

**Original Research Article**

TBSRTC in LBC Preparation of Thyroid Lesions– Preferred over the Conventional Cytology

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Abstract

Background: *Fine Needle Aspiration (FNAC) is simple, easy & cost effective method adopted worldwide as a pre-/ post-operative diagnostic tool for any thyroid lesion. Yet it has its limitation. Hence in 2007 The Bethesda System of Reporting Thyroid Cytopathology(TBSRTC) was framed by National Cancer Institute (NCI) to improvise the conventional cytology (CP) into Liquid Base Cytology (LBC)*

Material and Method: *Present prospective study was conducted in our Cytopathology section over a period of three years (from January 2015 – December 2017). Total 315 patients with visible and palpable thyroid swelling were aspirated after taking consent, by 22-23 Gauge needle with the help of an aspirator under all aseptic measures. Then 2-3 dry smears were made and 2-3 smears were fixed in alcohol for conventional smear study (CP). Dry smears were stained with Diff Quik stain and alcohol fixed smears were stained with Hematoxylin & Eosin (H&E) and papanicolau (PAP) stain. Rest of the samples were put in the preservative solution and then processed for Liquid Based Cytology (LBC) preparation and stained with PAP stained.*

Result: *Total 315 thyroid cases were sampled for CP study & LBC could be done for 156 patients. Yet total 250 cases could be correlated for histopathology. Out of 156 patients of LBC, one patient did not turn up for surgery & 10 cases were in TBS grade I category.*

In CP out of total 315 patients, only 250 cases were correlated and 15 cases were of grade I TBS category. Then specificity, sensitivity, accuracy, FPR and FNR were calculated for both CP & LBC methods and was analysed with other studies.

Conclusion: *LBC and TBS reporting system was found to be more comprehensive & communicative for Pathologist, Clinicians & patients with almost comparable sensitivity, specificity and accuracy.*

Keywords: *Thyroid, TBSRTC, LBC, CP.*

Introduction

Fine needle Aspiration Cytology (FNAC) is considered most important diagnostic test for thyroid lesions due to its safety, simplicity and

low cost. However it has limited role in discriminating benign from malignant follicular patterned lesions of thyroid. Liquid based cytology (LBC) for thyroid lesion is gaining

popularity for its excellent preservation and for the lack of undesired background. However neither LBC nor conventional cytosmears technique can substitute the histopathological diagnosis, but can be regarded as important tool for pre-operative diagnosis and post –operative follow up of thyroid lesions. The Bethesda system of reporting thyroid cytology (TBSRTC) was framed by National Cancer Institute(NCI) at Thyroid FNA of the Science conference and since then it has proved its utility in predicting cancer risk, improving clarity of communication among cytopathologists and physicians and for triage of patient with malignant thyroid lesions.¹

Aims and Objectives

The present prospective study was undertaken with aims and objectives to ascertain the utility of LBC over conventional cytosmears in the diagnosis of thyroid lesion using TBSRTC with special emphasis given on thyroid malignancy.

Materials and Methods

This prospective study was carried over a period of 3 years (from January 2015 to December 2017) in the department of Cytopathology of our institute, a tertiary care teaching institute. Sample was collected from the patients having thyroid swelling, referred by General Surgery and ENT department of our institute.

The study group comprised of total 315 random patients(n =315) having thyroid swelling who had undergone FNAC test, out of the total 7508 number of FNAC during that 3yr period. Out of 315 thyroid cases, 250 cases (n =250) were histologically correlated and 156 samples (n =156) were submitted for LBC. Patients of either sex with palpable thyroid lesion were included in the study (after informed consent). Samples were obtained for cytological study by FNAC technique² using 22 or 23 gauge needle by experienced cytopathologists. Conventional smears (CP) were prepared for each case. In all cases 2 to 3 smears were immediately fixed in 95% ethyl alcohol for 1 to 2 minutes and stained

for H&E or papanicolau stain. Rest of the conventional smears were air dried at room temperature for Diff Quick staining.

