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Sonographic-Pathologic Correlative Study of Spectrum of Thyroid Disorders in Tribal Hilly Wayanad of Kerala.

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ABSTRACT

Background: Thyroid nodules (TN) can alter the body metabolism, but the majority of thyroid nodules are asymptomatic and benign. TN are typically found on physical exam or incidentally when other imaging studies are performed. Malignant or symptomatic nodules that compress nearby structures warrant surgical excision. Ultrasound (US) is the preferred imaging modality for characterizing TN, and the ultrasound guided fine needle aspiration biopsy (FNAB) is the preferred method of tissue sampling. The present study aims to observe the diagnostic accuracy of US, in the assessment of TN compared to pathologic findings. **Methods:** This analytical, retrospective study was conducted on 200 patients that were referred for US scan in tertiary care hospital of tribal, hilly, Wayanad of Kerala, between February 2015 and Jan 2016. **Results:** : In our study the Sensitivity, Specificity, Positive predictive value (PPV) & Negative predictive value (PPV) of US, in detecting malignant TN, was found to be 80%, 97.8%, 80% and 97.8% respectively. The overall accuracy of US in detection of benign & malignant TN was found to be 96%. **Conclusions:** TI-RADS criteria combined with US guided FNAB, well correlated with pathological findings, increases the rate of detection of thyroid cancer and reduces the number of unnecessary surgical procedures and the overall cost of medical care.

Keywords: Colloid goiter, Fine needle aspiration biopsy, Multinodular goiter, Thyroid nodules, Thyroid carcinoma, Thyroiditis, TIRADS, Ultrasonography.

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INTRODUCTION

Thyroid nodules (TN) are common medical problem caused by a variety of thyroid disorders. They are found in 4-8% of adults by means of palpation, in 10-41% by means of US and in 50% by means of pathologic examination at autopsy.[1,2] The TN is a common entity with the majority of nodules are asymptomatic and only 5 - 10% of nodules being malignant, the decision to operate is made on therapeutic or diagnostic grounds.[3,4]

US plays a prominent role in the management of thyroid disease; it can detect clinically impalpable TN and characterize them as cystic, solid, or complex but determining that a nodule is definitively benign or malignant is difficult, and so when indicated, it is used to guide Fine Needle Aspiration Biopsy (FNAB), to determine whether the nodule is benign or malignant.[5-7]

The low specificity of US is mainly due to the considerable overlap between the sonographic findings of benign nodules and thyroid cancer. Hence, most solid and complex cystic nodules require FNAB to establish the true diagnosis. FNAB can diagnose the nature of TN with a sensitivity of 86% and a specificity of 85%.[8] US imaging studies and cytology from FNAB are the main tools used by the clinician to decide whether surgical excision of a TN is warranted.

The Purpose of this study were to describe the Sonographic findings of TN and categorize according to TI-RADS classification, based on a score modified according to ultrasound criteria for malignancy,[11] that would help to classify it as benign, suspicious or malignant and compare it with cytopathological results, and to demonstrate how US is integrated with the FNAB to provide valuable information that can be used to improve patient care.

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MATERIALS & METHODS

It was a cross sectional descriptive and analytical study carried out at a Tertiary Care Hospital of tribal, hilly Wayanad in Kerala, from February 2015 and Jan 2016, with retrospective data collection. Authorization for the study was obtained from the institutional review board. Inclusion criteria; Consecutive records of 200 patients from February 2015 to Jan 2016 with focal TN on US for which US-guided FNAB was performed and pathology results were available were selected for review.

Exclusion criteria; All records without available digital thyroid US images and those with indeterminate cytology/histology were also excluded. Patients ranged in age from 6 to 80 years (mean, 39.06 years). The mean age of male patients was 39 years (range, 13–65 years), and the mean age of female patients was 35.2 years (range, 6–80 years). Brief History, Clinical examination and relevant Biochemical investigations were obtained & recorded in all patients. All US scans of the thyroid gland and neck areas were performed by experienced radiologists using a linear array transducer (4 - 12 MHz) in a General Electric US scanner (Voluson S6; GE) using an optimized gain, in longitudinal and transverse planes. All TN were characterized according to the internal component (solid, mixed or cystic), the shape ,margins, echogenicity, location of the nodule, number, size, calcifications , retrosternal extension if any and relation or Invasion to surrounding structures .

Margins were classified as - well circumscribed, lobulated (regular) or irregular. A TN is illdefined when more than 50% of its border is not demarcated. The shape of the nodule was categorized as - taller-than-wide, round and irregular.

Echogenicity was classified as- hyperechogenicity, isoechogenicity, hypoechogenicity, mixed echogenicity and marked hypoechogenicity. Isoechogenicity was defined as an echogenicity similar to that of the adjacent healthy thyroid gland. A nodule was classified as marked hypoechogenicity, if the echogenicity was less than that of the superficial surrounding neck muscles.

Calcifications when present were categorized as microcalcifications (<1mm), macrocalcifications (>1mm) and rim calcification (egg shell). When a nodule had both types of calcifications (macrocalcifications, including rim calcifications, intermingled with microcalcifications), we regarded it as having microcalcifications.

Parenchyma interface- Invisible, complete hypoechoic halo, or incomplete halo. Halo or Hypoechoic rim around a TN is produced by a pseudo capsule of fibrous connective tissue, a compressed thyroid parenchyma, and chronic inflammatory infiltrates.

Vascularity-intrinsic hypervascularity (central) or diffused hypervascularity (central & peripheral) or perinodal vascularity (peripheral) or Avascularity (absent). Intrinsic vascularity is defined as the flow in the central part of the tumor greater than that in the surrounding thyroid parenchyma. Perinodal vascularity is defined as the presence of vascularity around at least 25% of the circumference of the nodule. Muscle and vascular invasion- present or absent.

Cervical Lymphadenopathy- present or absent. Distant metastasis- present or absent.

US findings of microcalcifications, irregular or microlobulated margins, marked hypoechogenicity, taller-than-wide shape and intrinsic vascularity are considered indicative of malignancy. Nodules showing at least one of the findings were considered suspicious for malignancy.

The classification system of the thyroid nodules TI-RADS (Thyroid Imaging Reporting and Data System) proposed by Horvath et al in 2009 is rarely used.[10] Hence we used a score modified according to ultrasound (US) criteria for malignancy [Table 1], in order to obtain a better application of this classification in daily practice.[11]

Table 1: Sonographic Suspicious criteria for Malignancy.[11]

- Hypoechogenicity
- Microcalcifications
- Partially cystic nodule with eccentric location of the fluid portion and lobulation of the solid component
- Irregular margins
- Perinodular thyroid parenchyma invasion
- Taller-than-wide shape
- Intranodular vascularity

Each criterion is assigned a point in the final score. If suspi¬cious cervical lymph nodes are detected, an additional point is added to the score for categorizing nodules on TI-RADS classification.[10]

Thyroid nodule was classified into a TIRADS category [Table 2] based on a modified score according to the US criteria for malignancy present in each case [Table 1].

Table 2: TI-RADS classification of thyroid nodules based on a scoring system according to Ultrasound criteria for malignancy.[11]

TI-RADS		
Category	**Description**	**Score**
1	Normal thyroid gland. No focal lesion.	
2	Benign nodules.Noticeably benign pattern (0% risk of malignancy).	Score -0
3	Probably benign nodules (<5% risk of malignancy).	Score -0
4a	Undetermined nodules (5-10% risk of malignancy).	Score -1
4b	Suspicious nodules (10-50% risk of malignancy).	Score -2
4c	Highly suspicious nodules (50-85% risk of malignancy).	Score -3-4
5	Probably malignant nodules (>85% risk of malignancy).	Score -5 or higher
6	Biopsy-proven malignancy.	

At our institution, US guided FNAB is performed on the TN with suspicious US features or the largest thyroid nodule, if no suspicious US features are detected.

US guided FNAB was performed with a 23-gauge needle attached to a 10 ml disposable plastic syringe. Materials obtained from aspiration biopsy were expelled onto glass slides, smeared and sent to the pathology laboratory. All smears were placed immediately in 95% alcohol for Papanicolaou staining. Cytopathologists of the hospital specializing in thyroid pathology interpreted the smears. During the study period, the cytology reports were classified as benign, suspicious for carcinoma, malignant, or inadequate. Histology was performed if cytology was suspicious or suggestive of malignancy.

Results of the examination were interpreted on the basis of these findings and diagnosis was proposed after considering history and physical examination.

