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Original Research Article

# Thyroid lesions reporting using TBSRTC reporting system and cytohistopathological correlation- An experience at a tertiary care hospital

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ABSTRACT

**Background:** Thyroid lesions are most common head and neck lesions and a study was conducted to analyze thyroid aspiration smears by using The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), it has standardized reporting and cytological criteria in thyroid aspiration smears.
**Aims and Objectives:** To analyze the thyroid aspiration cytology smears by using TBSRTC and categorize, subcategorize thyroid lesions according to the TBSRTC monograph and to correlate cytopathology and histopathology, wherever surgery was performed.
**Material and Methods:** The retrospective study of 390 patients who presented with various thyroid presentations. FNAC was performed, smears were stained and evaluation of smears and categorisation was done as per TBSRTC into non diagnostic/unsatisfactory (ND/UNS), Benign Atypia of undetermined significance/follicular lesions of undetermined significance (AUS/FLUS), Follicular neoplasms / suspicious of follicular neoplasms (FN /SFN), Suspicious of malignancy(SFM), and Malignant. Cytohisto correlation was done.
**Results:** Out of 390 thyroid FNAC's ND/UNS 14(3.5%), Benign 357(91.3%), AUS/FLUS 01 (0.23%), FN /SFN08 (2.05%), SFM04(1.02%), Malignant 06 (1.53%). Cytohisto correlation was done in 53 patients sensitivity, specificity were calculated.
**Conclusion:** TBSRTC is an excellent reporting system for thyroid which avoids the unnecessary surgeries for the benign thyroids and gives proper guidelines to the clinicians about the patient management.



## 1. Introduction

Thyroid lesions are the most common lesions manifested particularly in country like India where it is endemic for iodine deficiency disorders and with goitre prevalence of about 40%.[1] Patients clinically present with solitary thyroid nodule, multiple thyroid nodules, diffuse thyroid nodule, pressure symptoms and other clinical symptoms. The majority of clinically diagnosed thyroid nodules are nonneoplastic and neoplastic lesions constitutes 5-30% and these requires surgical intervention for further management.[2–6] Thyroid malignancy is the most common endocrine malignancy. Papillary carcinoma is most common among the malignancies followed by follicular carcinoma, medullary carcinoma, anaplastic carcinoma followed by lymphoma.[7] Most common benign lesion is colloid goiter. FNAC is a safe procedure which is easily available in low cost, simple, reliable and results are quickly obtained.[8] It doesn't need any prior preparation of the patients and anaesthesia. FNAC is performed on clinically palpable thyroid nodules and also using ultrasonographically in cases of abnormal thyroid nodules which enhances the diagnostic accuracy.[9,10] FNAC procedure plays a major role in decreasing the unwanted surgeries for benign lesions and increasing the need of surgical management for the malignant thyroid lesions upto 50%.[11] This procedure have

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its own limitations also, its accuracy is lowers in suspicious lesions like follicular neoplasms.[12–15] These limitations are mainly due to the sampling technique from the variable thyroid regions, skill of the person in performing the procedure and interpretation of the thyroid smears.[16]

The cytopathologists were facing a problem to communicate thyroid FNAC interpretation to referring physician in terms of succinct, unambiguous, and clinically helpful. There are various reporting formats for thyroid reporting system, which made it very difficult to clinicians in understanding the thyroid reports. To address these issues National cancer institute (NCI) hosted a state conference at Bethesda, Maryland. There are six committees dealt with different areas regarding thyroid cytopathology. Diagnostic terminology and morphological criteria was dealt in committee IV 2(2). The Bethesda system for Reporting thyroid cytopathology TBSRTC which includes definitions, diagnostic criteria/ morphological criteria, explanatory notes and a brief management plan for each category shown in Table 1. Aim of current study is to report the thyroid cytology smears by using TBSRTC and help the clinician for the better management of the patient and to study cytohisto correlation.

