Comparative Analysis of Routine Fine Needle Aspiration Cytology with Ultrasound Guided Fine Needle Aspiration Cytology in Thyroid Lesions

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ABSTRACT

Introduction: Fine needle aspiration cytology of thyroid lesions is the single most sensitive, specific and cost-effective method of investigation of thyroid nodules. Most palpable thyroid nodules can readily be aspirated without ultrasound guidance. However, non-palpable nodules/ complex nodules containing large areas of cystic degeneration are preferably aspirated under sonographic guidance to increase diagnostic accuracy. With this background we aimed to evaluate and compare the diagnostic yield of routine FNAC (R-FNAC) with Ultrasound guided FNAC (US- FNAC) in thyroid lesions.

Material and Methods: This was a cross sectional prospective study on all those patients who referred to the Department of Pathology for the evaluation of thyroid lesions from April 2016 to September 2016. Routine (R) FNAC and USG guided FNAC were conducted in randomly selected patient with thyroid lesions who give prior consent.

Results: A total of 65 patients were aspirated by both routine as well as USG guided FNAC during a six month period. Both smears were evaluated using Bethesda system for reporting thyroid cytopathology 2007. Overall the diagnostic sample rate was increased from 76.9% (R-FNAC) to 95.38% (US-FNAC). For benign lesions, the diagnostic accuracy was 74.94% and 94.54% for R-FNAC and US-FNAC respectively, with significant p value ($p<0.004$). With use of ultrasound guidance, the sensitivity, positive predictive value, and negative predictive value increased significantly. Among the malignant lesions, the diagnostic sample rates were 60% (R-FNAC) and 100% (US-FNAC) with a significant p value of <0.001. In addition, the inadequate specimen rate decreased from 23.1% (R-FNAC) to 4.62% (US-FNAC)

Conclusion: US-FNAC improved the cytological diagnostic accuracy, sensitivity, and positive predictive value and reduced the false-negative rate in comparison with R-FNAC. US-FNAC will also avoid unnecessary repeat FNAC in cases of unsatisfactory specimens.

Keywords: Routine FNAC, US-FNAC, Thyroid Lesions

INTRODUCTION

Thyroid lesions are a common clinical problem in the world. About 5% of the general population has palpable thyroid nodules and the prevalence increases to 10-55% with the use of ultrasonography[1] and thyroid malignancy occurs in 5-15% of the cases.[2] Generally, nodules more than 1cm has a greater potential to be a clinically significant cancer however non palpable nodules have the same cancer risk as palpable nodules with the same size;[3] Fine needle aspiration cytology of thyroid lesions is the single most sensitive, specific and cost-effective method of investigation of thyroid nodules.[4] Most palpable thyroid nodules can readily be aspirated without ultrasound guidance (palpation-guided FNAB). However, non-palpable nodules or complex nodules containing large areas of cystic degeneration are preferably aspirated under sonographic guidance to increase diagnostic accuracy;[5,6] With the use of Ultrasound, it can provide information regarding the location, number, size and echogenicity of thyroid nodules. The 2009 American Thyroid Association Management Guideline on Thyroid Nodule recommends fine needle aspiration biopsy (FNAB) for thyroid nodules greater than 0.5cm with high risk history (history of thyroid cancer in one or more first degree relatives, history of exposure to ionizing radiation during childhood or adolescence; prior hemi-thyroidectomy with discovery of thyroid cancer suspicious on sonographic features such as micro-calcifications, hypo-echoic lesion, increased nodular vascularity, infiltrative margins, absent halo and taller than wide on transverse view.[7]

Although FNAC is safely and widely recommended as the first line diagnostic test for the preoperative selection of patients in thyroid lesions. The major pitfall of this procedure is that routine FNAC cannot differentiate between follicular adenoma and follicular carcinoma and significant rate of false negative (missed neoplasms) cases. [8, 9]

Nowadays with the use of the Bethesda system for reporting thyroid cytology 2007, a flexible reporting framework which provides clinically relevant information that will assist referring physicians in the management of patients.[14]