LBC was performed in 156 cases by the Thin Prep technique. For this the sample from the syringe was ringed into 30 ml of cyto Lit solution. It was then centrifuged at 1200g for five minutes followed by discarding off of the supernatant. The remaining cell palate was then resuspended in Preserv Cyt solution and processed using the Thin Prep processor. All the Thin prep slide were then stained with the Papanicolau stain.

Then both CP & LBC stained smears were reported according to TBSRTC categories.

TBSRTC recommended diagnostic categories are Gr I – Non diagnostic / Unsatisfactory, Gr II – Benign (includes adenomatoid nodule, colloid nodule, Hashimoto's thyroiditis, subacute thyroiditis etc), Gr III – Atypia of undetermined significance (AUS) or follicular neoplasm of undetermined significance (FUS), Gr IV -- follicular neoplasm or suspicious for a follicular neoplasm, Gr V ---- Suspicious for malignancy (includes suspicious for papillary carcinoma / medullary carcinoma / metastatic carcinoma/ lymphoma), Gr VI--- Malignant(includes papillary carcinoma / medullary carcinoma / metastatic carcinoma/ anaplastic carcinoma/lymphoma)

After FNAC diagnosis, 250 thyroid patients (n=250) underwent surgery whose surgical samples were received by the histopathology department of our institute. The samples were processed and stained with routine Haemotoxylin and Eosin (H&E) and then

Referring histopathology as gold standard, cases were correlated with both CP(n=250) and LBC (n=156) individually.

Group I category patients of both CP & LBC & equivocal/non diagnostic cases of histology were excluded from the study.

Results

Between January 2015-December 2017, prospective analysis of 315 patients was done who

were having thyroid lesions and were referred to cytology section of our department. The mean age of presentation was 40. 12 years with a female preponderance (M:F = 1:7.2). Most of the patients (35 %) presented with a bilateral or diffuse involvement of thyroid gland. The thyroid swelling was palpable in all cases except in 3 patients and of all cases the smallest lesion was 2x1 cm and the size of the largest one was 7x5 cm. Maximum number of (35.6%) patients presented with duration of symptom being more than 10 months. Majority of the cases were non tender (85.34%) and soft to firm in consistency. More than half the number of thyroid FNACs (56.50 % =178cases) in our study was diagnosed as colloid nodule.

Majority of the cases out of total 315 thyroid cases diagnosed by *conventional cytosmears preparation (CP)*: were categorized as benign (group II) & was 81.60% (257) comprising of colloid nodule(n=178), adenomatoid goiter(n=63),

autoimmune thyroiditis (n=12)& granulomatous thyroiditis (n=4); followed by malignant lesion (group VI) comprised of 7.6 %(n=24) . Atypia with undetermined significance (group III) was diagnosed in 0.9 %(n=3). Suspicious for follicular neoplasm / follicular neoplasm (group IV) and suspicious for malignancy (group V) constituted 2.9 % (n=9)and 2.2 % (n=7) respectively. 4.8% (n=15) of the conventional cytosmears preparation were falling under inadequate / non diagnostic category(group I).[Fig.1A].

Out of the 156 cases of *LBC*: 71.15% (n= 111) were benign lesions (group II), followed by malignant lesions (group VI) i.e.12.8 %(n= 20) . Atypia with undetermined significance (group III) was the diagnosis in 0.64 % (n=1)where as 4.5 % (n=7) were diagnosed as each of suspicious for follicular neoplasm (group IV) or suspicious for malignancy (group V). The LBC preparation was inadequate or non diagnostic (group I) in 6.41% (n=10). [Fig.1B]

