

# Solitary Thyroid Nodules - Validity of Ultrasonography, Fine Needle Aspiration Cytology and Sestamibi in Detecting Thyroid Malignancies - A Cross-Sectional Study in Kerala

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## ABSTRACT

### BACKGROUND

The diagnosis of thyroid malignancies continues to remain a challenge, due to lack of specificity with various modalities, and intrinsic variability with clinical examination. Although histopathological diagnosis is confirmatory, there is a need for pre-surgical assessment and confirmation, which will prove to be useful in decision making regarding the course of management. The present study was carried out to evaluate the validity of various modalities for detection of thyroid malignancies.

### METHODS

This cross-sectional study was carried out among 40 patients who presented to the outpatient clinic with thyroid nodules. All the participants were evaluated by ultrasound, fine needle aspiration cytology (FNAC) and sestamibi scintigraphy. All the participants were taken up for surgery and the resected specimen was sent for histopathology for confirmatory diagnosis.

### RESULTS

Ultrasound and FNAC detected malignancy in 25 % of the participants, while sestamibi scintigraphy detected malignancy in 30 % of the participants. Based on histopathology, the gold standard confirmatory test, malignancy was detected in 35 % of the participants. It was observed that the sensitivity was highest for FNAC (75 %) followed by TC methoxyisobutylisonitrile (TC MIBI) (50 %). Specificity was highest for FNAC (95 %) followed by ultrasound (88 %) ( $P < 0.0001$ ).

### CONCLUSIONS

FNAC has the highest sensitivity and specificity while ultrasound and sestamibi have comparable specificity. There is a high probability of malignancy when the delayed image in sestamibi scintigraphy shows retention. MIBI may prove to be useful in differentiating benign and malignant follicular lesions.

### KEYWORDS

Papillary Carcinoma, Histopathology, Thyroid Nodule, Sestamibi, FNAC

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## BACKGROUND

Thyroid malignancies often present as nodules and are asymptomatic in nature. With increasing incidence reported worldwide, there is a growing need for making an early diagnosis for effective management. Presence of thyroid nodules are fairly common all over the world. It is estimated that approximately 5 % to 7 % of the adult American population has a palpable thyroid nodule, and autopsy and high-resolution ultrasonography studies suggest that up to 50 % of adults may have nodules within their thyroid gland.<sup>1,2</sup> In India, the prevalence of palpable thyroid nodules is been estimated to be 12.2 %, although the prevalence of thyroid malignancies is considerably rare, with an incidence of 8.7 per 100,000 population.<sup>3</sup> Because the overwhelming majority of thyroid nodules are benign, the diagnosis of thyroid malignancies through clinical examination has been a great challenge for clinicians. In the presence of solitary thyroid nodule, it is essential for the clinician to explore the risk factors for malignancy which includes prior neck irradiation, family history of malignancies, age, and, the physical characteristics of the nodule including size, consistency, mobility, presence of pressure symptoms including hoarseness of voice and presence or absence of lymphadenopathy.

In addition to clinical evaluation, there is a huge need to depend on radiological and histological confirmation of malignancies, as the thyroid function tests seldom show any variation.<sup>4</sup> Challenges continue to persist in terms of choosing the right course of action; while the surgeons recommend removal of all the nodules, endocrinologists prefer to proceed based on cytological finding obtained through fine needle aspiration cytology. The goal of diagnostic workup has always remained to select those patients for surgery who have a high likelihood of harbouring malignancy in the nodule. Among the several diagnostic modalities available, FNAC, ultrasound (USG) and radionuclide scan are commonly used to aid the clinical diagnosis. There are however drawbacks for each technique and arriving at a consensus regarding the appropriate course of action continues to elude the clinicians. The present study was undertaken to compare the findings of sonological, sestamibi thyroid scintigraphy, cytological and histopathological findings in discrete thyroid swellings and to evaluate the efficacy of these in differentiating between benign and malignant nodules.<sup>5</sup>

## Objective

This study was carried out to compare the findings of ultrasound, sestamibi scintigraphy, FNAC and histopathology in the evaluation of discrete thyroid nodules.

## METHODS

The present study was carried out as a cross sectional study in the Department of General and Endocrine Surgery of our tertiary care teaching institution for a period of eighteen months from January 2006 to July 2007. All the patients who

presented at the outpatient clinic with solitary and dominant thyroid nodules were selected for the study.

