

Study of the Efficacy of Triple Assessment in the Diagnosis of Thyroid Nodule

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Abstract

Background and Objectives: The management of thyroid nodules is multi-disciplinary and involves surgeons, pathologists, endocrinologists and radiologists. Here, we conducted a prospective correlational study of 50 patients who presented with solitary thyroid nodule to Basaveshwara Teaching and General Hospital during Nov 2016 to June 2018. The objectives were: 1. To study the clinical presentation, USG and FNAC findings of thyroid nodules. 2. To study the concordance and discordant results in the triple assessment. 3. To compare the results with the histopathological findings when available. **Methods:** All the patients who fit the inclusion criteria (n=50), underwent triple assessment i.e clinical examination, Ultrasound Examination and US guided FNAC of the thyroid nodule along with complete thyroid profile and routine investigations. The findings of the triple assessment were then compared with Histopathological Report, post-surgery. The concordance of the preliminary investigations was then assessed. **Results:** In this study, the peak incidence was noted in the age group of 31-40 with 34% of the patients (n=17). The youngest patient was 18 yrs old and the eldest, 70 yrs old. 88% (n=44) of the patients were females, whereas 12% patients were male. The most commonly accompanied symptom to the thyroid swelling was pain/discomfort (in 14 patients). Most patients (44%) were categorised into Bethesda Category II indicating benign swellings. The diagnostic accuracy of USG and FNAC were 92% and 98% respectively. **Conclusion:** • The incidence of thyroid cancer is 22% among the patients with thyroid

nodules. • There is a higher incidence of benign lesions (88%) most of which belonged to Bethesda Category II. • Sex profile of both benign and malignant lesions showed high female preponderance. • Ultrasound guided Fine Needle Aspiration Cytology showed high sensitivity and 98% diagnostic accuracy.

Keywords: Triple assessment; thyroid nodule; US guided FNAC.

Introduction

Thyroid swellings are one of the common problems seen in surgical practice. The management of thyroid nodules is multi-disciplinary and involves surgeons, pathologists, endocrinologists and radiologists [1].

The current approach to thyroid swellings has been revolutionized with the introduction of Thyroid ultrasonography (USG) and Fine Needle Aspiration Cytology (FNAC).

Ultrasound is easy to perform, widely available, does not involve ionizing radiation and is readily combined with FNAC [2]. Because of superficial location and good vascularisation of thyroid gland, high resolution real time grey scale and colour Doppler sonography can delineate and demonstrate the normal thyroid anatomy and pathological conditions with remarkable clarity.

The role of FNAC in pre-operative assessment of thyroid swellings has been well established in several studies. It has resulted in substantial improvements in diagnostic accuracy, cost reductions, and higher malignancy yield at the time of surgery [3].

It is therefore the ideal investigation of choice for evaluating thyroid nodules. Together, they can determine the nature of thyroid swelling and help in designing a rational treatment strategy.

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Triple assessment

Triple assessment means:

- i. History and physical examination including malignancy risk stratification.
- ii. Imaging, usually the ultrasonographic evaluation of the thyroid and the neck.
- iii. Image guided FNAC for confirmation; FNAC without image guidance has a false positive rate of 40% which can be avoided by guided FNAC [4].

However 10%-15% of the lesions cannot be categorized either as benign or as malignant by triple assessment alone. Bethesda system of the FNAC of the thyroid gland ensures uniformity of reporting so that the pathologist and surgeon are in the same frequency. It helps in the prognosis and management. Bethesda system is reported in six specific categories which are linked to the recommended management options.

Objectives

1. To study the clinical presentation, USG and FNAC findings of thyroid nodules.
2. To study the concordance and discordant results in the triple assessment.
3. To compare the results with the histopathological findings when available.

Methodology

A prospective correlational study was conducted on 50 consecutive patients who presented to the Department of General Surgery at Basaveshwara Teaching and General Hospital during the period of November 2016 to June 2018 which included patients presenting with thyroid enlargement to evaluate the efficacy of triple assessment of thyroid nodules.

