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A comparative study of sonographic evaluation of thyroid nodules, using TIRADS, with fine needle aspiration cytology

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***Abstract*---**Various imaging modalities have been used in the diagnosis of thyroid diseases. Ultrasonography followed by USG guided FNAC is usually done in evaluating any thyroid nodule that is palpable on physical examination. FNAC often used as the initial screening test for diagnosis of thyroid nodule. This study was a cross-sectional study where patients with palpable thyroid nodules or clinically evident thyroid disease (hypothyroidism/hyperthyroidism) were evaluated by ultrasound examination, which were correlated with FNAC of the patient. Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. It was concluded that conclusion high resolution ultrasound is an accurate technique to assess the morphology of thyroid nodules.

***Keywords*---**USG, FNAC, Thyroid, Nodules.

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Introduction

The thyroid gland is the first of the body's endocrine glands to develop, on approximately the 24th day of gestation. The normal thyroid gland consists of two lobes and a bridging isthmus uniting in front of second, third and fourth tracheal rings [1]. Various imaging modalities have been used in diagnosis of thyroid diseases. Thyroid volume can be calculated accurately by ultrasonography [2]. Sonographically, the normal thyroid parenchyma has a homogenous, medium to high level echogenicity. The capsule of the thyroid gland is represented by a thin hyperechoic line around the thyroid lobes. The capsule can become calcified in patients with uremia or in disorders of calcium metabolism [2]. On Sonographic evaluation majority of the thyroid nodules are asymptomatic and are detected incidentally [3-5] Ultrasonography followed by USG guided FNAC is usually done in evaluating any thyroid nodule that is palpable on physical examination. On computed topography the normal thyroid tissue is identified by its higher density compared to the adjacent structures. Sonographic features of malignant thyroid nodules include Micro calcifications [6-9] marked hypoechogenicity, irregular or microlobulated margins and intranodular central vascularity.

The Fine needle aspiration cytology (FNAC) is simple, cost effective, readily repeated and quick to perform procedure in the outpatient department with excellent patient compliance. Important factor for the satisfactory test includes representative specimen from the nodule and an experienced cytologist to interpret findings. It is often used as the initial screening test for diagnosis of thyroid nodule [10]. The main aim of FNAC is to identify nodules that require surgery and those nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign disease [11]. The main aims of this study were to assess the sonographic features of various thyroid nodules using grey scale and colour Doppler sonography and to correlate the ultrasound findings with Fine needle aspiration cytology.

Material and Methods

The present study was conducted in the Postgraduate Department of Radiodiagnosis and Imaging, Government Medical College, Srinagar, J&K, India over a period of 18 months, after obtaining ethical clearance from Institutional Ethics Committee and written consent from the patients. This study was a cross-sectional study where patients with palpable thyroid nodules or clinically evident thyroid disease (hypothyroidism/hyperthyroidism) were evaluated by ultrasound examination, which were correlated with FNAC of the patient. The diagnostic accuracy of ultrasound was evaluated and compared with FNAC findings.

Inclusion Criteria

All the patients referred to Radiology Department of Government Medical College, Srinagar with symptoms of lump in anterior aspect of neck with or without symptoms of hyperthyroidism or hypothyroidism will be included in the study, if they have met the following criteria.

- Patients with palpable lump with or without any symptoms of thyroid disease.
- Patients with non-palpable lesions in thyroid region detected by HRUSG.

Exclusion Criteria

- Previously diagnosed cases of benign disease and thyroid malignancies.
- Cases undergoing treatment.
- Diagnosed cases of carcinoma thyroid on follow up for residual disease or recurrence.