### **Inclusion Criteria**

1. All patients with a thyroid nodule of more than 1 cm in size
2. Those swellings which were solitary on clinical palpation but multi nodular on ultrasound were also included in the study.
3. Euthyroid state

### **Exclusion Criteria**

Recurrent goiter

### **Ethical Approval and Informed Consent**

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study (IEC number - not applicable). Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

### **Sample Size and Sampling**

Based on the literature,<sup>6</sup> considering the sensitivity of 88 % with 10 % precision and 95 % level of significance, the sample size required was 40 diseased subjects. The participants for the study were selected by consecutive sampling based on the selection criteria.

### **Data Collection**

All the patients were submitted to ultrasound, FNAC and then sestamibi thyroid scintigraphy. The results of FNAC were interpreted as benign, malignant, inadequate and suspicious. Ultrasound of the thyroid nodules was done by using a 7.5 mHz linear probe. Based on the ultrasound the nodules were evaluated by size, shape, echotexture, calcification, shape, vascularity and lymph nodes and were classified as benign, malignant and suspicious. All the patients were subjected to technetium 99 scan followed by sestamibi scintigraphy. The technetium scan was done to discriminate the suspected solitary thyroid nodule and to establish it is a cold nodule. About 5 to 10 mCi Tc 99 sestamibi injected intravenously. After 15 to 20 minutes, anterior neck images were taken and repeated again at after 1.5 to 2 hours for delayed image to look for washout/retention in the nodule. The images were obtained using Gamma camera. The results were interpreted as neoplastic, non-neoplastic and suspicious for malignancy. All the participants were subjected to surgery and histopathological examination of the specimens were obtained.

### **Data Analysis**

Data was entered and analysed using SPSS version 20 software. The histopathology reports were considered as the

gold standard and were correlated with the findings of FNAC, USG and Tc-MIBI scintigraphy in order to evaluate their sensitivity, specificity, accuracy, positive and negative predictive values by statistical methods.

### Operational Definitions

A solitary thyroid nodule was defined as a discrete thyroid swelling in an otherwise impalpable gland. Dominant nodule was defined as a similar swelling in a gland with clinical evidence of generalized abnormality in the form of a contralateral lobe or generalized mild nodularity.

### RESULTS

The present study was carried out among 40 participants. The mean age of the participants was 41 years and majority of the participants belonged to the age group of 40 - 49 years (30 %). Majority of the participants were females (75 %) and underwent total thyroidectomy (70 %). Out of the 40 participants, 14 were diagnosed with malignancy (35 %). Among those with malignancy, majority belonged to the age group of 40 - 49 years (28.6 %) and were females (71.4 %). (Table 1)

Sl. No.	Characteristics	Total Participants		Participants with Malignancy	
		Frequency (N = 40)	(%)	Frequency (N = 14)	(%)
Age (in years)	10 - 19	2	5	1	7.2
	20 - 29	5	12.5	3	21.4
	30 - 39	11	27.5	2	14.2
	40 - 49	12	30	4	28.6
	50 - 59	6	15	3	21.4
	60 - 69	3	7.5	0	0
	70 - 79	1	2.5	1	7.2
Sex	Male	10	25	4	28.6
	Female	30	75	10	71.4
Type of surgery	Hemithyroidectomy	12	30	3	21.4
	Total thyroidectomy	28	70	11	78.6

Table 1. Background Characteristics of the Study Participants

Sl. No.	Characteristics	Frequency	Percentage
Type	Solitary	33	82.5
	Dominant	7	17.5
Consistency	Cystic	13	32.5
	Solid	22	55
	Mixed	5	12.5

Table 2. Nodule Characteristics of the Study Participants

Sl. No.	Time of Uptake	Malignant n (%)	Benign n (%)	Total
1	Initial	14 (38.8)	22 (61.1)	36
2	Delayed	8 (53.3)	7 (46.7)	15

Table 3. Technetium<sup>99m</sup> Uptake Particulars among the Study Participants

In this study, ultrasound, FNAC, sestamibi and histopathology were the modalities used to detect malignancy. Ultrasound and FNAC detected malignancy in 25 % of the participants, while sestamibi scintigraphy detected malignancy in 30 % of the participants. Based on histopathology, the gold standard confirmatory test,

malignancy was detected in 35 % of the participants (Figure 1). The histopathological diagnosis of thyroid malignancies is given in figure 2. It was seen that majority of the malignancies were papillary carcinoma (86 %) followed by follicular and Hurthle's cell carcinoma (7 % each). Majority of the nodules were solitary (82.5 %) and were solid (55 %) cystic nodules were seen in 32.5 % of the cases. (Table 2) The sestamibi scintigraphy demonstrated that initial uptake was present in 36 cases, of which 14 (38.8 %) were malignant, while the uptake was delayed in 15 cases of which 8 (53.3 %) were malignant. (Table 3)

