

## Utility of Commonly Used Preoperative Diagnostic Tools in Detecting Malignant Thyroid Nodules

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### ABSTRACT

**Background:** Nodular thyroid disease is a common disorder and its incidence increases with age. They are three to four times more common in females than in males. The main risk of such nodules is the possibility of malignancy. In past decades, palpable thyroid nodules (TNs) were surgically excised to establish a tissue diagnosis, and in some instances completion thyroidectomy was needed if malignancy was detected which means more morbidity to the patients. On the same time the incidence of tissue diagnosed cancers in these nodules ranged from 12-20%; therefore it is logic to propose a more selective policy in choosing patients with thyroid nodules for whom surgery is required. Recently, advances in two diagnostic tools; namely ultrasonography (US) and fine-needle aspiration cytology (FNAC), and more recently the combination of both (Sonar Guided FNAC) served to revolutionize the treatment of TNs and to reduce the number of unnecessary surgeries for nodules that are predictably benign. **Aim of the work:** It was to evaluate the utility of the commonly used preoperative diagnostic tools in detecting malignancy in patients with TNs scheduled for surgery in our hospital by comparing its results to that of the gold standard investigation (postoperative histopathology). **Patients and Methods:** In General Surgery Department, Faculty of medicine, Zagazig University Hospitals, Zagazig, Egypt; one hundred patients with thyroid nodules were included in this study in the period from April 2012 to June 2016. They were 68 females and 32 males with mean age of  $40.77 \pm 14.9$ . Complete clinical, laboratory and ultrasonographic examinations were carried out for all patients but sonar guided FNAC was done only for patients who accepted it. CT examination was ordered for patients with clinically suspicious malignant TNs. After making the preoperative diagnosis for each patient; the suitable thyroid surgery was carried out and the preoperative diagnosis was compared to the postoperative histopathologic one. **Results** were statistically analyzed using SPSS version 20 and showed: the largest number of patients with TNs (35%) presented in the fourth decade of life while the lowest one presented in the age group below 20 years (1%). Histopathologically, 39% of cases were found to have malignant TNs and the remaining 61% had non-malignant TNs and the most frequent malignant lesion was papillary carcinoma 79.5% followed by follicular carcinoma 10.3% and the most frequent benign lesion was colloid nodules 54.1% followed by follicular adenoma 23%. The sensitivity, specificity and accuracy rates of US were 92.3%, 44.3% and 63.0% and those of CT were 88.0%, 43.5% and 66.7%, while those of FNAC were 100.0%, 97.6% and 98.6% respectively. **Conclusion:** There is a quite high prevalence of malignant nodules in patients suffering from nodular thyroid disease. US has an integral role in preoperative evaluation of TNs as well as long-term post treatment follow-up. Sonar guided FNAC is a safe, easy, quick to perform, highly sensitive and accurate tool in diagnosing thyroid malignancy and plays a crucial role in the selection of patients with TNs for operation. It is readily repeatable, and has excellent patient compliance. So, all thyroid swellings should be thoroughly investigated for malignancy considering FNAC.

**Key words:** Nodular thyroid disease, Ultrasound, Fine Needle Aspiration Cytology and Thyroid malignancy.

### INTRODUCTION

The incidence of thyroid nodules (TNs) increases with age; they are three to four times more common in females than in males. Wide

scale population surveys suggest nearly 8-15% of the adult population may harbor a clinically significant nodule requiring evaluation but ultrasonic based studies showed the true figure to be much greater with around 50% of adults

having nodules. In areas of severe iodine deficiency, the prevalence can be as high as 90%.<sup>(1)</sup> Incidentally detected thyroid nodules on CT and MRI of the head, neck, or chest often appear equally important.<sup>(1,2)</sup>

The commonest cause of these nodules is dietary but may be inflammatory (bacterial, viral or autoimmune), neoplastic or familial. People may also inherit the tendency to goitre from earlier generations. Cysts and benign neoplasms are often responsible for a single thyroid lump but malignant neoplasms may be responsible also in a considerable sector.<sup>(1,2,3)</sup>

Although often asymptomatic, TNs require meticulous evaluation primarily because of their risk of thyroid cancer and its potential dangers and secondly as patients become aware of this risk the anxiety associated with this disorder should not be underestimated. In most large-scale reports approximately 12-20% of thyroid nodules >1 cm in diameter prove to be cancerous. This incidence increased since the 1990s, which may be attributed primarily to improved nodule detection and more frequent nodule evaluation. Most well-differentiated thyroid cancers are indolent processes effectively treated with surgery and, when needed, adjunctive radioactive iodine therapy. In contrast, untreated thyroid cancers can rarely metastasize and threaten life. Therefore, patients with newly identified TNs should be subjected to thorough diagnostic evaluation.<sup>(2,4)</sup> Even if benign, large nodules may cause obstructive symptoms and hemorrhage which can spontaneously occur in cystic ones with its associated dangers.<sup>(1,3)</sup>

