Bangladesh J Otorhinolaryngol 2021; 27(1): 36-43

Original Article

Correlation of Ultrasonography Guided Fine Needle Aspiration Cytology with Postoperative Histopathology in Diagnosis of Thyroid Nodule

Md. Jaber-Al-Sayied[1], A Allam Choudhury[2], Sonia Jahan Bithi[3], Ashim Kumar Biswas[4], Riashat Azim Majumder[5], Md. Abdur Razzak[6], Md. Hasanul Haque[7], Md. Quamruzzaman[8]

Abstract:

Background*: Fine-needle aspiration cytology (FNAC) is recommended as a decisive diagnostic step in the workup of patients with nodular thyroid disease. Unfortunately, FNAC can miss malignancies in smaller and deeper nodule. Ultrasound guided FNAC (US-FNAC) can reduce this error in suspicious thyroid nodule.*

Objectives: *To find out the correlation of USG guided FNAC with postoperative histopathology in diagnosis of thyroid nodule.*

Methods: *After obtaining clearance and approval from Institutional Review Board, all 45 patients of thyroid nodule who were admitted in the Department of Otolaryngology – Head & Neck surgery of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from April 2017 to August 2018 and had fulfilled the inclusion and exclusion criteria were selected for the study. Each patient was assessed before surgery by USG guided FNAC and post operatively by histopathology.*

Results: *In this study mean age of the respondents was 33.33 yearswith SD±10.84. Male female ration was 1:5.4. USG guided FNAC was reported by 'The Bethesda System for Reporting Thyroid Cytopathology' (TBS-RTC).Of the 45 specimens 2 samples were nondiagnostic or*

1. Junior Consultant, Department of Otolayngology-Head & Neck Surgery, Mugda Medical College & Hospital, Dhaka, Bangladesh
2. Professor, Department of Otolayngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
3. Senior Consultant,Department of Dentistry, Central Police Hospital, Rajarbag
4. Associate Professor, Department of Otolayngology-Head & Neck Surgery,Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
5. Medical Officer, Department of Otolayngology-Head & Neck Surgery,Mugda Medical College & Hospital, Dhaka, Bangladesh
6. Junior Consultant, Department of Otolayngology-Head & Neck Surgery,Shahid Tajuddin Ahmed Medical College & Hospital, Dhaka, Bangladesh
7. Medical Officer, Department of Otolayngology-Head & Neck Surgery,Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
8. Junior Consultant, Department of Otolayngology-Head & Neck Surgery,250 Bedded general Hospital, Pabna, Bangladesh

Address of correspondence: Dr. Md. Jaber-Al-Sayied, Junior Consultant (ENT), Department of ENT & Head-Neck Surgery, Mugda Medical College & Hospital, Dhaka, Bangladesh. Mob: 01717796151, Email: mdjaberalsayied@gmail.com

unsatisfactory (Class I), 26 samples were benign (Class II), 2 samples were showing Atypia of Undetermined Significance or Follicular lesion of Undetermined Significance (Class III), 6 were showing follicular neoplasm or suspicious for a follicular neoplasm (Class IV), 5 samples were suspicious for malignancy (Class V) and 4 samples were positive for malignancy (Class VI).

On comparison of ultrasound guided FNAC with histopathology the sensitivity for correct diagnosis was 94%, specificity was 93%, positive predictive value was 88%, negative predictive value was 96% and accuracy was 93%. Pearson's correlation coefficient was 0.85 which is very strong for positive relationship.

Conclusion: *USG guided FNAC is the most accurate method for diagnostic evaluation of thyroid nodules.*

Key words: *USG guided FNAC, Thyroid.*

Introduction:

Thyroid nodules are common in adults, which may be detected by palpation in 3-7% of patients. The prevalence may be raise as high as70% or more, if sensitive imaging such as ultrasonography is being employed. Most of these thyroid nodules are benign in nature. To avoid unnecessary surgery ultrasono-graphy and FNAC is being used as a diagnostic tools to differentiate between malignant and benign lesions. Although accurate diagnosis between follicular carcinoma and follicular adenoma is difficult by FNAC[1].

In patients with nodular disease FNAC is widely recommended as an initial and crucial test to select those patients who require excision of the lesion and subsequent histologic diagnosis. If FNAC proves to be either suspicious or malignant, surgery is indicated. The optimal diagnostic strategy is aiming to avoid surgery in patients with benign thyroid disease, while at the same time performing prompt surgical treatment of patients with thyroid carcinoma. To achieve this, FNAC must score high on test characteristics. This can be achieved by USG guided aspiration.[2]

5-38% of clinically detectable thyroid nodules are malignant. Of the initial screening tests for patients with thyroid nodules, FNAC is widely used. It is used to differentiate benign from malignant thyroid nodules and helps preoperatively in selecting patients for surgery. But USG guided FNAC may increase its accuracy & will reduce unnecessary thyroid surgeries[3].

