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ROLE OF ULTRASONOGRAPHY & COLOR DOPPLER IN THE EVALUATION OF THYROID NODULES WITH HISTOPATHOLOGICAL CORRELATION

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ABSTRACT: PURPOSE OF THE STUDY: 1. To identify morphologic patterns on sonography, those are predictive of benign thyroid nodules and malignant thyroid nodules. 2. To evaluate the efficacy of sonography in differentiating benign and malignant thyroid nodules in comparison with histopathology. **MATERIALS AND METHODS:** HRS of thyroid was performed in 60 patients with clinically palpable STN, referred to Department of Radiodiagnosis, R. L. Jssalappa Hospital and Research Centre, Tamaka, Kolar, Karnataka over a period of 24months, using SIEMENS ACCUSON X 300 and SIEMENS G 50 with 5-10 MHz transducers. Thyroid sonographic findings relevant to benign or malignant thyroid nodules were recorded and these findings were compared with histopathology reports. **RESULTS:** Out of 60 cases of solitary thyroid nodules evaluated at sonography, 41 were diagnosed to be benign thyroid nodules. 19 were malignant thyroid nodules. After histopathological evaluation, 43 cases were found to be benign thyroid nodules and 17 were malignant thyroid nodules. Among benign thyroid nodules, follicular adenoma 55.8% (24 cases)was most common followed by nodular hyperplasia 27.9% (12 cases)and colloid nodule 16.3%(7 cases). Among malignant nodules, papillary carcinoma 88.2% (15 cases) was most common followed by follicular carcinoma 11.8% (2 cases). **CONCLUSION:** Thyroid nodules were more common in the females of age group 31 – 45 years. Sonography is a safe, fairly accurate investigation to differentiate benign from malignant thyroid nodules with sensitivity of 82.3 % and specificity of 88.3 %.
KEYWORDS: solitary thyroid nodule; high resolution sonography; histopathology.

INTRODUCTION: Thyroid nodule is a discrete lesion and a common clinical condition. Solitary thyroid nodules are commonly being present in up to 50% of the elderly population. Thyroid nodules are found in up to 20% clinically by palpation and in up to 70% on sonographic studies.[1] The thyroid gland is unique among endocrine glands, in that it is the first endocrine gland to appear in the fetus. It is the largest of all endocrine glands (Weighing about 25 gm) and is the only one which is amenable to direct physical examination because of its superficial location.[2] One or more additional non-palpable thyroid nodules may be found by sonography in about 50% of patients with a clinically palpable solitary nodule and they are also incidentally detected by imaging studies performed for various reasons.[3]

STN is one of the commonest thyroid disorders. STN is common in females than males with a ratio of 5:1 and prevalence mainly depends on age, sex, iodine intake, diet and environmental exposure, though STN is common in women, malignancy in STN is common in men.[4]

Sonography is a choice of investigation in evaluation of thyroid nodules. The high resolution sonography has resulted in discovery of large number of thyroid nodules which are obscured

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clinically. Many sonographic features have been described to differentiate benign nodules from malignant nodules.[5] For each thyroid nodule, gray scale and color Doppler ultrasound are used to evaluate the sonographic features, which include shape, echogenicity (Hypoechoic or isoechoic or hyperechoic), composition (Solid, purely cystic, cyst with thin septa, mixed and spongiform), margin, halo, as well as presence or absence of coarse / microcalcification, vascularity of the nodule and presence or absence of regional lymphnodes.[6]

Sonographic features which may be highly predictive of benign nodule on the basis of certain characteristics which includes wider than tall in shape, hyperechoic or isoechoic, solid nodule or purely cystic / cystic with thin septa / mixed / spongiform, well-defined margins, complete peripheral halo, coarse or egg shell peripheral calcification and perinodular vascularity.[7]