In earlier decades, palpable TNs were surgically excised to establish a tissue diagnosis, and in some instances completion thyroidectomy was needed if malignancy was detected which means more morbidity to the patients as such surgeries even with the best hands are attended with considerable morbidity (bleeding, recurrent and superior laryngeal nerves injuries and hypoparathyroidism). Recently, advances in two techniques, namely US and fine-needle aspiration cytology (FNAC), and ultimately the combination of both techniques served to revolutionize the treatment of thyroid nodules and to reduce the incidence of unnecessary surgery for nodules that are predictably benign.<sup>(4,5,6,7)</sup>

Advanced researches in molecular genetic testing represents the greatest hope for the

development of a highly accurate serum marker to detect malignant thyroid nodules. It is now possible to detect thyroid cancer cells in peripheral blood samples by measuring the mRNA of thyroid-specific genes, such as the mRNA of thyroglobulin and the thyrotropin receptor. In addition, microRNAs, which are small endogenous noncoding RNAs involved with the regulation of gene expression, can be detected in serum of patient's with thyroid cancer.<sup>(8)</sup>

## AIM OF THE WORK

This prospective study was carried out to evaluate the utility of commonly used preoperative diagnostic tools in detecting malignancy in patients with nodular thyroid disease scheduled for thyroid surgery in our hospital; by comparing its results to that of the gold standard investigation i.e. postoperative histopathology.

## PATIENTS AND METHODS

One hundred patients with nodular thyroid disease admitted for thyroid surgery in General Surgery Department of Zagazig University Hospitals were included in this study from April 2012 to June 2016. After approval of the ethical board and obtaining a full informed written consent all patients were subjected to:

### I- Preoperative evaluation :

- 1- Detailed history taking including family history of endocrinal malignancies and history of head, neck or chest exposure to irradiation.
- 2- Full clinical examination.
- 3- Laboratory investigations:
  - Preoperative thyroid function tests (TSH, T4, T3), serum Calcitonin, thyroglobulin and thyroid antibodies in some cases.
  - Routine preoperative laboratory investigations.
- 4- Imaging studies :
  - a. Neck ultrasound examination (using a high resolution LOGIQ Pro 6 GE device 7.5-10 MHz linear-array transducer) was done for all patients to detect and describe thyroid nodules regarding its size, side, number, presence of sonographic criteria suggestive of malignancy as micro-calcification, solid or heterogeneous cystic composition,

irregular or blurred nodular margins, absent or avascular halo sign, parenchymal hypoechogenicity or intranodular vascularization by doppler, fixity of the nodule to the thyroid tissue by dynamic palpation during US examination and also to check fixity of the thyroid to the surrounding structures e.g. the strap muscles, trachea or esophagus.<sup>(9)</sup> US was done also to detect enlarged cervical lymph nodes and to describe features suggestive of malignant deposits in it which are the same as those mentioned above.<sup>(9)</sup> The patient was considered as having suspicious malignant thyroid (+ve) if one or more suspicious criteria were detected in even one nodule or as having non-malignant one (-ve) if no suspicious criteria were detected.

- b. Sonar guided FNAC was performed for TNs and enlarged cervical lymph nodes (if present) of patients who accepted it. For solitary thyroid nodules; FNAC was done for solid or heterogeneous cystic nodules > 1 cm in maximum diameter and for the dominant nodules  $\geq 2$  cm in cases of multinodular goiters.<sup>(1)</sup> Fine needle aspiration biopsy was performed using 23 gauge needle and four slide smears were made for each case and immediately fixed in 95% ethyl alcohol for about 30 min. Two of the 4 slides were stained with hematoxylin and eosin (Hx & E) and others with Giemsa and Papanicolaou (Pap) stains. The remnants in the syringe were clotted or centrifuged then, fixed in neutral buffered formalin for 12 hours and processed as small cell-blocks.<sup>(10)</sup> The results of FNAC were expressed according to The Bethesda System for Reporting Thyroid Cytology (TBSRTC)<sup>(11)</sup>; as malignant (+ve), benign (-ve) or suspicious follicular neoplasm lesion (SFN).
- c. Plain X -ray PA and Lateral views on the Chest for patients preoperatively diagnosed as cancer thyroid to detect any pulmonary metastatic deposits.
- d. CT scan neck was performed using 16 channel Optima GE (General Electric company) device for patients with large cervical goiters causing local symptoms, substernal or suspiciously malignant ones. Some patients were referred to surgery clinic

after discovery of thyroid nodules in CT done for them because of other head, neck or chest complaints. The results of CT were expressed as being suspiciously malignant (+ve) or non-malignant (-ve).

