A COMPARATIVE STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY, ULTRASONOGRAPHY AND RADIONUCLIDE SCAN IN MANAGEMENT OF SOLITARY THYROID NODULE: A PROSPECTIVE ANALYSIS OF FIFTY CASES

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ABSTRACT: Solitary thyroid nodule is a common clinical entity encountered by the otorhinolaryngologist and physicians. The optimum diagnostic strategy for euthyroid patient with a solitary nodule thyroid is still a matter of debate. The goal of diagnostic workup now is to select those patients for surgery who have a high likelihood of harbouring malignancy in the solitary nodule. The present study was undertaken to evaluate the utility of FNAC in the pre-operative diagnosis of solitary thyroid nodule and to evaluate the efficacy of FNAC, USG, RNS in differentiating between benign and malignant nodules. It was found that FNAC is a safe, reliable and cost effective diagnostic modality with a high sensitivity of 83.3% and specificity of 100% and single best investigation for pre-operative evaluation of solitary thyroid nodules to differentiate between benign and malignant nodules.

KEY WORDS: Solitary thyroid nodule, Fine Needle Aspiration Cytology (FNAC), Ultrasonography (USG), Radionuclide Scan (RNS), sensitivity, specificity.

INTRODUCTION: The thyroid gland is unique among endocrine glands in that it is the first endocrine gland to appear in the fetus. It is the largest of all endocrine glands (weighing about 25g) and is the only one which is amenable to direct physical examination because of its superficial location. Autopsy studies have demonstrated that the thyroid nodularity is present in approximately 37% of the general population, of which 12% form the group with solitary thyroid nodules. The incidence of clinically apparent thyroid nodules in the general population is approximately 4-5%. The overall incidence of malignancy in solitary thyroid nodule ranges between 10% and 30% depending on the selectivity of surgical indications. Few subjects in surgery have generated as much controversy as the management of solitary thyroid nodule, the two major issues being the diagnostic workup and the extent of thyroidectomy. Because of the possibility of malignancy, some clinicians, especially those in the surgical subspecialties, recommend that all nodules be removed. On the other hand, endocrinologists recommend that FNAC be performed as the initial step of evaluation in order to avoid unnecessary surgery. Because thyroid nodularity is so common, it would be impossible to operate on every patient with a thyroid mass, as the incidence of malignancy is quite low compared with the overall incidence of thyroid nodularity. So, the goal of diagnostic workup now is to select those patients for surgery who have a high likelihood of harbouring malignancy in the nodule. At one extreme, the diagnosis of malignancy may be strongly suspected on clinical grounds and such patients generally require open exploration. On the other hand, one finds many patients in whom the history and clinical findings are not so conclusive. Many investigations are used to differentiate between benign and malignant nodules so as to avoid surgery in those who don't need it. Among

these, FNAC, USG and RNS are commonly used in association with clinical features but there are drawbacks of each technique and the final answer to the problem is still elusive. The present study was undertaken to evaluate the utility of FNAC in preoperative diagnosis of solitary thyroid nodule and to evaluate the efficacy of FNAC, USG and RNS in differentiating between benign and malignant nodules.

MATERIALS AND METHODS: A prospective study was carried out on 50 euthyroid cases of solitary thyroid nodule attending the Department of ENT, Vinayaka Mission Medical College and Hospital, Karaikal, during the period of may 2012 to July 2013. For the purpose of inclusion in this study, a solitary thyroid nodule was defined as a single clinically palpable discrete lesion involving either lobe or the isthmus of the thyroid gland. Then, all patients were submitted to FNAC, USG and RNS. The results of FNAC were interpreted as benign, malignant, suspicious and inadequate aspirate. The results of RNS were interpreted as cold and warm (hot nodules being excluded from the study). Sonographically, the nodules were evaluated for size, location, echotexture, margins, presence of halo, calcification, accessory nodules, associated cervical lymphadenopathy and consistency (solid, cystic or mixed) in order to differentiate between benign and malignant nodules. Then, all the patients were subjected to surgery and histopathological examination (HPE) of the specimens was obtained. Finally, the histopathology reports were correlated with the findings of FNAC, USG and RNS in order to evaluate their sensitivity and specificity by statistical methods.