Sonographic features which may be highly predictive of malignant nodule are taller than wide shape, predominantly hypoechoic or hyperechoic, solid nodule, ill-defined margins, incomplete peripheral halo, microcalcification, intranodular vascularity, regional lymphadenopathy and local invasion of adjacent structures.[8]

Prediction of malignancy using sonography still remains difficult. Since there is overlap of sonographic features between benign and malignant thyroid nodules, as it is not possible to distinguish a benign follicular adenoma from follicular carcinoma by sonography, FNAC, core biopsy and frozen sections, as vascular and capsular invasion can only be evaluated on histological specimen, so sonographic features are usually corroborated with histopathology results in differentiating various thyroid nodules.[9]

The goal in evaluating a thyroid nodule is to determine whether it is benign nodule or malignant nodule so that patients can undergo treatment at an earlier stage to reduce possible morbidity and mortality due to the disease, while avoiding unnecessary tests and surgery in patients with benign nodules.[11]

MATERIALS AND METHODS: All patients referred for HRS of the thyroid with clinically suspected STN to department of Radiodiagnosis at R. L. Jalappa Hospital and research centre, Kolar are taken for the study.

Total 60 cases who were diagnosed clinically with solitary thyroid nodule in R. L. Jalappa Hospital and research centre, Kolar, over a 24 months study period from December 2010 to November 2012.

INCLUSION CRITERIA:
- All patients with clinical diagnosis of solitary thyroid nodule who are 18 yrs of age and above.

EXCLUSION CRITERIA:
- Patient with diffuse thyroid disease.
- Patients with multinodular goiter.

Method of Performing Examination: Sonography of neck was performed by using SIEMENS ACCUSON X 300 & SIEMENS G 50 with 5-10 MHz transducers.

Thyroid ultrasound was performed with the patient in supine position and with a pillow placed between the shoulders to allow hyperextension of the neck and to elevate the thyroid gland

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away from sternal notch area. The entire thyroid was scanned from upper to the lower pole and the isthmus in the longitudinal and transverse planes.

Sonographic features of thyroid nodule were noted in the prepared proforma, with these sonographic features the thyroid nodule was predicted as benign or malignant, later these patients underwent surgery.

The data collected from these patients was analyzed using descriptive tools like specificity, sensitivity and predictive value of sonographic diagnosis on comparison with histopathological diagnosis.

RESULTS: The present study deals with results of sonography of the thyroid nodule regarding prediction of benign and malignant nodule in comparison with histopathological diagnosis.

	Number of cases (n=60)	Percentage (%)
Benign	41	68.3%
Malignant	19	31.7%
Total	**60**	**100**

TABLE 1: INCIDENCE OF NODULES ON SONOGRAPHY

Age (years)	Number of cases (n= 60)	Percentage (%)
21-30	13	21.7%
31-40	24	40%
41-50	14	23.3%
51-60	8	16%
61& above	1	2%
Total	**60**	**100%**

TABLE 2: AGE INCIDENCE OF STN ON SONOGRAPHY

Sex	Number of cases(n=50)	Percentage (%)
Female	51	85%
Male	9	15%
Total	**60**	**100%**

TABLE 3: SEX RATIO

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Location	Number of cases(n=50)	Percentage (%)
Right lobe	39	65%
Left lobe	19	31.7%
Isthmus	2	3.3%
Total	**60**	**100%**
TABLE 4: LOCATION OF NODULES ON SONOGRAPHY		

SL. No.	Morphologic Pattern	No. of cases	Benign	Malignant
1.	Spongiform	2	2	-
2.	Cyst with colloid clot	3	3	-
3.	Giraffe	-	-	-
4.	White knight	13	12	1
5.	Red light	4	1	3
6.	Hypoechoic	13	1	12
7.	Isoechoic without halo	8	2	6
8.	Isoechoic with halo	9	7	2
9.	Ring of fire	3	2	1
10.	Mixed	2	1	1
TABLE 5: MORPHOLOGIC PATTERNS ON SONOGRAPHY AS DESCRIBED(By waters et al)[5]				

