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Original Research Article

Evaluation of thyroid nodules by Gray scale and Doppler sonography and correlation with fine needle aspiration cytology

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ABSTRACT

Background: Nodular goiter is a worldwide disease and is encountered commonly in clinical practice by primary care physicians, endocrinologist, surgeons and otolaryngologists. The solitary thyroid nodule is common presentation & the incidence of carcinoma in single thyroid nodule is between 8-20% and in multinodular goiter is about 5%. Ultrasonography (USG), both Gray scale and color Doppler is useful in diagnosis of various thyroid lesions and can be utilized to correlate USG features with histopathological findings wherever possible.
Methods: The present study was conducted in the Department of Radio Diagnosis and Modern Imaging, Govt. Medical College, Kota, Rajasthan, India. Participants after understanding the study protocol and procedure, were asked to give their written consent for the study. Cross sectional study was conducted with 50 patients of all age group presenting with thyroid nodule. 50 patients of all age group attending outdoor and indoor of E.N.T. and other surgical department of this hospital presenting with thyroid nodule.
Results: Out of 50 cases, majority of patients were between 21-40 years of age, most of the malignant cases were in 41-50 years of age group. Majority had involvement of right lobe of thyroid (44%), 74% had single thyroid nodule. Lesions having multiple nodules were mostly benign in nature. Malignant lesions were mostly seen in single thyroid nodule. Higher resistive index (RI) value (in 83.3% cases) and lower peak systolic velocity (PSV) (in 100% cases) were found in malignant lesion as compared to benign lesion. Thus, pulse Doppler study has found to be very useful in deciding the nature of the lesion. Most common malignancies are anaplastic carcinoma and Squamous cell carcinoma. All cases diagnosed malignant on USG were proved to be malignant on fine needle aspiration cytology (FNAC) and vice versa.
Conclusions: An excellent correlation was seen in diagnosis of thyroid lesions between sonography (Gray scale, color Doppler flow Imaging (CDFI) and power Doppler (PD)) and histopathology. Sonography (Gray scale and Doppler together) was 98% sensitive in diagnosis of thyroid lesions.

Keywords: Carcinoma, Doppler, FNAC, Gray scale, Thyroid nodule, USG

INTRODUCTION

Thyroid gland is unique among endocrine glands in that it is the first endocrine gland to appear in the fetus, largest of all endocrine glands (Weighing about 25 gm) and because of its superficial location it is only one, which is amenable to direct physical examination. Thyroid is common site of both benign and malignant conditions

therefore early diagnosis is very important for better management and survival of patient.

Nodular goiter is a worldwide disease and is encountered commonly in clinical practice by primary care physicians, endocrinologist, surgeons and otolaryngologists. Nodular goiter is common in women than in men, with advancing age and after exposure to external irradiation. They may be asymptomatic with normal TSH (Nontoxic) or may be associated with systemic thyrotoxic symptoms (Toxic Multinodular goiter or Plummer's disease).

The solitary thyroid nodule is common presentation and the incidence of carcinoma in single thyroid nodule is between 8-20% and in multinodular goiter is about 5%. This concern is warranted as the most neoplasm originate in a focus of replicating cells and present as solitary thyroid nodule in early stage of malignancy. Various imaging modalities have been used in diagnosis of thyroid disease. Plain X-Ray film has a limited role in thyroid disorder, but may be useful in assessment of retrosternal extension and tracheal displacement. Radionuclide imaging provides functional information that complements the anatomical information obtained by ultrasound. Technetium - 99 m per technetate is most widely used thyroid imaging agent and is used as a 1st line diagnostic tool in the evaluation of the thyroid. Other agents used to image the thyroid are 123I, 131I, Thallium- 201, 99m Tc- MIBI, MIBG, and 99m Tc DMSA.