Inclusion criteria

1. Patients with clinically suspected thyroid nodules.
2. As a pre-requisite before surgery in patients with thyroid disease.

Exclusion criteria

1. Pregnant women with thyroid swellings.
2. Patients not willing to undergo Ultrasonography and FNAC.

Procedure

The qualifying participants were informed in detail regarding the risks and benefits of each procedure and written informed consent was obtained. All patients with Thyroid nodules were clinically evaluated and subjected for Ultrasonography of the thyroid nodule and neck. Then, FNAC of the thyroid nodule on the basis of the Ultrasonography findings was done. Thyroid Function Tests of the patients were also done to plan the further medical or surgical management. These observations were then compared with the histopathological findings.

Results

In our study, 88% (n=44) of the patients were females, whereas 12% patients were male. (Table 1).

Table 1: Age wise distribution of thyroid nodules

Age	Number	Percentage (In %)
<20	1	2
21-30	16	32
31-40	17	34
41-50	10	20
51-60	2	4
>60	4	8
Total	50	100

In this study, the peak incidence was noted in the age group of 31-40 with 34% of the patients (n=17), closely followed by the age group of 21-30 with 32% patients (n=16). The youngest patient was 18 yrs old and the eldest, 70 yrs old (Figure 1).

Table 2: Age wise distribution of benign and malignant thyroid nodules proven by HPE

Age in years	Benign		Malignant	
	number	percentage	number	percentage
<20	1	2%	0	0%
21-30	13	26%	3	6%
31-40	16	32%	1	2%
41-50	9	18%	1	2%
51-60	0	0%	2	4%
>60	0	0%	4	8%
Total	39	78%	11	22%

In this study, there was a trend towards malignancy with increasing age and most benign tumours were noted below the age of 50 yrs. All the patients above the age of 50, who presented to us, had malignant thyroid nodule (Figure 2).

A total of 40 patients (80%) were euthyroid at the time of presentation. 1 patient was hypothyroid and 9 were hyperthyroid.

All the 50 patients came to the OPD with complaints of swelling in the anterior aspect of the neck. Following that, the most commonly accompanied symptom was pain/ discomfort (in 14 patients) (Figure 3).

