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Original Research Article

Evaluation of the Efficacy of Ultrasound Guided Fine Needle Aspiration Cytology in the Diagnosis of Thyroid Lesions

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ABSTRACT

Aims and objectives: Our aim was to evaluate the efficacy of ultrasound guided fine needle aspiration cytology (USG-FNAC) in diagnosis of thyroid lesions by comparing it with standard fine needle aspiration cytology (S-FNAC)
Method: The study included 667 cases with thyroid lesions out of which 210 cases underwent S-FNAC and 457 cases underwent USG-FNAC, for which ultrasound findings were recorded simultaneously. Histopathology was available in 42 cases and 56 cases, in which initial diagnosis was obtained by S-FNAC and USG-FNAC respectively.
Results: Sensitivity, specificity and accuracy of S-FNAC were 50%, 97.36% and 92.85% respectively, while for USG-FNAC they were 87.5%, 100% and 98.21% in similar order. False negative and false positive rates for S-FNAC were 4.76% and 2.3% respectively, while for USG-FNAC they were 1.81% and 0% respectively. Inadequacy rates for S-FNAC and USG-FNAC were 19.05% and 3.72% respectively. Chi square test was employed and the difference was found to be statistically significant (p value < 0.05).
Conclusion: USG-FNAC significantly decreases the inadequacy rate thus increasing the diagnostic accuracy.
Key words: Fine needle aspiration cytology, ultrasound, guided, thyroid.

INTRODUCTION

Annual incidence rate of thyroid nodules is 4-8%. [1] However, autopsy and ultrasound data have shown that prevalence rate of thyroid nodules in normal individuals is 70%. [2] Most of these thyroid nodules are benign, with malignancy being detected in

only 5% cases. In addition to this, a very few of thyroid cancers are lethal.[3,4] As a result, differentiating benign from malignant thyroid disease is of utmost importance for deciding on medical versus surgical management.

FNAC has been established as a safe and cost effective first line investigation in distinguishing benign from malignant thyroid lesions, thus reducing the number of unnecessary surgeries.

However, one of the major limitations of FNAC thyroid has been found to be a high inadequacy rate, ranging from 6.4 to 32.4% in various studies. [5]

Although repeat aspiration and experience reduces the rate of inadequate aspirate, this increases the number of visits of the patient to the clinic, thereby, reducing the efficacy and cost effectiveness of the procedure. At the same time it reduces the treating clinician's confidence in the cytology report and adds to the apprehension and anxiety in the patient.

Since the introduction of USG-FNAC by Rizatto et al in 1973, several studies have reported that USG-FNAC not only reduces the inadequacy rate but also helps to accurately select the patients for surgery hence avoiding unnecessary diagnostic thyroidectomies. [6,7,8,9] It does this by selection of the biopsy site, avoiding cystic areas and coarse calcification. Its role has been found useful in detecting micro carcinomas, cystic carcinomas, cancer associated with benign nodules for example Hashimoto's thyroiditis or coarse calcification. [10] However to date, there is very little literature that has compared the efficacy of S-FNAC and USG-FNAC in a large series in India.

The present study was performed to compare the efficacy of S-FNAC and USG-FNAC in the diagnosis and management of thyroid diseases in a large series of patients.

MATERIAL AND METHODS

This was a prospective study including 617 patients with thyroid disease. All the cases from January 2004 to December 2004 were subjected to S-FNAC, while for all cases from January 2005 to September 2006, FNAC was done under ultrasound guidance.

210 cases underwent S-FNAC while in 457 cases USG-FNAC was done.

Histopathology was obtained in 98 cases, out of which 42 cases were initially diagnosed by S-FNAC and 56 cases were initially diagnosed by USG-FNAC.

Ultrasound findings were recorded whenever available i.e., in 457 cases. The nodules were evaluated for echogenicity, homogeneity of structure, micro calcification and their margins. Ultrasound scanner used was equipped with 7.5 MHz transducer.