Ultrasound was first used to study the thyroid gland in 1967, primarily to distinguish solid lesions from cystic lesions.[1] Ultrasonography is often first modality used to image the thyroid gland because it is convenient, inexpensive, quick and easy to perform without ionizing radiation. USG readily identifies and distinguishes between cystic and solid lesions. Limitations of USG include difficulties in evaluating ectopically located thyroid tissue, predicting the functional status of thyroid nodule and surveying the neck for metastatic lymphadenopathy. Addition of color Doppler and pulse Doppler sonography has further increased the diagnostic accuracy of thyroid disease by providing information about vascularity and morphology of lesion.

Computed tomography (CT) is excellent at characterizing density of thyroid lesion. Thus, defining presence of calcification, cysts, or hemorrhage. The borders of thyroid mass are usually well delineated by CT. An advantage of CT is that entire neck as well as mediastinum can be surveyed for metastatic lymphadenopathy and ectopic thyroid tissue. Computed tomography (CT) is inferior to Ultrasound for differential diagnosis of thyroid nodules.

Magnetic resonance imaging (MRI) of thyroid like CT can be used to evaluate the content of entire neck. Yousem et al concluded that advantage of MRI over CT includes improved soft tissue discrimination and lack of beam hardening artifacts; however, MRI is not superior in identification of malignant lymphadenopathy.[2]

The present study was undertaken to assess the usefulness of USG both gray scale and color Doppler in various thyroid lesions and to correlate these features with histopathological findings wherever possible.

METHODS

The present study was carried out in the department of Radio diagnosis, Govt. Medical College and Associated M.B.S. Hospital, Kota. The group under study was comprised of 50 patients of all age group attending outdoor and indoor of E.N.T. and other surgical departments of this hospital with a thyroid nodule.

The examination was conducted in the manner described below and details were recorded in predesigned performa.

Clinical assessment

Relevant history was taken about clinical symptoms and the presenting complaints. Physical examination was also carried out.

Radiological examination

Ultrasonography (USG)

Real time Gray scale USG and Color Doppler study was done using high frequency linear probe of 7-12 MHz on Siemens G-60S machine. The selected images in different planes were stored on hard disc. The examination was also extended laterally to include the region of carotid artery and jugular vein to identify enlarged jugular chain lymph nodes, superiorly to visualize submandibular adenopathy and inferiorly to define any pathologic supraclavicular lymph nodes. For Gray scale imaging, meticulous attention was given to set gains and time gain compensation (TGC) to prevent masking of pathology and to maximize contrast resolution respectively. There after Color Doppler flow Imaging (CDFI) was performed to depict flow in thyroid vessels. Superior, inferior thyroid vessels and intra parenchymal vessels were identified wherever possible the Doppler controls were optimized to detect low flow. The scale or pulse repetition frequency (PRF) was set as low as possible. The color gain was set high and then adjusted until background "noise" just disappears. Thereafter, power Doppler (PD) mode was applied to area of interest.

Sonographically the thyroid nodule was evaluated for size, shape, location, echotexture, margins, presence of halo, calcification, accessory nodules and associated cervical lymphadenopathy. Vascularity of nodule was evaluated by parameters like peak systolic velocity (PSV), end diastolic velocity (EDV), pulsality index (PI) and resistive index (RI). State of adjacent great vessels and neck muscles were evaluated.

Vascularity of lesions was evaluated with both color and power Doppler as follows:

- Type I: Absence of blood flow
- Type II: Perinodular blood flow
- Type III: Intranodular, with or without perinodular blood flow.

Computed tomography

CT neck and upper chest was done in patients with retrosternal goiter and metastatic lymphadenopathy.

Laboratory investigation

Relevant investigations like T3, T4 and TSH were done as required.

Finally, collected data were analyzed to arrive at definitive diagnosis. Ultra-sonographic findings were correlated with clinical and laboratory parameters to arrive at final diagnosis. All cases were properly followed up sonographically, surgically or pathologically as per indication to arrive at final diagnosis.