Image Aquisition
Ultrasonography (USG)

Ultrasound was performed with the USG in the department (GE LOGIQ TECH S8) using 5-10 MHz (7.5 MHz) transducer. The patient was examined in supine position with neck extended. Ultrasound gel (ULTRA CONOGEL) was applied to create smooth acoustic interface. The entire thyroid gland from upper to lower pole and the isthmus was examined in the longitudinal and transverse planes. Bilateral carotid arteries, jugular veins and supraclavicular fossa were examined. The lesions were evaluated as per TIRADS (thyroid imaging reporting and data system). Points were added from the different categories to determine TIRADS levels. The diagnosis was based on TIRADS as follows:

- **TIRADS 1:** normal thyroid gland
- **TIRADS 2:** Benign nodule
- **TIRADS 3:** Probably benign (<5% malignancy)
- **TIRADS 4:** Suspicious nodules (5-80% malignancy). Nodules in this group can be further categorised into 4a (5-10% malignancy) and 4b (10-80% malignancy).
- **TIRADS 5:** Probably malignant nodules (>80% malignancy)
- **TIRADS 6:** Biopsy proven malignancy.

Cytological Diagnosis

The following modalities were used to establish the cytological diagnosis of the patient.

FNAC

The neck was hyperextended, the skin cleansed with povidone iodine (betadine) solution. The transducer was also be cleansed with the same solution. Sterile gel was used as a coupling agent. The needle used was 25G non-cutting bevelled edge needle. The needle is attached to 10 ml syringe. After introducing the needle, the needle was moved gently up to the nodule centre under US guidance. Then, gentle suction was done by pulling the piston of the syringe. If the specimen contains much blood, a non- aspiration technique was used. In this, 25- gauge needle is inserted under ultrasound guidance into the thyroid gland and no suction is applied, and this needle is moved in back-and-forth excursions. Due to the capillary action the fluid of the cells from the nodule moves into the needle. Such specimen is often less bloody. Two drops of aspirate/fluid in the syringe are to be ejected over a clean slide. The aspirate on the first slide is to be spread on it to form a film coating on it. The slide making procedure was repeated once more and after smearing the second slide. The slides were fixed by air (in dry fixation), or subjected to wet fixation and stained in giemsa (in dry fixation), haemotoxylin and eosin or papanicolaou (for wet fixation). Slides were examined under microscope by pathologist and cytological diagnosis of thyroid was given. In a few select cases whose cytology came out to be follicular neoplasm, HPE follow up was taken for further categorisation into follicular adenoma and carcinoma.

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Graphically the data was presented by bar diagrams. Diagnostic accuracy (sensitivity, specificity, positive predicted value and negative predicted value) of ACR TIRADS was obtained for detection of various thyroid lesions, taking cytology/histopathology as gold standard.

Results

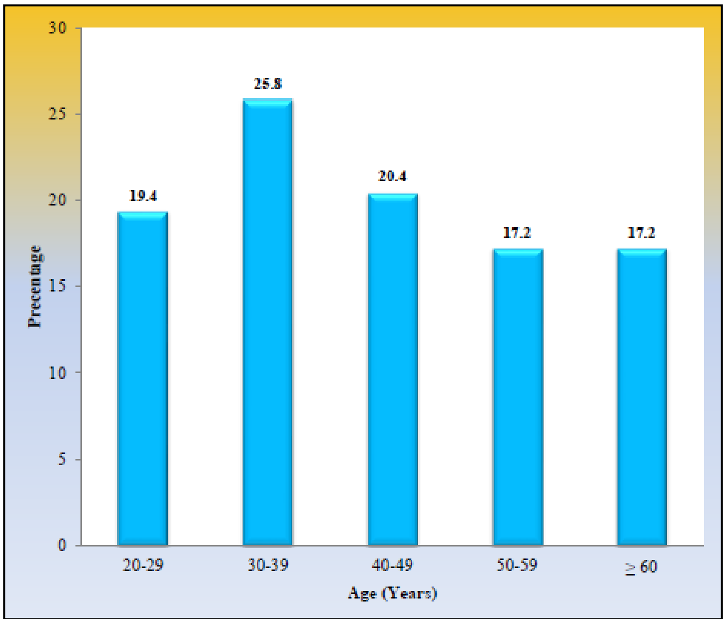


Figure 1. Shows Age Distribution of Patients

In present study, the age of patients ranged from 20-70 years. Majority of the patients were in age group of 30-39 years (25.8%) with mean age of presentation at 42.9 years as shown in Figure 1.