Category	AP/TRANS ratio		Total (%)
	< 1cm	> 1cm	
Benign	35(85.4%)	6(14.6%)	41(100%)
Malignant	4(21.1%)	15(78.9%)	19(100%)
TABLE: 6 DISTRIBUTION OF AP/TRANS RATIO ACCORDING TO SONOGRAPHIC DIAGNOSIS			

Category	Echotexture				Total (%)
	Hyperechoic	Isoechoic	Hypoechoic	Anechoic	
Benign	14 (34%)	17(41.6%)	3(7.3%)	7(21.2%)	41(100%)
Malignant	1(5.2%)	4(21.2%)	14(73.6%)	-	19(100%)
TABLE: 7 DISTRIBUTION OF ECHOTEXTURE ACCORDING TO SONOGRAPHY DIAGNOSIS					

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Category	Internal contents					Total (%)
	Solid	Purely cystic	Cyst with thin septa	Mixed	Spongiform	
Benign	34(82.9%)	1(2.4%)	3(7.3%)	1(2.4%)	2(6%)	41(100%)
Malignant	18(94.7%)	-	-	1(5.3%)	-	19(100%)
TABLE: 8 DISTRIBUTION OF COMPOSITION ACCORDING TO SONOGRAPHY DIAGNOSIS						

Category	Margin		Total (%)
	Well-defined	Ill-defined	
Benign	36(87.8%)	5(12.2%)	41(100%)
Malignant	2(10.5%)	17(89.5%)	19(100%)
TABLE: 9 DISTRIBUTION OF MARGIN ACCORDING TO SONOGRAPHY DIAGNOSIS			

Category	Halo		Total (%)
	Peripheral complete halo	Peripheral incomplete halo	
Benign	29 (90.6%)	3(9.4%)	32(100%)
Malignant	5(26.4%)	14(73.6%)	19(100%)
TABLE: 10 DISTRIBUTION OF HALO ACCORDING TO SONOGRAPHY DIAGNOSIS			

Category	Calcification			Total
	Coarse	Micro	Peripheral EGG shell	
Benign	6(67%)	1(11%)	2(22%)	9(100%)
Malignant	1 (6.7%)	14(93.3%)	-	15(100%)
Total	7	15	2	24
TABLE 11: DISTRIBUTION OF CALCIFICATION ACCORDING TO SONOGRAPHY DIAGNOSIS				

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Category	Vascularity		Total (%)
	Intranodular	Perinodular	
Benign	2 (7.7%)	24 (92.3%)	26(100%)
Malignant	15(78.9%)	4 (21.1%)	19(100%)
Total	**17**	**28**	**45**
TABLE 12: DISTRIBUTION OF VASCULARITY ACCORDING TO SONOGRAPHY DIAGNOSIS			

HISTOPATHOLOGICAL DIAGNOSIS

Benign nodules	Number of cases (35)	Percentage (100%)
Follicular adenoma	24	55.8%
Nodular hyperplasia	12	27.9%
Colloid nodule	7	16.3%
TOTAL	**43**	**100%**
TABLE 13: TYPES OF BENIGN NODULES		

Malignant lesions	Number of cases(15)	Percentage (100%)
Papillary carcinoma	15	88.2%
Follicular carcinoma	2	11.8%
Medullary carcinoma	-	-
TABLE 14: TYPES OF MALIGNANT NODULES		

|		HISTOPATHOLOGY		
H		**Benign**	**Malignant**	**TOTAL**
R	Benign	38	3	41
S	Malignant	5	14	19
	TOTAL	**43**	**17**	**60**
TABLE 15: COMPARISION OF SONOGRAPHY WITH HISTOPATHOLOGY				