Cystic fluid only (CFO -category 1) constitute 20-30% of the aspirate and there are 5% chance of intra-cystic papillary carcinoma which can be detected effectively by means of USG guided FNAC and categories 3 and 5 which are inconclusive and suspicious of malignancy respectively,

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where repeat aspiration or USG guided FNAC are advisable;[10] Several studies have suggested that the use of ultrasound guidance improves the diagnostic accuracy of aspiration biopsies in comparison with palpation guidance only.[5,11,12,13] The purposes of our study were to compare the cytological diagnostic accuracy of US-FNAC of thyroid lesions with that of Routine fine-needle aspiration cytology (R-FNAC) and to determine the sensitivity, specificity, positive and negative predictive value of USG-FNAC and Palpation guided FNAC in both benign and malignant lesions.

MATERIAL AND METHODS

This was a cross sectional prospective study on all those patients who referred to the Department of Pathology for the evaluation of thyroid lesions from April 2016 to September 2016. The Institutional Ethical Committee (IEC) approval will be taken prior to start of the research study as per protocol. Patient's informed consent will be taken in each case before including in the study and confidentiality will be maintained. Fine-needle aspirations of thyroid lesions were performed by both palpation guided routine(R-FNAC) as well as USG guided FNAC. All thyroid examinations, ultrasound imaging, and aspiration were performed in a similar manner by one pathologist and one radiologist. During this period, 65 patients (43 female and 12 male) underwent FNAC of thyroid lesions. All the patients of thyroid lesion coming to the Pathology department with routine requisition of FNAC. Patients, who do not give consent for complete study, already diagnosed, previously operated and with deranged INR (more than 2).

Study methods - Routinely, FNAC were done on solitary nodules or dominant nodules in multinodular glands. USG-FNAC was performed on all solitary palpable and non-palpable nodules according to US-based recommendations for thyroid nodules proposed by the American Thyroid Association;[7] the radiologist had preferentially select the thyroid nodule that shows at least one of the following malignant US findings: a taller-than-wide shape, a spiculated or microlobulated margin, marked hypoechogenicity, microcalcification, and/or macrocalcification. In contrast, US characteristics consistent with benignity include a pure cyst, a predominantly cystic or cystic nodule with reverberating artifacts and spongiform nodules.[15,16] In addition, colour Doppler US can be used to reveal any blood vessels in and around the nodule so that vascular injury can be avoided during the procedure;[17] Because most US-FNAs are well-tolerated and are not associated with significant patient pain or discomfort, routine use of local anaesthesia has not been recommended.[18]

All FNAC procedures were performed at BPS GMC (W), in accordance with standard techniques. The aspiration area was cleaned with use of povidone-iodine swabs. For each FNAC, we attempted a mean of 2 passes (range, 1 to 4) at different sites of a solid thyroid nodule by using 1½-inch-long 25-gauge, bevel-edged needles. For USG machine Philips HD 11XE was used and the transducer was cleaned with use of povidone-iodine swabs before USG-FNAC was performed. In the setting of a multinodular thyroid gland with multiple nodules ≥1 cm, 2 to 4 passes were attempted per nodule. We had used ultrasound characteristics to determine which nodules to aspirate in a multinodular goiter; rather than the size of the nodule. Nodules with cystic components were first aspirated of fluid, and then the solid component was aspirated. Smears of the specimens were made on site and evaluated for adequate cellularity by a cytopathologist. Smears were air-dried for Leishman staining and fixed immediately in 95% ethanol, and stained by using the method of Papanicolaou. If cellularity was inadequate, additional passes were undertaken. Direct manual compression at the biopsy site is essential to reduce the risk of procedure-related complication. Each FNAC of thyroid lesions was considered to have adequate cellularity if there were at least 5 groups of well-visualized follicular cells, with each group containing 10 or more cells. Cytological diagnoses were classified according to Bethesda system for reporting thyroid cytopathology.[14]

STAISTICAL ANALYSIS

Microsoft office 2007 was used for the analysis. Descriptive statistics like mean and percentages were used for the ananlysis. Student t test was used for the comparision.