RESULTS: Solitary thyroid nodules are very commonly seen in the general population. The cytological diagnosis of benign nodule was confirmed in 31 (96.87%) of 32 patients and was disputed in 1 (3.13%) which was shown to be malignant (Table – III). In 10 cytologically suspicious cases, HPE revealed benign lesion in 7 cases and malignant lesion in 3 cases. All 5 malignant interpretations on cytology were confirmed by HPE. All 3 inadequate specimens on cytology were shown to be benign on HPE (Tables I, II and III).

Table I: Results of FNAC

Classification of aspirate	Number (%)
Benign	32 (64%)
Suspicious	10 (20%)
Malignant	5 (10%)
Inadequate aspirate	3 (6%)

Table II: Results of Histopathological Examination

Histopathological diagnosis	Number (%)
Adenomatous goitre	20(40%)
Colloid goiter	14(28%)
Papillary carcinoma	8(16%)
Follicular adenoma	4(8%)
Thyroiditis	3(6%)
Follicular carcinoma	1(2%)

Table III: Correlation of FNAC with histopathological diagnosis

Histopathological diagnosis	FNAC				Total
	Benign	Suspicious	Malignant	Inadequate aspirate	
Benign	31	7	---	3	41
Malignant	1	3	5	---	9
Total	32	10	5	3	50

Table IV: Correlation of FNAC with Histopathological diagnosis in thyroid carcinoma

Histopathological diagnosis	Number	FNAC diagnosis	Number
Papillary Carcinoma	8	**Papillary Carcinoma**	5
		Suspicious	2
		Benign	1
Follicular carcinoma	1	**Suspicious**	1

Table V: Result of RNS

Type of Nodule	Number (%)
Cold	39 (78%)
Warm	11(22%)

Table VI: Correlation of RNS with Histopathological diagnosis

Type of nodule on RNS	Number	Histopathological diagnosis		% of malignancy
		Benign	Malignant	
Cold	39	30	9	23
Warm	11	11	0	0

Of the 8 cases (88.9%) of papillary carcinoma of thyroid, FNAC revealed papillary carcinoma in 5 cases with a concordance rate of 62.5%, suspicious in 2 cases (25%) and benign in 1 case (12.5%). Cytology revealed suspicious lesion for the only case of follicular carcinoma (Table – IV).

In radionuclide scan, 39 (78%) of the solitary thyroid nodules were found to be cold. All malignancies were found exclusively in the cold nodules. 9 out of 39 (23%) cold nodules were found to be malignant (Tables V and VI).

Table VII: Correlation of USG echotexture with malignancy

USG echo texture	Number	Histopathological diagnosis		% of malignancy
		Benign	Malignant	
Solid	38	32	6	15.8
Mixed	8	5	3	37.9
Cystic	4	4	0	0

Table VIII: Correlation of USG with histopathological diagnosis

Histopathological diagnosis	USG diagnosis			Total
	Benign	Suspicious	Malignant	
Benign	36	5	----	41
Malignant	2	2	5	9
Total	38	7	5	50

On ultrasonography, 4 (8%) of the 50 solitary thyroid nodules were cystic, 38 (76%) were solid and 8 (16%) were mixed. 6 (15.8%) out of 38 solid nodules and 3 (37.9%) of 8 mixed nodules were subsequently found to harbor malignancy. None of the cystic nodules showed malignancy (Table VII).

Taking into consideration the various ultrasonographical features, cases were classified into benign, suspicious and malignant categories. The ultrasonographic diagnosis of benign was confirmed in 36 (94.7%) out of 38 cases and was disputed in 2 (5.3%) cases by HPE which turned out to be malignant. In 7 Ultrasonographic suspects, HPE revealed benign lesion in 5 cases and malignant lesion in 2 cases. All malignant interpretations on USG were confirmed by HPE (Table VIII).

All cases in the study had solitary thyroid nodule on clinical examination. USG revealed multiple nodules in 16 (32%) of the 50 cases. RNS revealed multiple nodules in 12 (24%) of the 50 cases. Preoperatively, 19 (38%) glands were found to have multiple nodules. Thus, USG is most sensitive diagnostic modality to detect nodularity (Table IX).

It was observed that FNAC is 83.3% sensitive and 100% specific in detection of malignancy in solitary thyroid nodules whereas USG is 71.4% sensitive and 77.7% specific in the same regard.