RESULTS

A total of 200 records of patients who fulfilled the inclusion criteria were selected for the study.

Age range of our study was between 6-80 years, youngest patient was 6 years old female and eldest was 80 years old female. Most of the patients are females (90.5%) and remaining are males (9.5%).

The nodules assessed in our study ranged from 3 mm to 55 mm. The TN were single in 16% & multiple in 84% patients. The mean nodule size was 22.9 mm with a range of 3–55 mm.

In our study 13% TN were hypoechoic, 14% isoechoic, 28% nodules were hyperechoic and 45% were mixed echoic. Central & peripheral vascularity was present in 25% patients and peripheral vascularity was seen in 75% patients. No calcification was iden¬tified in 91% patients, macrocalcification was seen in 8% patients and microcalcification was seen in 1% patients.

Table 3: Baseline characteristics of Studied group of patients & Thyroid nodules.

Baseline characteristics	**Category**	**Number**	**Percentage (%)**
Age	1-10	1	0.5
	11-20	10	5
	21-30	34	17
	31-40	43	21.5
	41-50	61	30.5
	51-60	31	15.5
	61-70	13	6.5
	71-80	7	3.5
Gender	Male	19	9.5
	Female	181	90.5
Number of lesions	Single	32	16
	Multiple	168	84
Size of lesion (mm)	<10	34	17
	10-19	51	25.5
	20-39	95	47.5
	40 or more	20	10
Lobe	Right	26	13
	Left	10	5
	Isthmus	2	1
	Both lobes & isthmus	162	81
Shape	Round or Oval	176	88
	Taller than wide	14	7
	Irregular	10	5
Margin	Regular	190	95
	Irregular	10	5
Echotexture	Hypoechoic	26	13
	Hyperechoic	56	28
	Isoechoic	28	14
	Mixed echoic	90	45
Calcification	Egg shell (Rim)	6	3
	Coarse (macro)	10	5
	Micro calcification	2	1
Hypoechoic Halo	Absent	33	16.5
	Complete	163	81.5
	Incomplete	4	2
Vascularity	Absent	0	0
	Peripheral (Rim)	150	75
	Central & peripheral	50	25
Local invasion	Present	1	0.5
	Absent	199	99.5
Distant Metastasis	Present	6	3
	Absent	194	97
Lymphadenopathy	Present	197	98.5
	Absent	3	1.5

Table 4: Distribution of Benign and Malignant lesions according to Consistency.

Type of lesion	Benign	Percentage	Malignant	Percentage	Total
Cystic	7	3.5	0	0	07
Solid	83	41.5	9	4.5	92
Mixed	98	49	3	1.5	101
Total	188	94	12	6	200

Table 5: Distribution of thyroid disease according to Age.

Age Yrs	Benign nodule	%	Colloid goitre	%	Thyroiditis	%	Carcinoma	%	Thyroglossal cyst	%
1-20	0	0	02	01	6	3	2	1	1	0.5
21-30	1	0.5	21	10.5	10	5	1	0.5	1	0.5
31-40	3	1.5	31	15.5	6	3	2	1	1	0.5
41-50	1	0.5	52	26	7	3.5	1	0.5	0	0
51-60	1	0.5	24	12	3	1.5	3	1.5	0	0
61-70	0	0	12	06	0	0	1	0.5	0	0
71-80	0	0	05	2.5	0	0	2	1	0	0
Total	6	3	147	73.5	32	16	12	6	3	1.5

Table 6: TI-RADS classification of thyroid nodules based on modified score according to ultrasound criteria for malig¬nancy (Table 1 & 2).

Score according to US criteria for Malignancy	TI-RADS Category	Number of Patients	Malignancy	Positive Predictive Value (PPV)
0	TI-RADS 1	3	0	0
0	TI-RADS 2	87	0	0
0	TI-RADS 3	71	0	0
1	TI-RADS 4a	22	2	9%
2	TI-RADS 4b	11	5	45.4%
3 or 4	TI-RADS 4c	5	4	80%
5 or more	TI-RADS 5	1	1	100%
6	TI-RADS 6	0	0	

Cystic TN were identified in 3.5% patients, Solid TN in 46% patients and mixed TN in 50.5%. It was observed that 4.5% of solid nodules and 1.5% of mixed nodules were malignant.

The incidence of TN was most common in the age group of 31- 50 years (50.5%) and least between 61-80 years (8.5%). Normal thy¬roid background was present in 6.5% (13) patients; colloid/ adenomatous hyperplasia changes were seen in background thyroid in 77.5% (155) patients and thyroiditis was seen in 16% (32) patients. Regarding the malignant TN, the prevalence was highest in age group of 51-80 years (50%). Three males with TN had thyroid cancer (15.7%) and nine females with TN had thyroid cancer (4.9%). Four patients of thyroid carcinoma (33.3%) had solitary nodule and eight patients (66.6%) had multiple thyroid nodules. The prevalence of thyroid cancer was higher in patients with solitary nodules (25%) than in patients with a multiple nodules (9.5%).

The types of thyroid cancer were 66.6% (8) papillary, 16.6% (2) follicular, 8.3% (1) medullary and 8.3 % (1) undifferentiated carcinoma. Regarding the benign TN, the prevalence was highest in age group of 41-50 years (30%). 14.8 % (28) of benign nodules had solitary nodule and 85.1% (160) had two or more thyroid nodules, while 91.5% (172) of benign TN were in females and only 8.5% (16) were in males. Most common US diagnosis is Colloid goitre (73.5%), followed by Thyroiditis (16%) and least Thyroglossal cyst (1.5%).

The benign nodules, encountered in our study were 4 cases of Follicular adenoma (2%) & 2 cases of hyperplasic nodule (1%). The US features of each thyroid nodule were characterized and classified into different TIRADS categories, as shown in [Table 6]. The TIRADS 2 & 3 category was dominant, accounting for 79% cases (158).

The different TIRADS categories were confronted with the results of pathology and the risk of malignancy was calculated [Table 7].

The score in all benign (TIRADS 2) or probably benign (TIRADS 3) thyroid nodules was zero. The scores of TIRADS 4a, 4b and 4c were one, two and three to four points, respectively with malignancy rates of 9%, 45.4% and 80% respectively. TIRADS 5 TN had a score of five or more points with a malignancy rate of 100% in this study. The risk of malignancy was found to increase from TIRADS 4 to 5.

Among the 200 patients included in this study, only 12 patients (6%) had thyroid carcinoma while 178 patients (89%) had benign pathological results and 10 patients (5%) had suspicious pathological results.

The following US features showed a significant association with malignancy- solid component, hypoechogenicity, microlobulated or irregular margins, microcalcifications, intrinsic vascularity and taller-than-wide shape. As the number of suspicious US features increased, the probability and risk of malignancy also increased.

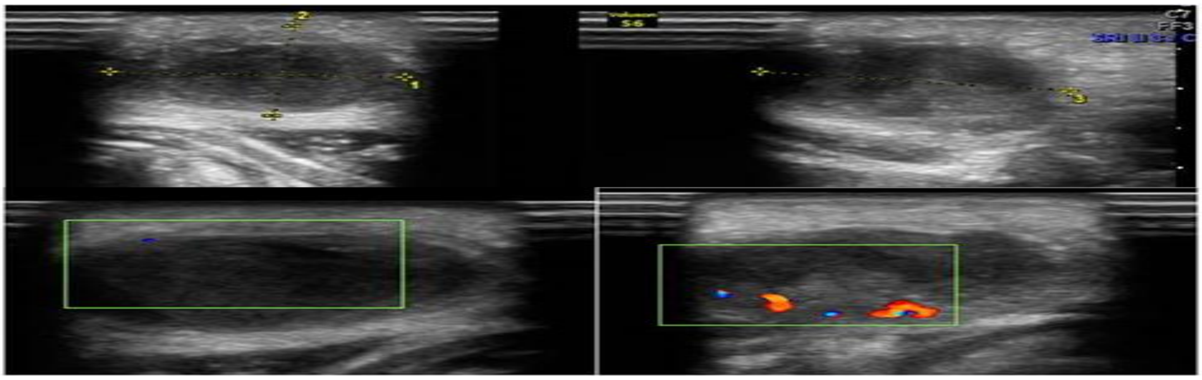

Figure 1: (A-D). 6 years old female child with infected thyroglossal cyst (TIRADS-1). Longitudinal & Transverse US sections reveal a hypoechoic heterogenous thick walled, suprahyoid midline cyst (18x11x19mm) showing no internal vascularity. Normal thyroid gland was seen on US.

