Smears were reviewed and cytological reporting was done according to both conventional and Bethesda systems. **Result:** Most of the patients were females (177, 87.6%) with a mean age of 37.4 years. 4.0% were non diagnostic, 91.1% were benign, 1.5% were atypia/follicular lesion of undetermined significance, 1.0% were suspicious for follicular neoplasm/ follicular neoplasm and 2.4% were malignant. Radiological findings were available in 100 cases and showed diagnostic deviation in 2 cases with cytological findings. Histopathological correlation was present in 16 cases and revealed minor deviation in one case. **Conclusion:** The Bethesda System for Thyroid Cytology is a useful method in reporting different thyroid lesions. In our study a definite interpretation for lesions in category I and III was provided by following specific criteria. Standardising the reporting methodology increases the reproducibility of diagnosis.

**Keywords:** Cytology; Correlation; Conventional; Bethesda System; Radiological; Biochemical; FNAC.

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### Introduction

Thyroid lesions are frequent with an annual incidence rate of 4-8% [1]. Fine needle aspiration cytology (FNAC) of the thyroid is a widely utilized tool for the diagnosis of thyroid lesions with high degree of sensitivity, specificity and diagnostic accuracy. It provides a more rapid and accurate diagnosis of thyroid lesions than any other combination of clinical and laboratory tests. Terminology for thyroid FNA has varied from one laboratory to another due to lack of standardised system of reporting [2]. Pathologists were using different terminologies and diagnostic criteria thus creating much confusion [3].

For clarity of communication and uniformity of terminology, the National Cancer Institute (NCI) proposed the Bethesda System for Reporting Thyroid Cytology (TBSRTC) in 2007 that has attempted to standardize the diagnostic approach of reporting by laying down cytomorphological criteria. It entails the format of report, evaluation of adequacy and diagnostic categories. The adoption of this system will facilitate better communication among the pathologist and clinician and also allows easy and reliable sharing of data among laboratories [4,5].

The present study was undertaken to report the thyroid cytology smears by TBSRTC, compare it with the existing system in an attempt to standardize the reporting system and aid in patient management.

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### Material and Methods

A prospective study was conducted on 202 patients who underwent FNAC of thyroid gland over a period

of 2 years from July 2014 to June 2016. Ethical clearance from institutional ethic committee was taken prior to study. Informed consent for FNAC procedure was obtained. FNAC was performed using fine 24 gauge needle by aspiration or non-aspiration technique. Air dried smears stained with May Grunwald Giemsa (MGG) stain and wet fixed (ethyl alcohol) smears stained with Papanicolau (Pap) and Hematoxylin and Eosin (H&E) stain were prepared. Cytological reporting on stained smears was done according to conventional method and later categorised according to Bethesda system for reporting thyroid cytology in a blinded manner by 2 pathologists. In case of discrepancy opinion of third pathologist was taken. The six diagnostic categories of Bethesda system- Non diagnostic or unsatisfactory (ND/UNS); Benign; Follicular lesion of undetermined significance (FLUS)/ Atypia of undetermined significance (AUS); Suspicion for Follicular neoplasm (SFN) / Follicular neoplasm (FN); Suspicion for malignancy (SFM) and Malignant [6,7].

Further correlation with radiological and histopathological findings were done wherever available.

## Results

A total of 202 patients were included in the study. Age of patients ranged from 11 to 92 years with the mean age of 37.4 years. There was female predominance with 87.6% cases and 12.3% cases being males. The male to female ratio was 1:7.1. Majority of the patients (28.2%) were in 2<sup>nd</sup> decade. 98% patients presented with palpable thyroid lesion

and in 2% cases ultrasound guided FNA was done. 98% patients presented with swelling as most frequent chief complaint. Other complaints were of anxiety and difficulty in deglutition in 67.3% and 65.8% cases respectively. 54.5% had diffuse enlargement of thyroid gland and 45.5% showed nodular lesion.

Most commonly benign lesions were diagnosed followed by lesions in other categories (Table 1).

Eight cases were reported in category 1 with 4 (2.0%) showing only cyst fluid followed by non- diagnostic in 3 (1.6%) and unsatisfactory in 1/8 (0.4%) (Figure 1).