RESULTS

In this study, 65 patients (57 female and 8 male) underwent FNAC of thyroid lesions. The mean age of patient was 40.34 ± 14years, with an age range of 15 to 67 years and M:F::1:7. Out of 8 males, four show benign lesions and four show features of papillary carcinoma and out of 57 females, fifty one females show benign lesions and six show features of papillary carcinoma.On comparison of the two methods, there was decrease in the inadequate sample rate (category 1) and increase in the pickup of benign as well as malignant lesion with the use of USG- FNAC and on comparing the two methods by means of paired t-test the p value was highly significant <0.001. (Table 1)

Detailed distribution of category wise cases by two methods

Category	Number and (%) of cases (R-FNAC)	Number and (%) of cases (USG-FNAC)
1	15 (23.1%)	3 (4.61%)
2	44 (67.69%)	52(79.99%)
5	5 (7.69%)	-
6	1 (1.53%)	10 (15.38%)

Table-1: Category wise distribution of thyroid lesions with routine FNAC and USG FNAC using Bethesda reporting system

Type of lesion	Number of cases (15)	Number of cases (3)
Colloid only	8	1
Blood only	4	-
Colloid with cystic macrophages	2	2
Few follicular cells	1	-

Table-2: Comparison of Bethesda category 1 lesion by R-FNAC and USG-FNAC

were as follows (Table 2,3,4)

The inadequate specimen rate decreased from 23.1% (15/65) by R-FNAC to 4.62% (3/65) by USG-FNAC. Out of 15 inadequate specimens, 11 cases (73.33%) were reported as benign lesion category 2 and one case (6.66%) was reported as malignant (category 6).

For Non-neoplastic lesions (Bethesda category 2), the most common lesion is colloid goitre followed by lymphocytic thyroiditis and hyperplasia of thyroid. The sensitivity was 74.94% and 94.54% for R-FNAC and US-FNAC respectively, with significant p value ($p<0.004$) by using Fisher Exact $\chi 2$ test (Table 5). The cytological microphotographs of smears show increase in cell yield and proper characterisation of lesion. [Figure 1a and 1b]

For Neoplastic lesions (Bethesda category 6), In R-FNAC 6 cases were reported under malignant category out of which 5 were suspicious for papillary carcinoma (Bethesda category 5) and 1 case was of papillary carcinoma (Bethesda category 6). While by USG guided FNAC ten cases were diagnosed. Out of 10 cases, 6 patients were female and 4 patients were male, M:F ratio was 2:3. Out of four male patients three patients were in 5th -6th decade while one was in 3rd decade. While all female patients were in 3rd -4th decade.

One case of multinodular colloid goitre and one case of cystic fluid only turned out to be papillary carcinoma on USG-FNAC (Case 6 and 9) (Figure 2a, 2b, 2c, 2d, 2e). Clinically two patient's presents with lymph node metastasis and on USG guided FNAC show sub-centimetre thyroid lesions and solid cystic lesion (Case 7 and 8), (Figure 3a, 3b, 3c and Figure 4a, 4b,4c). One case was a rare presentation of intra-cystic papillary carcinoma which was missed on R-FNAC reported as cystic fluid only (category 1) (Case 7) (Figure 5a, 5b).