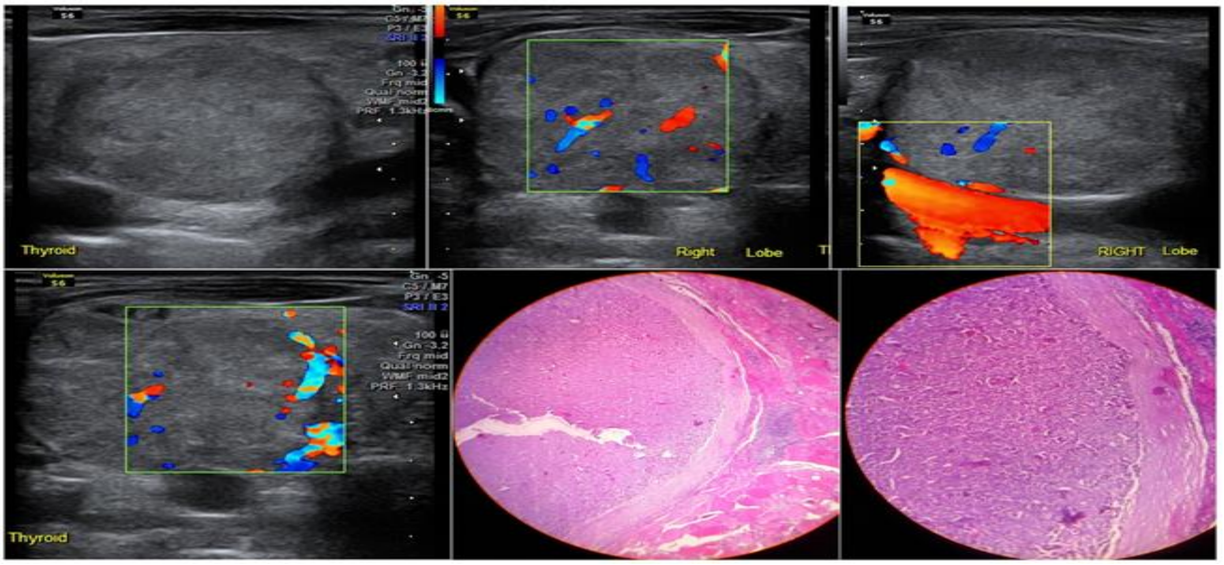

Figure 2: (A-F). 39 years aged female patient with benign Follicular adenoma (TIRADS-2). (A-D).Longitudinal & Transverse US images of right lobe of thyroid show solitary large, solid, iso to hyperechoic, homogenous oval nodule (28x22mm) with a hypoechoic halo around it. The lesion has a rim of vessels entering it's central area.(E,F).HPE -Show small thyroid follicles with scanty or absent colloid surrounded by a capsule. Capsule does not show invasion by follicles.

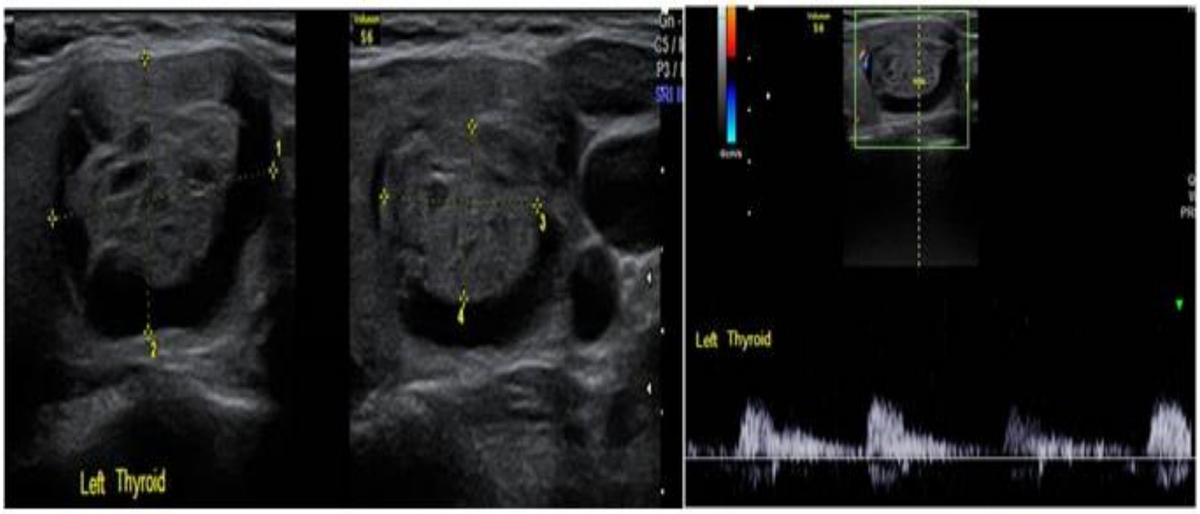

Figure 3: (A-C). 26 years old female with Hyperplastic colloid nodule (TIRADS-2). A. The nodule is round, has regular borders, 70 % solid (18x10mm), isoechoic with peripheral crescentic cystic component measures 26x17mm.C.Colour doppler show blood flow within the solid component.

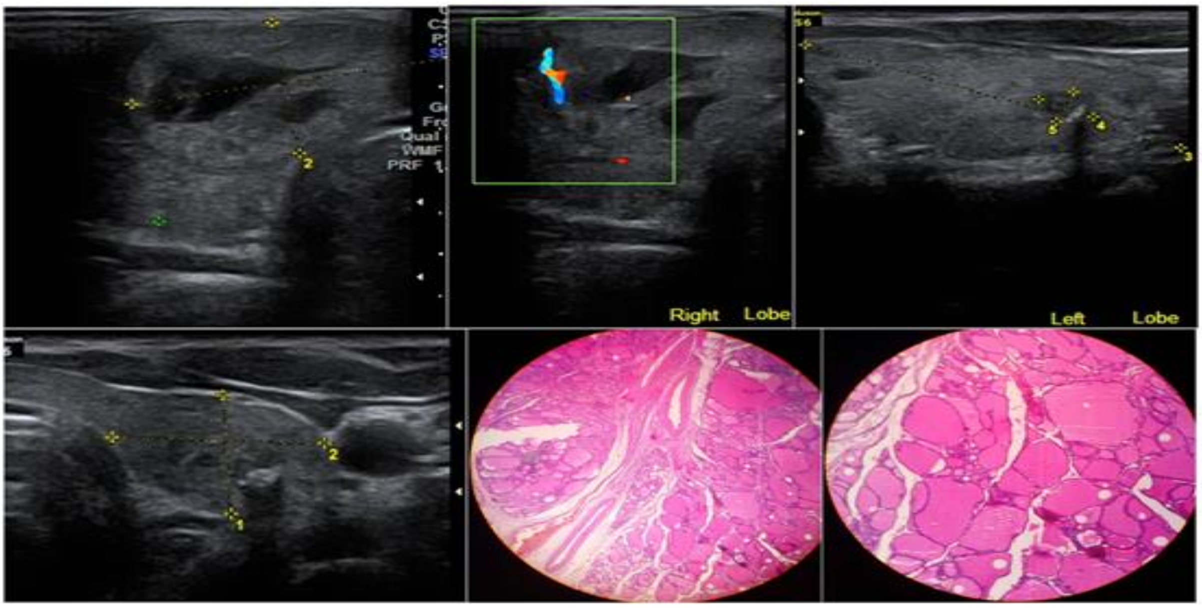

Figure 4: (A-F).A 40-year-old man with a multinodular colloid goiter (TIRADS-2).(A)Tranverse US image depicts a solid isoechoic nodule (27x15mm) with central cystic degeneration & a hypoechoic halo around it.(B).Minimal perinodular vascularity (< 25% of nodule circumference) is demonstrated on the colour flow imaging.(C,D).Longitudinal & Transverse section gray-scale image of left lobe, depicts a small, solid hypoechoic nodule (5x4mm) with a marginal coarse calcific focus.(E,F).HPE reveal thyroid parenchyma divided by fibrous septa into nodules. The follicles are of varying sizes filled with dense colloid & lined by flattened epithelium. Foci of aggregates of lymphocytes seen.

Table 7: TIRADS categories, Diagnostic performance of US & Risk of Malignancy.