## 2. Materials and Methods

The present study was conducted in department of pathology ESIC Medical College, Hyderabad, India during study period April2016 to April 2018. Patients with thyroid nodule referred to the cytology department from General medicine, General Surgery, Endocrinology departments. After the local examination of swelling and detailed explanation of FNAC procedure aspiration, consent was taken and procedure was done carefully with 23G needle, smears were prepared and fixed in 95% alcohol solution and stained with haematoxylin and eosin stain. Air dried smears were studied using May-Grunwalds Giemsa. If the aspirate yields fluid it was cytocentrifuzed and the smears prepared from sediment and those are stained with haematoxylin and eosin stains. Cytological features were evaluated and reporting was done according to TBSRTC (Table 1) whenever histopathological specimen available collected in 10% formalin in fresh state and allowed to fix for 24 hours. Detailed gross examination was done and bits were given paraffin embedded H&E stained sections were obtained and studied under light microscopy. Correlation of histopathological findings was performed with FNAC. Sensitivity, Specificity and Accuracy were calculated.

## 3. Results

The present study includes a total number of 390 cases. Patients age range from 11years to 75 years, most patients with female predominance. In the present study non-neoplastic lesions were more common than neoplastic lesions. Cytological categorization was done by using BETHESDA SYSTEM shown in Table 2 **.** Of the 390 cases, surgery was done for 53 cases only, it includes 2/14 category I cases, 42/357 category II cases, 0/1 category III cases, 3/8 category IV, 3/4 of category V cases, 3/6 category VI cases. Table 3 represents the Histopathology diagnosis of each category. There were 2 cases of Bethesda I category (nondiagnostic) with histological follow up both are benign. Bethesda II category includes 357 cases of which histological follow up in 42 cases, 40 were benign, except 2-one case was focal papillary thyroid carcinoma, one case papillary thyroid carcinoma showing the malignancy rate of 4.7%. Bethesda III category includes 1 case with no histopathology followup. Bethesda IV category includes 8 cases of which histological follow up in 3 cases 2 follicular carcinomas and one case was adenomatoid goiter with malignancy rate of 66%. Bethesda V category includes 4 of which histopathology followup in 3 cases all of them show papillary thyroid carcinoma with malignancy rate of 100%. Bethesda VI category includes 6 cases of which histopathology follow up in 3 cases all of them show papillary thyroid carcinoma with malignancy rate 100%.

## 4. Discussion

Thyroid cytopathology reporting requires standard, consistent and reproducible reporting system. There are many classification systems were there before adapting the TBSRTC. Main advantage of this system is the standardization of terminologies used for thyroid reporting. The 6 Categories of TSBRTC clearly specify the implied risk of malignancy rate in each category, and recommendation for surgical and clinical management. TSBRTC does not recommend surgery for the category I, II, III. It recommends excision of nodule or nodules, partial, complete thyroidectomy for category IV, V, VI.

In the present study among total of 53 patients 40 (77%) were female and 13(22%) were males with F:M ratio 3:1 and most of the patients belongs to 21-40 years. Mechanism underlying thyroid lesions most common in female patients not understood. Based on thyroid cytological findings these Thyroid lesions have been divided into two major groups, Non –Neoplastic 44(88%) and Neoplastic 6(12%). Most of them are Non neoplastic lesions it include colloid goiter 23(50%), adenomatoid nodule 11(6%). Lymphocytic Thyroiditis 8(16%), Neoplastic lesions includes follicular neoplasms 3(6%), Papillary carcinoma 3(6%), Unsatisfactory 2(4%).

These findings are correlating with the other studies in Gopal Krishna damle study[17] of 54 patients histopathological correlation 36 cases were goiters, 4 hurthle cell thyroiditis, 3 thyroiditis, follicular neoplasms 4, papillary carcinoma 3, thyroid neoplasms 2 cases. Handa U et al,[18] reported a study of FNAC in 434 thyroidswelling