The diagnosis of malignant lesion were missed on R-FNAC cytology in 4 out of 10 patients with malignant nodules but all the suspected malignant lesions on USG were picked up

Thyroid lesion	Types	Number of cases (44) R-FNAC		Number of cases (51) USG-FNAC	
Goiter	Colloid goiter with cystic change Adenomatous goitre	19 4	23	24 4	28
Hyperplastic thyroid nodule	Hyperplastic thyroid nodule with colloid goiter with cystic change Thyroid hyperplasia	2 8	10	2 10	12
Lymphocytic thyroiditis		11		11	

Table-3: Comparison of diagnosis in Bethesda category 2 by R-NAC and USG-FNAC

Type of lesion	No of cases	Report on R-FNAC	Report on USG-FNAC
Multinodular goiter	6	Category 5 in five cases and Category 2 in one case	Category 6
Papillary carcinoma with lymph node metastasis	2	Category 2 –solid cystic thyroid lesion and lymph node show cystic changes other case have lymph node metastasis with impalpable thyroid swelling	Category 6
Intra-cystic papillary carcinoma	1	Category 1	Category 6
Solitary thyroid nodule	1	Category 6	Category 6

Table-4: Comparison of Bethesda category 6 [malignant cases (n=10)] by R-FNAC and USG-FNAC

Parameters	R- FNAC	USG- GUIDED FNAC
Senstivity	74.54%	94.54%
Specificity	70%	100%
Positive Predictive Value	93.18%	100%
Negative Predictive Value	33.33%	76.92%

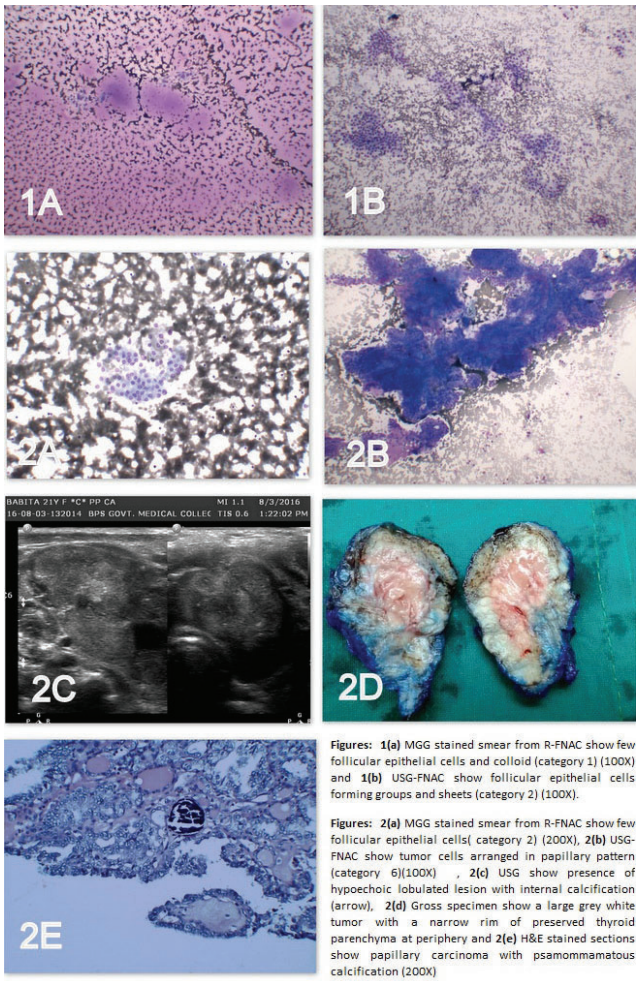
Table-5: Statistical parameters for R-FNAC with USG-FNAC for benign thyroid lesion

Parameters	R-FNAC	USG-FNAC
Sensitivity	60%	100%
Positive Predictive Value	100%	100%
Negative Predictive Value	93.22%	100%
Percentage Of False Negative Cases	40%	0%

Table-6: Statistical parameters for R-FNAC with USG-FNAC for malignant thyroid lesion