**II- Surgical interventions:** Preoperative investigations of each patient were reviewed and the patient was diagnosed as having a malignant thyroid lesion if one or more diagnostic tool showed that. Surgical procedures were tailored accordingly and included: Hemithyroidectomy for non-malignant unilateral lesions, Bilateral subtotal or near-total thyroidectomy for bilateral non-malignant lesions, Total thyroidectomy for suspiciously malignant lesions without lymph node enlargement and Total thyroidectomy plus selective (lateral  $\pm$  central) neck dissection for suspiciously malignant lesions with lymph node enlargement.

**III- Histopathology:** All operative specimens were sent for histopathological examination to make the final diagnosis which was compared to the preoperative one.

**IV- Postoperative care and follow up:** Early postoperative care was offered to all patients in department of general surgery with good analgesia, close observation of vital signs near a source of oxygen and for drain output. Oral fluids were started two hours after complete recovery and light diet after six hours. Serum calcium was checked up on second postoperative day. Drains were removed on second postoperative day but after 3-5 days in cases of neck dissection. Patients were discharged on 2<sup>nd</sup> or 3<sup>rd</sup> postoperative day but in cases of neck dissection on the 7<sup>th</sup> postoperative day and those with postoperative complications remained admitted in hospital for care according to type of complication as will be mentioned later. Discharge medications included oral analgesics and Eltroxine oral tablets but it was postponed in malignant cases when I<sup>131</sup> scan or suppressive dose were planned. Follow up period ranged from 8 - 41 months during which there were neither recurrent neck masses nor other eventful complications. It included clinical, laboratory and ultrasonographic evaluations.

**Statistical Analysis:**

Standard methods using Software Package of Social Science (SPSS) version 20 for windows, Student t-test and Chi-square were used in appropriate situation. P. value  $\leq 0.05$  was considered the level of significance.

**RESULTS**

One hundred patients with nodular thyroid disease were included in this study. They were 68 females and 32 males (female: male ratio = 2.13 : 1), their ages ranged from 14 - 69 years with mean age of  $40.77 \pm 14.9$  years. The largest number of patients with thyroid nodules were in the fourth decade of life (35) followed by the third decade (32) then the fifth decade (19), followed by the sixth decade (8) and less frequency was above 60 years (5 patients) and the least was below 20 (one patient). None of them had past history of head, neck or chest irradiation also non had family history of thyroid malignancy or multiple endocrine neoplasia. Fifteen patients were referred to surgery clinic from other clinics with CT scans done for head, neck or chest conditions with incidentally discovered thyroid nodules. Of the other eighty five patients; 37 presented with asymptomatic thyroid swelling/s and the remaining were having thyroid swelling/s

associated with: dyspnea in 16 patients, local pain in 10 patients, cough in 9 patients, dysphagia in 11 patients and hoarseness of voice in 2 patients.

**Results of Ultrasonographic examinations** (Tables 1,2 and Photos 1-4):

- Solitary thyroid nodules were found in 44 patients (44%) [Right lobe; in 25 patients (56.8%) and left lobe; in 19 patients (43.2%)]. These nodules were solid hypoechoic in 26 patients and heterogeneous cystic in 18 patients.
- Multiple nodules were found in 56 patients (56%) which involved one lobe in two patients and both lobes with or without the isthmus in 54 patients with retrosternal extension in 11 of them. Various nodular characters (solid, heterogeneous cystic and pure cystic) were represented in each patient.
- The greatest diameter of thyroid nodules by US ranged from 2.4 - 8.5 cm. with mean of  $5 \pm 3.5$  cm.
- Seventy patients (70%) showed suspiciously malignant thyroid (+ve) and the remaining thirty patients (30%) showed non-malignant thyroid (-ve).
- Enlarged cervical lymph nodes were found in 34 patients; 31 of them had suspiciously malignant nodes (+ve) and 3 were non-malignant (-ve).

**Table (1) : Ultrasonographic findings:**

Findings	Character of Nodule or lymph node		No. of pts. & %	No. of pts. with +ve criteria by US
Thyroid Nodules	Solitary 44%	Rt.	25 (56.8%)	25
		Lt.	19 (43.2%)	19
	Multiple 56%	Bilateral	54 (96.4%)	26
		Unilateral (Rt.)	2 (3.6%)	0
Lymph node	Enlarged		34 (34.0%)	31

No.= number. Pts.= patients. +ve= suspiciously malignant. US= Ultrasound examination. Rt.= Right lobe. Lt.= Left lobe.