Majority of the cases were in Category II 184 (91.1%). They included 136 cases of benign follicular nodule with 95 cases (47.0%) of colloid goitre followed by 29 cases (14.4%) of hyperplastic nodule and 12 (5.9%) cases of nodular goitre. Thyroiditis was reported in 48 cases with 28 (13.9%) cases of chronic thyroiditis and 20 (9.9%) of lymphocytic thyroiditis (Figure 2).

Category III included 3 cases (1.5%) (Figure 3). Two cases were categorised into category IV (Figure 4) and 5 cases were malignant: 4 were papillary carcinoma and 1 was medullary carcinoma (Figure 5), None of the cases was diagnosed as suspicious for malignancy.

Radiological findings could be correlated in 100 cases. Non-neoplastic diagnosis on radiology was given in 98% cases. Out of which on FNA 94.0% (92/98) were categorised into BFN (category II), 4.0% (4/98) were non diagnostic (category I) and 2.0% (2/98) cases were of FLUS (Category III). One lesion in category IV and VI, each was given an impression of suspicious for malignancy on radiology. On

Table 1: Bethesda categorisation of thyroid lesions

	Bethesda Category	Cases	%
I	Non-diagnostic/unsatisfactory	8	4.0
II	Benign	184	91.1
III	Atypia / follicular lesion of undetermined significance	3	1.5
IV	Follicular neoplasm/suspicion for follicular neoplasm	2	1.0
V	Suspicion for malignancy	0	0.0
VI	Malignant	5	2.4
	<b>Total</b>	<b>202</b>	<b>100</b>

Table 2: Comparative diagnostic analysis according to conventional and Bethesda reporting system

S. No.	Conventional Method	Cases	Bethesda system
1.	Colloid goitre	2	Category I (Unsatisfactory)
2.	Could be neoplastic	1	Category III (FLUS)
3.	Hyperplasia/ possibility of follicular neoplasm	1	Category III (FLUS)
4.	Excessive hurthle cell change (? Neoplastic)	1	Category III (FLUS)

comparing USG findings with FNAC in benign cases; sensitivity and specificity were 85.7% and 88.8% respectively.

Histopathological diagnosis was available in 7.9% (16/202) of cases, 15/16 of the cases show cyto-histopathological concurrence. One of the cases which was reported as colloid goitre on cytology was reported as colloid goitre with associated thyroiditis on histopathology.

On correlating the reporting terminology, Bethesda system provided a specific category. (Table 2) 2 cases reported as colloid goitre conventionally were reclassified into category I, as on review microscopically cellularity did not meet the adequacy criteria. 3 cases which were diagnosed as suspicious for neoplasm conventionally were reclassified into category III as FLUS. 2 of these cases had moderate amount of cellularity with sheets and clusters of follicular cells exhibiting anisonucleosis and

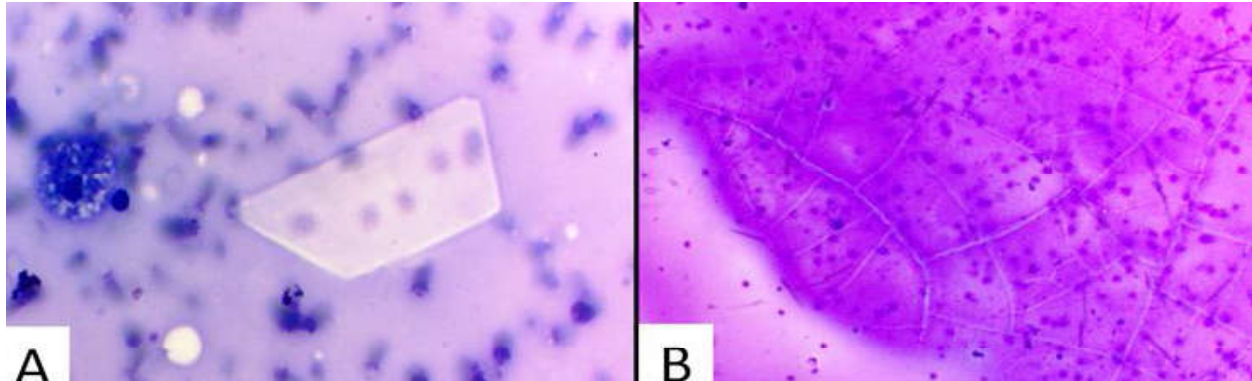


Fig. 1: Category I- A. Cyst fluid only: Blood mixed thin colloid with haemosiderin laden macrophage and cholesterol crystal. (MGG, X 400) B. Unsatisfactory aspirate: Thin colloid exhibiting pavement artifact. Follicular cells absent. (MGG, X100)