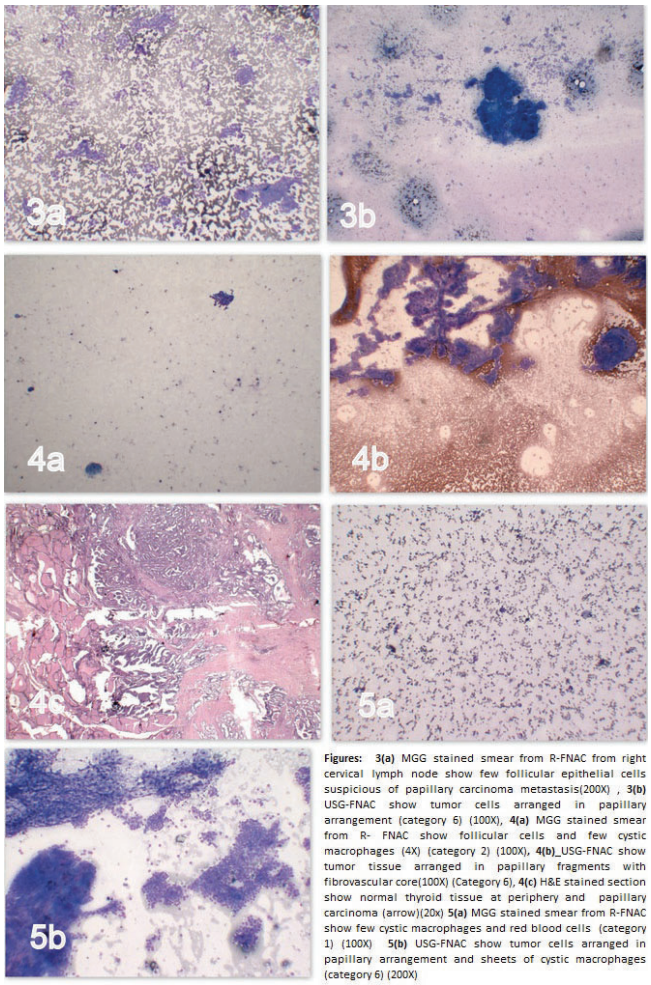
References	Duration of study	Cases	Malignancy rate	Sensitivity	Specificity	Inadequate sample rate
Danese et al;[5] Italy (1998)	15 years	1075	-	91.8 vs 97.1	68.8 vs 70.9	8.7 vs 3.5%
Izquierdoetal.;[13] USA (2006)	47 months	276	-	60.9vs 80	-	11.2 vs 7.1%
Carmeci et al;[21] USA (1998)	5 years	497	40%vs 59%	89 vs 100%	69 vs 100%	16 vs 7%
Our study India (2016)	6 month	65	For malignant lesions 60% vs 100%	For benign lesions 74.54% vs 94.54%	70% vs 100%	23.1%vs 4.62%

Table-7: Comparison of our results with the results of previous studies: Palpation Guided versus Ultrasound guided FNAB



Figures: 1(a) MGG stained smear from R-FNAC show few follicular epithelial cells and colloid (category 1) (100X) and **1(b)** USG-FNAC show follicular epithelial cells forming groups and sheets (category 2) (100X).

Figures: 2(a) MGG stained smear from R-FNAC show few follicular epithelial cells(category 2) (200X), **2(b)** USG-FNAC show tumor cells arranged in papillary pattern (category 6)(100X) , **2(c)** USG show presence of hypoechoic lobulated lesion with internal calcification (arrow), **2(d)** Gross specimen show a large grey white tumor with a narrow rim of preserved thyroid parenchyma at periphery and **2(e)** H&E stained sections show papillary carcinoma with psamommamatous calcification (200X)



Figures: 3(a) MGG stained smear from R-FNAC from right cervical lymph node show few follicular epithelial cells suspicious of papillary carcinoma metastasis(200X) , **3(b)** USG-FNAC show tumor cells arranged in papillary arrangement (category 6) (100X), **4(a)** MGG stained smear from R- FNAC show follicular cells and few cystic macrophages (4X) (category 2) (100X), **4(b)**_USG-FNAC show tumor tissue arranged in papillary fragments with fibrovascular core(100X) (Category 6), **4(c)** H&E stained section show normal thyroid tissue at periphery and papillary carcinoma (arrow)(20x) **5(a)** MGG stained smear from R-FNAC show few cystic macrophages and red blood cells (category 1) (100X) **5(b)** USG-FNAC show tumor cells arranged in papillary arrangement and sheets of cystic macrophages (category 6) (200X)