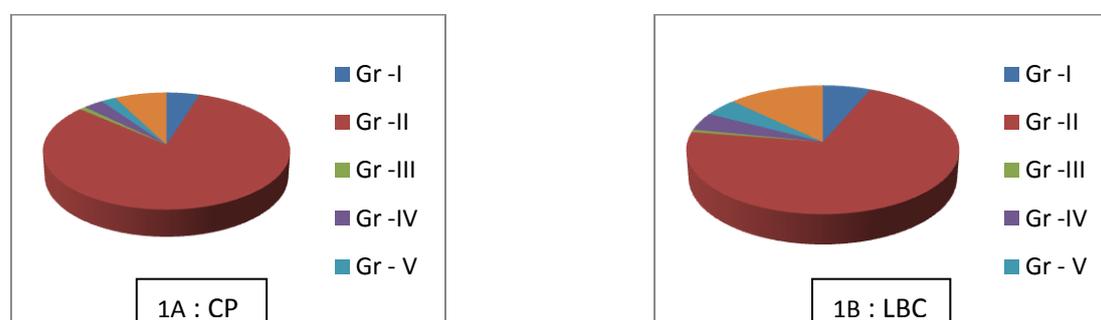


Figure 1A, B --Pie chart showing distribution of cases (in % age) in different groups, in both CP and LBC

In *CP and Histology correlation*: out of total 250 cases; Unanimous CP and Histology correlation was done in 204 cases as benign (group I) and 5 cases were found to be *false negative* (3 of which were actually medullary carcinoma and 2 were papillary carcinoma of thyroid). Out of total 31 malignant cases reported in CP (group V & VI) , only 24 papillary carcinoma of thyroid(Fig.3B), 3 medullary carcinomas, 2 anaplastic carcinomas where as 1 case reported as papillary carcinoma turned out to be hurthle cell adenoma (*false positive*) and another 1 case was equivocal & was excluded from the study. 5 follicular

neoplasm were found to be *true positives* i.e follicular carcinoma (Fig.2A).out of total 12 cases of (group III & IV); and rest 6 cases were reported as follicular adenoma histopathologically. 1 case reported as suspicious for follicular neoplasm in CP turned out to be non-diagnostic in HP study & was excluded.[Table1]

In *LBC and Histology correlation*: A total of 145 LBC –histology correlation could be done. Out of total31cases carcinoma of thyroid (group V & VI) in LBC; 25 cases were confirmed as papillary carcinoma of thyroid by HP-TBSRTC study (Fig.3A); whereas 1 case turned out as hurthle cell

adenoma (*false positive*), another 1 case did not turn up for surgery, only 1 case of anaplastic carcinoma could be correlated and no case (n=0) of medullary carcinoma was correlated. Out of 8 cases from group III & IV in LBC; 4 cases were found to be follicular carcinoma (Fig.2B) and 4 cases were follicular adenoma (*true negatives*). Out of total 111 benign cases of group II in LBC, 5 cases turned out to be *false negative* and reported

as 3 cases of medullary carcinoma and two cases of papillary carcinoma of thyroid in histology. Rest 106 cases were correlated well. [Table2] Hence sensitivity, specificity, positive predictive value (PPV), false positive rate (FPR), false negative rate(FNR) and accuracy was calculated for both the methods taking histopathology as gold standard and correlated with other studies.[Table3&4]

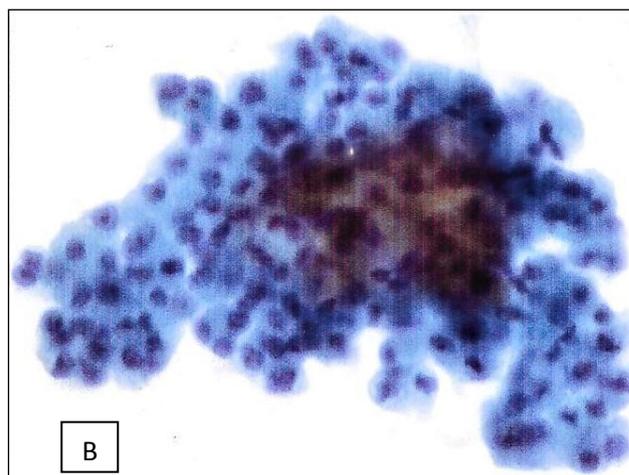
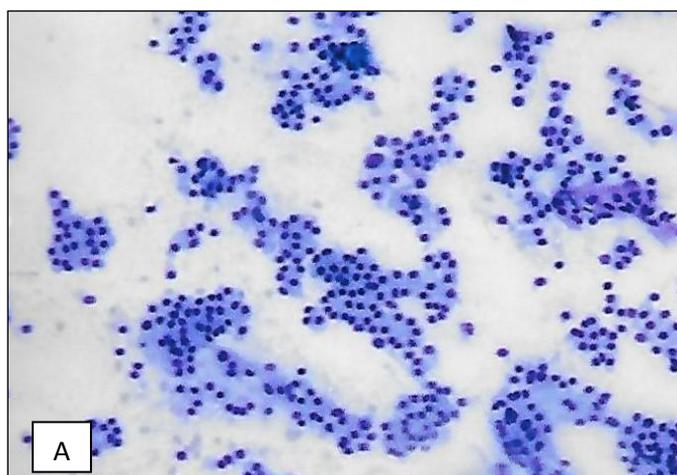