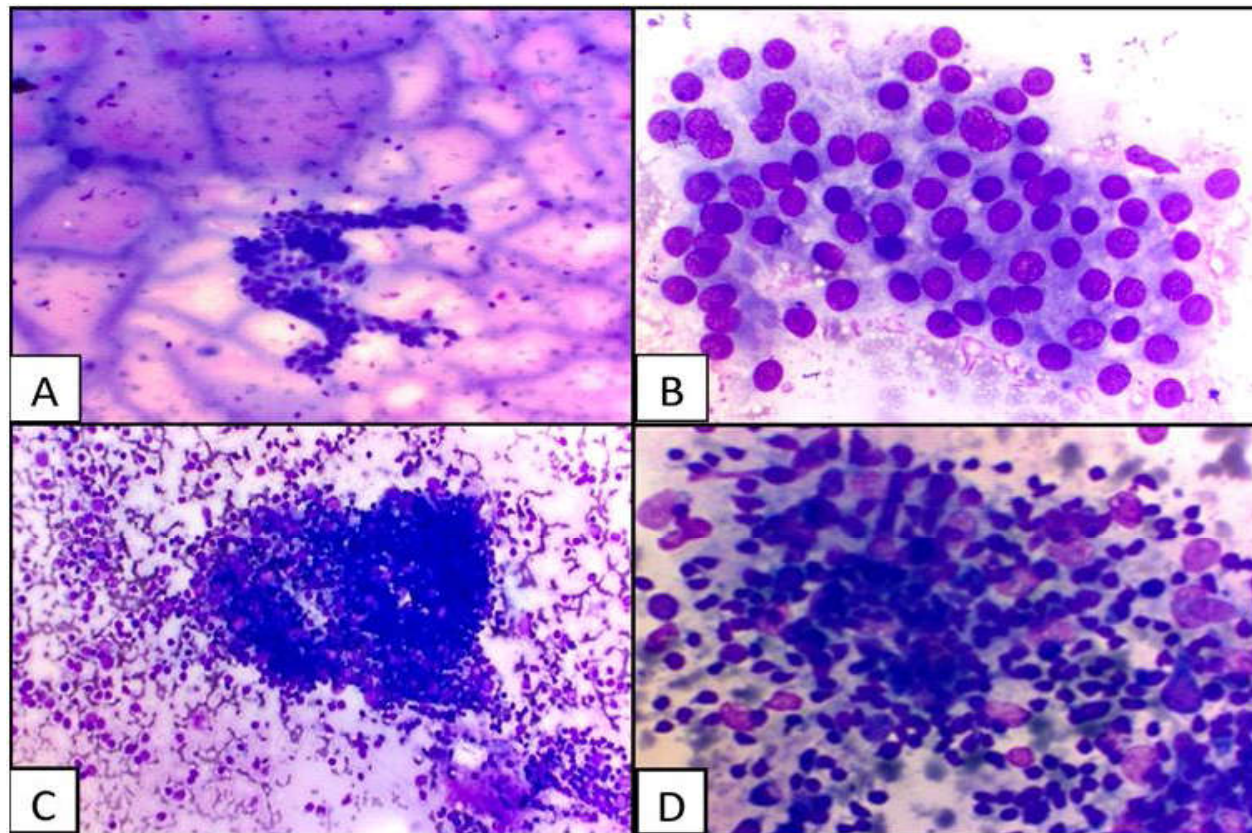
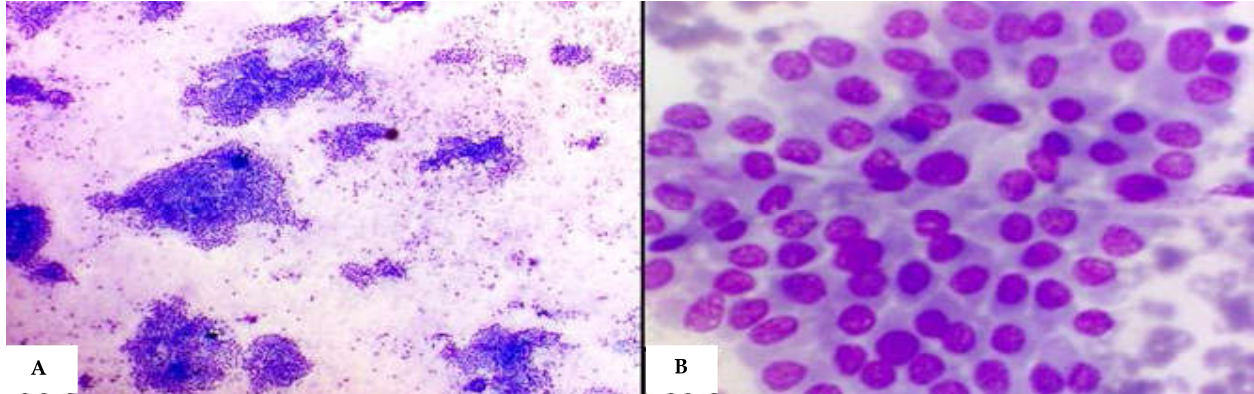
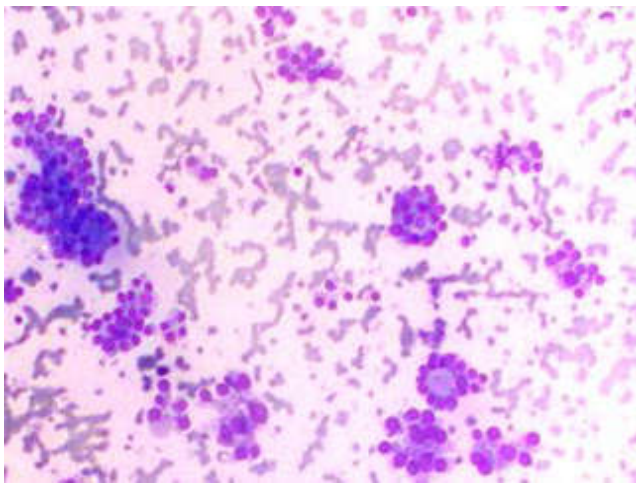