TI-RADS Category	Pathology		Total	Risk of malignancy (%)
	Benign	Malignant		
TIRADS 1,2,3,	161	0	161	0
TIRADS 4a	20	2	22	9
TIRADS 4b	06	5	11	45.4
TIRADS 4c	01	4	05	80
TIRADS 5	0	1	01	100
Total	188	12	200	-

Table 8: Sonographic findings of Thyroid nodules & Pathologic results (FNAB) correlation.

USG	Pathology			Total
	Benign	Suspicious	Malignant	
Benign	166	7	3	176
Suspicious	08	3	1	12
Malignant	04	0	8	12
Total	178	10	12	200

Statistical analysis of US in detection of Benign and Malignant TN was done .Sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of US were estimated [Table 9].

The accuracy of US in detection of benign & malignant TN was found to be 96%.

Table 9: Statistical results of Ultrasound & Pathology in detection of Benign and Malignant Thyroid nodules.

Parameter	Diagnosis	
	Benign	Malignant
True Positive (TP)	184	8
False Positive (FP)	4	4
True Negative (TN)	8	184
False Negative (FN)	4	4
Sensitivity (Se)	97.8%	80%
Specificity (Sp)	80%	97.8%
Positive Predictive Value (PPV)	97.87	80%
Negative Predictive Value (NPV)	80%	97.8%
Accuracy	96%	96%

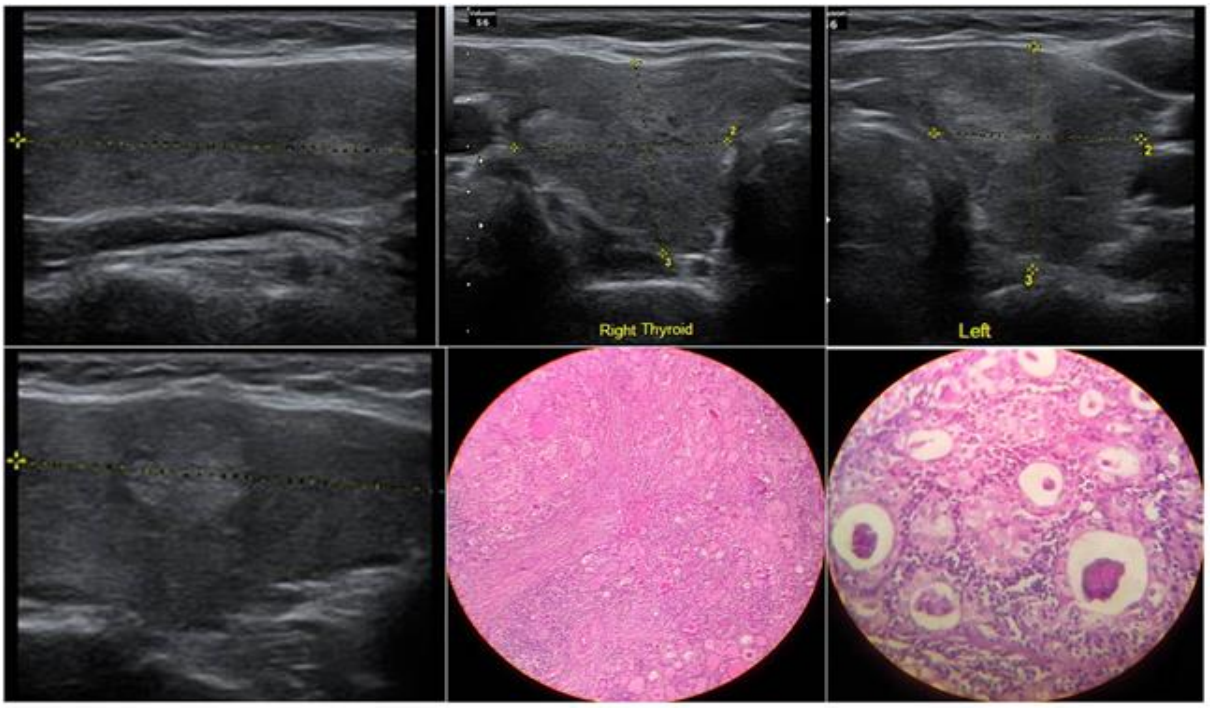

Figure 5: (A-F).A 49 years aged female with diffuse Hashimotos thyroiditis and nodular Thyroiditis (TIRADS-3). (A-D).Longitudinal & Transverse US sections reveal hypoechoic enlarged right (40x21x20mm) & left lobe (42x21x24mm) of thyroid with coarse echotexture and coexistent hyperechoic nodule.(E,F).HPE shows follicular destruction by lymphoctic infiltration with nuclear changes of lining epithelium and thyroid parenchymal fibrosis.

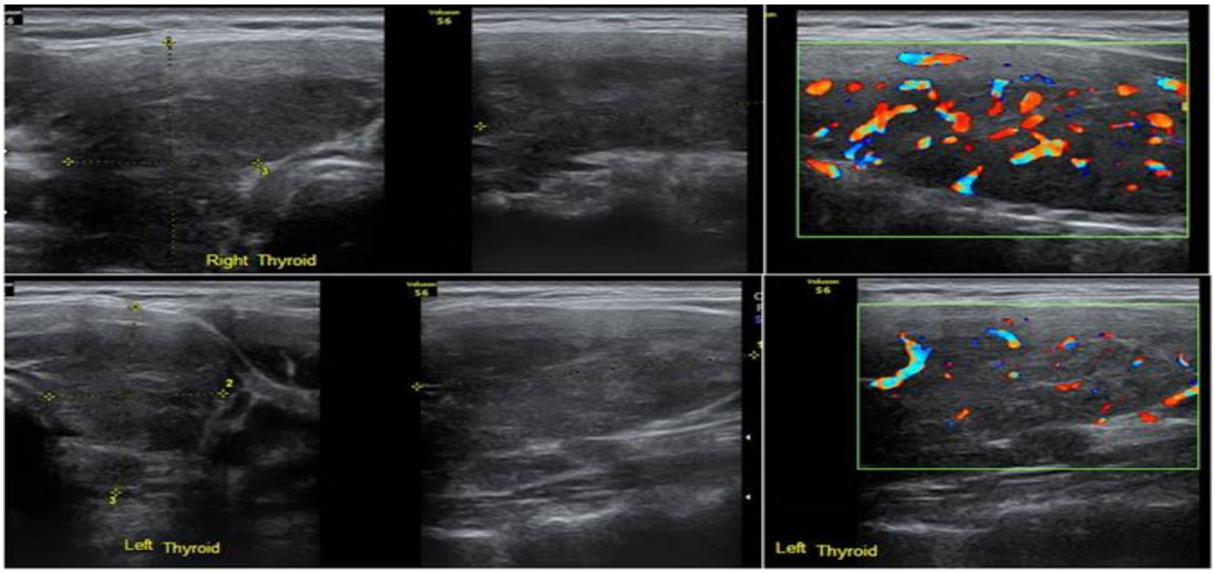

Figure 6: (A-F).27 years aged female patient with Lymphocytic thyroiditis (TIRADS-3). Transverse & Longitudinal US sections reveal diffusely enlarged inhomogenous hypoechoic thyroid gland (right lobe 40x16x27mm, left lobe 39x20x27mm) with augmentation of the vascularity.

DISCUSSION

Multiple pathologic processes, both benign and malignant, may affect the thyroid.