SENSITIVITY- 82.3%
SPECIFICITY- 88.3%
POSITIVE PREDICTIVE VALUE-73.6%
NEGATIVE PREDICTIVE VALUE-92.6%

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SONOGRAPHY MORPHOLOGIC FEATURES OF BENIGN NODULES

Case 1: 45 year male with colloid clot. Transverse sonographic image of the left thyroid lobe shows cyst with colloid clot (arrow) which does not shows vascularity on color Doppler image and also showing comet- tail artifacts (arrow head).
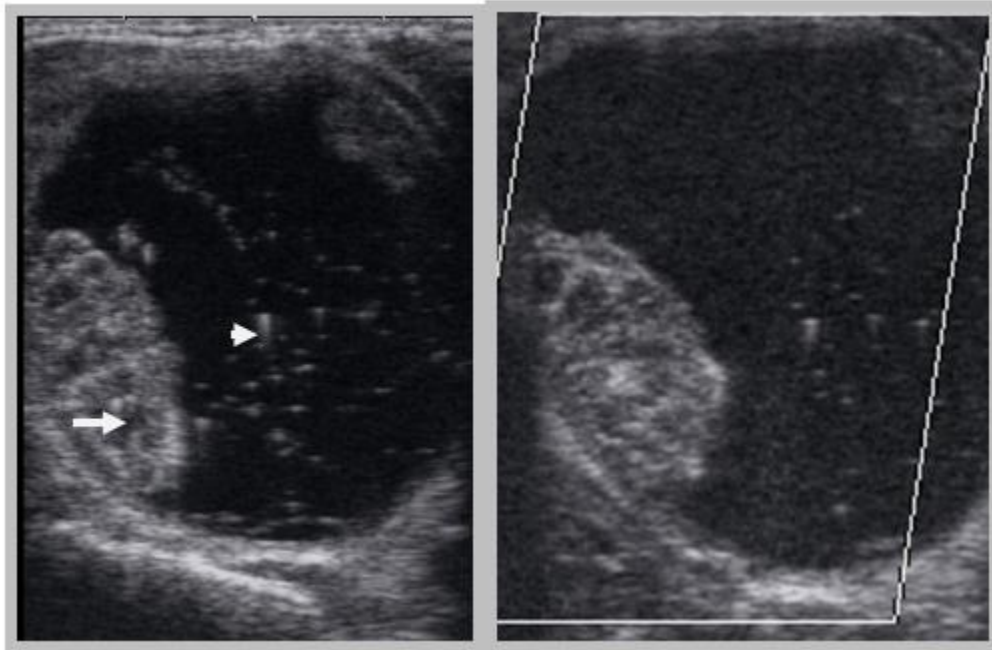
Case 1

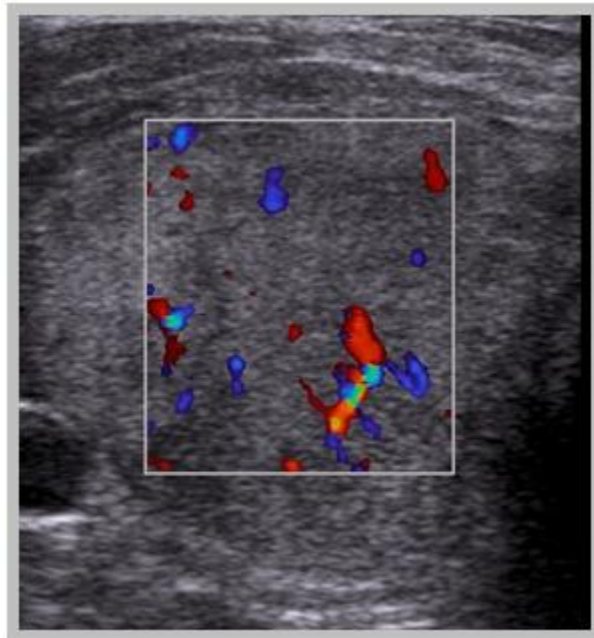**Case 2:** 30 year female. Transverse gray scale sonographic image of the right thyroid lobe shows mixed nodule (Both cystic and solid) suggestive of benign nodule.