Table 1
Shows gender distribution of the patients

Gender	Number	Percentage
Male	25	26.9
Female	68	73.1
Total	93	100

Among these 93 patients, 68 were female (73.1%) and 25 were males (26.9%) as shown in Table 1.

Table 2
Composition of lesion in study patients

Composition	Number	Percentage
Cystic or predominately cystic	1	1.1
Spongiform	6	6.5
Mixed solid-cystic	47	50.5
Solid or predominately solid	39	41.9
Total	93	100

Out of 93 nodules, 39 were predominantly solid (41.9%), 47 demonstrated mixed solid cystic nature (50.5%). 6 (6.5%) of the nodules were spongiform in nature and only one (1.1%) was a cystic nodule as shown in Table 2.

Table 3
Shows echogenicity of lesions in study patients

Echogenicity	Number	Percentage
Anechoic	6	6.5
Hyperechoic or isoechoic	37	39.8
Hypoechoic	50	53.8
Very hypoechoic	0	0.0
Total	93	100

In our study, 6.5% (n=6) of nodules were anechoic, 39.8%(n=37) nodules were hyperechoic, 53.8%(n=50) nodules were hypoechoic as shown in Table 3

Table 4
Shape of the lesions in study patients

Shape	Number	Percentage
Wider than tall	76	81.7
Taller than wide	17	18.3
Total	93	100

Out of the 93 nodules evaluated, 76 were wider than tall (81.7%), and 17 nodules were taller than wide (18.3%) as shown in Table 4.

Table 5
Margins of lesions in study patients

Margins	Number	Percentage
Smooth	67	72.0
Ill defined	0	0.0
Lobulated/irregular	18	19.4
Extra-thyroidal extension	8	8.6
Total	93	100

67 nodules among the 93 nodules had smooth margins (72%), 18 had lobulated/irregular margins (19.4%), 8 had extra-thyroidal extension (8.6%) as shown in Table 5.

Table 6
Echogenic foci of lesions in study population

Echogenic foci	Number	Percentage
None/Comet tail artifact	77	82.8
Macrocalcifications	3	3.2
Peripheral rim calcifications	2	2.2
Punctate echogenic foci	11	11.8
Total	93	100

82.8% of cases (n=77) either showed no echogenic foci or comet tail artifacts as shown in Table 6.

Table 7
Risk of malignancy for individual USG feature included in ACR TIRADS 2017

USG feature		Benign lesions	Malignant lesions	Total lesions	Risk of malignancy (%)
Composition	Cystic or predominately cystic	1	0	1	0.0
	Spongiform	6	0	6	0.0
	Mixed solid-cystic	27	20	47	42.6
	Solid or predominately solid	27	12	39	30.8
Echogenicity	Anechoic	6	0	6	0.0
	Hyperechoic or isoechoic	30	7	37	18.9
	Hypoechoic	25	25	50	50.0
Shape	Wider than tall	61	15	76	19.7
	Taller than wide	0	17	17	100.0
Margins	Smooth	52	15	67	22.4
	Lobulated/irregular	8	10	18	55.6
	Extra-thyroidal extension	1	7	8	87.5
Echogenic foci	None/Comet tail artifact	57	20	77	26.0
	Macrocalcifications	3	0	3	0.0
	Peripheral rim calcifications	1	1	2	50.0
	Punctate echogenic foci	0	11	11	100

Among these 57 came out benign and 20 were malignant on FNAC with risk of malignancy 26%. 3 of the cases showed macrocalcifications and all of them turned out to be benign on FNAC. Out of 2 cases which showed peripheral rim calcification, one was benign, and one was malignant on FNAC with malignancy risk of 50%. 11.8% (n =11) cases showed punctate echogenic foci on ultrasonography and all of the cases turned out to be malignant on FNAC, thus carrying a malignancy risk of 100% as shown in Table 7.