Historically, the diagnostic criteria and reporting nomenclature of FNAC is varied internationally. These are epitomizedby the North American National Cancer Institute(Bethesda) terminology (2007), Italian (2007, 2014), Australian (2014), Japanese (2013) and British Thyroid Association/Royal College of Pathologists guidelines (2002, 2007, and 2016). The terminology for non-diagnostic, benign, malignant and suspect for malignancy is similar across each of these classifications with minor differences inemphasis for the equivocal/indeterminate category. Numerical categories increase accuracy, aid local audit, allow comparison with other centers including internationally and can guide discussion on further management[4].

The aim of this study was to identify the correlation of USG guided FNAC with postoperative histopathology in thyroid nodule. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of USG guided FNAC was also evaluated after the surgical removal and histopathological diagnosis.

Methods:

This prospective observational study was performed on 45 patients in the Department of Otolaryngology – Head & Neck surgery, Department of pathology, Department of radiology & imaging, Bangabandhu Sheikh Mujib Medical University, Dhaka from April

2017 to August 2018.After obtaining clearance and approval from Institutional Review Board, all patients of thyroid nodule who were admitted into Department of Otolaryngology – Head & neck surgery of the concerned institution and fulfill the inclusion and exclusion criteria was recruited as subjects in the study. Patients with thyroid nodule, age ranging from 20 to 70 years was included in the study. Patients not ready for surgery, with already diagnosed thyroid lesions by histopathology & all toxic goiters confirmed by clinical evaluation were excluded from the study. Diagnosis of thyroid nodule was done by clinical examination, USG of thyroid and USG guided FNAC of thyroid. FNAC was carried out under ultrasound guidance so that the needle position can be controlled and samples can be regarded as representative, even within very small nodules. A written "informed consent" was taken. Experienced radiologist performed an ultrasonography guided fine needle aspiration with the use of 10 ml disposable syringe with 23-gauge needle by using a perpendicular puncture. When the needle tip reached the target nodule, the needle was observed as a small echogenic spot within the nodule on the US monitor. After placing needle tip in the appropriate area of the target nodule, sampling was commenced. After obtaining a sample, the specimen was mounted immediately onto a glass slide. Specimens were fixed with 95% ethanol and were sent for cytological evaluation. Reporting was done by "the Bethesda system for reporting Thyroid Cytopathology" (TBS- RTC). Then all other relevant investigations were done &informed written consent was taken from all patients for surgery except Bethesda class I. Patients with non-neoplastic FNAC diagnoses underwent surgery because of pressure symptoms or unwillingness to carry out follow-up. All patients, reported as Bethesda class II - VI were operated under general anesthesia. Postoperative histopathology report was obtained & correlation was done with preoperative USG guided FNAC. Data were collected by interview and by laboratory investigation using structured data collection sheet.

Statistical Analysis:

Data were processed and analyzed using Microsoft Excel 2016(Microsoft office professional plus 2016). Correlation of USG guided FNAC with histopathology was done by Pearson's correlation coefficient.

Results:

The mean age of the respondents was 33.33 years with SD±10.84. Most of them were female, house-wife& living in rural areas. Highest number of respondents were diagnosed as Bethesda class II in USG guided FNAC.

Table I :

Distribution of different lesions diagnosed by histopathologist (n=45)

Group by classes		USG guided FNAC	Histopathology	
			Benign	Malignant
I	Non-diagnostic or unsatisfactory	2 (4.44%)	Not operated	Not operated
II	Benign	26 (57.72%)	25	1 (PTC)
III	Atypia of undetermined significance or follicular lesion of undetermined significance	2 (4.44%)	1 (FA)	1 (FTC)
IV	Follicular neoplasm or suspicious for a follicular neoplasm	6 (13.32%)	1 (FA)	5 (FTC)
V	Suspicious for malignancy	5 (11.10%)	0	5 (PTC)
VI	Malignant	4 (8.88%)	0	3 (PTC) 1 (MTC)
Total		45	27 (60%)	16 (36%)

Key PTC: Papillary thyroid carcinoma, FA: Follicular adenoma, MTC: Medullary thyroid carcinoma, FTC: Follicular thyroid carcinoma

The table shows 2 samples (4.4%) were class I, 26 (57.72%) were class, 2 (4.4%) were class III, 6 (13.32%) were class IV, 5 (11.1%) were class V, 4 (8.88%) were malignant class VI. There were 2 false positive cases from correct diagnosis and only 1 smear was false negative when compared with histopathology. True positive was 15 cases & true negative was 25 cases.