Case 2

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Case 3: 32 year female with follicular adenoma. Transverse Doppler sonographic image of the right thyroid lobe shows hypervascular nodule.

Case 3

Case 4: 21 year female with nodular hyperplasia. Transverse gray scale sonographic image of the right thyroid lobe shows circumscribed homogenous isoechoic nodule with complete hypoechoic peripheral halo.
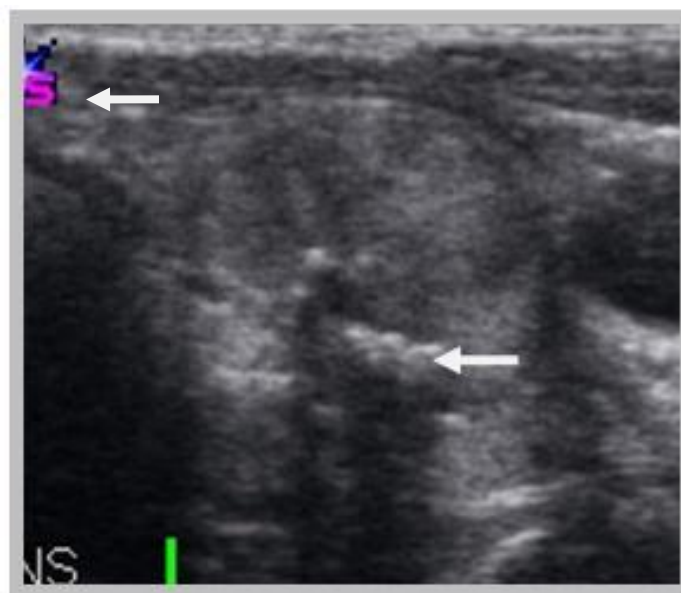

Case 4

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Case 5: 35 year female. Transverse gray scale sonographic image of the left thyroid lobe shows peripheral egg shell calcification (Arrow) suggestive of benign nodule.

Case 5

Case 6: 42 year male. Longitudinal gray scale sonographic image of the left thyroid lobe shows circumscribed homogenous isoechoic nodule with coarse calcifications (arrow) suggestive of benign nodule.
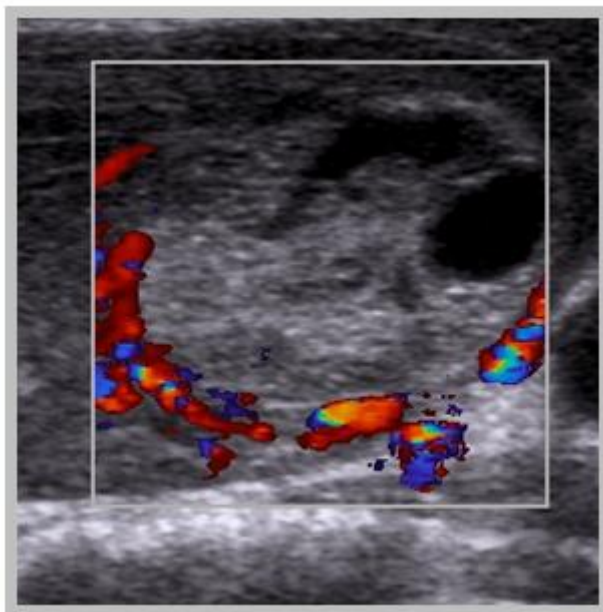

Case 6

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Case 7: 55 year female with hyperplastic nodule. Longitudinal Doppler image of the left thyroid lobe shows peripheral hypervascularity.

Case 7

## SONOGRAPHIC MORPHOLOGIC FEATURES OF MALIGNANT NODULES

Case 8: 41 years female with papillary carcinoma. Transverse gray scale sonographic image of the right thyroid lobe shows a circumscribed hypoechoic nodule with incomplete peripheral halo (arrow).