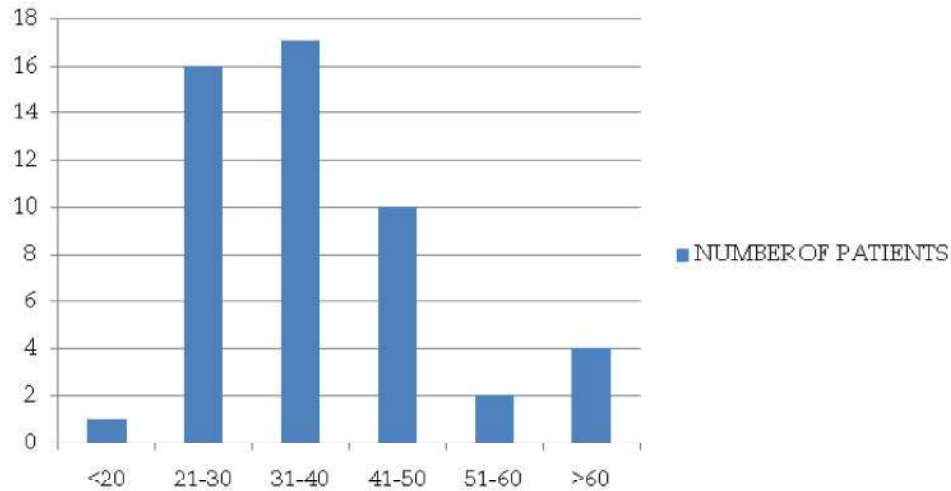


Fig. 1: Graphical representation of age wise distribution

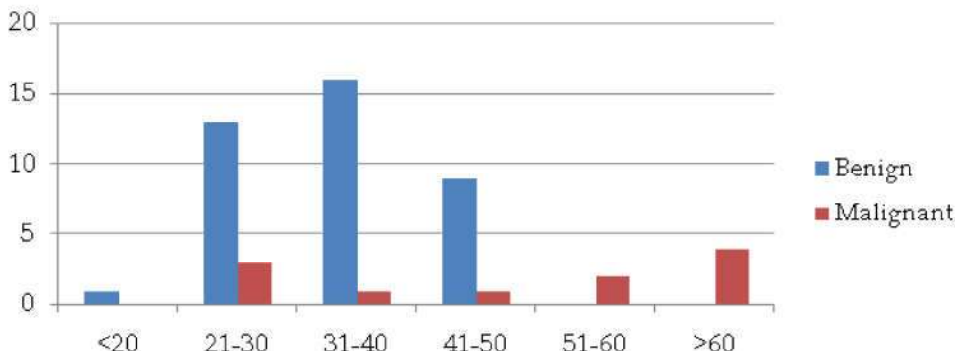


Fig. 2: Graphical Representation of Age wise distribution of benign and malignant thyroid nodules proven by HPE

Presenting Symptoms

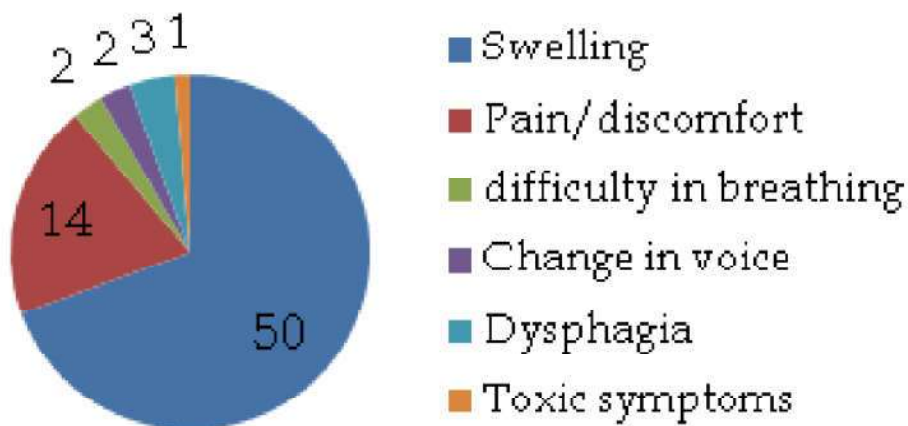


Fig. 3: Distribution of patients according to presenting symptoms

In our study, most patients (44%) were categorised into Category II indicating benign swellings (Figure 4).

Table 3: Distribution of patients based on Bethesda categories of the nodules on FNAC

Category	Diagnostic Category	Number	Percentage (%)
I	Nondiagnostic or Unsatisfactory	7	14
II	Benign	22	44
III	Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	8	16

IV	Follicular Neoplasm or Suspicious for a Follicular Neoplasm	3	6
V	Suspicious for Malignancy	6	12
VI	Malignant	4	8

Table 4: Comparative characters of nodules by various methods

	Benign	percentage	Malignant	percentage
Physical examination	45	90%	5	10
Ultrasound examination	44	88%	6	12%
US guided FNAC	40	80%	10	20%
HPE	39	78%	11	22%