Fig-2A & B –Cytosmears of Follicular Neoplasm of Thyroid in CP (DIFF,100x) & LBC (PAP,400x)

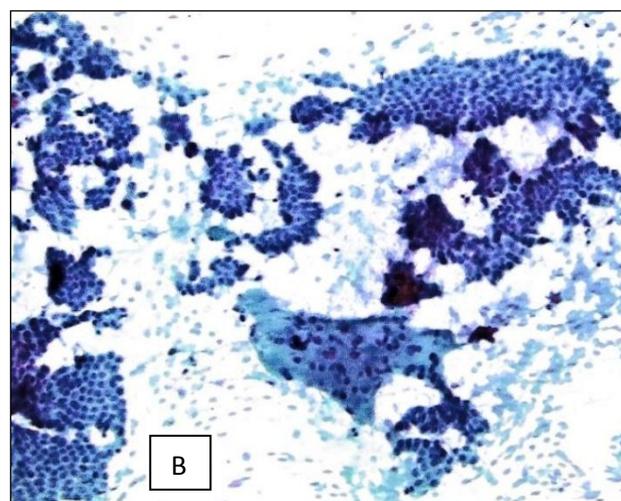
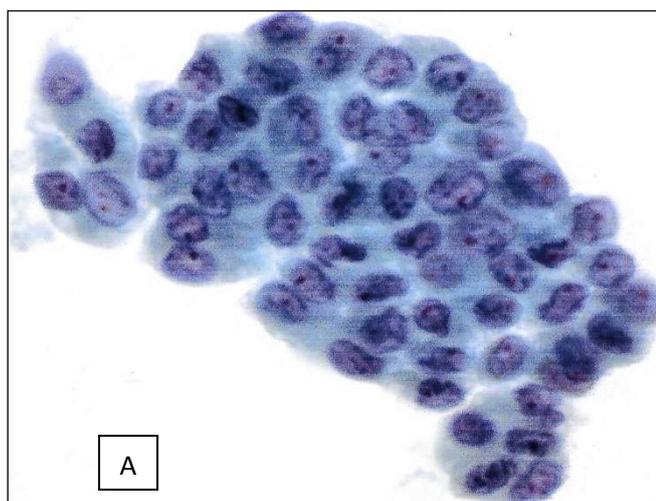


FIG-3A & B – Cytosmears of Papillary Carcinoma of Thyroid in LBC (PAP,400x) & CP (DIFF,100x)

Table 1: Correlation of morphological patterns in CP with histology

Pattern	CP	Histology	True Positive	True Negative	False Positive	False Negative
Benign nodule (Gr II)	209	209	0	204	0	5
Atypical / Suspicious FN (Gr III & IV)	11(3+8)	11	5	6 (3+3)	0	0
PTC (Gr V & VI)	25(18+7)	25	24	0	1	0
MC (Gr VI)	3	3	3	0	0	0
AC (Gr VI)	2	2	2	0	0	0
TOTAL	250	250	34	210	1	5

Table 2: Histological correlation of different morphological patterns as per TBS in LBC