Thyroid nodules and thyroid malignancy have a female predilection of 4:1 and 2–3:1, respectively. In general, the probability of malignancy in a nodule is higher for men and for patients under 15 years or over 45 years of age. Mortality from thyroid cancer increases when the patient is over 45 years old.[12]

Ideally, the diagnosis of TN should be made with knowledge of the patient's history, physical examination and thyroid function tests. Patients at high risk of thyroid cancer are generally those with childhood exposure to radiation, family history of cancer, multiple endocrine neoplasia (MEN) syndrome and a history of thyroid cancer.[13]

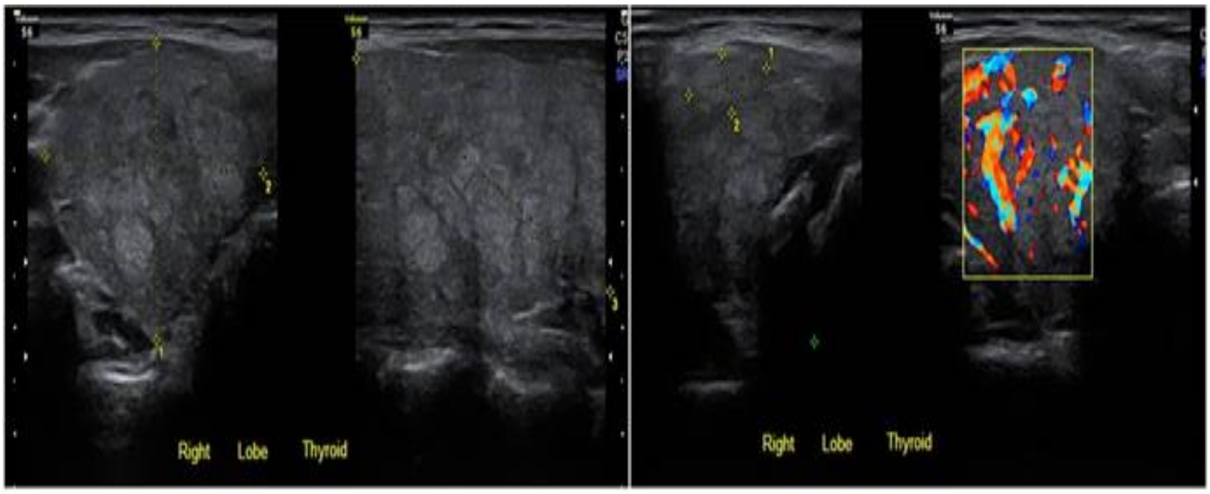

Figure 7: (A-D). 50 year old female with Nodular Hyperplasia in colloid goiter (TIRADS-4a). Transverse & Longitudinal US images show enlarged right lobe of thyroid with round isoechoic nodules showing increased vascularity.

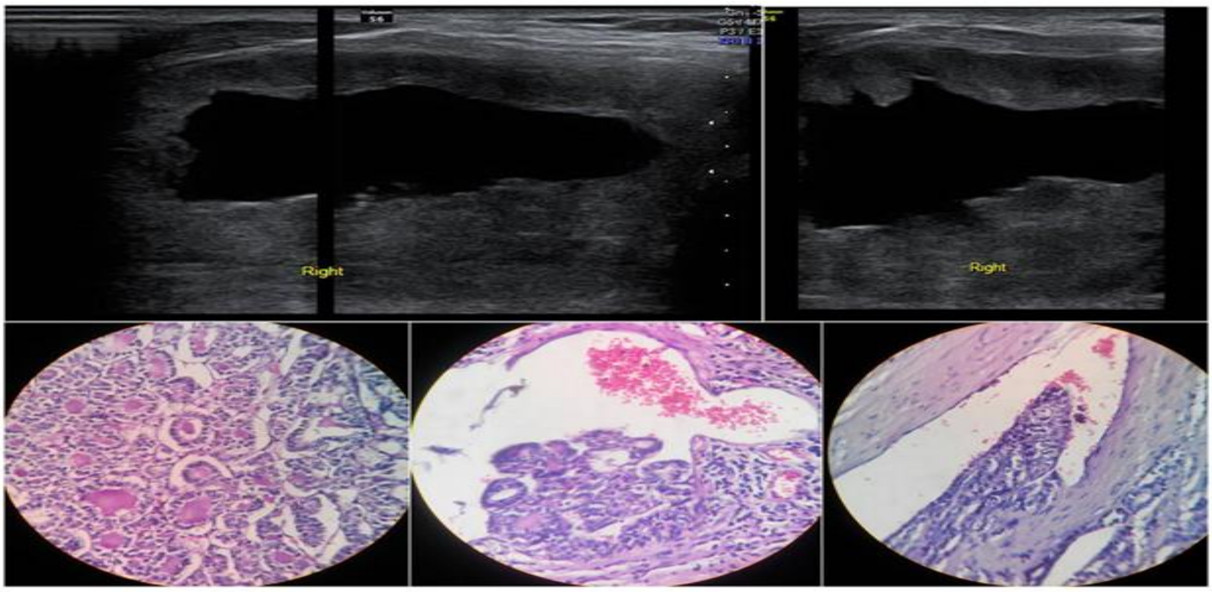

Figure 8: (A-E). 53 year old male with Follicular carcinoma (TIRADS-4b).(A,B).LS & TS of Right lobe reveal large oval isoechoic solid nodule (57x24x43mm) with irregular borders & central cystic area.(C-E).Photomicrograph reveals follicular carcinoma invading through and through capsule & vascular invasion.

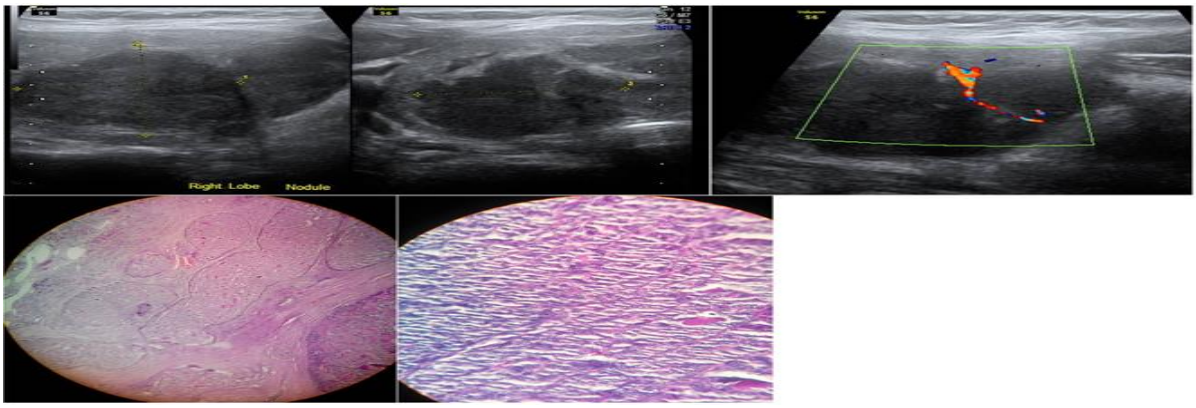

Figure 9: (A-E).62 year old female with Poorly differentiated carcinoma (TIRADS-4c).(A-C).Longitudinal & Transverse US image shows a irregular, hypoechoic, heterogenous, illdefined solid nodule (28x22x24mm) with central vascularity in right lobe. (C,D).Photomicrograph shows cells arranged in small follicles with scanty colloid, trabecular arrangement and foci of insular arrangement.

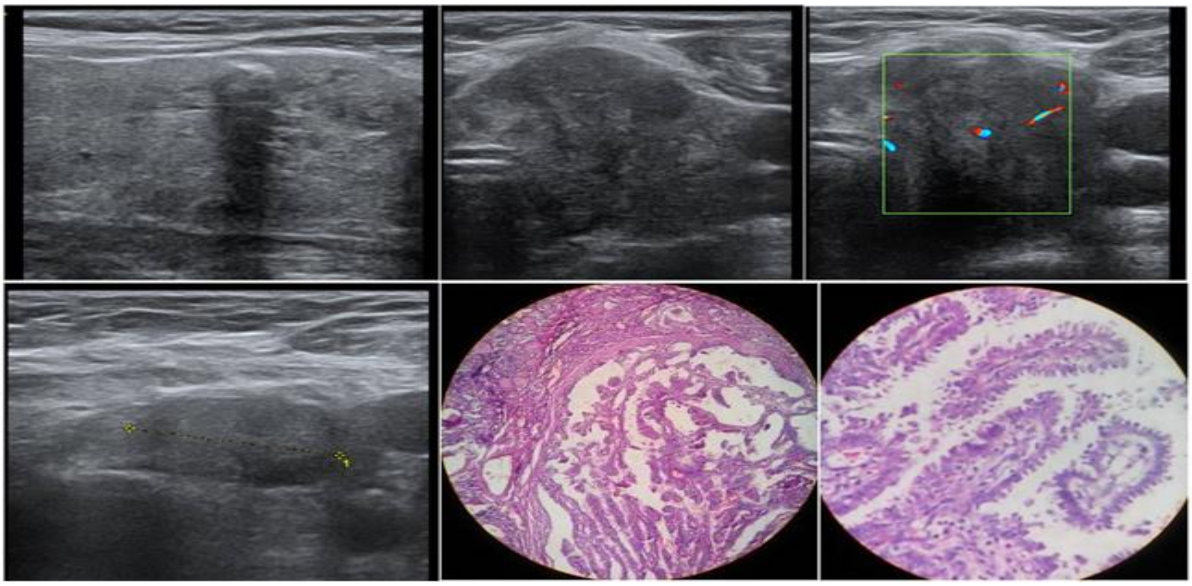

Figure 10: (A-F).74 years old female with Papillary carcinoma (TIRADS-5).(A,B).Longitudinal & transverse sections of left lobe of thyroid reveal large hypoechoic, taller than wide ,infiltrating mass with poorly defined margins & absence of clear hypoechoic halo around the mass.(C).CFI shows increased central vascularity.(D).LS of enlarged deep cervical lymphnode with altered morphology.(E,F).HPE depicts papillary arrangement with fibrovascular cores. The neoplastic epithelium, lining fibrovascular cores shows ground-glass appearance, grooving, crowding and nuclear overlap.