Table 8
Histopathological diagnosis of thyroid nodules

Histopathological Diagnosis	Number	Percentage
Benign	61	65.6
Malignant	32	34.4
Total	93	100.0

In our study out of 93 cases, 65.6% (n =61) were benign and 34.4% (n=32) were malignant as shown in Table 8.

Table 9
Distribution of malignant thyroid nodules

Malignant thyroid nodules	Number	Percentage
Papillary carcinoma	17	18.3
Follicular carcinoma	10	10.8
Anaplastic carcinoma	2	2.2
Epithelial carcinoma	1	1.1
Medullary carcinoma	1	1.1
Hurthle cell neoplasm	1	1.1
Total	32	34.4

Among the malignant lesions, papillary cancer was the predominant finding (n=17), in 18.3% of cases. Follicular Cancer was the next common finding (n=10) in 10.8% of cases. Anaplastic carcinoma was found in 2.2%, epithelial cancer in 1.1%, medullary carcinoma in 1.1% cases and hurthle cell neoplasm in 1.1% cases as shown in Table 9.

Table 10
Risk of malignancy according to ACR TIRADS 2017 category

TIRADS category	Benign lesions	Malignant lesions	Total lesions	Risk of malignancy (%)
1	4	0	4	0.0
2	18	0	18	0.0
3	29	4	33	12.1
4	10	18	28	64.3
5	0	10	10	100

All the lesions graded as TIRADS 1 and 2 were found to be benign (risk of malignancy 0%). 33 lesions were graded as TIRADS 3, among them 29 were benign and 4 malignant on FNAC, with risk of malignancy upto 12.1%. 28 lesions were graded as TIRADS 4, among them 18 were malignant nodules and 10 benign with overall risk of malignancy about 64%. Among lesions graded as TIRADS 5 (n=10), all 10 lesions were malignant (risk of malignancy 100%) as shown in Table 10.

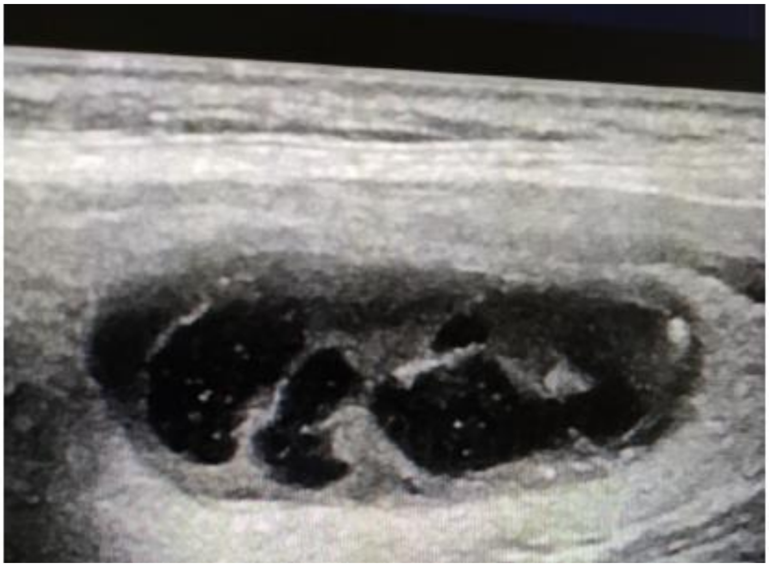
Table 11
Diagnostic accuracy of ACR TIRADS in predicting thyroid lesions

Variable	Value	95% CI
Sensitivity	87.5	71.93-95.03
Specificity	83.6	72.39-90.84
Positive predictive value	73.6	57.99-85.03
Negative predictive value	92.7	82.74-97.14
Diagnostic accuracy	84.9	76.30-90.82

It was observed that USG by TIRADS classification has a sensitivity of 87.5%, specificity of 83.6%. Positive predictive value of 73.6%, negative predictive value of 92.7% and diagnostic accuracy of 84.9%. The p value observed is 0.0001 which is statistically significant as shown in Table 11.