TBS.	LBC	Histology correlation	True Positive	True Negative	False Positive	False Negative
GR II	111	111	0	106	0	5
GR III & IV	8	8 (7 + 1)	4	4 (1 + 3)	0	0
GR V & VI	25	25 (18 + 7)	24	0	1	0
GR V (MC)	0	0	0	0	0	0
GR V (AC)	1	1	1	0	0	0
TOTAL	145	145	29	110	1	5 (3+2)

Table 3: Statistical correlation of our study with other authors in CP

Sl no.	Study	Sensitivity	Specificity	Accuracy
1	Ko HM et al ^[13]	78	98	84
2	Ko HM et al ^[14]	79	98	87
3	Aravinthan T et al ^[10]	80	97	98
4	Guhamallick M et al ^[8]	93	98	
5	Mamoon N et al ^[15]	85	73	76
6	Sharma C et al ^[12]	89.5	98	97
7	Sinna EA et al ^[16]	92.8	94.2	93.6
8	Present study	87.17	99.52	97.6

Table 4: Statistical correlation of our study with other authors in LBC

Sl no.	Study	Sensitivity	Specificity	Accuracy
1	Afify AM et al ^[17]	70	95	88
2	Stamataki M et al ^[18]	88	99	98
3	Geer C et al ^[19]	77	81	80
4	Cochand PB et al ^[20]	81	60	72
5	Present LBC	85.29	99.09	95.86

Discussion

Thyroid lesions have always been a diagnostic challenge in clinical practice. Histopathology is the gold standard for accurate diagnosis of thyroid lesions, but it requires an operative procedure, is expensive and time consuming.

FNAC is considered the primary investigation of choice in evaluation of palpable thyroid nodule due to its safety, simplicity and low complication rate^[3,4] Aspiration cytology done by conventional smear method is accurate^[5] but has its own limitations owing to sampling errors and its inability to distinguish between benign and malignant follicular lesions. LBC is gaining popularity as a collection of pre-operative technique for needle aspiration due to its lack of air drying artifacts and clean background. In the past 10-15 years, LBC has been implemented as a complement to conventional smear. The study was carried out to ascertain the utility of LBC over conventional cytosmears, especially in diagnosing malignant thyroid lesions using TBSRCT.

A total of 315 cases with thyroid lesions were studied with the mean age of presentation of being 40.12 years which was comparable to the study by Rangaswamy M et al.^[6] The male: female ratio in our study was 1:7.2 which is closes to Handa U. et al (2008).^[3] The present study agrees with Kapilla K et al.^[7] that bilateral/diffuse involvement of the thyroid gland was the most common presentation. FNAC of thyroid swelling in our study yielded satisfactor y smear in 95.2 % of cases which is comparable and closest to the study of Guhamallick et al^[8]

Histopathological correlation was possible in 250 cases of conventional smear and 145 cases of LBC. Referring histopathology as the gold standard, false positive rate (FPR), false negative rate(FNR), sensitivity, specificity, PPV and accuracy was calculated for both conventional preparation & LBC and was compared with other studies.

Dean DS and Gharib H in their study have suggested that Hashimoto thyroiditis is probably

the most common cause of false positivity followed by follicular and hurthle cell adenoma which are often misdiagnosed as PTC^[9]. The most common cause of false negative error is inadequate or improper sampling. The false positive rate (FPR) in the present study was 0.48% in CP and 0.91% in LBC which was lower than most of the studies^[4,8,10,11,13] and was comparable to the study of Guhamallick et al^[8] and Sharma C^[12]. False negative rate (FNR) in our study was 12.83% in CP and 14.71% in LBC, which was higher than most of the studies and was comparable to the study by Sharma C^[12].

Sensitivity of thyroid cytology by conventional smear (CP) ranged from 78% to 93% and specificity ranged from 73% to 99.52% in various studies. In the present study the sensitivity to diagnose malignancy was 87.17% and the specificity was 99.52%. This result is comparable to other studies^[8,10,12,13,14,15,16] and agrees with the study by Sharma C. The PPV was 87.17% & accuracy in our study was 97.6% and it is closest to the study by Aravinthan T et al^[10].

In the present study LBC had sensitivity of 85.29% and specificity of 99.09% and with an accuracy of 95.86% & PPV 96.66% .