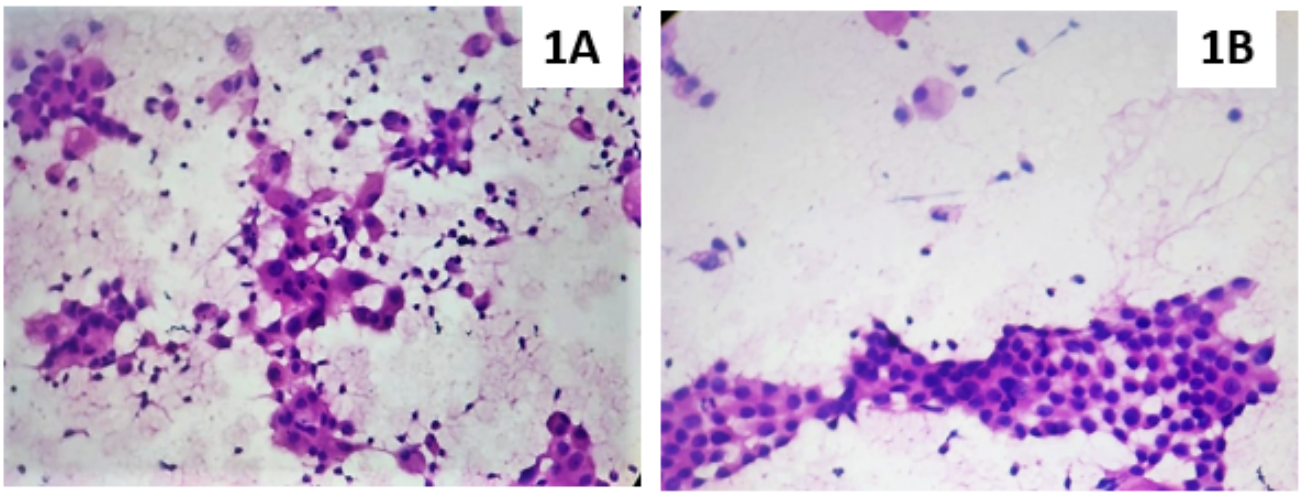


**Fig. 1: A:** Photomicrography shows Cystmacrophages in cystic fluid 40x H&E stain. **B:** 2 monolayred sheets of thyroid follicular cells and cyst macrophages in colloid goiter 40 x H&E

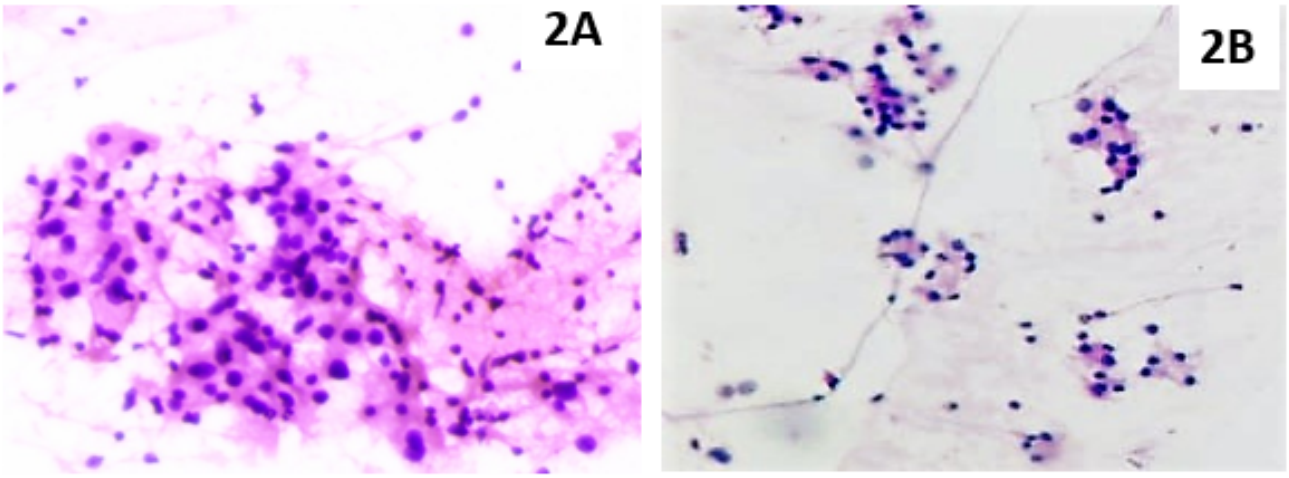


**Fig. 2: A:** Photomicrography shows cellular smear with Hurthle cell change and lymphocytic impinging on thyroid follicular cells 40x H&E; **B:** Pauci cellular smear with micro follicular pattern in (AUS/FLUS) 10x H&E

cases, out of which 57.60% FNAC reports was Colloid goiter followed by 27.41% thyroiditis, 2.30% adenomatous goiter. In 7.14% neoplastic group, 1.38% reported as follicular neoplasm and 3.91% as malignant.