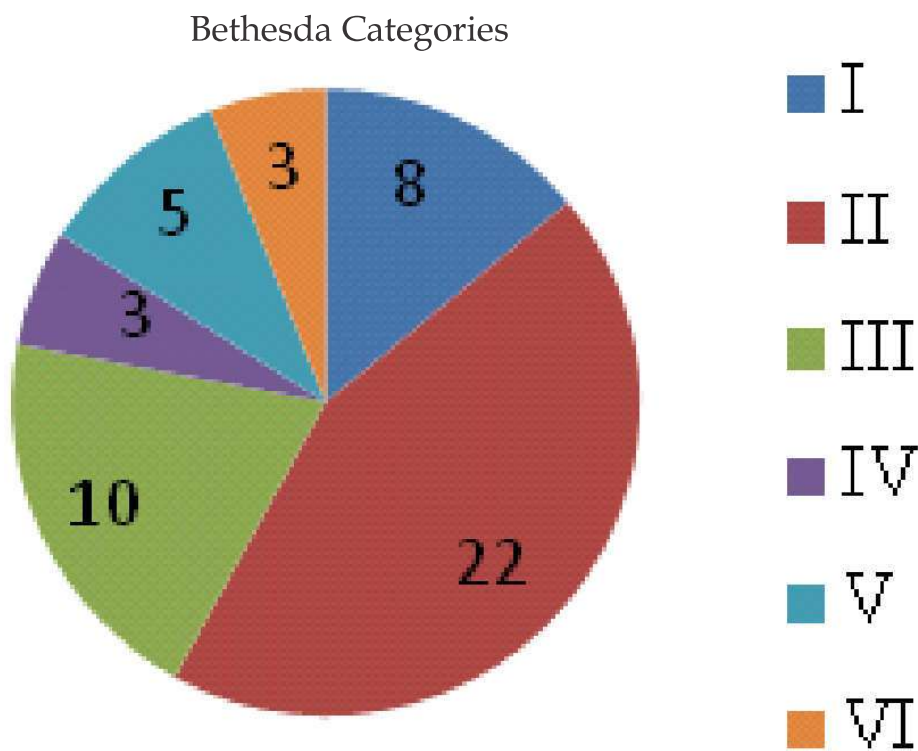


Fig. 4: Graphical representation of distribution of patients according to Bethesda categories

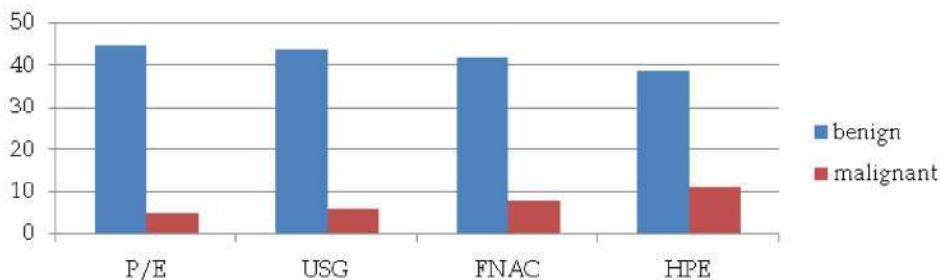


Fig. 5: Graphical Representation of Comparative characters of nodules by various methods

*P/E = Physical Examination

Table 5: USG and HPE correlation

Malignant		Histopathological Examination		
		Benign	Total	
Ultrasound Examination	Malignant	8(a) True positive	1(b) False positive	7
	Benign	3(c) False negative	38(d) True negative	43
	Total	11	39	50

Sensitivity: $TP/TP+FN \times 100 = 72.7\%$

Specificity: $TN/TN+FP \times 100 = 97.4\%$

PPV: $TP/TP+FP \times 100 = 88.8\%$

NPV: $TN/TN+FN \times 100 = 90.4\%$

Diagnostic Accuracy: $(TP+TN)/FP+FN+TP+TN \times 100 = 92\%$

Table 6: FNAC and HPE correlation

Malignant		Histopathological Examination		
		Benign	Total	
US guided FNAC	Malignant	10(a) True positive	0 (b) False positive	8
	Benign	1 (c) False negative	39 (d) True negative	42
	Total	11	39	50

There were no inconclusive reports on FNAC.