Technique of USG-FNAC [11, 12]

Procedure was done with patient in supine position with neck extended. Ultrasonography was done with an ultrasound scanner equipped with 7.5 MHz transducer and findings were noted. Sterile gel was used as a coupling agent and no local anaesthesia was given. Procedure was performed by the Pathologist. Under the guidance of radiologist 23 G needle was introduced directly in the lesion through the skin. The needle was inserted obliquely along a path parallel to the scanning plane, so that tip and shaft of the needle were continuously visualised. When the needle reached the target, the technique of capillary sampling was employed. 4 passes were made, needle withdrawn, material expressed on slides and thin smears were prepared.

Half of the slides were immediately fixed in 95% ethyl alcohol for Haematoxylin and Eosin and Papanicolaou stain. Half

slides were air-dried for May- Grunwald-Giemsa stain. Standard FNAC was carried out with a similar proceduresas described above except ultrasound guidance was not used.

Following precautions were strictly followed during the procedure:

1. In case of cystic lesions the aspirated fluid was centrifuged and smears prepared from the sediment. If a residual mass was palpated, it was sampled and slides labelled separately.
2. In case of multinodulargoiter, if more than 2 nodules measuring > 1 cm were present, FNAC was done from the most suspicious nodule. If more than 2 nodules were present and both appeared benign, then larger one was aspirated.

All cases were classified into five categories.

1. Benign (Negative): Included simple goiter, colloid goiter with cystic change, adenomatous goiter, Grave's disease, thyroglossal cyst, colloid cyst and thyroiditis.
2. Indeterminate: Follicular neoplasm and Hurtle cell neoplasm in which differentiation between benign and malignancy was not possible**.**
3. Suspicious: Included cases in which FNAC smears showed high cellularity, microacinar pattern, anisonucleosis, nucleomegaly, some but not all features of papillary carcinoma and scant to absent colloid.
4. Malignant (Positive): Included papillary carcinoma, medullary carcinoma and anaplastic carcinoma.
5. Inadequate: Adequacy criteria- Smears should have at least six follicular cell clusters, each cluster having at least ten follicular cells, spread on at least two separate smears.

Chi- square test was employed for statistical analysis.

RESULTS

Age of the patients ranged from seven to 80 years, with maximum number of cases belonging to fourth decade. Thyroid disease was more common in females i.e., 567 cases (85%).

Table 1 shows the cytologic diagnostic categories in 667 cases. Table 2 shows the ultrasound findings in the 457 cases. On ultrasound, 39 of the lesions were cystic and 418 cases were solid. 40 (8.75%) nodules were hypo echoic and showed micro calcification. Remaining 417 (91.24%) cases showed mixed echogenicity and no micro calcification. Irregular margins were seen in 57 (12.47%) of the cases. 26 cases (5.68%) were given a malignant diagnosis on FNAC, of these 13 (50%) were hypoechoic with irregular margins and micro calcifications. Out of 431 (94.31%) cases diagnosed as benign on FNAC, 19 (4.51%) cases presented with hypo echoic appearance, irregular margins and micro calcification. Thus malignant lesions were more frequently associated with hypo echoic appearance, irregular margins and micro calcification on ultrasound than benign lesions. However out of 40 cases with hypo echoic appearance, irregular margins and micro calcification on ultrasound, only 13 cases were confirmed as malignant on FNAC.

Table 3 shows cytological diagnosis of 40 cases suspected as malignancy on ultrasonography**.** There were 14 cases with non-palpable thyroid nodules. One of these underwent ultrasound for pyrexia of unknown origin and was found to harbour a hypo echoic lesion of four mm in the right lobe of thyroid. FNAC of this lesion under ultrasound guidance revealed a papillary carcinoma.