Broadly the thyroid diseases are classified into three categories: (i) benign thyroid nodules, (ii) malignant tumors of thyroid gland, and (iii) diffuse thyroid enlargement. Approximately 60%–70% of thyroid nodules in which FNAB is performed are reported to be benign and most commonly represent benign follicular nodules or thyroiditis.[14,15]

Benign follicular nodules include nodular goiter, adenomatoid or hyperplastic nod¬ules, colloid nodules, nodules in Graves disease, and macrofollicular subtype follicular adenoma.[15]

Thyroiditis is inflammation of the thyroid. It can be categorized as chronic lym¬phocytic thyroiditis (including autoimmune and Hashimoto thyroiditis), de Quervain (subacute or granulomatous) thyroiditis, acute (infec¬tious) thyroiditis and Riedel (fibrous) thyroiditis. Of these subtypes, chronic lymphocytic thyroiditis is the most common. At US, Hashimoto thyroiditis often demonstrates a diffusely heterogeneous echotexture and diffuse increased vascularity but it may also mani¬fest as one or more nodules.

Follicular adenoma is a benign neoplastic proliferation of follicles surrounded by a complete capsule. Hürthle cell adenoma is considered a variant of follicular adenoma in which over 75% of cells show oncocytic or Hürthle cell changes. Follicular adenoma and follicular carcinoma cannot usually be dis¬tinguished with FNAB alone and are reported as a follicular neoplasm.[19] When a nodule is reported to be a follicular neoplasm at FNAB, there is a 70%–85% chance of its being a follicu¬lar adenoma and a 15%– 30% risk of malignancy.[15] The histologic distinction between follicular adenoma and fol¬licular carcinoma can be made only upon surgical excision, by assessing for the absence (adenoma) or presence (carcinoma) of capsular-vascular invasion.[19]

Most malignant lesions are primary thyroid carcino¬mas, which include Papillary carcinoma , follicular carcinoma, medullary carcinoma, and anaplastic carcinoma with Secondary malignant thyroid lesions, lymphoma and metastatic tumor being much less common. Papillary carcinoma represents 80% of all primary thyroid malignan¬cies.[15] Follicular carcinoma represents 11%, and medullary carcinoma represents 4% of all primary thyroid malignancies.[12] Primary thyroid lymphoma is a malignant clonal proliferation of lymphocytes and accounts for 1%–5% of thyroid malignancies.[14] Metastatic tumor represents 5.5% of biopsied thyroid malignan¬cies usually originating from primary lung, breast, or renal cell carcinoma.[14,19]

Of the primary thyroid malignancies, papillary and follicular carcinomas have a rela¬tively good prognosis, medullary carcinoma has an intermediate prognosis, and anaplastic carcinoma has a dismal prognosis.[16]

TN have been conventionally evaluated on real-time high resolution Ultrasound (US). US identify nodules too small to be palpated, the presence of multiple nodules, central, or lateral neck lymphadenopathy, and provides accurate measurements of nodule diameter for interval monitoring. Additionally, it allows characterization of nodules by sonographic features which suggest malignancy. While they do not obviate the need for biopsy, these features are extremely useful in selecting the site within a nodule for FNAB in order to improve diagnostic yield, or to select appropriate nodules to aspirate within a multinodular thyroid.[3]

The accuracy of US-guided FNAB (68%) is higher than that of palpation-guided FNAB (48%).[17] FNAB increases the rate of detection of thyroid cancer and reduces the number of unnecessary surgical procedures and the overall cost of medical care.[17,18]

US features that suggest Benignity include - a TN with a uniform halo, predominantly cys¬tic composition, and avascularity, as well as an enlarged thyroid with multiple nodules.

Specific US features of a TN that raise suspicion for Malignancy - include microcalcifications, exten¬sion beyond the thyroid margin, cervical lymph node metastasis, taller-than-wide shape in the transverse plane, and marked hypoechogenicity. Less specific US features that may raise suspicion include lack of a halo, an ill-defined or irregular margin, solid composition, and increased central vascularity.[19]

Microcalcifications represent psammoma bodies, which are round, laminar calcific de¬posits.[20] They appear as punctate echogenic foci less than 1 mm in size and without acous¬tic shadowing. In contrast, macrocalcifications are coarse calcifications greater than 1 mm in size and may demonstrate acoustic shadow¬ing.[20,23,24] If tiny bright reflectors with a clear cut comet tail artifact were present at conventional US, were considered as colloid.[9] Microcalcifications are typical of papillary thyroid carcinoma, whereas macro¬calcifications (including rim calcifications) are less ominous but may be seen in both medullary and papillary carcinoma.[23,24]

The internal content of a thyroid nodule may be predominantly solid (> 50%–100% solid) or predominantly cystic (0%–49% solid). The solid component of the nodule may be hypoechoic, isoechoic or hyperechoic to the surrounding normal-appearing thyroid parenchyma. The nodule is termed as 'markedly hypoechoic' if it is of lower echogenicity than the overlying strap muscles, and is thus highly suspicious for malignancy.[22]

Some solid nodules may have a spongiform appearance, identified as an aggregation of multiple microcystic components in more than 50% of the volume of the nodule.[22] Bonavita et al likened this appearance to a 'puff pastry' pattern (similar to the ultra-thin layers of flaky pastry in desserts such as napoleons),[25] which is found to be characteristic of colloid nodules or goiter.

A pure cystic nodule is highly unlikely to be malignant.[23] These are usually benign nodules that have undergone cystic or haemorrhagic degeneration. A cystic nodule containing a central plug of avascular colloid is the sign of a colloid nodule.

Metastasis to regional cervical lymph nodes occurs in 19% of all thyroid malignancies, especially papillary car¬cinoma and also medullary carcinoma; it rarely occurs in follicular carcinoma.[20]

Thyroid gland US Elastography is used to study hardness/elasticity of the TN to differentiate malignant from benign lesions by utilizing external compression technique. It determines the amount of tissue displacement at various depths, by assessing the ultrasound signals reflected from the tissues before and after compression. A benign nodule is softer and deforms more easily, whereas the malignant nodule is harder and deforms less when compressed by ultrasound probe. Dedicated software then provides an accurate measurement of tissue distortion and displays it visually as an elastographic image. Real time shear elastography is a latest technique; that characterizes and quantifies tissue stiffness better than conventional elastography.[26,27]

Contrast enhanced ultrasound (CE-US) is a newly developed technique that helps in characterizing a benign & malignant TN. Ring enhancement is predictive of benign lesions, whereas heterogeneous enhancement is helpful for detecting malignant lesions. However, overlapping findings seem to limit the potential of this technique in the characterization of thyroid nodules.[28] Use of specific contrast (e.g. Sono Vue) and pulse inversion harmonic imaging further improves the efficacy of ultrasound in diagnosing a malignant thyroid nodule.[29,30]

Radioisotope scanning can be used to determine if a thyroid nodule is functioning, but it does not provide an accurate measurement of size. Thyroid scintigraphy may be performed using either technetium-99m pertechnetate or an iodine-based radionuclide (I 123 or I 131). I 131 is useful for whole-body imaging performed to evaluate for residual thyroid tissue or metastatic disease after thyroidectomy or thyroid ablation.[31] About 80 to 85% of thyroid nodules are cold, and about 10% of these nodules represent a malignancy. Hot nodules account for 5% of all nodules, and the likelihood of malignancy is less than 1% for these nodules. Taken together, the sensitivity for the diagnosis of thyroid cancer is 89 to 93%, specificity is 5%, and the positive predictive value of malignancy is only 10%.[32] Although 18FDG-PET/CT does not play a role in the workup of a nodule, any 18 FDG-avid thyroid nodule found incidentally deserves a thorough work up for malignancy.[34]

Computed tomography (CT) and magnetic resonance imaging (MRI) have almost no role in the initial evaluation of a thyroid nodule, and are rarely indicated in the initial workup. However, they are both excellent (100%sensitivities) for evaluating the extent of large substernal goiters which may be compressing nearby structures.[33] Of note, iodinated contrast material utilized for CT scan should be avoided because its use prevents scintigraphy or administration of radioactive iodine (RAI) therapy for a period of 1 to 2 months. Gadolinium contrast used with MRI does not interfere with thyroid uptake of radiotracer, but it is significantly more expensive than CT or ultrasound.