Sl. No.	Parameters	Diagnostic Modalities		
		Ultrasound	FNAC	TCMIBI
1	Sensitivity (%)	21.4	75	50
2	Specificity (%)	88	95	80.9
3	Positive predictive value (%)	50	90	58.3
4	Negative predictive value (%)	66.6	86.3	75
5	False positive (%)	12	5	19.1
6	False negative (%)	78.6	25	50
7	Accuracy (%)	71.4	80	80
	P value	0.04*	< 0.0001*	< 0.003*

Table 4. Validity of Various Diagnostic Parameters in Detecting Thyroid Malignancies

\*statistically significant

Sl. No.	Parallel Testing	Sensitivity Rate	Specificity Rate
1	USG "and" FNAC "and" TCMIBI	0.078	1.9612
2	USG "or" FNAC "or" TCMIBI	1.3825	0.6688

Table 5. Combined Predictive Validity of the Tests

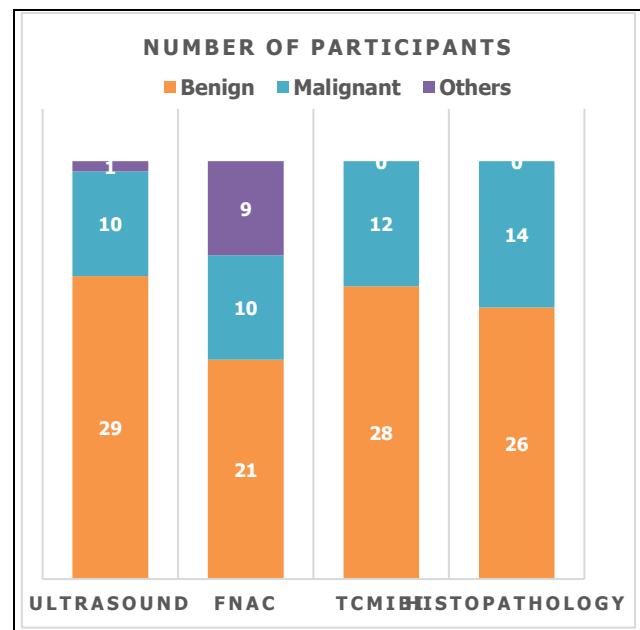
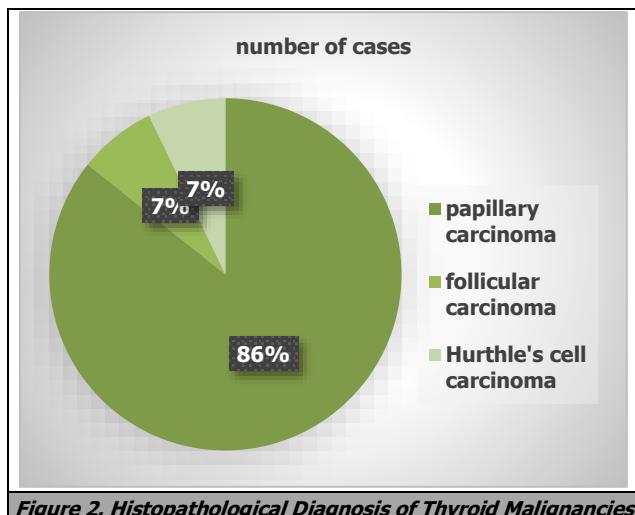


Figure 1. Malignancy Detected through Various Modalities

The validity parameters were analyzed for each of the diagnostic modality. It was observed that the sensitivity was highest for FNAC (75 %) followed by TCMIBI (50 %). Specificity was highest for FNAC (95 %) followed by ultrasound (88 %). Both positive and negative predictive value was highest for FNAC (90 % and 86.3 % respectively). False positivity was lowest for FNAC (5 %) and highest for TCMIBI (19.1 %), while false negatives were lowest for FNAC (25 %) and highest for ultrasound (78.6 %). Overall, it was observed that FNAC showed statistically significant difference in the validity parameters compared to other

modalities ( $P < 0.0001$ ). While evaluating the combined validity of these three methods through parallel testing, higher specificity was observed when evaluated in an "and" manner (1.9612) compared to sensitivity (0.078). However, on evaluating in an "or" manner the overall sensitivity was higher (1.3825) compared to specificity (0.6688). (Table 5)