**Sonar guided FNAC:**

Eighty patients (80%) accepted FNAC including 27 out of 34 patients with lymph node enlargement (79.4 %). The rest of patients (20%) refused FNAC including the remaining 7 patients (20.6%) with lymph node enlargement (Photos 5,6,7).

Thyroid FNAC showed (Table 2):

- 30/80 patients (37.5%) showed smears (+ve) for malignancy.
- 41/80 patients (51.25%) showed smears (-ve) for malignancy.

- 9/80 patients (11.25%) showed suspicious follicular neoplasm (SFN) smear.

Lymph node FNAC showed (Table 2):

- 24/27 (88.9%) showed malignant smears (+ve).
- 3/27 (11.1%) were (-ve) for malignancy.

**CT scan** was done for 48 patients and showed; suspiciously malignant (+ve) lesions in 35 patients (72.9%) and non-malignant lesions (-ve) in 13 patients (27.1%); (Table (2 and Photos 8,9).

**Table (2) :** Results of individual preoperative diagnostic tool regarding suspicion of malignancy:

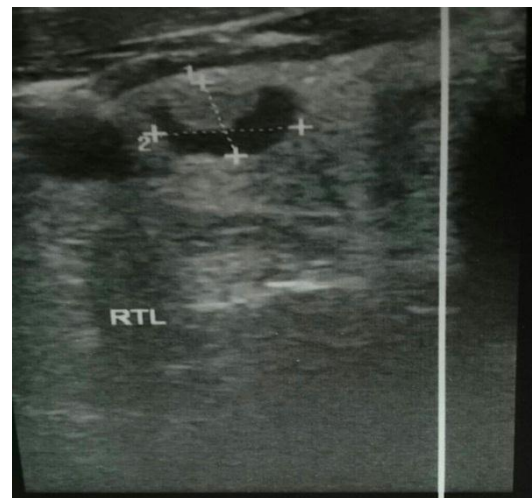
Diagnostic tool & number of patients subjected to it & its result	No.	%	
US done for all (100) patients	-ve	30	30.0%
	+ve	70	70.0%
CT done for 48 patients	-ve	13	27.1%
	+ve	35	72.9%
Thyroid FNAC done for 80 patients	-ve	41	51.25%
	+ve	30	37.5%
	SFN	9	11.25%
LN FNAC done for 27 out of 34 patients	-ve	3	11.1%
	+ve	24	88.9%

US= ultrasound. CT= computerized tomography. FNAC= fine needle aspiration cytology.

LN= lymph node. SFN= suspicious follicular neoplasm. +ve= suspiciously malignant. -ve = benign.



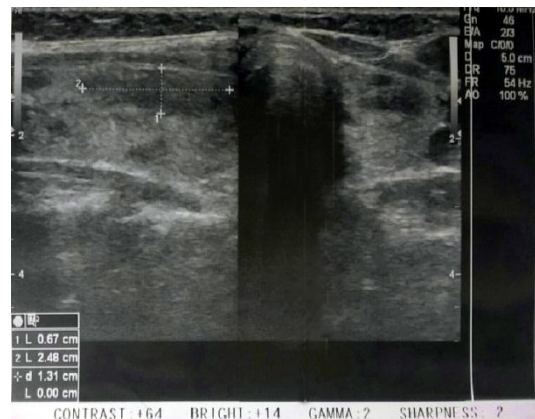
**Photo (1) :** Thyroid US; left lobe solitary nodule 2.7 cm x 2.2 cm with dots of microcalcification



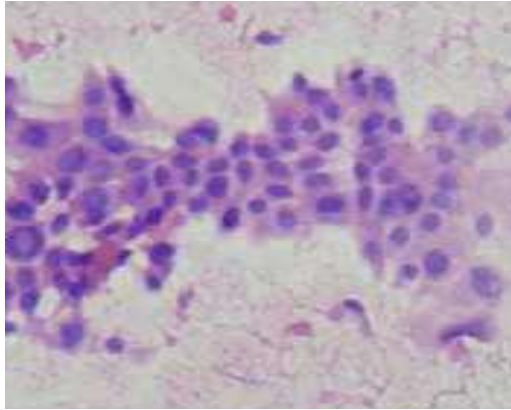
**Photo (2):** Thyroid US; right lobe nodule harboring small solid isoechoic component inside in female patient 27 years old