Table 1: Cytologic diagnostic categories in 667 cases

S. No.	Cytologic diagnostic categories	Number of cases	Percentage
1	Negative/Benign	565	84.70
2	Indeterminate	20	2.99
3	Suspicious	2	0.29
4	Positive/Malignant	23	3.44
5	Inadequate	57	8.54
	Total	667	100

Table 2: Ultrasonography findings in 457 cases

S. No	Ultrasonography findings	Number of cases	Percentage
1	Echo structure		
	1. Solid	418	91.46
	2 .Cystic	39	8.53
2	Echogenicity		
	1. Hypo echoic	40	8.75
	2. Mixed echogenicity	417	91.24
3	Calcification		
	1. Presence	40	8.75
	2. Absence	417	91.24
4	Margins		
	1. Regular	400	87.52
	2. Irregular	57	12.47
	Total	457	100

Table 3: Cytology diagnosis of 40 cases suspected as malignant on ultrasonography

S. No.	Cytology diagnosis	Number of cases	Percentage
I	Benign		
	1. Colloid goiter	13	32.5
	2. Adenomatous goiter	3	7.5
	3. Thyroiditis	3	7.5
II	Indeterminate		
	Follicular neoplasm	3	7.5
III	Suspicious	2	5
IV	Malignant		
	1. Papillary carcinoma	3	7.5
	2. Medullary carcinoma	3	7.5
	3. Anaplastic carcinoma	7	17.5
V	Inadequate	3	7.5
	Total	40	100

Table 4 compares the adequacy rate of S-FNAC with that of USG-FNAC. 40 (19.05%) cases yielded inadequate aspirate when S- FNAC was used, while only 17 (3.72%) cases were inadequate when USG-FNAC was used. Chi-Square test was applied for comparison of the inadequacy rate in which $X^2 > 42$, df=1 and *p* value was less than 0.05 and this was statistically significant.

Table 4: Comparison of adequacy and inadequacy rate in S-FNAC and USG-FNAC

S. No.		S-FNAC	USG-FNAC
1	Number of adequate smears	170 (80.95%)	440 (96.28%)
2	Number of inadequate smears	40 (19.05%)	17 (3.72%)
	Total	210	457

Chi square test was employed
$X^2 > 42$, df=1 and *p*value was less than 0.05 and this was statistically significant.

Cases with inadequate aspirate were excluded in calculating statistical values.
Histopathology was obtained in 98 cases out of which 42 cases were initially diagnosed by S-FNAC and 56 cases by USG-FNAC. Cyto-histological correlation is shown in Table 5.

Table 5: Correlation of cytologic with histopathologic diagnosis in all the cases

S. No.	Histopathology	Number of cases (percentage)	S-FNAC		USG-FNAC	
			Consistent	Non Consistent	Consistent	Non Consistent
1	Nodular colloid goiter	69 (70.40)	28	-	41	-
2	Multinodulargoiter	3 (3.06)	1	1	1	-
3	Colloid cyst	1 (1.02)	-	-	1(Inadequate on FNAC)	
4	Thyroglossal duct cyst	4 (4.02)	2	-	2	-
5	Lymphocytic thyroiditis	1 (1.02)	1	-	-	-
6	Hashimoto's thyroiditis	3 (3.06)	-	2	1	-
7	Follicular adenoma	5 (5.10)	3		2	-
8	Hurthle cell neoplasm	1 (1.02)	-		1	-
9	Follicular carcinoma	5 (5.10)	-		3	1
10	Papillary carcinoma	5 (5.10)	2		2	-
11	Medullary carcinoma	1 (1.02)	-		1	-
	Total	98 (100)	37	5	54+1*	1

*Inadequate – Not included in calculation

Out of 42 cases of S-FNAC for which histopathology were available, correlation was obtained in 37 cases. Non consistent diagnosis was obtained in five cases. Two cases of colloid cyst at S-FNAC proved to be Hashimoto's thyroiditis on histopathology. The small solid foci were missed at FNAC. There was one false positive case of adenomatous goitre which was misdiagnosed as follicular neoplasm at FNAC. There were two false negative cases – one case of follicular carcinoma was misdiagnosed as adenomatous goiter at FNAC. Another was a case of papillary carcinoma with cystic change which was misdiagnosed as colloid goiter at FNAC.