Fine needle aspiration biopsy (FNAB) is the most important step in the workup of the thyroid nodule, as cytology is the primary determinant in whether thyroidectomy is indicated. Its use has dramatically decreased the number of thyroidectomies performed, and improved the yield of malignancy in glands that have been extirpated.[35] FNAB can be performed with or without US guidance, but diagnostic accuracy is improved using sonographic needle localization due to a decreased number of inadequate specimens and false negative results.[36]

Benign lesions on FNAB have an approximate 3% risk of malignancy and may be followed clinically with US or with a repeat FNAB which, if also benign, decreases the risk of a false negative to 1.3%.[37] The use of genetic biomarkers to assist in interpretation of FNAB samples is likely to greatly enhance the ability to distinguish benign from malignant thyroid nodules in conjunction with cytology.

The larger group of patients (52%) in our study were in 31-50 yrs age group. A similar demography was reported in the study conducted by Mary C et al who studied 1985 patients of which 1742 occurred in women and 203 were males and most of patients was in the age group of 30-50.[38]

In general, TN are four times more common in women than in men.[33] In our study of TN, the occurrence among males and females was 9.5% and 90.5% respectively. This correlated with study by Kimoto et al of 10% and 90% respectively.[39]

The rate of malignancy in the current study was 6% which is consistent with the proportion of thyroid cancers in reported series which varies from 4% to 32%.[2,3,33,41]

In our study, the rate of cancer in males with TN (15.7%) was higher than in females with TN (4.9%), these results were comparable with those reported in previous studies by Hegedus L et al, Tuttle RM et al and Mohammed A et al.[2,12,41]

Among the 200 patients included in this study, only 6% patients had thyroid carcinoma while 89% patients had benign pathological results and 5% patients had suspicious pathological results which correlates with the study by Qays A.Hassan et al,[42] Among the 66 patients included in his study, only 9% patients had thyroid carcinoma while 84.84% patients had benign pathological results and 6.1% patients had suspicious pathological results.

In our study the prevalence of thyroid cancer was higher in patients with solitary nodules (25%) than in patients with a multiple nodules (9.5%), which are near in comparison to study by Qays A.Hassan et al of 20% and 2.44% respectively.[42]

The types of thyroid cancer in our study were 66.6% papillary, 16.6% follicular, 8.3% medullary and 8.3 % undifferentiated carcinoma. These results were comparable statistically with those reported in studies by Ogilvie JB et all and Mohammed A et al and similar to the results by Qays A.Hassan et al of papillary carcinoma (66.7%),[40-42] follicular carcinoma (16.7%) and undifferentiated carcinoma (16.7%). Our study did not show strong relation between size of the thyroid nodule detected by US and final pathological results and this corresponds with the study by Ross L Titton et al and Amer AM Ali et al.[43,44]

In his work, Horvath suggested a malignant risk of less than 5% for TIRADS 3, 5% - 10% for TIRADS 4a, 10% - 80% for TIRADS 4b and greater than 80% for TIRADS 5.[10]

The risk of malignancy in our study for TIRADS 4a, 4b, 4c and TIRADS 5 are 9%, 45.4%, 80% and 100% respectively. From our results, the risk of malignancy significantly increased from TIRADS 4 to 5. Our findings are within this range suggested by Horvath and similar to that obtained by J.Fernández Sánchez with malignancy rates for TI-RADS 4a, 4b, 4c and TI-RADS 5 were 9.5%, 48%, 85% and100% respectively.[11]

So if properly classified on US the probability of a particular nodule being malignant can be inferred from the TIRADS category with a certain level of confidence and appropriate measures for management can be initiated.

TI-RADS is a merely sonographic classification. The final evalu¬ation and therapeutic decision making in the presence of a TN cannot be limited to the results of a thyroid ultrasound. In addition to the standard laboratory tests for the evaluation of thyroid function, measurement of thyroglobulin, calcitonin and diverse anti-thyroid antibodies is also important, as well as the thyroid scintigraphy using 99mTC-sodium pertechnetate.[11]

Different range of Sensitivity & Specificity of US for detecting malignant thyroid nodules are reported in various studies. The Sensitivity & Specificity of US in detecting malignant thyroid tumors ranged from 80-100% and from 40-91% respectively.[45]

In a study by Tahmasebi MM et al the Sensitivity,[46] Specificity, Positive predictive value (PPV), Negative predictive value (PPV) and Accuracy in detecting malignant TN was found be 100%, 93.2%, 37.5% ,100% and 93.4% respectively and 88.4%%, 73.3%, 74% ,88% and 80.3% respectively in another study by Anuradha kapali et al.[47]

In our study the Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (PPV) and Accuracy in detecting malignant TN, was found be 80%, 97.8%, 80%, 97.8% and 96% respectively, which nearly correlated with studies by Tahmasebi MM et al & Anuradha kapali et al.[46,47]

The limitations of our study include retrospective data collection and the fact that histology was not available for all of the TN, as those with a benign cytology were not operated for ethical reasons. However, this can be compensated by the high NPV of cytology.

CONCLUSION

Thyroid nodules are common entities that are found through physical examination or incidentally through imaging modalities performed for other reasons. The majority of thyroid nodules are benign, but they warrant surgical excision when they are large enough to be symptomatic or if there is concern for malignancy. US is a sensitive and specific primary imaging modality by which the thyroid gland is studied with good overall accuracy. Nodules one centimeter or larger or sonographically suspicious subcentimeter nodules warrant cytologic analysis through FNAB to determine the risk of malignancy. A TI-RADS classification based on a score according to the number of suspicious US criteria defined for malignancy can be applied in daily practice. The risk of malignancy was found to increase from TIRADS 4 to 5. All TNs with a TIRADS score of 5 or higher are malignant. US guided FNAB increases the rate of detection of thyroid cancer and reduces the number of unnecessary surgical procedures and the overall cost of medical care.

Detecting malignancy preoperatively allows total thyroidectomy in a single operation without the need for frozen section or removal of the thyroid remnant in a second surgery.