Present study had 14 cases in ND/UNS Category. The number of cases in this category is dependent on the aspirator experience. These cases are repeated after 3 month to prevent false positive interpretations due to reparative changes, reactive changes. Histopathology specimen were available for 2 cases with diagnosis of colloid goiter on histopathology.

The Benign category had 357 cases with (91.3%), in recent studies with 7-14. The diagnostic criteria for this category was clearly mentioned in TBSRTC monograph. 42 cases were operated 40 cases were benign and 2 cases turned out into malignant.

Most of the lesions which are benign colloid nodules were correctly identified in cytology only 2 cases on histology which are turned to be nodular goiter with lymphocytic thyroiditis may be because of aspirate from the cystic areas of the lesion and also sample is not aspirated from multiple sites because of this we missed out the diagnosis. One previous study on the solitary thyroid lesion Gagneten study[19] enlightens the importance of performing multiple aspirations to obtain representative material from different areas since the thyroid can be affected by more than one disease process.

False negative cases constitutes about 4% in our study 2 cases of adenomatoid goiter histology one case turned out to be focal papillary thyroid carcinoma and one case papillary

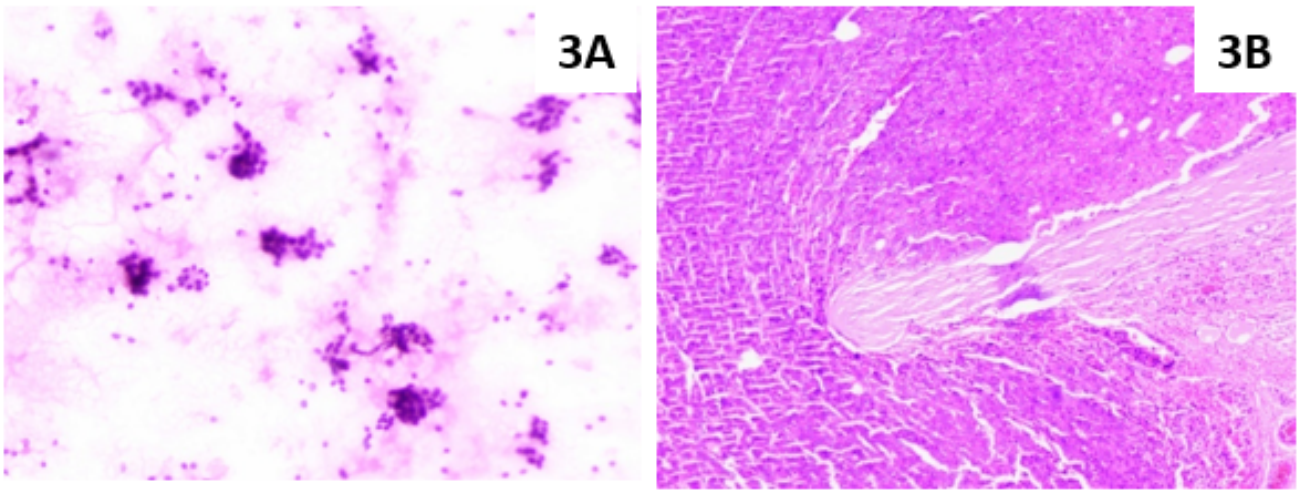


**Fig. 3: A:** Highly cellular smear with repitative microfollicles in SN/SFN 10X H &E; **B:** Histopathology section shows capsular breeching in Follicular carcinoma 40X H &E