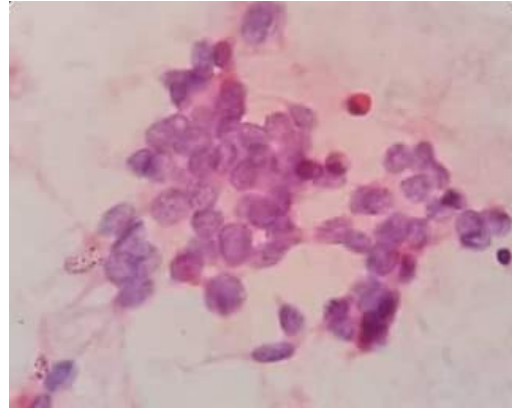
**Photo (3) :** Same patient in photo 2 showing abnormal vascular signal flow on doppler study



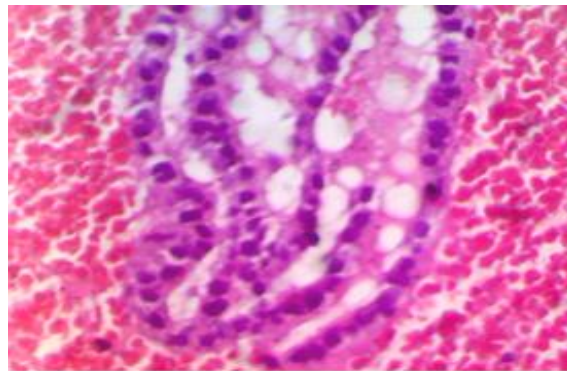
**Photo (4) :** Thyroid US; benign multinodular goiter



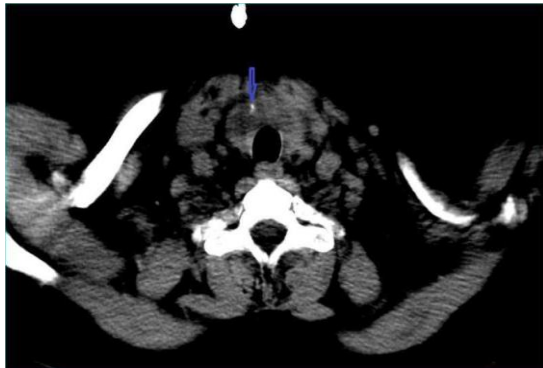
**Photo (5):** FNAC smear of papillary carcinoma, pleomorphic open face nuclei



**Photo (6):** FNAC smear of papillary carcinoma; powdery chromatin nuclei



**Photo (7):** FNAC, cell block, of papillary thyroid carcinoma, note the papillary structure, and nuclear pleomorphism



**Photo (8):** Axial CT at level of thyroid showing ill defined hypodense thyroid nodule harboring small calcified focus within its Rt. lobe (blue arrow) proved follicular carcinoma by pathology. In a female patient 32y



**Photo (9):** Female 55y CT axial enhanced, left lobe hypodense non-enhanced focal nodule (red arrow) (benign nodule)

### Surgical procedures:

Hemithyroidectomy was done for 2 patients with unilateral multiple nodules but in one of them completion thyroidectomy was carried out on the 5<sup>th</sup> postoperative day because of malignant histopathology. Early in the study bilateral subtotal thyroidectomy was done for 13 patients with preoperative diagnosis of multinodular goiter but completion thyroidectomy was indicated and carried out for 3 patients of them because of malignant histopathology since then, near total thyroidectomy was done for 18 patients with multinodular disease. Total thyroidectomy alone was done for 36 patients because of a suspicious nodule and total thyroidectomy with selective neck dissection (lateral ± central) was done for 31 patients because of suspiciously malignant nodule/s and preoperatively suspected lymph node involvement.

Postoperative complications occurred in 8 patients (8%) and included; reactionary hemorrhage in one patient after total thyroidectomy which mandated immediate reopening the wound and controlling the bleeding source, reinsertion of a drain and closure of the wound. The patient was discharged home after another 24 hours after removal of the drain. Transient postoperative tetany in 5 patients (2 after completion thyroidectomy and 3 after total thyroidectomy) it was diagnosed clinically and laboratory on second postoperative day, the patients improved within 3 months postoperatively during which they received calcium and vitamin D. Two patients suffered hoarseness of voice after completion

thyroidectomy; which improved to satisfying extent within the first six postoperative months. There were no mortalities in our study.