Sensitivity: $TP/TP+FN \times 100 = 90.9\%$

Specificity: $TN/TN+FP \times 100 = 100\%$

PPV: $TP/TP+FP \times 100 = 100\%$

NPV: $TN/TN+FN \times 100 = 97.5\%$

Diagnostic Accuracy: $(TP+TN)/FP+FN+TP+TN \times 100 = 98\%$

**Image 1:**

Discussion

According to Khalid et al, the mean age of presentation of Thyroid nodule is 32.2 ± 11.58 years with a range of 13 to 90 years [5]. In retrospective, consecutive analysis by Hee-Nee Pang and Chung-Ming Chen, the mean age of patients with nodular goitres was 48.1 years and the mean age of presentation for malignant thyroid tumours was

49.25 years [6]. A study done by Aghini Lombardi et al on an iodine deficient community showed that thyroid nodularity was 0.5% in children and progressively increased with age to 28.5% in the 56- to 65 yr old group [7]. According to Edino ST et al the ages of the patients with carcinoma ranged from 16 to 65 years, with a mean age of 38.8 years [8].

In this study, the age incidence for the benign lesions ranged from 18 years to 64 years. The age incidence for the malignant lesions ranged from 31 to 72 years. The most common age group for benign lesions was between 41 to 50 years. This study shows an increase in malignancy rate with age; with 36.3% of malignant cases noted in >60 yr olds with mean age of presentation of malignant thyroid tumours being 49.36%.

Sex: The present study observed female preponderance in both benign and malignant tumours. It was observed that out of 50 cases, 44 (88%) were females and 6 (12%) were males. The female to male ratio was 7:1. The female to male ratio for malignancy was 2.6:1. In females, 36 (81.8%) of the thyroid nodules were benign in nature and 8 (18.1%) were malignant. whereas in males, 3 (50% of male patients) were benign and 3 (50%) were malignant.

72.7% (n=8) of all malignancies were found in females and 27.3% (n=3) in males. Thus most of the thyroid nodules were benign irrespective of the sex. The malignancy rates were higher in males as compared to females.

Mulandzi et al., in his study in 2001, observed female preponderance in both benign and malignant tumors in the ratio of 6:1 [9].

Yeole BB et al., in his descriptive epidemiological study of thyroid cancer in Bombay stated that they are three times more frequent among women than men [10]. In another data report in Luxemburg by Mark Keipes, et al., the ratio of male to female was 1:4 [11].

Study by Hee-Nee Pang and Chung-Ming Chen showed that 79.1% with nodular goitres were females [6].

Edino et al. states that 72% of malignant patients are females, and 28% are males [8]. Thus our study correlates with these values.

Clinical Profile

Present study shows that the duration of symptom before seeking medical attention varies from 1 month to 11 years. Thus majority of the patients with benign disease had symptoms for 1 month to as long as 11 years. Majority of the patient with malignant disease had duration of symptoms ranging from 2 months to 5 years.

In the present study, all [100%] the patients presented with thyroid swelling, of which 72% did not have any symptoms other than swelling. 28% of the patients complained of pain or discomfort in the neck. Pressure symptoms like dysphagia was present in only 6% of the patients, difficulty in breathing, change of voice was present in 4% patients each.

Study by Hee-Nee Pang and Chung-Ming Chen showed that most of the thyroid nodules were asymptomatic. 6.7% complained of painful nodules, 6.0% patients noted hoarseness of voice and another 6.0% gave a history of dysphagia. According to Khalid et al dyspnoea was the most common symptom [20.5%], followed by thyrotoxic symptoms in 18.9%, dysphagia in 16.6%, pain in 8.2%, hypothyroid symptom in 6% and hoarseness of voice in 5.2% of the patients. 21.87% of the patients presenting with toxic symptoms had anxiety and palpitations. Next most common symptom was heat intolerance [17.18%] followed by weight loss [14.06%]. Menstrual disturbance and excessive sweating were the other toxic symptoms in that order.

Ultrasonography was found to be very useful in

the evaluation of Thyroid malignancy. In the present study, ultrasonography diagnosed 9 (18%) patients with adenoma and 6 (12%) with adenoma along with cystic degeneration. 10 (20%) patients were diagnosed to have colloid cyst and 14 (28%) with colloid goitre. Multinodular goitre was noted in 6 (12%) patients. USG diagnosed accurately 5 (10%) patients with malignancy, indicating a sensitivity of 72.7%.