Statistical analysis was done by standard statistical methods.

RESULTS

Maximum number of cases were seen in 31-40 years of age group, all of which were benign. Most of the malignant cases were seen in 41-50 years of age group. 40 patients are female and 10 patients are male. Out of 40 female patients, 37 had benign and 3 had malignant lesion and out of 10 male patients, 7 have benign and 3 have malignant lesion.

Table 1: Age wise distribution of cases.

Age (in years)	No. of cases (n=50)			Percentage
	Benign	Malignant	Total	
0-10	0	0	0	0
11-20	3	0	3	6
21-30	14	0	14	28
31-40	18	0	18	36
41-50	5	3	8	16
51-60	4	1	5	10
61-70	0	1	1	2
71-80	0	1	1	2

In maximum number of cases (22), right lobe of thyroid was involved. In one case, whole gland was affected. Single thyroid nodule was present in 37 patients out of them, 32 were benign and 5 were malignant. Lesions having multiple nodules are mostly benign in nature.

Most common echotexture pattern was mixed echoic which was seen mostly in benign cases. Malignancy was more common in hypoechoic nodule. Isoechoic, cystic and hyperechoic nodules were mostly benign. 45 patients were having nodules with regular margins, out of those 44 cases were benign and one case was malignant. Irregular margins of thyroid nodules were seen in 5 patients, which were all malignant. Nodular calcification was found in 3 patients out of these, 2 cases were benign and one case was malignant. Fine calcification was found in 3 patients. Out of these, 2 cases were malignant and one case was benign. Coarse calcification was found in 3 patients, which all were benign. Halo in thyroid nodule was absent in 32 patients. Out of these, 26 cases were benign and 6 cases were malignant while Halo was present in 18 patients, which all were benign in nature.

Table 2: Echotexture of thyroid nodules.

Echotexture	No. of cases				Total
	Benign		Malignant		
	No.	%	No.	%	
Mixed echoic	26	52%	1	2%	27
Hypo-echoic	3	6%	5	10%	8
Iso-echoic	8	16%	0	0%	8
Cystic	6	12%	0	0%	6
Hyper-echoic	1	2%	0	0%	1

Table: 3: Color Doppler of thyroid nodule.

Type of blood flow	No. of cases				Total (%)
	Benign		Malignant		
	No.	%	No.	%	
Absent blood flow	25	50%	0	0%	25 (50%)
Perinodular blood flow	10	20%	0	0%	10 (20%)
Intranodular with or without Perinodular blood flow	9	18%	6	12%	15 (30%)

Table 3 shows that absent blood flow was noted in 25 patients, which all were benign and Perinodular blood flow was noted in 10 patients, which all proved benign. Intranodular with or without perinodular blood flow was noted in 15 patients. Out of those 9 cases were benign and 6 cases were malignant.

Table 4: Pulse Doppler of thyroid nodule.

Spectral analysis	No. of cases				Total
	Benign		Malignant		
	No.	%	No.	%	
R.I. >0.75	0	0%	5	10%	5
<0.75	44	88%	1	2%	45
PSV(Cm./Sec.)					
> 20.4	44	88%	0	0%	44
<20.4	0	0%	6	12%	6

Cut off value of RI for malignant nodule was > 0.75 which was seen in 5/6 malignant cases.

Cut off value of PSV for malignant nodule was < 20.4 cm/sec. which was seen in all malignant cases (Table4).

Out of 6 malignant cases, regional lymphadenopathy was absent in 2 malignant cases and was present in 4 cases.

Table 5: Distribution of benign cases (n=44).

Diagnosis	No. of cases	Percentage
Colloid goiter	32	72.72%
Nodular goiter	6	13.63%
Thyroid cyst	1	2.27%
Follicular adenoma	3	6.81%
Hashimoto's thyroiditis	2	4.54%

This table shows that most common benign lesion is colloid goiter.