Table IX: Assessment of nodularity by various techniques

Modality	Nodulartiy	
	Solitary	Multiple
Clinical	50	0
RNS	38	12
USG	34	16
Preoperative	31	19

Table X: Sensitivity and Specificity of various diagnostic modalities

Diagnostic modality	Sensitivity	Specificity
FNAC	83.3%	100%
USG	71.4%	77.7%
RNS	100%	23%

Although RNS is 100% sensitive (as all malignancies were found in cold nodules only), it has a very low specificity (23%) in the identification of malignancy in solitary thyroid nodules (Table X).

DISCUSSION: The overall incidence of malignancy in solitary thyroid nodules varies from 10% to 30% according to various studies. In our study, the overall incidence of malignancy in solitary thyroid nodules was 18 %.

FNAC is the cornerstone of the laboratory evaluation of solitary thyroid nodules, and its use in recent years has resulted in a significant decrease in the number of surgeries being performed, while increasing the yield of malignant lesions of patients who have undergone surgery. As it distinguishes between the benign and malignant lesions quite effectively preoperatively, it has been proposed as the preoperative screening method of choice. Colloid containing aspirates almost always indicate the presence of a benign nodule. We found that out of 41 cases found to be non-malignant on HPE, 31 were correctly identified negative for malignancy on FNAC. The overall accuracy was 71.1% in our series, whereas in various other series it has varied from 79% to 98%. Depending on the experience of the physician performing FNAC and the experience of the cytologist interpreting the cytologic findings, its accuracy may be as high as 98%. The diagnosis is correct in about 90% of undifferentiated carcinomas and medullary thyroid carcinomas and in about 80% of papillary carcinomas. For follicular carcinomas, however, its accuracy in the hands of many cytologists is only about 40% because it is very difficult to distinguish between benign and malignant follicular neoplasms by FNAC.

When FNAC reports of 9 patients with thyroid carcinoma were checked, it was found that 5 out of 9 cases had a correct preoperative diagnosis and 2 cases were reported as suspicious and 1 as benign. A 62.5% concordance between the histologic and cytologic diagnosis was found which rose to 87.5% on inclusion of the suspect cases as positive cases. Altavilla & Pascale et al (1999) reported in their series a 45.83% concordance between the histologic and cytologic diagnosis which on including the suspect cases as cytologically positive rose to 70%.

The overall sensitivity of FNAC in our series was 83.3% while the overall specificity was 100% as all malignancies reported on FNAC were correctly confirmed by final HPE. The sensitivity and specificity of FNAC were 71.43% and 100% respectively according to Altavilla et al (1990), 98% and 99% according to Goellner et al (1987), 93.5% and 75% according to Bouvet et al (1992).

FNAC has certain limitations because of scanty sample and suspicious diagnosis. In our series, 6% of the specimens were inadequate and 10% were found to be suspicious. Out of 7 suspicious cases, 3 were found to be malignant on final HPE. Thus, an overall malignant rate of about 42.8% for the suspicious group was found. Because of this high incidence of malignancy in suspicious lesions, surgical removal of these nodules should be strongly considered in these cases.

Pitfalls in FNAC of the thyroid as mentioned by Shaha (2000)

- Adequacy of specimen (quantitative & qualitative)
- Accuracy of specimen (nonhomogeneity of needle placement)
- Accuracy of cytopathologic interpretation
- Cysts (difficulties with degenerative nodules)
- Follicular lesions (benign vs. malignant)
- Hurthle cell lesions (benign vs. malignant)
- Lymphocytic lesions (lymphocytic thyroiditis vs. lymphoma)

All patients in this study were also evaluated by RNS preoperatively. The scan showed a cold nodule in 39 (78%) cases and a warm nodule in 11 (22%) cases.

Patients having a hyperfunctioning or hot nodule were excluded from the study. The overall incidence of malignancy in this study was 18% (9/50). As the majority of the nodule were cold (78%), the risk of malignancy in a cold nodule was 23%. The RNS had 100% sensitivity in our series in the detection of malignancy but the specificity was very low (23%). Marshall & Cox et al (1991) reported an overall incidence of 73% of cold nodules in their series out of which 12.2% were found to be malignant. The overall sensitivity of detecting malignancy in their series was 100%nbut specificity was only 12.2%. Kapur & Sarin et al (1982) reported in their series 16% incidence of malignancy in cold nodules. It was observed in a study by Sharma et al (1999) that radionuclide perfusion study is useful to differentiate benign from malignant solitary thyroid nodules with a high degree of sensitivity (95%) and specificity (87.9%).