In current study pearson's correlation coefficient is 0.85. Which reflects USG guided FNAC has very strong positive relationship with post operative histopathology. Performance of USG guided FNAC reveals Sensitivity 94%, Specificity 93%, Positive predictive value 88%, Negative predictive value 96%, Accuracy 93%.

Table II :

Distribution of malignant lesion in histopathology.

Malignant lesions (n= 16: 36%)	Histopathology	USG guided FNAC	
Papillary carcinoma	9	Suspicious formalignancy(PTC)	5
		Malignant (PTC)	3
		Benign	1
Follicular carcinoma	6	Follicular neoplasm	5
		Atypia of undetermined significance	1
Medullary carcinoma	1	Malignant (MTC)	1
Total	16	16	

On histopathology of these smears, there were 16/45 cases with malignant thyroid lesions.

Table III :

Distribution of benign lesion in histopathology.

Benign lesions (n= 27: 60%)	Histopathology	USG guided FNAC	
Colloid goiter	16	Benign	23
Multinodular goiter	7	(Consistent with a benign follicular nodule)	
Follicular adenoma	2	Atypia of undetermined significance	1
		Follicular neoplasm	1
Hashimoto's thyroiditis	2	Benign	2
		(Consistent with lymphocytic thyroiditis)	
Total	27		27

On histopathology 27/45 (60%) specimens were benign lesions.

Table IV :
Correlation of USG guided FNAC with Histopathology.

US FNAC Category	N	Histopathology						
		Colloid goiter	Multinodular goiter	Follicular adenoma	Hashimoto's thyroiditis	PTC	FTC	MTC
Non diagnostic	2							
Benign	26	16	7		2	1		
Atypia of undetermined significance	2			1			1	
Follicular neoplasm	6			1			5	
Suspicious for malignancy	5					5		
Malignant	4					3		1

Key: US FNAC= USG guided fine needle aspiration cytology, PTC= Papillary carcinoma of thyroid, FTC= Follicular carcinoma of thyroid, MTC= Medullary carcinoma of thyroid.

Table showing US FNAC findings were in concordance with histopathology.

Discussion:

USG guided FNAC is a least invasive, simple and most accurate method to evaluate thyroid nodule. Ultrasound guidance allows continuous visualization of the needle during insertion and sampling with resulting in pinpoint accuracy with a high level of safety.

In the present study, age of the patients ranged from 18-65 years with a mean age of 33.33years with SD±10.84 years. These findings are in conformity with Irfan*et al.* 2014. They reported mean age 33.35 ± 11.77 years[5]. This finding may be due to prevalence of endemic goiter is more in younger age group.

In our study most of the respondents were female. This finding is similar to the finding of Haberal *et al*.2008.where 83.8% respondents were female and 16.2% respondents were male[6]. Goiter is predominantly present in female as there is estrogen receptor in thyroid which stimulates goitrogenesis.

We found that occupation of the most of the respondents were housewife. This finding has concordance with Kocak *et al*. 2013. where Goiter prevalence was highest in agricultural workers (35.3 %) and housewives (32.2 %), and lowest in the unemployed (3.5 %). They concluded that there was significant difference between occupational groups and goiter prevalence[7]. Our most of respondents were female and goiter is more common among them. This may explain why goiter is common in housewives.

In our study most of respondents were from rural area. It defer from study of Irfan *et al*. 2014. where 68.75 % respondents were from urban area and 31.25% respondents were from rural area[5]. Lack of health education, more consumption of goitrogen may be the cause of higher goitrogenesis in rural areas.

In the present study, USG guided FNAC of thyroid lesion result was interpreted as per Bethesda system. Most of our respondents belong to Bethesda class II, which is similar to a meta analysis on The Bethesda System for Reporting Thyroid Cytopathology (TBS RTC) of Massimo *et al*. 2012.Where 59.3% of 25445 patients reported as Bethesda class II. Bethesda class II is benign lesion, most of thyroid lesions are benign[8].