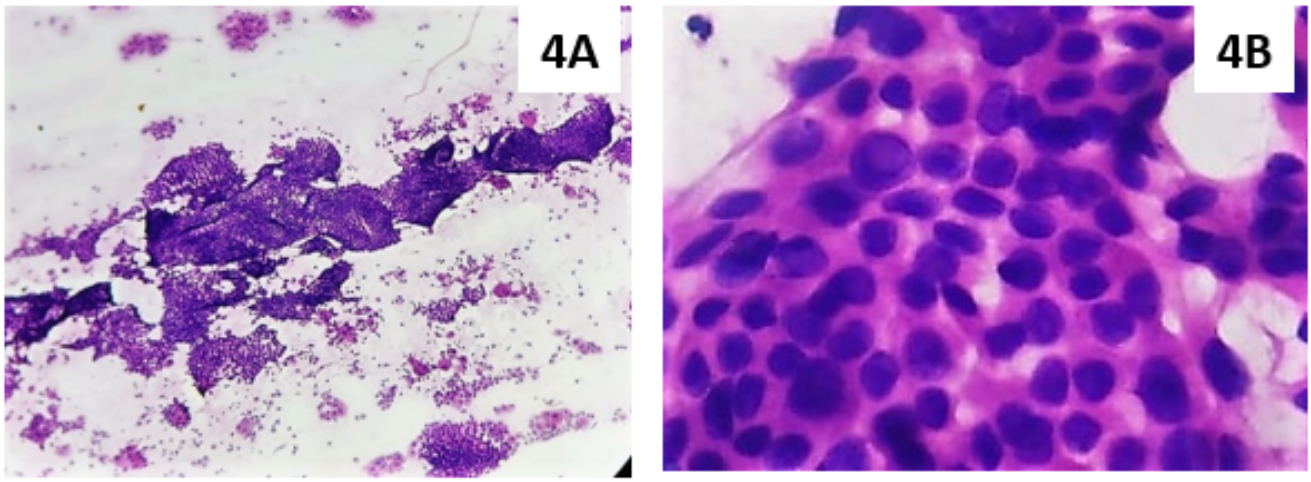


**Fig. 4: A:** Highly cellular smear with papillary pattern arrangement of thyroid follicular cells10X H &E; **B:** Intra nuclear inclusions in papillary carcinoma thyroid 40X H &E

thyroid carcinoma both these cases also show cystic areas in the thyroid lesions. Over all 40% of cystic neoplastic lesions missed in FNAC mainly cystic papillary carcinoma of thyroid. In Amatya et al.[20] study and Fernandes H et al[21] Shakuntala Sunil Aramani et al.[22] study also found a similar misdiagnosis.

Maral Mokhtari et al[23] in his study mention that cystic lesions in thyroid caused by both benign and malignant conditions. Adenomatoid (nodular) colloid goiter is the most common cause of benign cystic lesion of the thyroid gland[24] and 23% of the thyroid cystic lesions are caused by malignancy.[25] Suspicious cystic thyroid evaluation done carefully, if needed guided FNAC shall be done on cystic lesions. 25% of primary papillary carcinomas, 20% of follicular neoplasms and in 26% of follicular carcinomas of thyroid show cystic change and/or haemorrhage in neoplasms.[26]

Cytologic differentiation of Cystic Papillary Thyroid Carcinoma from cystic adenomatoid nodules was very difficult. Maral Mokhtari et al[23] in his study mention that presence of monolayer sheets and papillary clusters with central hyaline cores were seen only in CPTC, nuclear grooves and inclusions, foamy macrophages, atypical histiocytes, anisonucleosis, multinucleated giant cells, and calcification and the other findings specific to CPTC were as follows- small clusters with scalloped margins, cellular swirls, and clusters with a cartwheel pattern.

The false negative results are the poorly cellular sample in a cystic papillary carcinoma due to the thick fibrous capsule. The diagnostic error was most commonly due to inadequate specimens and cystic lesions.