### The histopathological results (Tables 3,4):

Histopathology diagnosed malignant nodules in 39 patients (39%) which were either solid (28/39 = 71.8%) or heterogeneous cystic nodules (11/39 = 28.2%) and the most frequent form was papillary carcinoma (31 patients; 79.5%) most of them in the 3<sup>rd</sup> decade of life, followed by follicular carcinoma (4 patients; 10.3%) all of them in the 4<sup>th</sup> decade of life. Anaplastic carcinoma had been found in 2 patients (5.1%) in their sixties and medullary carcinoma in 2 patients (5.1%) in 5<sup>th</sup> and 6<sup>th</sup> decades of life. These results showed clear predominance of papillary carcinoma over other encountered thyroid cancers (Table 3) and showed also more frequency of thyroid malignancy in males than in females (65.63 % versus 26.47 %; table 6). Histopathology also showed malignant deposits in lymph nodes of 26 out of 34 patients with enlarged cervical lymph nodes, those patients included 19 with preoperative +ve FNAC and the remaining seven patients were those who refused FNAC preoperatively. Nonmalignant nodules were diagnosed in 61 patients (61%). The commonest form was colloid nodule which was found in 33 patients (54.1%) followed by the follicular adenoma in 14 patients (23%), then follicular hyperplasia in 8 patients (13.1%) and the least was Hashimoto's thyroiditis in 6 patients (9.8%) (Table 3).

**Table (3) :** Postoperative histopathological diagnosis and its frequencies

Pathological category & its frequency	Histopathology	No. of pt.	% per category
Malignant nodules 39%	Papillary carcinoma	31	79.5%
	Follicular carcinoma	4	10.3%
	Medullary carcinoma	2	5.1%
	Anaplastic carcinoma	2	5.1%
Nonmalignant nodules 61%	Colloid nodule	33	54.1%
	Follicular adenoma	14	23.0%
	Follicular hyperplasia	8	13.1%
	Hashimoto's thyroiditis	6	9.8%

By comparing the preoperative diagnosis of different tools (table 2) with the histopathologic diagnosis (Table3) we found the following results (table 4): Histopathology has confirmed malignancy in only 36 out of 70 patients

diagnosed as suspiciously malignant (+ve) nodules by US (+ve predictive value = 51.43%) while the remaining 34 were non-malignant (false +ve) and out of 30 patients with (-ve) nodules by US; histopathology confirmed true negativity in



27 (-ve predictive value = 90%) while the other 3 were malignant (3 false -ve). US showed sensitivity of 92.31%, specificity of 44.3% and Accuracy of 63%. Histopathology confirmed benign nodules in all benign thyroid FNAC (41 patients) (-ve predictive value= 100%) and confirmed malignancy in 29 out of 30 patients with malignant thyroid FNAC (+ve predictive value= 96.7%) while disproved malignancy in one patient (one false +ve). The nine patients who underwent FNAC and showed suspicious cellular follicular neoplasms proved to be adenomas (-ve) by histopathology (undetermined diagnostic ratio= 11.25%). These nine patients were excluded when calculating the statistical values of FNAC of thyroid nodules as the diagnosis of malignancy in follicular neoplasms depends upon capsular and/or vascular invasion which is beyond the ability of FNAC. Thyroid FNAC showed sensitivity, specificity and accuracy of 100%, 97.6% and 98.6% respectively. Histopathology

confirmed malignancy in lymph nodes of 19 patients out of 24 with malignant lymph node FNAC smears (+ve predictive value=79.2%) while the nodes in the other 5 were non-malignant (false +ve) and the remaining 3 patients were negative by histopathology as primarily diagnosed by FNAC (-ve predictive value= 100%). Lymph node FNAC showed sensitivity of 100% and specificity of 37.5% and accuracy of 81.5%. Out of 35 patients with suspicious malignant nodules by CT; histopathology confirmed this in only 22 patients (+ve predictive value= 62.9%) and the other 13 were non-malignant (13 false +ve). Non-malignant nodules were confirmed by histopathology in 10 out of 13 patients diagnosed by CT as non-malignant (-ve predictive value= 76.9%) and the other 3 patients were malignant (3 false -ve). CT showed sensitivity of 88%, specificity of 43.8% and accuracy of 66.67% (Tables 4&5).

**Table (4):** Comparing the results of individual preoperative diagnostic tool with histopathologic one regarding presence or absence of malignancy:

Individual tool & number of patients subjected to it & its result and number		Histopathology		X <sup>2</sup>	Kappa agreement	P value
		-ve	+ve			
US done for all patients	-ve in 30 patients	<b>27</b> (90.0%)	3 10.0%	15.1 5	0.37	0.00**
	+ve in 70 patients	34 (48.6 %)	<b>36</b> (51.4%)			
CT done for (48 patients)	-ve in 13 patients	<b>10</b> (76.9%)	3 (23.1%)	6.01	0.26	0.01*
	+ve in 35 patients	13 (37.1%)	<b>22</b> (62.9%)			
Thyroid FNAC done for (80 patients)	-ve in 41 patients	<b>41</b> (100%)	0 (0.00%)	75.21	0.81	0.00**
	+ve in 30 patients	1 (3.3%)	<b>29</b> (96.7%)			
	SFN in 9 patients	9 (100%)	0 (0.00%)			
Lymph node FNAC Done for (27 patients)	-ve in 3 patients	<b>3</b> (100%)	0 (0.00%)	8.01	0.38	0.004*
	+ve in 24 patients	5 (20.8%)	<b>19</b> (79.2%)			

US= ultrasonography. CT= computerized tomography. FNAC= fine needle aspiration cytology. -ve= benign. +ve= malignant. SFN= suspicious follicular neoplasm. \* = Significant. \*\* = High Significance.