Case 8

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Case 9: 62 year male with papillary carcinoma. Longitudinal gray scale sonographic image of the right thyroid lobe shows homogenous hypoechoic nodule with ill-defined borders and shows internodular vascularity.
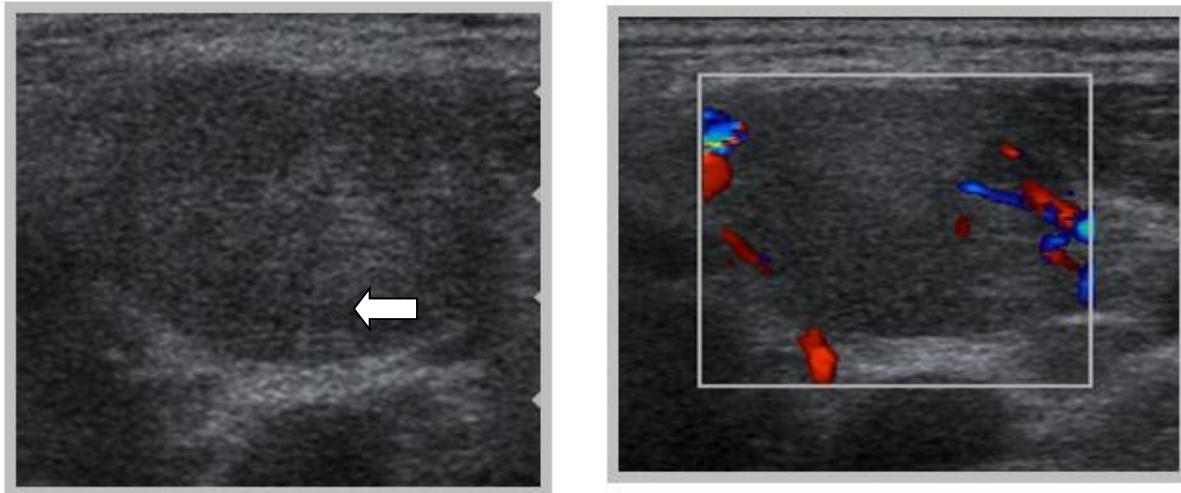

Case 9

Case 10: 45 year female with papillary carcinoma. Longitudinal gray scale sonographic image of the left thyroid lobe shows micro-calcifications and refractive shadows from edge of a solid nodule (arrow).

Case 10

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Case 11: 25 year female with follicular neoplasm. Longitudinal sonographic image of the left thyroid lobe shows solid homogenous egg shaped nodule with thin capsule with intranodular vascularity on color Doppler image which proved to be follicular carcinoma on histopathology.
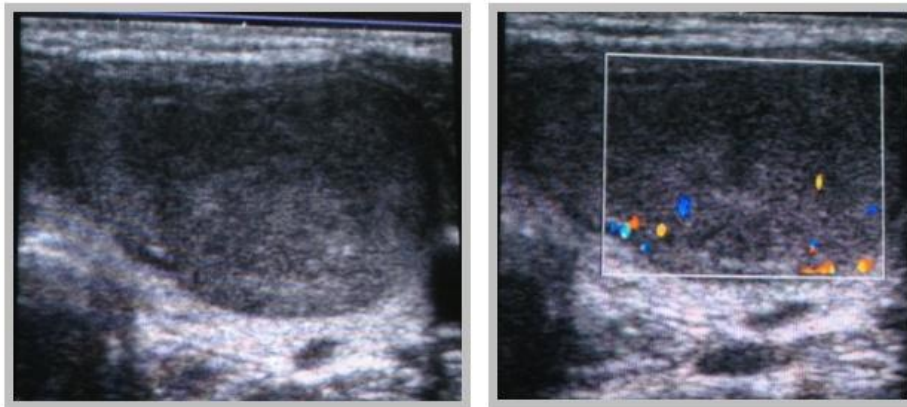
Case 11

HISTOPATHOLOGY IMAGES

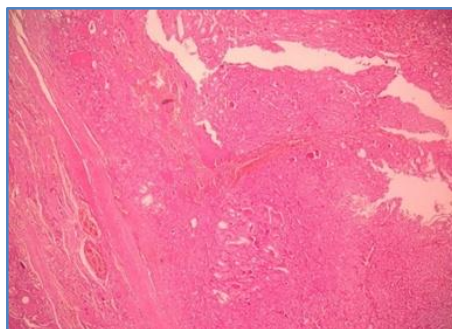**FIG. 1:** Microphotography showing Nodular Hyperplasia.