Representative Cases

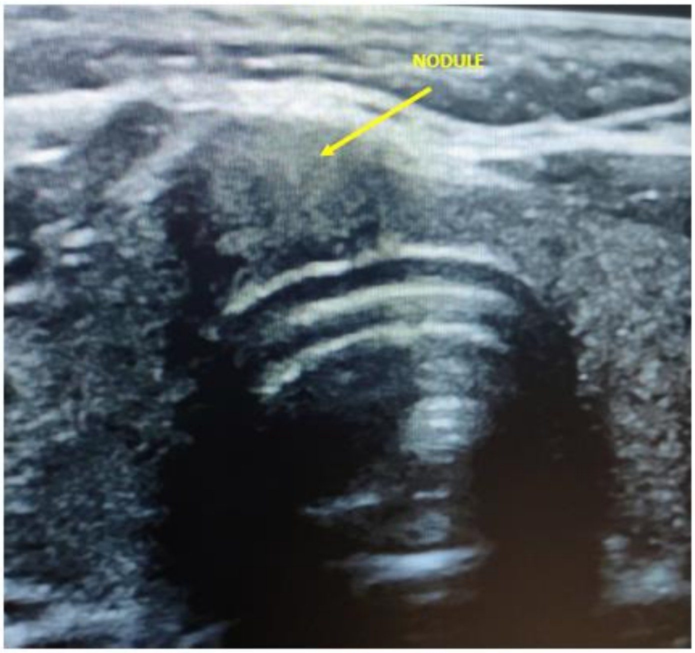
CASE – 1



TIRADS SCORING:

Well defined/smooth:	0
Mixed solid/cystic:	1
Wider than taller:	0
Hyperechoic (solid component):	1
Comet tail artifacts:	0
Total:	2
TIRADS:	2
FNAC finding:	Colloid nodule

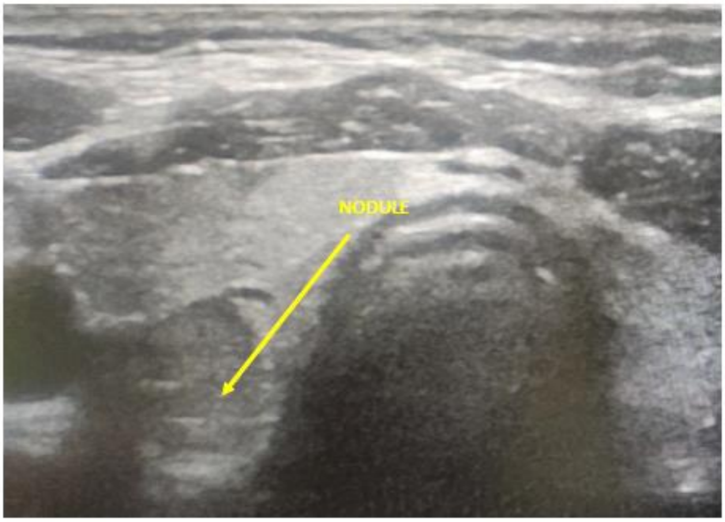
CASE 2:



TIRADS SCORING:

Well defined/smooth:	0
Solid:	2
Taller than wider:	3
Iso/hyperechoic:	1
No echogenic foci:	0
Total score:	6
TIRADS:	4
FNAC finding:	Papillary carcinoma

CASE – 3



TIRADS SCORING:

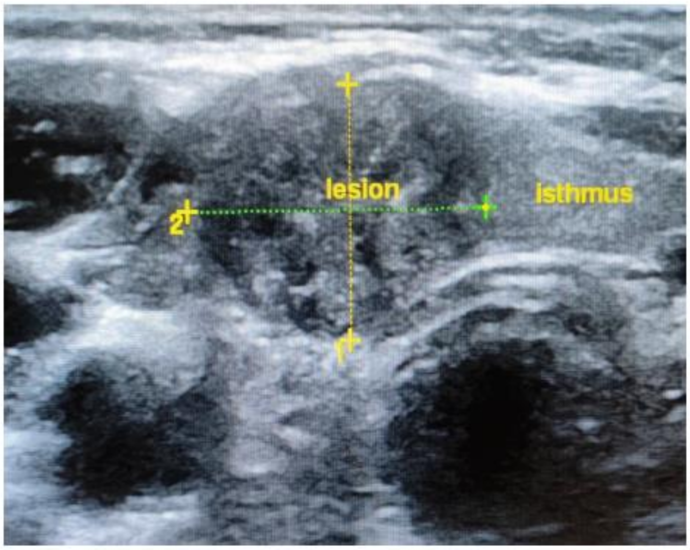
Well defined:	0
Solid:	2
Taller than wider:	3
Hypoechoic:	2
No echogenic Foci:	0
Total score:	7
TIRADS Score:	5
FNAC finding:	Follicular neoplasm

CASE – 4

TIRADS SCORING:

Extra-Thyroidal extension:	3
Solid Score:	2
Iso/Hyperechoic:	1
Taller than wider:	3
Punctate echogenic Foci:	3
Total Score:	12
TIRADS:	5
FNAC finding:	Medullary Carcinoma

CASE – 5



TIRADS SCORING:

Well defined:	0
Solid:	2
Wider than tall:	0
Hypoechoic:	2
Punctate echogenic foci:	3
Total:	7
TIRADS:	5
FNAC finding:	Hurthle cell neoplasm

Discussion

The incidence of thyroid cancers has doubled in the last 30 years, most likely due to advanced screening methods. Therefore, careful screening for timely diagnosis is of utmost importance. The incidence of malignancy in our study was 34.4%. The high incidence of malignancy in our study can be attributed to the fact that suspicious nodules underwent FNAC more frequently. Out of 32 malignant nodules, 17 (18.3%) were papillary carcinoma, 10 were follicular carcinoma (10.8%), 2 were anaplastic carcinoma (2.2%), 1 was epithelial carcinoma (1.1%), 1 was medullary carcinoma (1.1) and 1 was hurthle cell carcinoma (1.1%). Therefore, the most common thyroid malignancy was papillary carcinoma which is also shown by Patil et al [12]. This is also in line with studies conducted by Razmpa et al [13], Papini et al [14] and Khoo et al [15].

In a study conducted by Patil et al [12]it was stated that the risk of malignancy increased from TIRADS category 2 to category 5. They stated that TIRADS category 2 has 0% risk of malignancy. TIRADS 3, 4 and 5 had 6.8%, 21.3% and 80% risk of malignancy respectively. This risk of malignancy in our study for TIRADS category 2, 3, 4 and 5 were 0%, 12.1%, 64.4% and 100% respectively. The results are corresponding to previous studies. In a study by Srinivas MN et al [16] the risk of malignancy in various TIRADS categories was found to be in concordance with our study. Similar findings were seen in a study Bhatnagar S et al [17]. In the study conducted by Patil et al [12] it was observed that risk of malignancy in a nodule of solid composition was 32.6% which is comparable to our study, which showed a malignancy risk of 30.8% in solid nodules. The sensitivity, specificity, positive predictive value for solid composition in our study was 37.5%, 55.7% and 30.8%, which is comparable to a study conducted by Aggarwal SK et al [18]. We also found a higher risk of malignancy in our study for solid-cystic nodules. This can be explained by the fact that in our population iodine deficiency disorders are highly prevalent, thus presence of cystic changes in background thyroid gland is common.