In our study Bethesda class-I was 4.44%, Class II -57.72%, class -III 4.44%, class IV - 13.32%, class V -11.1%, class VI -8.88% (Table I) which is in concordance with a meta analysis of Massimo *et al*. 2012 where class I-12.9%, class II-59.3%, class III 9.6%, class IV 10.1%, class V 2.7%, class VI 5.4%[8]. In class I & class V it is different from our study. This difference may be due to their inclusion of free hand as well as USG guided FNAC. In our study ultrasound guidance reduce rate of non-diagnostic rates. Al Sindi *et al*. 2013.evaluated USG guided FNAC in thyroid lesion, they also categorize their subjects as Bethesda system. They had class I -8.5%, class II-72.5%, class III – 10%, class IV- 3%, class V- 3.5%, class VI- 2.5%. USG guidance reported low non-diagnostic value in this study[9]. Major problems associated with free hand FNAC are significant false negatives (missed neoplasms) and difficulties in accurate identification of follicular lesions leading to wrong FNAC diagnoses[10]. In our study we observe 2 false positive cases and both are of follicular adenoma. Al Sindi *et al*. 2013.reported that all of their false positive cases were follicular adenoma. Though false positive cases are much lower in USG guidance[9]. Mustafa et al.2006 reported 33.3% false positive cases in palpation guided or free hand FNAC where as in USG guidance FNAC it was much lower (25%). This finding is due to the fact that FNAC has a limitation to differentiate follicular adenoma from follicular carcinoma[11].

The accuracy of FNAC depends crucially on the technique, operator-performing the aspiration and the cytopathologist-analyzing it. Even under optimal conditions, the false negative rate for thyroid neoplasms can vary from 1% to 6% due to wrong diagnosis or sampling errors. In our study there is a false negative case 1/45. It is similar to Daniele *et al*. 1998.[12]Who reported false negative in 1% cases of USG guided FNAC. He observed the false negative rate much lower for US-FNAC when compared with free hand FNAC. These false negative cases are may be microcarcinoma (<1cm) which may be missed by USG. Microcarcinoma is usually papillary carcinoma and our false negative case was confirmed as papillary carcinoma by histopathology. Other cause may be the fact that cystic lesion harbor occult malignancy in 10% of cases. USG guided aspirates are usually done in solid component of nodule.

A review of studies that evaluated the role of US-FNAC in the detection of thyroid cancer revealed a sensitivity of 76%–98%, specificity of 71%–100%, false-negative rate of 0%–5%, false-positive rate of 0–5.7%, and overall accuracy of 69%–97%.[12] Our results have shown Pearson's correlation coefficient was 0.85. Which reflects USG guided FNAC has very strong positive relationship with post operative histopathology& in our study sensitivity and specificity of US-FNAC was 94% and 93% respectively. The PPV 88%, NPV 96% and the diagnostic accuracy was 93%.

In our study most of the malignant lesion was papillary carcinoma (9), rest are follicular carcinoma (6) and medullary carcinoma (1%).(Table 2&4).which is similar to the Pannersalvam *et al*. 2013[13] where papillary carcinoma was 61.5%. Daniele *et al.*[11] 1998 reported papillary carcinoma 71.7%, follicular carcinoma 7.6% and medullary carcinoma

1.9%.Among 9 cases of our study 5 were suspicious for malignancy (PTC), 3 were malignant (PTC) and 1 was benign in USG guided FNAC; Among 15 reported cases of Al Sindi et al. 2013 in USG guided FNAC 5 were suspicious for malignancy, 3 were malignant and 1 was benign lesion[9]. In our study 6/16 cases were follicular carcinomas among them 5 were follicular neoplasm and 1 was atypia of undetermined significance in USG guided FNAC; Al Sindi *et al.*2013 reported 4/15 cases were follicular carcinomas among them 2 were follicular neoplasm and 2 was atypia of undetermined significance in USG guided FNAC; in our study 1/16 case was of medullary carcinoma which was reported as malignant (MTC) in USG guided FNAC which is similar to Al Sindi *et al.* 2013[9]. In our study most of the benign lesion of histopathology was colloid goiter (16/27) multinodular goiter was (7/27) both were reported as benign in USG guided FNAC (Table 3&4). Which is in consistent with Irfan *et al.* 2014 where most of benign lesion reported as colloid goiter (51%)[5].

Some of the potential advantages of US-FNAC in the evaluation of nodular thyroid disease is guiding the needle to take samples from non-palpable nodules. The major benefit of this technique is accurate sampling of small or multiple nodules. Certain sonologic features of thyroid lesions are predictive of malignancy and hence such lesions can be accurately aspirated[14]. Another crucial benefit of using US-FNAC is significant reduction in the number of inadequate aspirates[11]. It is possible that reduced number of inadequate aspirates may potentially lead to increase in the yield of cancer and the diagnostic accuracy of FNAC. The rate of inadequate specimens in our study was 4.4 % (2 out of 45 samples), which is comparable to the above quoted studies. (Table I & IV)

We categorized cytological results into six classes according to Bethesda description for thyroid cytology. Such categorization of FNAC smears results is necessary to allow clinicians to use cytology results to guide patient management with specific reference to the need for thyroidectomy. Our study showed that use of better reporting system (Bethesda methods) there was relatively low rate of non diagnostic or inadequate smears, allowing it to be useful method for determining the treatment plan for non palpable smaller thyroid nodules. In our study the incidence of adequate specimens was 43/45 (96%) with US- FNAC as compared to the Kim *et al.* 2009 who found it 81% in his series of 201patients[15].