Study done by Mary C. Frates, Benson C.B., Doubilet P M, et al. noted that the presence of any calcification within nodule raises the likelihood of malignancy. In particular, microcalcification in a predominantly solid nodule is associated with approximately threefold increase in cancer risk as compared with solid nodule without calcification [12].

L. Solbiati et al. in 1985 showed that margin was ill-defined and irregular in 69.7% and well-defined in 30.3%. Thyroid lesion with well-defined margin suggests benign pathology [13]. However, results are unequivocal in the present study.

FNAC was found to be very useful in the evaluation of thyroid nodule. In majority of the cases where the FNAC was benign it proved to be benign thyroid nodule on postoperative histopathological examination. 78% of the thyroid lesions were diagnosed as benign by FNAC and 20% were diagnosed as malignant.

In present study, FNAC is reported according to Bethesda system. In all cases, samples were collected from image guided FNAC. 44% of patients were categorised by Bethesda system as category-II, 16% as category-III, 14% as category-I, 12% as category-V, 8% as category- VI and 6% as category-IV.

Most of the malignant lesions were Bethesda category-V and VI on FNAC. One patient was diagnosed with category-IV. Benign nodule was the most common diagnosis made by FNAC [44%].

Table 7: Comparison of FNAC with other studies

	Saddique et al. [14]	Bagga & Mahajan [15]	Yaarubi et al. [16]	The present study
Benign	83.33%	90.6%	64%	78%
Malignant	16.66%	12%	6%	20%
Suspicious	-	6.7%	12%	2%

Histopathology showed 39 [78%] out of 50 patients had benign thyroid lesion. Remaining 11 [22%] patients had malignancy.

Edino et al in their study of 160 multinodular goiters, 24 (15.0%) had histologically diagnosed cancer. Well differentiated follicular carcinoma was the predominant histological type in 13 (52%)

cases, followed by papillary in 10 (40%), medullary carcinoma in 1 (4%) and anaplastic carcinoma in 1 (4%) patient [8].

Table 8: Comparison of histopathological diagnosis to other studies

	Saddique et al. [14]	Bagga et al. [15]	Yaarubi et al. [16]	The present Study
Benign	81.66%	81.25%	81%	78%
Malignant	18.33%	18.75%	18%	22%

Analysis of the cytological reports in various series confirms the very high diagnostic accuracy of fine needle aspiration cytology.

Fine needle aspiration cytology revealed that the nodule was benign in 40 patients, suspicious in 1 and malignant in 10 patients. 10 out of total 11 malignant cases were diagnosed by FNAC. One case of Bethesda category-VI was diagnosed as Bethesda category-IV by FNAC, thus giving a false negative report.

The overall sensitivity of fine needle aspiration cytology in Goiter in the present study was 90.9%, specificity was 100%, positive predictive value of 100%, negative predictive value of 97.5% & diagnostic accuracy of 98%.

Thus, FNAC is a valuable investigation to aid clinical examination and evaluation of a patient with goiter. Due to its high accuracy, specificity and sensitivity, FNAC is a reliable investigation in preoperative diagnosis of malignancy in a thyroid swelling. Our values are comparable with other similar studies.

Table 9: Validity tests of FNAC by various studies

Name of the study	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Muhammed Saddique et al. [14]	75%	95.83%	81.31%	93.81%
Bagga & Mahajan [15]	66%	100%	100%	96%
Mundasad et al. [17]	52.6%	86.6%	38.4%	90.4%
Present Study	90.9%	100%	100%	97.5%

Conclusion

In the current prospective study of 50 patients:

The incidence of thyroid cancer is 22% among the patients with thyroid nodules.

There is a higher incidence of benign lesions (88%)

most of which belonged to Bethesda Category II.

Regarding age incidence, benign lesions commonly presented in the 4th decade.

Sex profile of both benign and malignant lesions showed higher female preponderance.

Ultrasound guided Fine Needle Aspiration Cytology proved to be a useful first line investigation for malignant lesions of thyroid as it showed high sensitivity and 98% diagnostic accuracy.

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