Out of 56 cases of USG-FNAC, in which histopathology was available, it correlated with cytodiagnosis in all except one case of follicular carcinoma, which was misdiagnosed as adenomatous goitre at USG-FNAC (false negative). There was one case of colloid cyst diagnosed at histopathology, FNAC smears of which were inadequate for interpretation. There was no false positive case.

Table 6 depicts the final diagnosis of cases where histopathology was not consistent with the cytodiagnosis.

Table 7 depicts comparison of sensitivity, specificity and accuracy in S-FNAC and USG-FNAC. Sensitivity, specificity and accuracy of S-FNAC were 50%, 97.36% and 92.85% respectively and for USG-FNAC they were 87.5%, 100% and 98.21% respectively in similar order.

No complications were encountered during the procedure throughout the study.

Table 6: Final diagnosis of cases non-consistent on FNAC

S. No	S-FNAC diagnosis	Histopathologic diagnosis	Number of Cases
1	Colloid goiter with cystic change	Papillary carcinoma	1
2	Adenomatous goiter	Follicular carcinoma	1
3	Follicular Neoplasm	Multinodulargoiter	1
4	Colloid cyst	Hashimoto's thyroiditis	2
	US Guided FNAC diagnosis		
1	Adenomatous goiter	Follicular carcinoma	1

Table 7: Sensitivity, specificity and accuracy of S-FNAC and USG-FNAC

	Sensitivity	Specificity	Accuracy
S-FNAC	50%	97.36%	92.85%
USG-FNAC	87.50%	100%	98.21%

DISCUSSION

FNAC has been established as a first line of investigation in the diagnosis of thyroid disease. Thyroid nodules are seen in 70% of the normal individuals as detected by ultrasonography. [2] Most of the thyroid nodules are benign, malignancy being prevalent in only 3- 5% of these cases. [3,4] FNAC allows careful selection of patients for surgery reducing the diagnostic thyroidectomies.

However, the two major pitfalls of S-FNAC are inadequate aspirates seen in 6.4 to 32.4% cases and indeterminate results, especially in differentiating adenomatous nodules of multinodulargoiter from follicular neoplasms.

Major causes of inadequate aspirations are cystic papillary carcinomas, technical error and the variable criteria adopted for adequacy in different institutions. [13] Complexity in the thyroid nodules adds to the problem especially when

the lesions are cystic, calcified, fibrosed or difficult to access. [14]

Since its introduction by Miskin et al in 1973, ultrasound has been used extensively to characterize thyroid nodules with an attempt to distinguish benign from malignant nodules. [15]

Papini Enrico used ultrasound and USG-FNAC to evaluate 494 consequent patients with non-palpable thyroid nodules. They found that hypo echoic lesions with irregularmargins and micro calcification were independent risk factors for predicting malignancy. They recommended that USG-FNAC be performed on 8-15 mm nodule with at least one of the above ultrasound features. Predictive value of ultrasound is good only when multiple signs are used in combination in context of a single nodule, albeit at the expense of low sensitivity. [16, 17] In the present study, hypo echoic lesions with micro calcification was good predictors of malignancy. However, FNAC is must to confirm malignancy in these cases.

Later, Rizzato et al first used USG-FNAC as a diagnostic modality. [6] Since then several studies have documented its effectiveness in reducing the inadequacy rate as compared to when S-FNAC was used.

USG-FNAC is useful in cases of cystic lesions wherein sampling can be done from solid portion of partially cystic masses, yielding highly cellular aspirates by avoiding dilution with cystic fluid. Hashimoto's thyroiditis can sometimes present as cystic nodule, this possibility should be kept in mind lest an erroneous diagnosis of malignancy can be made. [18] Two of our cases of Hashimoto's thyroiditis presented as cystic nodule which were wrongly interpreted as colloid cyst at S-FNAC. In such cases, USG-FNAC allows precise sampling from any solid area. Cystic change in a papillary carcinoma is a major cause of false negative report. In our series there was one case of papillary carcinoma with cystic change which was missed at S-FNAC as smears showed only cyst macrophages. 50% of papillary carcinoma demonstrates cystic change. Areas of calcification and fibrosis can be traversed and needle positioned in solid portion under ultrasound guidance. About 5% of multinodulargoiter harbor malignancy. In these cases sampling can be done from all nodules, especially highly suspicious nodules which are hypo echoic and show micro calcification. [19]