Fig. 2: Category II: Benign A. Colloid goitre (MGG, X 100) B. Hyperplastic Nodule: mild anisonucleosis, delicate fragile cytoplasm showing fire flares (MGG, X 400) C. Lymphocytic thyroiditis. (MGG, X 100) D. Chronic thyroiditis Hurthle cells being destroyed by lymphocytes (MGG, X 400)

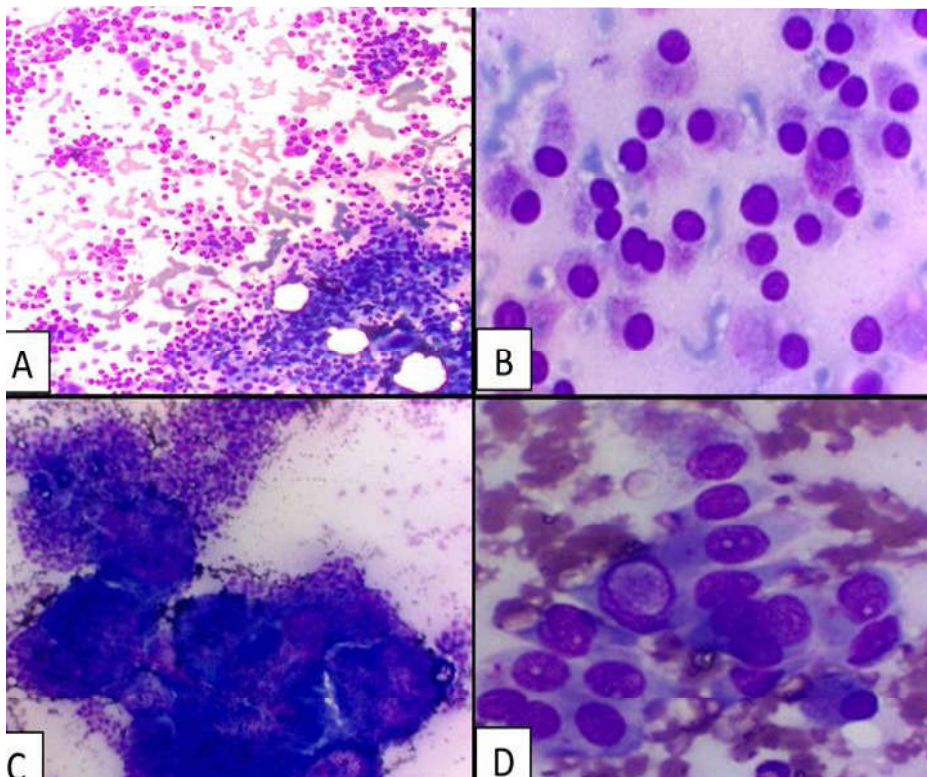




**Fig. 3:** FLUS: **A.** Clusters and sheets of large follicular epithelial cells (MGG, X 100) **B.** exhibiting anisonucleosis with extensive Hurthle cell change (MGG, X 400)



**Fig. 4:** Follicular neoplasm: Architectural atypia with micro-follicle formation.(MGG, X 100)



**Fig. 5:** Medullary carcinoma: **A.** Cellular smear with clusters and discretely lying follicular cells. (MGG X 100). **B.** Plump to oval cells with eccentric nuclei and eosinophilic granular cytoplasm. (MGG, X 400) Papillary carcinoma: **C.** Papillary arrangement (MGG, X 100) **D.** Plump cells having round to oval vesicular nuclei with intranuclear inclusions. (Arrow) (MGG, X 400)

overlapping. Other case had moderate cellularity consisting of hurthle cell change with scant colloid. However these findings were not sufficient to classify it as Hurthle cell neoplasm (HCN).

## Discussion

Thyroid lesions are the most common lesions subjected to the cytopathology as fine needle aspiration cytology is one of the first line investigation apart from biochemical and radiological investigations. Few borderline thyroid lesions often create confusion on cytopathological examination. To eliminate this confusion Bethesda system for reporting thyroid cytopathology (TBSRTC) has been implemented with main objective being to standardise the diagnostic terminology [8].

It thus reduces inter-observer variation and provides definite management guidelines thus minimizing the unnecessary surgical procedures for thyroid swellings and helps to determine better patient prognosis [9]. This system has separate category for indeterminate lesions that is FLUS/AUS; as thyroid aspirates with marked cellularity and focal features of atypia cellularly or architecturally are difficult to classify as observed in present study wherein 3 cases reported as suspicious for malignancy were reclassified into FLUS. There is a need for large study with histopathological correlation for predicting the incidence of malignancy in heterogenous categories as cases are unlikely to be operated [10].

Female sex has a predilection for thyroid disorders [11]. In present study there was female predominance with 87.6% cases, male to female ratio is 1:7 This is comparable to other studies [7,8,12].

Patients presenting with palpable or radiologically detected thyroid swelling were included in the study. Amongst 202 subject, 98% (198/202) of patients presented with swelling as the most frequent chief complaint followed by anxiety and difficulty in deglutition.

Mangshetty SS et al [13] observed 92.3% patients presented with slow growing midline neck swelling. Sreeramulu PN et al [14] concluded in a large series of patients that about 52% had presented with compressive symptoms including difficulty in swallowing, shortness of breath and change in voice.

Our study observed benign lesions were most frequent accounting for 91.1% of cases followed by non diagnostic/ unsatisfactory cases. Similar findings were observed by other authors [3,7,8] 2.0% cases were

cyst fluid only (CFO) followed by non diagnostic in 1.6% cases. Similar findings were observed by Mehra P et al [10] and Renuka V et al [15]. Two lesion diagnosed as benign category according to conventional system were reclassified into category I of Bethesda. Cystic fluid containing macrophages and no epithelial cell does not rule out possibility of cystic neoplasm. It is important to re-aspirate the lesion under ultrasound guidance as cystic change is commonly associated with 25% of papillary carcinomas and 20% of follicular neoplasms [16,17]. Two subsequent thyroid aspirates have a significantly lower risk of malignancy than patients with single non diagnostic aspirates [18].