Conclusion:

USG guided FNAC isnearly as accurate as histopathology in diagnosis of thyroid nodule.

Recommendation:

Small and suspicious thyroid nodule on USG should undergo an USG guided FNAC.

Inadequate smears from free hand FNAC yields accurate result by USG guided FNAC.

References:

1. Lin J, Huang B, Weng H, Jeng L and Hsueh C. Thyroid ultrasonography with fine needle aspiration cytology for the diagnosis of thyroid cancer. Journal of Clinical Ultrasound.1997; 25(3):111-118
2. Giard R, Hermans J. Use and accuracy of fine needle aspiration cytology in histologically proven thyroid carcinoma. Cancer. 2000;90(6):330-334.
3. DE VOS TOT Nederveen, Cappel R, Bouvy N, Bonjer H, VAN Muiswinkel J, Chadha S. Fine needle aspiration cytology of thyroid nodules: how accurate is it and what are the causes of discrepant cases?. Cytopathology. 2001;12(6):399-405

4. Haugen B, Alexander E, Bible K, Doherty G, Mandel S, Nikiforov Y et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016; 26(1):1-133.

5. Irfan khan, Mohsinulrasool, Imran Khan, Sajad Hamid. Comparison of demographic distribution of colloid goiter on USG-guided biopsy with free guided biopsy and confirm the same with cytohistopathological diagnosis in a study population. Medical Science.2014;15(59):14-20.

6. Haberal A, Toru S, Özen Ö, Arat Z, Bilezikçi B. Diagnostic pitfalls in the evaluation of fine needle aspiration cytology of the thyroid: correlation with histopathology in 260 cases. Cytopathology. 2009;20(2):103-108.

7. Kocak M, Erem C, Deger O, Topbas M, Ersoz H, Can E. Current prevalence of goiter determined by ultrasonography and associated risk factors in a formerly iodine-deficient area of Turkey. Endocrine. 2014;47(1):290-298.

8. Bongiovanni M, Spitale A, Faquin W, Mazzucchelli L, Baloch Z. The Bethesda System for Reporting Thyroid Cytopathology: A Meta-Analysis. Acta Cytologica. 2012; 56(4):333-339.

9. Al-Sindi K, Bukhari M, Saba K, Ali W, Arshad M, Zaidi N. Evaluation of non-palpable thyroid nodules by ultra sound guided fine needle aspiration cytology. Natural Science. 2013;05(02):214-220.

10. Kopald K. Clarifying the Role of Fine-Needle Aspiration Cytologic Evaluation and Frozen Section Examination in the Operative Management of Thyroid Cancer. Archives of Surgery. 1989; 124(10):1201.

11. Cesur M, Corapcioglu D, Bulut S, Gursoy A, Yilmaz A, Erdogan N et al. Comparison of Palpation-Guided Fine-Needle Aspiration Biopsy to Ultrasound-Guided Fine-Needle Aspiration Biopsy in the Evaluation of Thyroid Nodules. Thyroid. 2006;16(6):555-561.

12. Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic Accuracy of Conventional Versus Sonography-Guided Fine-Needle Aspiration Biopsy of Thyroid Nodules. Thyroid. 1998;8(1):15-21.

13. Panneerselvam S, Rajan K Vaithianathan, Ramachandran Santhanam. Accuracy of ultrasound guided fine needle aspiration cytology in the evaluation of thyroid nodules. International Journal of Current Research and Review.2013; 05 (02):223-30.

14. Kovacevic O, Smetana Škurla M. Sonographic diagnosis of thyroid nodules: Correlation with the results of sonographically guided fine-needle aspiration biopsy. Journal of Clinical Ultrasound. 2007; 35(2):63-67.

15. Kim D, Park A, Lee E, Choo H, Kim S, Lee S et al. Ultrasound-Guided Fine-Needle Aspiration Biopsy of Thyroid Nodules Smaller Than 5 mm in the Maximum Diameter: Assessment of Efficacy and Pathological Findings. Korean Journal of Radiology. 2009;10(5):435.