by USG guided FNAC. Out of 10 cytologically detected cases of papillary carcinoma 5 patients had undergone thyroidectomy and all of them were reported as papillary carcinoma on histopathologic examination (Figure 2e and 4c). Among the malignant lesions, the sensitivity rates were increased from 60% (R-FNAC) to 100% (USG-FNAC) with a highly significant p value of <0.001 by using Fisher Exact $\chi 2$ test (Table 6)

Overall the results of the routine and ultra sound guided FNAC were analysed by using SPSS version 22.0 statistical software, STUDENT PAIRED "t" TEST was applied and the difference observed between routine and ultrasound guided FNAC is highly significant with p value < 0.001

DISCUSSION

Out of 65 patients, 12.3% (8/65) were males and 87.69% (57/65) were females with age ranging from 15 to 67 years, and male to female ratio of 1:7. One of the advantages of USG-FNAC of thyroid nodules / lesions is a significant decrease in inadequate specimens. The inadequate cytological diagnosis rate of P-FNAB in the literature approximates 15%;[20] Carmeci et al reported a significant reduction in the inadequate specimen rate from 16% with the use of P-FNAB to 7% with the use of US-FNAB;[21] With continued improvement in ultrasound performance skills over time, this rate will likely decrease even further. We should assess the cellularity and in as much as additional passes could be made after initial cytology assessment if the cytological specimen was deemed inadequate. Danese et al reported an inadequate sample rate of only 3.5% with US-FNAB;[5]

In our study the routine FNAC group, 15/65 (23.1%) FNAC were non diagnostic (Bethesda category 1) while in ultrasound guided group, 3 (4.61%) FNAC were non diagnostic. In details the 12 patients (80%) were successfully reported by USG guided FNAC and 11 cases (73.33%) were of category 2 and the main concerned is of one case which turned out to be papillary carcinoma (Category 6) which implies a risk of 6.5% chances of malignancy in category 1 lesions which lies in concordance with the implied risk of malignancy in category 1 lesions according to Bethesda system for reporting thyroid cytopathology;[14]

For Non-neoplastic lesions (Bethesda category 2), the R-FNAC group, 44 (67.69%) FNAC were benign while in ultrasound guided group, 51 (78.46%) FNAC were benign. The sensitivity and specificity of detecting benign lesions were 74.54% and 70% in R-FNAC and 94.54% and 100% in USG-FNAC. There is increase in positive predictive value and negative predictive value in USG-FNAC group. The diagnostic accuracy was 74.94% and 94.54% for R-FNAC and US-FNAC respectively, with significant p value ($p<0.004$) by using Fisher Exact $\chi 2$ test

For malignant lesions, 4 out of 10 cases of papillary carcinoma were missed in R-FNAC and they were diagnosed with the

help of USG- FNAC. In R-FNAC,out of four undiagnosed cases, one present with the background of multninodular goitre, one patient presented with isolated lymph node enlargement with metastasis and on USG guided FNAC show sub centimetric thyroid lesions and other one show lymphnode involvement with cystic change and solid cystic lesion in thyroid and the fourth case was of cystic fluid only turned out to be intra-cystic papillary carcinoma on USG-FNAC and on histopathology, it was a rare presentation of intra-cystic papillary carcinoma which was missed on R-FNAC reported as cystic fluid only (category 1). Among the malignant lesions, the diagnostic sample rates were 60% (R-FNAC) and 100% (US-FNAC) with a highly significant p value of <0.001 by using Fisher Exact $\chi 2$ test