Fig. 1

FIG. 2: Microphotography showing Follicular adenoma.
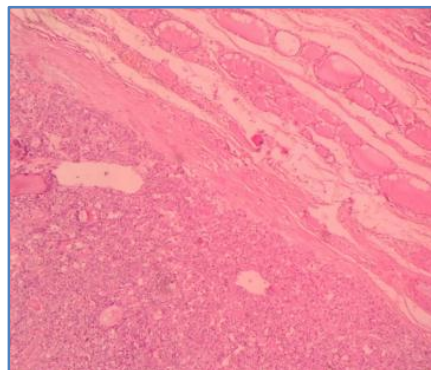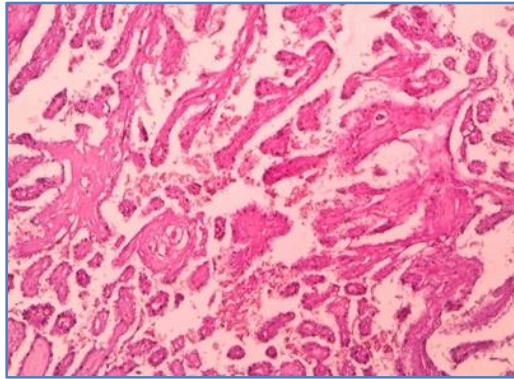

Fig. 2

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FIG. 3: Microphotography showing Papillary Carcinoma.

Fig. 3

DISCUSSION: Sonography is a choice of investigation in evaluation of thyroid nodules. The high resolution of ultrasound has resulted in discovery of large number of thyroid nodules which are obscured clinically. Many sonographic features have been described to differentiate benign and malignant nature of the nodule. The present study was done on 60 patients.

The study done by Burch HB et al showed that highest age incidence thyroid nodule is between 21-50 years, the maximum being 31-40 years.[12] In the present study the commonest age group affected was 31-40 years.

The study done by Tsegaye et al showed that females are more commonly affected than males with male to female ratio was about 1:4.1.[13] In present study female predominance (85%) was noted with a male to female ratio of 1:5.6 and correlates with the above study.

The study done by Horwath E et al showed that 71% of nodules commonly occur in right thyroid lobe.[14] In the present study 65% of nodules occurred in right thyroid lobe and followed by 31.7% in left thyroid lobe.

The study done by Watters et al showed that four specific morphologic features such as spongiform configuration, Cyst with colloid clot, Giraffe pattern and diffuse hyperechogenicity are predictive of benign thyroid nodules and had 100% specificity for benignity that do not require biopsy.[5] In the present study, nodules with spongiform configuration, cyst with colloid clot and diffuse hyperechogenicity were diagnosed as benign lesions on HRS and were confirmed by histopathology reports which correlates with the above study. There is no giraffe pattern in the present study.

The study done by Grabe SK et al showed that AP/TRANS ratio < 1was noted in 95.3 %of benign nodules and AP/TRANS ratio > 1 was noted in 83.7 % of malignant nodules.[15] In present study AP/TRANS ratio < 1 was noted in 85.4 % of benign nodules and AP/TRANS ration > 1 was noted in 78.9 % of malignant nodules which correlates with the above study.