Another major pitfall of FNAC is the follicular and hurthle cell neoplasm-indeterminate category. Smears with microfollicular pattern are a grey zone area and most of the erroneous diagnoses are related to distinguishing benign and malignant follicular neoplasm. Difficulties in distinguishing follicular carcinoma from adenoma and at times adenomatous goitre are well documented in literature and are unavoidable in clinical practice. [20,21] Studies suggest that aspiration from multiple sites, USG-FNAC and adhering to strict criteria may improve diagnostic accuracy in this setting. However criteria of capsular and vascular invasion are needed for satisfactory diagnosis in histopathology. [22]

In suspicious category about 25% are found to be malignant at surgery. In these cases USG-FNAC allows positioning of the needle in most suspicious area. [23] In the present study, the number of cases in suspicious category was 0.29%. This was lower as compared to those reported in literature. This can be explained by the fact that most studies include follicular neoplasm and hurthle cell neoplasm in suspicious category. [22, 23, 24] We could not reach at the final diagnosis in these cases as the patients were lost for follow up.

Due to continuous visualization of needle tip by ultrasound throughout the procedure,

acute complications can be reduced to minimal.

Takashima et al reported that sensitivity, specificity, accuracy and negative predictive value of USG-FNAC for malignancy were not significantly different from that of S-FNAC. However the initial failure rate for S-FNAC was significantly higher than for USG- FNAC. [19] As per Hatada et al, sensitivity, specificity and accuracy was higher for USG-FNAC as compared to S-FNAC, especially in patient with tumour < 2 cm. [11]

In present study, 20% of patients were referred for surgery when S-FNAC was used, while the referral rate dropped to 12.5% when USG-FNAC was used. These values for USG-FNAC are lower than that reported as documented in the literature. [25,26] Thus we were successful in achieving our goal of reducing number of thyroidectomies at our institution. Similarly the rate of malignancy picked up by USG-FNAC of 12.5% was higher than when S-FNAC was used i.e., of 9.5%. It is well documented that greater number of thyroid cancer can be detected by USG-FNAC as compared to S-FNAC. USG- FNAC is a powerful technique in detecting micro carcinomas, cystic carcinomas, cancer associated with benign nodule for example Hashimoto's thyroiditis or coarse calcification. [10]

Limitations of the study: Two separate groups were taken and compared.Comparison of FNAC from the same case with and without US guidance would have resulted in better results.

CONCLUSION

The authors conclude that USG-FNAC reduces the inadequacy rate significantly thus increasing the diagnostic accuracy. At the same time it reduces the number of unnecessary surgeries.

REFERENCES

1. Cramer H. Fine needle aspiration cytology of the thyroid: an appraisal. Cancer Cytopathol 2000;90:325–9.
2. Brander A, Viikinkoski P, Nickels J, et al. Thyroid gland: US screening in a random adult population. Radiology 1991;181:683 –7
3. Hegedüs L, Karstrup S. Ultrasonography in the evaluation of cold thyroid nodules. Eur J Endocrinol 1998;138:30-1.
4. Belfiore A, La Rosa GL, La Porta GA, et al. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. Am J Med 1992;93:363-9.
5. Cochand-Priollet B, Guillausseau PJ, Chagnon S, et al. The diagnostic value of fine-needle aspiration biopsy under ultrasonography in nonfunctional thyroid nodules: a prospective study comparing cytologic and histologic findings. Am J Med 1994;97:152-7.
6. Rizzatto G, Solbiati L, Croce F, et al. Aspiration biopsy of superficial lesions: ultrasonic guidance with a linear-array probe. Am J Roentgenol 1987;148:623-5.
7. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993;328:553-9.
8. Caruso D, Mazzaferri EL: Fine needle aspiration biopsy in the management of thyroid nodules. Endocrinologist 1991;1:194-202,
9. García-Mayor RV, Pérez Mendez LF, Páramo C, et al. Fine-needle aspiration biopsy of thyroid nodules: impact on clinical practice. J Endocrinol Invest 1997;20:482-7.