The majority of histologic thyroid carcinomas in our study (>50%) were found in multinodular glands, an observation that is in agreement with recent reports that have demonstrated similar rates of malignant involvement in multinodular and solitary nodular disease;[3,20] Marqusee et al;[11] provided evidence for the usefulness of ultrasonography in the management of nodular thyroid disease by showing that thyroid ultrasonography altered the clinical management of 63% of their patients who were referred to their thyroid nodule clinic because the prevalence of occult thyroid cancer in the general population is approximately 4%;[22]

Hence, the routine use of thyroid ultrasonography in the evaluation of suspected thyroid nodular disease and in patients with abnormal findings on thyroid examinations but no discrete nodules is recommended to avoid misdiagnosis of nodules of substantial size (50% of which were larger than 2 cm in our study) that may be cancerous. Studies have been reported that thyroid nodules >1 cm or <1 cm have the same rates of local/regional as well as distant metastatic involvement in differentiated thyroid cancer; that nodule characteristics, not size, should be determinates or criteria for FNAB consideration;[23,24] and that biopsy samples should be obtained irrespective of characteristics in nodules >2 cm. Our study demonstrated that US-FNAC has greater diagnostic accuracy, sensitivity, and positive and negative predictive values than does R-FNAC. These results correspond to those of Danese et al;[5] and Hatada et al,;[25] who also reported greater diagnostic accuracy, sensitivity, and positive and negative predictive values with use of US-FNAB than with P-FNAB. The reason mainly for the higher incidence of malignant cytopathology in the ultrasound guided FNAB is that they were able to choose the thyroid nodule with suspicious ultrasonographic features and that they were able to biopsy the non palpable nodules (nodules that are less than 1 cm and are posteriorly located.[26] The result of our study is comparable with other previous studies in that ultrasound guided FNAB is more sensitive and accurate with lesser percentage of inadequate specimens compared with palpation guided FNAB. To our knowledge, this is the first study comparing the diagnostic yield of ultrasound guided FNAC and R-FNAC in our country. However, because of the short duration of our study, we only had smaller number of patients compared with other studies (Table 7). Hence to summarise results of USG-FNAC were promising because USG guidance allows continuous visualisation of needle during insertion and sampling hence increase the diagnostic yield and sensitivity, help in selecting the suspicious thyroid nodule in MNG hence reduces false negative (malignant cases), guiding the needle to take sample from non-palpable nodules and avoid unnecessary repeat FNAC for proper characterisation

CONCLUSION

Hence to conclude, our experience has shown that routine use of thyroid ultrasonography and USG guided FNAC can be done efficiently and effectively, and it decreases the inadequate sample rate, false negative malignant cases, unnecessary repeat FNAC for proper characterisation and improves the diagnostic yield and accuracy rate. In future, the study will likely be having positive implications in cytological evaluation of patients with thyroid lesions with precise and rational diagnostic usage of Routine and Ultrasound guided FNAC and will help us avoiding unnecessary repeat FNACs in thyroid lesions.

REFERENCES

1. Sipos JA. Advances in ultrasound for the diagnosis and management of thyroid cancer. Thyroid 2009; 19: 1363-1372.
2. Hegedüs L. Clinical practice. The thyroid nodule. N Engl J Med 2004; 351:1764-1771.
3. Hagag P, Strauss S, Weiss M. Role of ultrasound-guided fine-needle aspiration biopsy in evaluation of nonpalpable thyroid nodules. Thyroid 1998; 8: 989-995.
4. Polyzos SA, Kita M, Avramidis A. Thyroid nodules - stepwise diagnosis and management. Hormones (Athens) 2007; 6: 101-119.
5. 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: 15-21.
6. Braga M, Cavalcanti TC, Collaço LM, Graf H. Efficacy of ultrasoundguided fine-needle aspiration biopsy in the diagnosis of complex thyroid nodules. J ClinEndocrinolMetab 2001; 86: 4089-4091.
7. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 19: 2009; 1167-1214
8. W. Lawrence Jr. and B.J.Kaplan. Diagnosis and management of patients with thyroid nodules. Journal of Surgical Oncology, vol. 80, no. 3, pp. 157–170.
9. A.N. Khalid, C.S. Hollenbeak, S.A.Quraishi, C.Y. Fan, and B.C. Stack Jr. The cost-effectiveness ofiodine131 scintigraphy, ultrasonography, and fine-needle aspiration biopsy in the initial diagnosis of solitary thyroid nodules. Archives of Otolaryngology—Head and Neck Surgery 2006;132:244–250.
10. Cesur M, Corapcioglu D, Bulut S, Gursoy A, Yilmaz AE, Erdogan N, Kamel N. Comparison of palpation-