It must be pointed out, however, that most of the thyroid nodules are cold, including cysts, colloid nodules, benign follicular lesions, hyperplastic nodules and nodules of Hashimoto's thyroiditis. Nodules that appear to be warm (without suppression of uptake in surrounding tissue) or isofunctioning may be malignant. With the exception of autonomously functioning or hot nodules, which are almost always benign, the thyroid scan does not help in differentiating between the benign and malignant thyroid lesions.

One of the main roles of the USG in the assessment of solitary thyroid nodules is to distinguish non-operatively between solid and cystic lesions. In our study, there were 4 cystic nodules (8%), 38 solid nodules (76%) and 8 mixed (16%). When the results of USG were compared with the final HPE report, we found that none of the cystic nodules harboured malignancy. Out of the 38 solid nodules, 6 (15.8%) were found to be malignant and out of 8 mixed nodules, 3 (37%) were found to be malignant. The nodules were sub divided into 3 groups – benign, suspicious and malignant on the basis of various sonographic features. Features suggestive of malignancy on USG are – hypoechoic pattern (almost always), incomplete peripheral halo, irregular margins, internal microcalcification, presence of cervical lymphadenopathy and peripheral degeneration in mixed nodules. Features suggestive of benign diseases on USG are – halo sign (transonic uniform rim surrounding the mass), variable echogenicity, multinodularity, large cystic lesion, diffusely nodular in homogenous gland and peripheral calcification.

USG correctly diagnosed malignancy in 2 patients in whom FNAC failed to achieve the correct diagnosis. On the other hand, FNAC revealed malignancy in 3 patients in whom USG indicated a benign lesion. In our study, all 5 malignancies recognized by USG were confirmed on HPE later on. In 2 patients, in which USG gave a false negative diagnosis of benign disease, HPE revealed papillary carcinoma. Both of these patients USG gave diagnosis of thyroiditis on the basis of diffuse echo pattern with multiple diffuse hypoechoic areas. Thus, it is not possible to differentiate between thyroiditis and malignancy. Katz and Kane et al (1984) also found that USG was unable to differentiate between thyroiditis and malignant lesion. Halo sign is not characteristic of benign lesions as it was seen in only 3 out of 4 (75%) cases of follicular adenoma and was absent in 1 case of follicular adenoma.

In our study, we found the sensitivity and specificity of USG to be 71.4% and 77.7% respectively for differentiating between the benign and malignant nodules. In consistency with our study, Watters et al (1992) found that the sensitivity and specificity of USG in suggesting a malignant

lesion were 74% and 83% respectively. They interpreted an USG report as suggestive of malignancy if the nodule was solid or of a mixed solid-cystic variety and a hypoechoic and no haloed lesion. They emphasized that the USG has added advantage of allowing the whole gland to be examined rather than the dominant nodule but was limited by the fact that no features were pathognomonic for malignancy so that it should be regarded as a complementary rather than an alternative investigation to FNAC in the management of solitary thyroid nodules. Jones et al (1990) found the sensitivity and specificity of USG to be 75% and 61% respectively.

It has been a consistent observation, according to published literature, that the risk of thyroid cancer is less with multiple nodules than with the solitary nodules. High resolution real-time USG is far better than clinical examination in detecting thyroid nodularity. Walker et al (1985) have shown that the prevalence of multinodularity in clinically solitary thyroid nodules is between 20% and 40% and it has been observed that for a thyroid nodule to be detected by palpation, it must be atleast 1 cm in diameter while USG detects nodules as small as 3 mm in diameter. Simeone et al (1982) stated that the detection of more than 1 lesion with USG reduces the probability of malignancy to 1-6%.

CONCLUSION: The present study was undertaken to evaluate the usefulness of FNAC, USG and RNS in the management of solitary thyroid nodules. The sensitivity and specificity of various diagnostic modalities were evaluated and it was found that while RNS and FNAC have a high sensitivity, FNAC and USG have a high specificity. In our study, the sensitivity and specificity of FNAC, USG and RNS were 83.3% and 100%, 71.4% and 77.7% and 100% and 23% respectively. An ideal test should have a sensitivity and specificity of 100%. The closest method to the ideal test is thus, FNAC which gives a sensitivity of 83% and specificity of 100%. However, a combination of various diagnostic modalities, rather than any single modality, will give optimal results and avoid unnecessary surgery in a great number of patients without missing any malignancy.

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