The study done by Kim et al showed that 55% of hyperechoic, 42% isoechoic nodules and 3% of hypoechoic are benign nodules and 80% of hypoechoic nodules and 20% of isoechoic nodules are malignant nodules.[16] In the present study, 34% of hyperechoic nodules, 41.6% of isoechoic nodules and 7.3% of hypoechoic nodules were benign.73.6%of hypoechoic nodules and 21.2% of isoechoic nodules were malignant.

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The study done by Hegde A et al showed that most benign and malignant nodules are solid, making it difficult to use this criterion for differentiating the two.[17] In present study shows 82.9% of benign nodules were solid, whereas 94.7% of malignant nodules were solid.

The study done by Papini E et al showed that nodule had well defined margin were benign and nodule had ill-defined margin were mostly malignant nodules. [18] In the present study, 87.8% of nodules had well-defined margins and 5% of nodule had ill-defined margins were benign nodules and 89.5% of the nodules had ill-defined margins and 10.5% well-defined margins were malignant nodules.

The study done by Wienke JR et al showed that 93.7% had peripheral complete halo in benign nodules and 83.3 % had peripheral incomplete halo in malignant nodules.[19] In the present study 90.6% of the nodules which had peripheral complete halo were benign nodules and 73.6% of the nodules which had peripheral incomplete halo were malignant nodules.

The study done by Wienke JR et al showed that coarse calcification seen in 72% and peripheral egg shell calcification seen in 35% of benign nodules, whereas microcalcification seen in 16% of malignant nodules.[19] In present study coarse calcification were seen in 67 % and peripheral egg shell calcification in 22 % of benign nodules and microcalcification was seen in 93.3 % of malignant nodules.

The study done by Propper RA et al showed that perinodular vascularity is seen in benign nodules and intranodular vascularity is seen in malignant nodules.[20] In the present study perinodular vascularity was seen in 92.3 % of benign nodules and 21.1% of malignant nodules, whereas intranodular vascularity was seen in 78.9 % of malignant nodules.

In the present study of 60 cases of solitary thyroid nodules, Sonographic diagnosis was made as benign in 41 cases, 38 cases were confirmed as benign by histopathology. Remaining 3 cases were diagnosed as malignant by histopathology. Sonologically these 3 cases showed features of benign nodule such as AP/TRANS ratio < 1, isoechoic nodule, well defined, peripheral thick complete halo.

In the present study of 60 cases, Sonographic diagnosis was made as malignant in 19 cases, 14 cases were confirmed as malignant by histopathology. Remaining 5 cases were diagnosed as benign by histopathology. Sonologically these 5 cases showed features of malignant nodule such as AP > 1, isoechoic nodule, peripheral complete halo and intranodular vascularity.

The sonographic mismatch of predicting benign and malignant nodules in the present study was mainly noted in cases of follicular adenoma and follicular carcinoma. They both differ only in the vascular and capsular invasion which is very difficult to diagnose on sonography. Hence in such cases histopathological examination only gives the correct diagnosis.

The study done by Jones et al showed that sonography has sensitivity of 75 % and specificity of 83 % in differentiating benign from malignant nodules.[21] In present study, sonography was able to differentiate benign from malignant nodules with sensitivity of 82.3% and specificity of 88.3 % which correlates with above study.

CONCLUSION: The incidence of STN was more common in female population. The peak incidence of STN was found in the age group of 31-40 years.

From the present study it was noted that sonographic features such as wider than tall in shape, isoechogenicity / hyperechogenicity, purely cystic nodule / cystic with thin septa / spongiform appearance, well defined margins, peripheral complete halo, egg shell / coarse calcification, comet tail artifact and perinodular vascularity are highly predictive of benign nodules.

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Sonographic features such as taller than wide shape, markedly hyperechogenicity / hypoechogenecity, ill-defined margins, peripheral incomplete halo, microcalcification and intranodular vascularity with or without perinodular vascularity are highly predictive of a malignant nodule.

Sonography is specific (88.3%) and sensitive (82.3 %) in differentiating benign from malignant nodule.

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