Table 6: Distribution of malignant cases (n=6).

Diagnosis	No. of cases	Percentage
Anaplastic carcinoma	2	33.333%
Squamous cell carcinoma	2	33.33%
Medullary carcinoma	1	16.66%
Papillary carcinoma	1	16.66%

In present study, common malignancies were anaplastic carcinoma and Squamous cell carcinoma.

Table 7: Correlation between USG and FNAC.

Pathology	Number of cases at final diagnosis by FNAC / HPE	Correct diagnosis at USG
Benign	42	42
Malignant	6	6
Inflammatory	2	1

Figure 1: Papillary carcinoma.

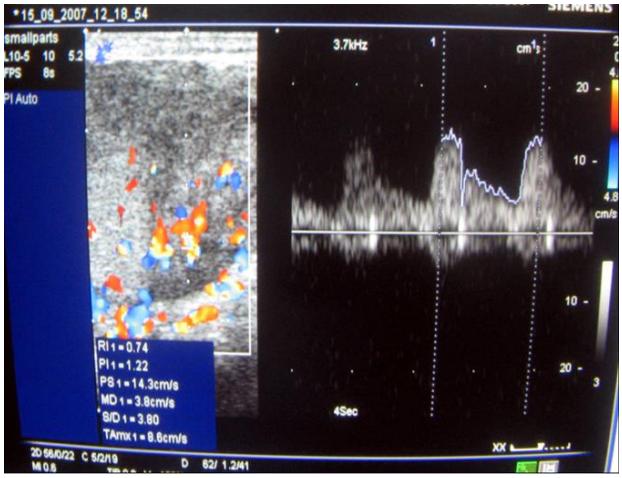


Figure 2: Colour Doppler increased intranodular blood flow. Pulse Doppler shows RI-0.74, PSV-14.3 cm/sec.

Squamous cell carcinoma

Figure 3: US Image shows hypoechoic lesion with irregular margin in left lobe of thyroid.

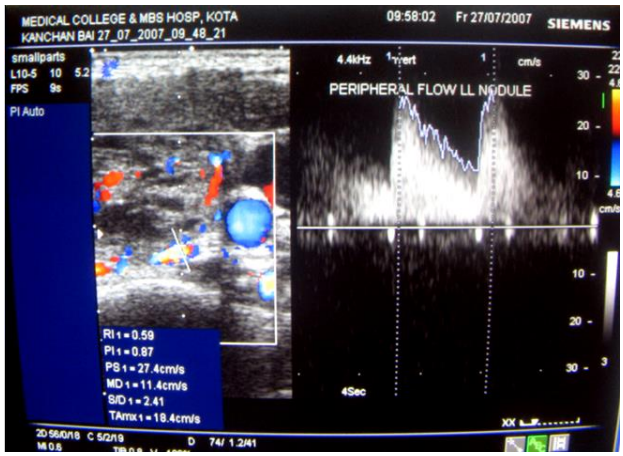
Figure 4: Pulse Doppler image shows RI 0.90 and PSV 20.2 cm./sec.

Anaplastic carcinoma

Figure 5: US Image shows hypoechoic lesions with irregular margins in left lobe of thyroid.

Colloid goiter

Figure 6: US Image shows well defined rounded mixed echoic lesion with cystic area showing nodular calcification.



CDI. Pulse Doppler shows RI - 0.59, PSV - 27.4cm/sec.

Figure 7: Nodule shows peripheral and intra-nodular blood flow on

All benign and malignant lesions were correctly diagnosed by USG, but inflammatory lesions could not be reliably distinguished on USG.

DISCUSSION

The present study was undertaken to evaluate thyroid nodules by high resolution sonography, CDFI and Power Doppler. All cases were properly followed up sonographically, surgically or pathologically wherever indicated to arrive at final diagnosis. Out of 50 patients, 88% cases were having benign, and 12% as malignant lesion. The youngest patient in this study was 18 years of age and the oldest being 75 years. Majority of the patients were between 21-40 years of age and the predominant group in the study was 31 to 40 years comprising of 18 patients (36%), which were all having benign lesion.