**Table 1:** The Bethesda System for reporting thyroid cytopathology: recommended diagnostic categories, implied risk of malignancy, and recommended clinical management

| Diagnostic category | Risk of malignancy (%) | Usual managementa |
|---|---|---|
| **(I) Nondiagnostic or unsatisfactory (ND/UNS)** | | |
| Cyst fluid only<br>Virtually acellular specimen<br>Other(obscuring blood, clotting artifactsetc) | | Repeat FNA with ultrasound guidance |
| **(II) Benign** | | |
| Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule etc.)<br>Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context<br>Consistent with granulomatous (subacute) thyroiditis<br>Others | 0-3% | Clinical follow up |
| **(III) Atypia of undetermined significance or follicular lesion of undetermined significance (AUS / FLUS)** | 5-15% | Repeat FNAC |
| (IV) Follicular neoplasm or suspicious for follicular neoplasm (FN/SFN)<br>-specify if Hurthle cell (oncocytic) type | 15–30% | Surgical lobectomy |
| **(V) Suspicious for malignancy (SFM)** | | |
| Suspicious for papillary carcinoma<br>Suspicious for medullary carcinoma<br>Suspicious for metastatic carcinoma<br>Suspicious for lymphoma<br>Other | 60–75% | Near-total thyroidectomy or surgical lobectomy |
| **(VI) Malignant** | | |
| Papillary thyroid carcinoma<br>Poorly differentiated carcinoma<br>Medullary thyroid carcinoma<br>Undifferentiated (anaplastic) carcinoma<br>Squamous cell carcinoma<br>Carcinoma with mixed features (specify)<br>Metastatic carcinoma<br>Non-Hodgkin lymphoma<br>Other | 97–99% | Near-total thyroidectomy |

**a:** Actual management may depend on other factors (e.g., clinical and sonographic) besides the FNA interpretation. **b:** Estimate extrapolated from histopathologic data from patients with "repeated atypicals" **c:** In the case of "suspicious for metastatic tumor" or a "malignant" interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated

In one study 3 PTC was incidental finding because it was less than 1cm and no abnormality in ultrasonography, no lymphnodes it was missed during aspiration. Incidentalomas remain silent. In an autopsy study conducted by Harach et al. found that there was 30% prevalence of these incidentalomas.

Lymphocytic thyroiditis seen in 8 cases, all were confirmed histologically.

The Bethesda category III AUS /FLUS is reserved for specimens that meet the one of the following criteria cells with architectural and/ or nuclear atypia that not sufficient to be classified as suspicious for malignancy, according to 2009 Bethesda Criteria, sparse cellular smears cells that are arranged predominantly in microfollicles, sparse cellularity and scant colloid predominance of hurthle cells. Drying, preparation artifacts that hinders the interpretation of cells but atypia still present, moderate or marked cellularity with vast majority being hurthle cells but clinically has lymphocytic thyroidits or nodular goiter, benign appearing sample with focal features suggestive of papillary carcinoma, smears with atypical cyst lining cells, follicles with large nuclei and prominent nucleoli due to treatment change, reparative changes due to cystic degeneration or haemorrhage, atypical lymphoid population, not otherwise specified. 5-15% of Malignancy risk and these cases were repeated after three months.In our study only one case was reported with no histopathology followup. An AUS result has been reported in 3.2-29% of thyroid cases.TBSRTC suggested the range of AUS approximately 7% all thyroid neoplasms but no literature

**Table 2:** Cytological distribution of cases

| Bethesda classification | Total number of cases | Percentage |
|---|---|---|
| 1. Non – diagnostic or unsatisfactory Cystic fluid only Virtually acellular smears Other (obscuring blood, clotting artifactsetc) | 07<br>02<br>05 | 3.5% |
| 2.Benign | | |
| Adenomatoid nodule | 40 | 10.2% |
| Colloid nodule | 187 | 47.9% |
| Lymphocytic thyroiditis | 130 | 33.3% |
| Granulomatous thyroiditis | | |
| Others | | |
| 3. Atypia of undetermined significance or follicular lesion of undetermined significance (aus / flus) | 01 | 0.23% |
| 4. Follicular neoplasmor suspicious for follicular neoplasm | 08 | 2.05% |
| 5. Suspicious for malignancy Suspicious for papillary carcinomasuspicious for medullary carcinomasuspicious for metastatic carcinomasuspicious for lymphomaother | 04 | 1.02% |
| 6. Malignancy Papillary thyroid carcinomapoorly differentiated carcinomamedullary thyroid carcinomaun differentiated (anaplastic) carcinomas quamous cell carcinoma carcinoma with mixed features (specify) metastatic carcinomanon-hodgkin lymphomaother | 06 | 1.53% |
| Total | 390 | 100% |