N.B: **The bold figures are true values whether +ve or -ve**, while the fine figures are false values whether +ve or -ve



**Table (5):** Sensitivity and Specificity of diagnostic tools

Diagnostic tool	Sensitivity	Specificity	+ve Predictive	-ve Predictive	Accuracy
US	92.31%	44.3%	51.43%	90%	63.0%
CT	88%	43.5%	62.9%	76.9%	66.67%
FNAC	100%	97.6%	96.7%	100%	98.6%
LN FNAC	100%	37.5%	79.2%	100%	81.5%

**Table (6):** Association between socio-demographic data and malignancy

Socio-demographic data		Malignant cases	Total	X <sup>2</sup>	P	
Sex	Female	No.	18	20.1	0.00**	
		%	26.47%			68.0%
	Male	No.	21			32
		%	65.63%			32.0%
Age	Mean	43.6667 (in 39 patients)		T	0.122	
	SD	19.45620		1.565		

No.= number. \*\* High significance. SD= standard deviation.

**Table (7):** Association between lymph node enlargement and malignancy

Lymph node enlargement		Malignancy	Total	X <sup>2</sup>	P
Enlarged	No.	26	34	30.4	0.00**
	%	66.7%	34.0%		

## DISCUSSION

Nodular thyroid disease occurs in 8-15% of the adult population based on palpation and in 20-76% based on ultrasound examination.<sup>(1,2)</sup> The major challenge in managing patients with this problem remains; to which surgical excision is required and which can be followed conservatively. Adopting a selective policy can avoid unnecessary extensive procedures and diagnostic thyroidectomies, which carry potential adverse effects to these patients.<sup>(12)</sup> In this work we studied the utility of different preoperative diagnostic tools in detecting malignancy in 100 patients with thyroid nodular disease scheduled for surgery based on preoperative diagnosis made by these tools. The preoperative diagnosis of each tool was compared to the final histopathologic one and hence its utility in terms of sensitivity, specificity and accuracy were calculated. Females to males ratio in this study run in agreement with those found by **Rahman** and **Mustafa**<sup>(13)</sup>, **Welker** and **Orlov**<sup>(14)</sup>, **Zuberi et al.**<sup>(15)</sup> and **Nazmul Huque** and **Colleagues**<sup>(16)</sup>; where this ratio was (5:1), (4:1), (2.5:1) and (2.1:1) respectively. This female preponderance is present in all studies including ours. The cause of high female to male ratio in

our study can be explained by the fact that most of patients were from non-endemic areas. The age related frequency of thyroid nodules in our study was similar to those found by **Nazmul Huque** and **Colleagues**<sup>(16)</sup> who studied 118 patients; with nearly similar demographic data; females: males ratio was 2.1:1, the age ranges from 11 to 60 years with a mean age of 32.5 years; where they found the highest frequency of thyroid nodules was in the fourth decade of life (54 patients). These results did not interfere with the fact that the incidence of thyroid nodules increases with age as these studies are not wide scale population surveys.<sup>(1)</sup>

In our study, all malignant thyroid nodules were more than 2 cm in diameter, but the matter of nodular size and risk of malignancy is somewhat debatable between different authors; e.g. it is not considered a predictive risk factor for malignancy as regarded by **Tai** and **Colleagues**<sup>(17)</sup> who found that there were no great significances between nodule size larger than 4 cm and nodule size less than 4 cm ( $P= 0.5$ ) while others like **Kamran et al.**<sup>(18)</sup> observed that increasing thyroid nodule size impacts cancer risk in a nonlinear fashion and a threshold is detected at 2.0 cm, beyond which cancer risk is unchanged.

In our study: the finding of preponderance of right lobe affection than left one (Table 1) was reported also in **Al-Robbani**<sup>(19)</sup> study; where out of 100 cases; 65 nodules were found in the right lobe and 35 in the left lobe. There is yet no reported predilection for any specific site and no reason has been put forward for such a predilection.