In our present study, we also analysed the sensitivity, specificity, positive predictive value and the negative predictive value for irregular/microlobulated margins. These values are 31.3%, 86.7%, 55.6% and 70.7% respectively with odds ratio of 3.01. Bhatnagar S et al [17] reported the sensitivity, specificity, positive predictive value, negative predictive value for irregular contours as 44.4%, 94.12%, 57.14%, 90.5% respectively. In the study by Patil et al [12] the reported sensitivity, specificity, positive predictive value, and negative predictive value of irregular margins as 21%, 97.6%, 66.6%, 84.6%. Bhatnagar S et al [17] reported that the nodules with taller than wider shape had sensitivity, specificity, positive predictive value, and negative predictive value of 22.22%, 100%, 100% and 87.93% respectively. This is in agreement with our study wherein we found out that taller than wider shape of a thyroid nodule had a sensitivity of 53.1%, specificity of 100%, PPV of 100% and NPV of 87.3%. Patil Y et al [12] reported sensitivity, specificity, positive predictive value and negative predictive value of 42.1%, 97.6%, 80%, 88.3% respectively.

The p-value for taller than wider shape in our study was <0.0001 which is statistically significant. In our study the presence of hypoechogenecity has sensitivity, specificity, positive predictive value and negative predictive value of 78.1%, 59.1%, 50.0% and 83.7% respectively. The p value for hypoechogenecity was <0.0001 which was statistically significant. The odds ratio for hypoechogenecity was 5.14 which means that nodules with hypoechoic nature have five times more risk of being malignant. According to Bhatnagar S et al [17], the sensitivity, specificity, positive predictive value and negative predictive value for hypoechogenecity was 78%, 70.89%, 31.82%, and 94.7% respectively. In the study by Patil et al [12] the sensitivity, specificity, poisitive predictive value and negative predictive value for hypoechogenecity was 84.2%, 88.2%, 61.5% and 96.1 % respectively. Both these studies conclude that a nodule with hypoechoic character has increased risk of malignancy which is in agreement with our study. A study by Preeti D et al [19] observed that TIRADS classification has a sensitivity of 85.7%, specificity of 96.36%, PPV of 75% and NPV of 98.14%. Another study by Tamer YM et al [20] observed the sensitivity, specificity, PPV, NPV of TIRADS to be

83.3%, 92.9%, 83.3% and 92.9% respectively. Our study concluded that USG by TIRADS has a sensitivity of 87.5%, specificity of 83.6%. Positive predictive value of 73.6%, negative predictive value of 92.7% and diagnostic accuracy of 84.9%. The p value observed is 0.0001 which is statistically significant.

According to the present study, TIRADS category 1 and 2 have 0% risk of malignancy with the risk of malignancy in TIRADS categories 3, 4 and 5 being 12.1%, 64.3% and 100% respectively. So, the nodules which fall in TIRADS category 3 and less than 3 do not need FNAC. They need a short term follow up every 6 months to determine the stability of the lesions. Follow up of atleast 2 years is recommended as thyroid malignancies tend to grow slowly. Only the nodules included in TIRADS 4 and 5 need FNAC to differentiate between benign and malignant thyroid nodules. The sonographic features like irregular margins, microlobulated margins, marked hypoechogenicity, micro-calcification and taller-than-wider shape are all associated with increased risk of malignancy. We also saw increased risk of malignancy in solid cystic nodules due to increased prevalence of pre-existing iodine deficiency disorders in our population. Sonographic features like completely cystic nodule, isoechogenicity or hyperechogenicity, macrocalcification are predictive of benignity. In conclusion high resolution ultrasound is an accurate technique to assess the morphology of thyroid nodules. Describing the findings using standard lexicon and categorizing using TIRADS achieves the following; It ensures objectivity in reporting, malignant lesions are identified with high accuracy, aids in clinical decision making, prevents unnecessary FNACs and avoids unnecessary patient discomfort, cost and wastage of resources.

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