**Table 3:** Comparision between results of FNAC and histopathology diagnosis

| Bethesda Classification | FNAC Diagnosis | Histopathology Diagnosis | False negative & positive percentage |
|---|---|---|---|
| 1. Non – diagnostic or unsatisfactory | 02 | 02 cases turned to colloid goiter | 02 true negatives |
| 2.Benign | | | |
| Adenomatoidgoiter | 11 | 09 adenomatoidgoiter, 01 focal papillary thyroid carcinoma, 01 ptc | 02 false negative 09 true positive |
| Colliodgoiter | 23 | 21 colloid goiter, 02 nodular goiter with lymphocytic thyroiditis | 20 true positive, 03 true negative |
| Lymphocytic thyroiditis | 08 | 08 lymphocyticthyroiditis | 08true positive |
| Granulomatous tyroiditis | | | |
| 3. Atypia of undetermined significant | | | |
| 4. Follicular neoplasm or suspicious for follicular neoplasm | 03 | 02 follicular carcinoma, 01 adenomatoidgoiter | 2 true positives 01 false positive, |
| 5. Suspiciousfor malignancy | 03 pct | 03 pct | 03 true positives |
| 6. Malignancy | 03 pct | 03 pct | 03 true positives, |
| Total | 53 | 53 | |

**Table 4:** Comparison of present study with other studies

| Studies | Year | Sensitivity | Specificity | Accuracy |
|---|---|---|---|---|
| C Gupta et al [27] | 2010 | 80 | 86.6 | 84 |
| Pinkey Panday et al [28] | 2012 | 57.14 | 90 | 80.28 |
| Parik et al [29] | 2012 | 71.43 | 100 | 90.24 |
| Ranjan et al [30] | 2014 | 82.14 | 86.8 | 83.60 |
| Gamit et al [8] | 2015 | 92.85 | 98.48 | 97.5 |
| Sarathbabu Kumara rama [7] | 2016 | 80-100% | 100 | 94.0 |
| Shakuntala Sunilaramani [22] | 2017 | 96.36 | 100 | 96.66 |
| Gopalkrishna Damle [17] | 2017 | 87.5 | 95.6 | 94.4 |
| Present study | 2018 | 95% | 83% | 94% |

to support this recommendations.

The Bethesda category IV FN/SFN recent studies shown that 2.2-16.1% in this category. In our study we received 1case of goiter misdiagnosed as follicular neoplasm in FNAC, it is because smears from the microfollicular areas in a goiter may show a repetative pattern of microfollicles similar to follicular neoplasm, in this cases differentiation from follicular neoplasms is very difficult. [31]

In another study they found that the majority of FN/SFN cases turn out to be FAs or adenomatoid nodules of multinodular goiter, both of which are more common than FC. Of those that prove to be malignant, many are follicular carcinoma but a significant proportion are follicular variants of papillary carcinoma. [32–35]

The Bethesda V SFM we had 3 cases suspicious for papillary carcinoma thyroid. On histopathology all are confirmed. Recent studies its range varies from 1.3-10. [7–14]

The Bethesda VI Malignant we had 3 cases of papillary carcinoma thyroid. 3 papillary carcinoma all are confirmed histologically. Different studies by Heimann A and Gritsman A suggest that different criteria for cytological diagnosis of papillary carcinoma of thyroid, combination of a intranuclear cytoplasmic inclusion, papillary structure with or without adherent blood vessels and dense metaplastic cytoplasm were the three most important variables. [31]

In the present study cytohistological correlation found to be, statistical analysis also shows sensitivity, specificity, positive productive value, negative productive value respectively.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None

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