guided fine-needle aspiration biopsy to ultrasound-guided fine-needle aspiration biopsy in the evaluation of thyroid nodules. Thyroid. 2006;16:555-61.
11. Marqusee E, Benson CB, Frates MC, et al. Usefulness of ultrasonography in the management of nodular thyroid disease. Ann Intern Med. 2000;133:696-700.
12. Senthil panneerselvam et al. Accuracy of ultrasound guided fine needle aspiration cytology in the evaluation of thyroid nodules. Int J Cur Res Rev, 2013;5:94.
13. Roberto Izquierdo et al. Comparison of palpation guided versus ultrasonography-guided fine needle aspiration biopsies of the thyroid nodules in an outpatient endocrinology practice. Endocr Pract. 2006; 12:609. 5.
14. Edmund S. Cibas, and Syed Z. Ali The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol 2009; 132:658-665 658.
15. Moon WJ, Baek JH, Jung SL, Kim DW, Kim EK, Kim JY, et al. Ultrasonography and the ultrasound-based management of thyroid nodules: consensus statement and recommendations. Korean J Radiol 2011;12:1-14.
16. Anderson TJ, Atalay MK, Grand DJ, Baird GL, Cronan JJ, Beland MD. Management of nodules with initially nondiagnostic results of thyroid fine-needle aspiration: can we avoid repeat biopsy? Radiology 2014;272:777-784.
17. Rausch P, Nowels K, Jeffrey RB Jr. Ultrasonographically guided thyroid biopsy: a review with emphasis on technique. J Ultrasound Med 2001;20:79-85.
18. Baloch ZW, Cibas ES, Clark DP, Layfield LJ, Ljung BM, Pitman MB, et al. The National Cancer Institute Thyroid fine needle aspiration state of the science conference: a summation Cytojournal 2008;5:6.
19. Cibas ES, Alexander EK, Benson CB, de Agustín PP, Dohert GM, Faquin WC, et al. Indications for thyroid FNA and pre-FNA requirements: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagn Cytopathol 2008;36:390-399.
20. Tollin SR, Mery GM, Jelveh N, et al. The use of fine-needle aspiration biopsy under ultrasound guidance to assess the risk of malignancy in patients with a multinodular goiter. Thyroid. 2000; 10:235-241.
21. Carmeci C, Jeffrey RB, McDougall IR, Nowels KW, Weigel RJ. Ultrasound-guided fine-needle aspiration biopsy of thyroid masses. Thyroid. 1998;8:283-289.
22. Leinung MC, Gianoukakis A, Lee DW. Ultrasonography in management of nodular thyroid disease [letter]. Ann Intern Med. 2001;135:383.
23. Papini E, Guglielmi R, Bianchini A, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. J Clin Endocrinol Metab. 2002;87:1941-1946.
24. Kim EK, Park CS, Chung WY, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. Am J Roentgenol. 2002;178:687-691.
25. Hatada T, Okada K, Ishii H, Ichii S, Utsunomiya J. Evaluation of ultrasound-guided fine-needle aspiration biopsy for thyroid nodules. Am J Surg. 1998s; 175:133-136.
26. Celeste Ong Ramos and Roberto C Mirasol. Ultrasound Guidance Improves the Diagnostic Yield and Accuracy of Fine Needle Aspiration Biopsy of Thyroid Nodules in Detecting Malignancy. Thyroid Disorders Ther 2014, 3:2

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