REFERENCES

1. Wiest PW, Hartshorne MF, Inskip PD, Crooks LA, Vela BS, Telepak RJ, et al. Thyroid palpation versus high-resolution thyroid ultrasonography in the detection of nodules. J Ultrasound Med. 1998;17:487-496.
2. Hegedus L, Bonnema SJ, Bennedbaek FN. Management of simple nodular goiter: current status and future perspectives. Endocr Rev. 2003;24:102-132.
3. Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. J Clin Endocrinol Metab 2002;87(5):1941–6. [PubMed: 11994321].
4. Nam-Goong IS, Kim HY, Gong G, Lee HK, Hong SJ, Kim WB, et al. Ultrasonography Guided fine needle aspiration of thyroid incidentaloma: correlation with pathological findings. Clin Endocrinol (Oxf) 2004;60(1):21–8. [PubMed: 14678283].
5. Watters DA, Ahuja AT, Evans RM, Chick W, King WW, Metreweli C, et al. Role of ultrasound in the management of thyroid nodules. Am J Surg. 1992;164:654–657.
6. Hansen JT. Embryology and surgical anatomy of the lower neck and superior mediastinum. In: Falk SA, ed. Thyroid Disease. Endocrinology, Surgery, Nuclear Medicine and Radiotherapy. 2nd ed. New York: Lippincott Raven; 1997.pp. 19–20.
7. Rufini V, Satta M. Embryology and anatomy of the thyroid. In: Troncone L, Satta MA, Shapiro B, et al, eds. Thyroid diseases. Basic science, pathology, and clinical laboratory diagnoses. London: CRC Press;1994. pp. 5–8.
8. Nadia K, Tammy A, Karen SJ. Ultrasound of the thyroid and parathyroid glands. Ultrasound Quarterly. 2003;19:162–176.
9. Anderson L, Middleton WD , Teefey SA , et al .Hashimoto thyroiditis. I. Sonographic analysis of the nodular form of Hashimoto thyroiditis. A,JR Am J Roentgenol 2010 ; 195 (1):208 – 215.
10. E. Horvath, S. Majlis, R. Rossi, C. Franco, J. P. Nied-mann, et al., "An Ultrasonogram Reporting System for Thyroid Nodules Stratifying Cancer Risk for Clinical Management," The Journal of Clinical Endocrinology & Metabolism, Vol. 95, No. 5, 2009, pp. 1748-1751. doi:10.1210/jc.2008-1724 .
11. J. Fernández Sánchez TI-RADS classification of thyroid nodules based on a score modified according to ultrasound criteria for malignancy. Rev. Argent. Radiol. 2014;78(3): 138-148.
12. Tuttle RM, Ball DW, Byrd D, et al. National Comprehensive Cancer Network clinical practice guidelines in oncology: thyroid carcinoma.Version 2.2013. http://www.nccn.org/professionals/physician gls/pdf/thyroid.pdf. April 9, 2013. Accessed June 25, 2013.
13. Amogh Hegde, MD, FRCR, Anil Gopinathan, MD, FRCR, Rafidah Abu Bakar, MMedUS, BSc, Chin Chin Ooi. A method in the madness in ultrasound evaluation of thyroid nodules. Singapore Med J 2012; 53(11): 766–773.
14. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correla¬tions. Cancer 2007;111(5): 306–315.
15. Ali SZ, Cibas ES. The Bethesda system for report¬ing thyroid cytopathology. New York, NY: Springer, 2009; 1–165.
16. Sacks W, Braunstein G. Papillary thyroid cancer. In: Braunstein G, ed. Thyroid cancer. New York, NY: Springer, 2012; 133–155.
17. Kim MJ, Kim KE, Park S, et al. US-guided fine-needle aspiration of thyroid nodules: indications, techniques, results. Radiographics 2008; 28:1869-86.
18. Hamberger B, Gharib H, Melton LJ, Goellner JR, Zinsmeister AR. Fine needle aspiration biopsy of thyroid nodules: impact on thyroid practice and cost of care. Am J Med 1982; 73:381-4.
19. Arun C. Nachiappan, MD Zeyad A. Metwalli, et al The Thyroid: Review of Imaging Features and Biopsy Techniques with Radiologic-Pathologic Correlation .RadioGraphics 2014; 34(2) :276–293.
20. Hoang JK, Lee WK, Lee M, Johnson D, Farrell S. US features of thyroid malignancy: pearls and pit¬falls. RadioGraphics 2007;27(3):847–860; discus¬sion 861–865.
21. Kwak JY, Han KH, Yoon JH, et al. Thyroid imag¬ing reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk. Radiology 2011;260(3):892–899.
22. Moon WJ, Jung SL, Lee JH, et al. Benign and ma¬lignant thyroid nodules: US differentiation—multi¬center retrospective study. Radiology 2008;247(3): 762–770.
23. Frates MC, Benson CB, Charboneau JW, et al. Management of thyroid nodules detected at US: So¬ciety of Radiologists in Ultrasound consensus con¬ference statement. Radiology 2005;237(3):794–800.
24. Desser TS, Kamaya A. Ultrasound of thyroid nod¬ules. Ultrasound Clin 2009;4(2):87–103.
25. Bonavita JA, Mayo J, Babb J, et al. Pattern recognition of benign nodules at ultrasound of the thyroid: which nodules can be left alone? Am J Roentgenol 2009; 193:207-13.
26. Hall TJ. AAPM/RSNA physics tutorial for residents: topics in US: beyond the basics: elasticity imaging with US. Radiographics. 2003;23:1657–71. [PubMed: 14615571]
27. Friedrich Rust M, Sperber A, Holzer K, Diener J, Grünwald F, Badenhoop K, et al. Real time elastography and contrast enhanced ultrasound for the assessment of thyroid nodules. Exp Clin Endocrinol Diabetes. 2010;118:602–9. [PubMed: 19856256].
28. Zhang B, Jiang YX, Liu JB, Yang M, Dai Q, Zhu QL, et al. Utility of contrast enhanced ultrasound for evaluation of thyroid nodules. Thyroid. 2010;20:51–7.[PubMed: 20067379].

29. Chaudhary V, Bano S. Imaging of the thyroid: Recent advances. Indian J Endocrinol Metab. 2012;16:371–6. [PMCID: PMC3354842] [PubMed: 22629501]
30. Gharib H, Papini E, Valcavi R, Baskin HJ, Crescenzi A, Dottorini ME, et al. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules Endocr Pract. 2006;12:63–102.[PubMed: 16596732]
31. Loevner LA. Imaging of the thyroid gland. Semin Ultrasound CT MR 1996;17(6):539–562.
32. Cases JA, Surks MI. The changing role of scintigraphy in the evaluation of thyroid nodules Semin Nucl Med 2000;30(2):81–7. [PubMed: 10787188].
33. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993;328(8):553–9. [PubMed: 8426623].
34. Razfar A, Christopoulos A, Lebeau SO, Hodak S, Carty SE, Escott EJ, Branstetter BF, Ferris RL.Clinical Utility of PET-CT in Recurrent Thyroid Carcinoma. Archives of Otolaryngology. 2009 in press.
35. Sidawy MK, Del Vecchio DM, Knoll SM. Fine-needle aspiration of thyroid nodules: correlation between cytology and histology and evaluation of discrepant cases. Cancer 1997;81(4):253–9.[PubMed: 9292740]
36. Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic accuracy of conventional versus sonography-guided fine-needle aspiration biopsy of thyroid nodules Thyroid 1998;8(1):15–21. [PubMed: 9492148].
37. Chehade JM, Silverberg AB, Kim J, Case C, Mooradian AD. Role of repeated fine-needle aspiration of thyroid nodules with benign cytologic features. Endocr Pract 2001;7(4):237–43. [PubMed:11497473].
38. Mary C. Frates, Carol B. Benson et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. The Journal of Clinical Endocrinology and Metabolism. 2006; 91 (9): 3411-3417.
39. Kimoto et al the efficiency of performing FNAC following mass gaining for thyroid tumors to avoid unnecessary surgery, surge today 29(9) 880-3, 1999.
40. Ogilvie JB, Piatigorsky EJ, Clark OH. Current status of fine needle aspiration for thyroid nodules. Adv Surg 2006;40:223–238.
41. Mohammed A. Kadhim, Basim S. Ahmed, Qahtan A. Mahdi. The frequency of thyroid carcinoma in patients with solitary and multiple nodules utilizing ultrasound guided fine needle aspiration cytology (FNAC): A prospective study (Thyroid carcinoma and U/S guided FNA). J Fac Med Baghdad. 2010;52:134-138.
42. Qays A. Hassan, Abdullateef A. Asghar and Mohammad A. Hadi. Sonographic-pathologic correlation in an ultrasound-guided fine needle aspiration of a thyroid nodule: Concordant or discordant? International Journal of Medical Research & Health Sciences, 2016, 5, 10:148-158. ISSN No: 2319-5886
43. Ross L Titton, Debra A Gervias, Giles W Boland, Michael M. Maher, Peter R. Mueller Sonography and snographically guided fine needle aspiration biopsy of thyroid gland: indications and technique, pearls and pitfalls. AJR. 2003;181:267-271.
44. Amer AM Ali, Abdulkader H Hasan, Tahir A Hawrami. The role of conventional ultrasound in the assessement of the thyroid nodules in Al-Sulaimanyia territory. Bas J Surg 2009;15:34.
45. G. Russ, C. Bigorgne, B. Royer, A. Rouxel and M. Bien-venu-Perrard, “The Thyroid Imaging Reporting and Data System (TIRADS) for Ultrasound of the Thyroid,” Journal of Radiology, Vol. 92, No. 7-8, 2011, pp. 701-713. doi:10.1016/j.jradio.2011.03.022.
46. Tahmasebi M, Dezfouli MRB,Gharibvand MM, Jahanshahi A, Nikpur N, Rahim F. Diagnostic Accuracy of Sonography in Assessment of Thyroid massesin comparison with pathology. Russian Open Medical Journal 2016;5(1) Article CID e0103. DOI;10.15275/rusomj.2016.0103.
47. Anuradha kapali, Jaipal BR, Raghuram P, Ravindra Bangar,Sateesh kumar Atmakuri. Role of Ultrasonography in Thyroid nodules with pathological correlation. International Journal of Contemporary Medical Research 2016;3(5);1451-1453.

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