Majority of patients with malignant lesion (50%) were between 41 to 50 years of age. These observations were consistent with those of Kapur et al who found maximum number of solitary thyroid nodules in 3rd, 4th and 5th decade.[3] The usual victims of thyroid enlargement were females as indicated in this study where 40 patients were females constituting 80% of total cases and 10 patients were males constituting 20% of total cases. Female to male ratio being 4:1. Belfiore et al, also reported 84.8% females and 14.2% males in their series.[4] Out of 80% females' patients, 74% cases were having benign thyroid nodule and 6% cases were having malignant thyroid nodule. Out of 20% male patients, 14% cases were having benign nodule and 6% cases were having malignant nodule. Main complaint was swelling neck in all the patients (100%).

Side of involvement of thyroid lobes

In the present study, right lobe of thyroid was involved in maximum number of cases (44%) followed by left lobe in 26%, both lobes in 20%, Isthmus in 8% and whole gland was involved in 2% of cases. However, in literature no significance has been attached to side of involvement. A higher involvement of right side appears to be a coincidence.

Malignancy and nodularity

It present study, 74% cases were having single thyroid nodule. Out of this, 64% cases were benign and 10% were malignant. 2 thyroid nodules were found in 16% of cases, all of which were benign. Multiple thyroid nodules were found in 10% cases out of them 8% cases were having benign and 2% cases had malignant lesion. Malignant lesions (5/6) were mostly seen in single thyroid nodules. There has been a consistent observation in literature, that the risk of thyroid cancer is less with multiple nodules than with the solitary nodule. Brown reported in his series that ultrasonography revealed multiple nodules in 28% glands and none of the gland

with multiple nodules was discovered as being malignant.[5]

Echotexture of thyroid nodule and malignancy

In study series, 54% cases had mixed echoic nodules. Out of this, 2% cases were having malignant lesion and 52% cases were having benign lesion. Out of 52% cases with benign mixed echoic lesion, 22% cases were mixed echoic, 20% cases were mixed echoic with cystic areas, 6% cases were having cystic nodule with fine septations, 2% cases were having cystic lesion with thick septa, 2% cases were having cystic lesion with mural nodule. Showing clearly that mixed echotexture alone does not point to malignant nature of lesion. 16% cases were having hypoechoic nodules. Out of this, 10% cases were having malignant lesion and 6% cases were having benign lesion. Showing very clearly that hypoechoic nodule is suggestive of malignancy. 16% cases were having isoechoic nodules, all of which were benign. 12% cases were having cystic nodules, all of which were benign. 2% cases were having hyperechoic nodule, which was benign.

Incidence of malignancy was more in hypoechoic nodules as compared to hyperechoic and isoechoic nodules. Cystic nodules were benign. Solbiati et al reported in his series that 62% hypoechoic nodules were malignant.[6] Percentage of benign nature of cystic, hyperechoic, mixed echoic and isoechoic nodules were 100%, 96%, 89%, 74% respectively. These observations are similar to our observations.

Margins of thyroid nodule

In present study, 90% cases were having well defined, regular margins of thyroid nodules. Out of this, 88% cases were having benign lesion and 2% cases were having malignant lesion. 10% cases were having irregular margins of thyroid nodules, all of which were malignant. Showing that irregular border suggests malignant nature of lesions. Similarly, Solbiati et al found that 82% thyroid nodules with regular margins were benign and 55% thyroid nodules with irregular margins were malignant.[6]