**Figure 2. Histopathological Diagnosis of Thyroid Malignancies**

## DISCUSSION

In this study, all the patients were evaluated by all the three tests prior to thyroidectomy. All the tests were compared with histopathology, which is considered as the gold standard in the diagnosis of thyroid malignancies. The incidence of thyroid nodules was found to be higher in females. The 40 patients included in the study were of the age range of 17 - 79 years with a mean age of 41 years. The indications for surgery were predominantly cosmetic reasons (40 %) and pre-operative diagnosis of malignancy (35 %). The prevalence of thyroid malignancy in this study was 35 %. The incidence of malignancy was higher in males with 40 % (4 out of 10 cases) showing malignancy. In females, the incidence of malignancy was found to be 33 % (11 out of 30 cases). The incidence of malignancy was maximum in the age group of 40 - 49 showing 28.6 % malignancy.

On evaluating various modalities for screening, the present study observed that FNAC had higher validity compared to other modalities in terms of sensitivity and specificity (76.9 % and 95.5 % respectively). The sensitivity and specificity of ultrasound was found to be 46.6 % and 84 % respectively for differentiating benign and malignant nodules. In this study, sestamibi showed a sensitivity of 66.6 % and specificity of 84 %. The sensitivity and specificity were comparable to other studies – 97 % and 100 % respectively according to Handa U et al. 76.5 % and 95.9 % respectively according to Aggarwal et al. while the accuracy was similar to the study done by Rout et al.<sup>7-9</sup> The accuracy was 88.5 %, positive predictive value was 90.9 %, and the negative predictive value was 87.5 %. In literature, an accuracy of 80 %, positive predictive value of 46 %, and a negative predictive value of 97 % are reported for FNAC.<sup>10</sup> On comparing the sestamibi findings with other published

literature, a study done by Sharma et al. showed a sensitivity of 84.4 % and specificity of 95.4 %, higher than our study findings.<sup>11</sup> Similar findings were seen in studies published by Sundaram FX et al.<sup>12</sup>

As far as ultrasound is concerned, it is useful for evaluation of thyroid nodules because of its safety, non-invasiveness, non-radioactivity and effectiveness. Studies emphasized that 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.

The results of sestamibi scintigraphy were based on the uptake of MIBI in the initial and delayed images. Presence of uptake in the initial images with retention or washout classified the tumour as neoplastic, while its absence with no retention in the delayed image classified the tumour as non-neoplastic. However, when the initial uptake was present with delayed image retention, it was interpreted as highly suspicious of malignancy. In the present study, there were a total of 14 malignancies and all of them showed uptake in the initial image. MIBI may be helpful in follicular neoplasms in differentiating benign and malignant lesions. It is most effective in the management of patients with low risk of malignancy or in cases where the role of cytological examination is limited, as in the case of follicular neoplasms.<sup>13</sup>

According to literature, FNAC is the safest, cost-effective, and most reliable technique available to differentiate between benign and malignant diseases of the thyroid.<sup>14</sup> It is highly accurate, inexpensive and has low morbidity. Processing time is usually only a few days. It is estimated that FNAC aids in reducing the number of thyroidectomies by half and the overall cost of medical care by one quarter while doubling the surgical confirmation of carcinoma.

FNAC has certain limitations that include the failure of the test due to inadequate sample in some cases and the occurrence of suspicious diagnosis in others. Though FNAC has been proposed as a preoperative screening method, it has some limitations. These are due to inadequate samples and accuracy of cytopathological interpretation. However, FNAC still remains the most useful investigation in the diagnosis of thyroid nodules owing to its high sensitivity.

## CONCLUSIONS

FNAC has the highest sensitivity and specificity. Ultrasound and sestamibi have comparable specificity. FNAC has the highest positive and negative predictive value, followed by MIBI and ultrasound. Accuracy was found to be highest in FNAC while sestamibi is useful in differentiating neoplastic and non-neoplastic lesions. There is a high probability of malignancy when the delayed image in sestamibi scintigraphy shows retention. MIBI may prove to be useful in differentiating benign and malignant follicular lesions.

Data sharing statement provided by the authors is available with the full text of this article at [jebmh.com](http://jebmh.com).

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Disclosure forms provided by the authors are available with the full text of this article at [jebmh.com](http://jebmh.com).

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