Category II lesions were most common comprising of 67.3% (136/202) cases of benign follicular nodule and 23.7% (48/202) cases of thyroiditis which is similar to studies conducted by Sinna EA et al [12].

The cytological appearance of nodular goitre can overlap with that of follicular neoplasm, selective sampling of microfollicles with absence of colloid in nodular goitre may make distinction from follicular neoplasm difficult. Also, Cystic papillary carcinomas may often contain abundant colloid causing diagnostic difficulties if smears are poorly cellular. Careful analysis of nuclear features allows correlation in diagnosis [17].

Aspirates of hashimoto's thyroiditis when dominated by lymphocytes at various stages of maturation and the smear may resemble an aspirate of hyperplastic lymph node. Presence of hurthle cells and follicular cell clusters differentiates it from lymph node. Hurthle cells in hashimoto's thyroiditis should be differentiated from hurthle cell neoplasm. In thyroiditis the oncocytes are large, atypical and pleomorphic whereas hurthle cell tumours usually show monotonous cells and presence of lymphocytes is also uncommon [16,17]. 1.5% (3/202) cases were categorised into group III. One of the cases had excessive hurthle cell change and two showed marked cellularity with follicular cells exhibiting anisonucleosis and overlapping. Frequency of lesions in this category is comparable to data of other studies [14].

Three cases (Table 2) in present study were reclassified into FLUS as there was marked cellularity but cytological features were not sufficient to classify as a neoplastic process. The new incorporation of category III in Bethesda system increased reproducibility of diagnosis in the present study. Incorporation of this diagnostic category has increased the FNA sensitivity and decreased false positive and false negative rates. Estimate of the risk

of malignancy in indeterminate thyroid lesions is limited by the fact that not all nodules undergo surgery [19]. 1.0%(2/202) cases were categorised into group IV of follicular neoplasm as microscopically there was architectural atypia with microfollicle formation. Cytological diagnosis of follicular neoplasm (FN)/ hurthle cell neoplasm (HCN) remains controversial for clinicians differentiating benign and malignant is not possible and surgical resection is mandatory for the diagnosis of follicular carcinoma/ hurthle cell carcinoma. FNAC may be useful method in primary FN/HCN screening because if Follicular neoplasm is diagnosed by FNAC, the rate of histologic FN diagnosis is relatively high [20]. 2.4% (5/202) were categorised into group VI as malignant. There were 4 cases of papillary carcinoma of thyroid (PTC) and a single case of medullary carcinoma(MTC). This is similar to the findings of other studies [8].

Papillary carcinoma is most common type of thyroid cancer occurring predominantly in females most often in third to fifth decades. Combining clinical and cytological criteria and US-guidance while needing minimize false negative diagnosis [5].

Radiological findings correlated with cytological findings in 98% cases (98/100 cases). On comparing USG findings with FNAC in benign cases; sensitivity was 85.7% and specificity 88.8%. However Sreeramulu PN et al [13] in his study on 200 patients reported sensitivity 85.2% and specificity 60%. This variation could be due to difference in number of benign and malignant cases. In present study only in 2 cases radiological findings were suspicious for malignancy on USG.

Mamatha M et al [9] observed on comparing conventional and Bethesda system both sensitivity and specificity were significantly high for Bethesda and concluded TBSTC is more superior.

In present study histopathological diagnosis was available in 16 cases. Concordance was observed in (15/16) cases with minor deviation in one case reported as colloid goitre on cytology showed additional finding of colloid goitre with thyroiditis on histopathology. This could be because of the fact that FNAC is a blind procedure. In one case of category IV cyto-histopathological correlation was available. It was reported as follicular neoplasm on cytology and hurthle cell variant of follicular carcinoma on histopathology. Other studies have shown high concordance in reporting of category II, IV and VI. However minor discrepancy has been observed in other diagnostic categories.

## Conclusion

TBSRTC brings standardisation in reporting thyroid FNAC thus reducing inter-observer variation and providing definitive management guidelines. Incorporation of category III in Bethesda system increased reproducibility of diagnosis in the present study. Histopathology is not required in most of the cases and patients can remain on follow up of FNA [9]. Further studies and meta-analysis of cytological reporting by Bethesda system and histopathology need to be conducted to determine more specific morphological criteria as has been done for cervical cytology reporting by Bethesda categorisation.

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