10. Yokozawa T, Fukata S, Kuma K, et al. Thyroid cancer detected by ultrasound-guided fine-needle aspiration biopsy. World J Surg 1996;20:848-53
11. Hatada T, Okada K, Ishii H, et al. Evaluation of ultrasound-guided fine-needle aspiration biopsy for thyroid nodules.Am J Surg 1998;175:133-6.
12. Orell RS, Sterrett FG, and Whitaker D. Thyroid. In: Orell RS, Sterrett FG and Whitaker D, editors. Fine Needle Aspiration Cytology. 4th ed. Elsevier Missouri: Churchill Livingstone; 2010. p. 125-64.
13. Can AS, Peker K.Comparison of palpation-versus ultrasound-guided fine-needle aspiration biopsies in the evaluation of thyroid nodules. BMC Res Notes 2008 1:12.
14. Baloch ZW, Tam D, Langer J, et al. Ultrasound-guided fine-needle aspiration biopsy of the thyroid: role of on-site assessment and multiple cytologic preparations. DiagnCytopathol 2000;23:425-9.
15. Miskin M, Rosen IB, Walfish PG. B-mode ultrasonography in assessment of thyroid gland lesions.Ann Intern Med 1973;79:505-10.
16. E Papini, R Guglielmi, ABianchini, et al. Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and Color-Doppler Features. J ClinEndocrinolMetab 2002; 87:1941–46.
17. T Rago, P Vitti, L Chiovato, et al. Role of conventional ultrasonography and colour flow Doppler sonography in predicting malignancy in 'cold' thyroid nodules. Eur J Endocrinol 1998;138:41–6.
18. Singh A, Kahlon KS, Chahal SK, et al . Hashimoto's thyroiditis: An unusual presentation as cystic solitary nodule-a diagnostic dilemma. Journal of cytology 2000.20:193-5.
19. Takashima S, Fukuda H, Kobayashi T. Thyroid nodules: clinical effect of ultrasound-guided fine-needle aspiration biopsy. J Clin Ultrasound 1994;22:535-2.
20. Löwhagen T, Willems JS, Lundell G, et al. *Aspiration biopsy cytology in diagnosis of thyroid cancer*. World J Surg 1981;5:61-70
21. Jan F. Silverman , R. Lee West , Ernest W. Larkin , et al. The role of fine-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. Cancer 1986;57:1164–70.
22. Davoudi MM, Yeh KA, Wei JP. Utility of fine-needle aspiration cytology and frozen-section examination in the operative management of thyroid nodules.Am Surg1997 ;63:1084-9.
23. Leenhardt L, Hejblum G, Franc B, et al . Indications and Limits of Ultrasound-Guided Cytology in the Management of Nonpalpable Thyroid Nodules.Journal of Clinical Endocrinology and Metabolism 1999; 84:24-8.
24. Mikosch P, Gallowitsch HJ, Kresnik E, et al. Value of ultrasound-guided fine-needle aspiration biopsy of thyroid nodules in an endemic goitre area. Eur J Nucl Med 2000;27:62-9.
25. Ogawa Y, Kato Y, Ikeda K, et al. The value of ultrasound-guided fine-needle aspiration cytology for thyroid nodules: an assessment of its diagnostic potential and pitfalls. Surg Today2001 ;31(2):97-101.

26. Mittendorf EA, Tamarkin SW, McHenry CR.The results of ultrasound-guided fine-needle aspiration biopsy for evaluation of nodular thyroid disease.Surgery2002 ;132:648-53.

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