It was compared with other studies^[17,18,19,20] and was in accordance with the Stamataki M et al^[18].

References

- Mufti ST, Molah R. The Bethesda system for reporting thyroid Cytopathology: A five year retrospective review of one center experience. *Int J health Sci (Qassim)* 2012;6(2);159-173
- Orell SR, Vielh P. The Techniques of FNA Cytology: i) Basic techniques, Miscellaneous Techniques.
- Handa U, Garg S, Mohan H, Nagarkar N. Role of Fine Needle Aspiration Cytology in diagnosis and Management of thyroid Leison: A Study of 434 Patients, *Journal of Cytology*. 2008;25(1):13-17.
- Sing P, Chopra R, Calton N, Kapoor R. Diagnostic Accuracy of Cytology of thyroid Leisons. *Journal of Cytology* 2000;17(3):135-9
- Silverman JF, West RL, Finley JL, Larkin EW, Park HK, Swanson MS, Fore WW. Fine Needle Aspiration versus Large Needle Biopsy or Cutting Biopsy in Evaluation of Thyroid Nodules. *Diagnostic Cytopathology*. 1986;2:25-30.
- Rangaswamy M, Narendra KL, Patel S, Gururajprasad C, Manjunath GV. Insight to Neoplastic Thyroid Lesions by Fine Needle Aspiration cytology. *J Cyto*. 2013;30(1):23-26.
- Kapila K Pathan SK, George SS, Haji BE, Das Dk, Qadan LR. Fine Needle aspiration cytology of the thyroid in children and adolescents: Experience with 792 aspirates, *acta cytol*. 2010;54(4):569-74
- Guhamallick M, Sengupta S, Bhattacharya NK, Basu N Roy S, Ghose AK, Chowdhury M. Cytodiagnosis of thyroid lesions – usefulness and pitfalls; A study of 288 cases, *J cytol*. 2008;25(1):6-9
- Dean DS, Gharib H. Fine needle aspiration biopsy of thyroid gland. [updated 2015 april 26]
- Aravinthan T, Banagala A, Gamage K. use of fine needle aspiration cytology on thyroid lumps, *Galle Medical journal* 2009;12(1):25-27
- Mandal S, Barman D, Mukherjee A, Mukherjee D, Saha J, Sinhas R. Fine needle aspiration cytology of thyroid nodules-evaluation of its role in diagnosis and management, *J Indian med association*, 2011;109(4);258-61.
- Sharma C. Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant cases. *J Egypt Cancer institute* 2015; 27:147-53.
- Ko HM, Jhu IK, Yang SH et al. Clinicopathologic analysis of fine needle aspiration of the thyroid: A review of 1613 cases and correlation with histopathologic diagnosis, *Acta cytol*. 2003;47:727-32.

- 14 Ko HM, Gavriel H, Zahab S et al. Accuracy and consistency of fine needle aspiration biopsy in the diagnosis and management of solitary thyroid nodules, *IsrMedical association J*,2005;7(6):371-73
- 15 Mamoon N, Jamy R, Khan AH, Evaluation of fine needle needle aspiartion cytology in thyroid as a screening tool in thyroid lesions, *J Pak Med association* 201;63(9):1120-23
- 16 Sinna EA, Ezzat N, Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions, *J Egypt canc Inst* 2012;24:63-70
- 17 Afify AM, LIU J, Al Khafaji, BM Cytologic artifacts and pitfalls of thyroid fine needle aspiratin using thin prep: A comparative retrospective review *ancer* 2001;93(3):179-86
- 18 Stamataki M et al. The role of liquid based cytology in the investigation of thyroid lesions. *Cytopathology* 2008;19(1):11-18
- 19 Geer C, Bourgain C, liquid based FNAC of the thyroid : a 4 year survey with Surepath. *Ancer Cytopathology*, 2011;119(1):58-67
- 20 Cochand Priolett-B, et al. Thyroid fine needle aspiration: The morphological features on Thinprep slide preparation, eighty cases with histological control. *Cytopathology*, 2003;14(6):343-49.