In our study; the finding that the malignant lesions were either solid or heterogeneous cystic nodules is similar to that reported by **Tarrar et al.**<sup>(20)</sup> where out of 60 patients they found 43 patients had solid hypoechoic nodules, 12 had heterogeneous cystic nodules and 5 had homogeneous cystic nodules, most of malignant lesions 7/8 patients (87.5%) were solid nodules and 1/8 patients (12.5%) were heterogeneous cystic nodules. It is also similar to study of **Nazmul Huque and colleagues.**<sup>(16)</sup>

Enlarged cervical lymph nodes in our patients whether hand palpable or sonar detected were highly suggestive of malignancy (P =0.00, Table 7) which goes in agreement with those reported by **Kelly and Meyers.**<sup>(8)</sup>

In our study US examination of thyroid for detecting malignancy showed sensitivity, specificity, positive predictive value, negative predictive value and accuracy comparable to those of **Cox et al.**<sup>(5)</sup>

In our study thyroid FNAC could not definitely differentiate follicular adenoma from adeno-carcinoma in (11.25%) and were diagnosed as suspicious cellular follicular neoplasm according to TBSRTC<sup>(11)</sup> and all were proved by histopathology to be follicular adenoma. Similar results were reported by **Nazmul Huque and his colleagues**<sup>(16)</sup>; who found out of 118 patients; 35 smears (29.66%) were suspicious cellular follicular lesion of which 31 (88.57%) proved to be follicular adenoma, and four (11.42%) were carcinoma. This can be explained by the fact that cytological distinction between follicular adenoma and carcinoma is almost impossible as it depends on capsular and/or vascular invasion on histological examination.<sup>(21)</sup>

In our study the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of thyroid FNAC (table 5) are in agreement to a great extent with those reported by **Senna and Ezzat**<sup>(22)</sup> whose results showed a sensitivity of 92.8% and a specificity of 94.2%, a diagnostic accuracy of 93.6%, a positive predictive value of

94.9%, and a negative predictive value of 91.8% and with those of **Shere and his colleagues**<sup>(23)</sup> study, where the sensitivity and specificity were 100%, 98.6 respectively. Our results were comparable also to published data by **Cap et al.**<sup>(24)</sup> where FNAC of thyroid is reported to have a sensitivity ranges from 65% to 98%, a specificity of 72% to 100%, a positive predictive value of 34% to 100%, and a negative predictive value of 83% to 100%.

The frequency of malignancy in our study was higher than those reported by **Rahman and Mostafa**<sup>(13)</sup> who studied the frequency of malignancy in both solitary and multinodular thyroid swellings and also higher than those reported by **Tarrar and Colleagues**<sup>(20)</sup>, who studied the frequency of cancer in solitary thyroid nodules only and found it 13.3%, but ours frequency was lower than that of **Renu et al.**<sup>(24)</sup> who found it 79.8% in 248 patients. This can be explained by that; our hospital provides medical service to large sector of population and the study included all nodular thyroid swellings whether solitary or multiple and whether clinically evident or incidentally discovered on CT scans of head, cervical spines and chest done for patients while were looking for medical care for other reasons and referred to us from other clinics.

In their study; **Tarrar and Colleagues**<sup>(20)</sup> found papillary carcinoma was the commonest type (50%) followed by follicular carcinoma (25%) then anaplastic and medullary carcinoma (12.5%) each, most cases of malignancy was between 31-40 years and more common in female. Our results were in agreement with their results except that of early age of occurrence in the third decade of life in our patients and that of feminine predilection of cancer in their study. Male predilection of malignancy in our study was comparable to published data by **Cap et al.**<sup>(25)</sup> and in a study by **Abul Hossain et al**<sup>(26)</sup>.

In the present study the non malignant lesions were similar to those reported by **Gupta and Colleagues**<sup>(27)</sup>; who found among 60 patients with benign lesions (from total 75 patients), the commonest pathological lesion was colloid nodule followed by the follicular adenoma .

The postoperative complication rates in our study were similar to those reported by **Ali and Colleagues**<sup>(28)</sup>, who found fewer complication rates after hemithyroidectomy when compared to near total or total thyroidectomy; as regard risk of

recurrent laryngeal nerve injury and / or hypoparathyroidism.

## CONCLUSION & RECOMMENDATIONS

There is a high prevalence of malignant thyroid nodules. Ultrasound has a crucial role in evaluating thyroid nodules especially as a guide to FNAC. Sonar guided FNAC is a good and trustful tool in diagnosing thyroid malignancy as it proved to be safe, easy, highly sensitive and 98.6% accurate. We recommend that all Thyroid nodules should be carefully examined and thoroughly investigated for malignancy using sonar guided FNAC. We recommend also more researches in the area of molecular genetic testing which may develop diagnostic tests for the evaluation of solitary thyroid nodules.

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