Calcification in thyroid nodules

Calcification can be detected in about 10-15% of all thyroid nodules, but the location and pattern of calcification have a more predictive value in distinguishing benign from malignant lesions Solbiati et al.[6] Peripheral or eggshell- like, calcification is perhaps the most reliable feature of a benign nodules, but unfortunately it occurs in only a small percentage of benign nodules. When calcifications are large and coarse, the nodule is more likely to be benign. When the calcifications are fine and punctate, malignancy is more likely. Pathologically, these fine calcifications may be caused by psammoma bodies, which are commonly seen in papillary cancers. Medullary thyroid carcinoma often exhibits bright echogenic foci either within the primary tumor or within metastatically involved cervical lymph nodes Gorman et al.[7]

In present study, also coarse and nodular calcification was seen more commonly in benign lesions and fine calcification more in malignant lesions. In study series calcification was found in 9 cases (18%) out of 50 patients. 33.33% cases were showing nodular calcification. 22.22% cases out of this, were benign and 11.11% cases were malignant. 33.33% cases were showing fine calcification. Out of this, 22.22% cases were malignant and 11.11% cases were benign. 33.33% cases were showing coarse calcification, all of which were benign.

Halo in thyroid nodules

Solbiati et al in their series reported that halo was found in 36% of thyroid nodules and by far more frequently in benign then in malignant abnormality (86% versus 14%).[6]

Halo is thought to represent compressed normal thyroid parenchyma, especially for rapid growing thyroid cancers, which often have thick, irregular and incomplete halo that are hypovascular or avascular on color Doppler scans. Color and power Doppler imaging have demonstrated that thin, complete peripheral halo, which is strongly suggestive of benign nodules, represents blood vessels coursing around the periphery of the lesion (the "basket pattern"). Study have also noted similar observations. In present study halo was present in 36% cases and all of which were benign.

Color doppler and pulse doppler of thyroid nodules

Fobbe et al demonstrated that 80-90% of hyperplastic, goitrous and adenomatous nodules display peripheral vascularity where as 70% to 90% of thyroid malignancy display internal vascularity with or without a peripheral component.[8] In present study also similar findings have been noted. In our series 50% cases were showing absent blood flow (type -1), all of which were benign. 20% cases were showing perinodular blood flow (type-2) all of which were benign. 30% cases were showing intranodular with or without perinodular blood flow (type-3). Out of this, 18% cases were benign and 12% cases were malignant. 79% of benign cases (35/44) were showing absent or perinodular blood flow.

All of malignant cases (6/6) were showing intranodular with or without perinodular blood flow. Thus, color Doppler flow has shown to be very useful in differentiating benign from malignant lesion.

In this study RI > 0.75 was seen in 83.3% malignant cases and < 0.75 was seen in 100% benign cases, 16.66% malignant cases. We have noted higher RI value and lower PSV in malignant lesion as compared to benign

lesion. PSV > 20.4 cm/sec. was seen in 100% benign cases and <20.4 cm/sec. was seen in 100% malignant cases. The RI (Resistive Index) is a good spectral Doppler parameter for assessing thyroid nodules because it is not dependent on the angle of insonation. With respect to vascular resistance, Holden reported mean RI value of 0.76 in carcinomas, 0.66 in adenomas and 0.57 in colloid nodules.[9] Cerbone et al reported similar results and found an RI greater than 0.75 in 18 of 21 carcinomas and in two of 232 benign nodules.[10] In more recent studies, many authors reported similar findings and concluded that RI value in malignant nodules were higher than in benign nodules.

Thus, pulse Doppler study has been found to be very useful in deciding the nature of lesion.

Lymphadenopathy

In this study, lymphadenopathy was seen in 4 malignant cases (66.66%). Lymphadenopathy was absent in 2 malignant cases (33.33%). Presence of Lymphadenopathy with thyroid nodule is highly suggestive of malignant nature of thyroid nodule.

Papillary and medullary carcinoma have high incidence of metastatic involvement of lymph nodes. Gorman et al found metastatic cervical lymph nodes with US in 80% of patients with medullary thyroid carcinoma.[7] Wunderbaldinger et al found that cervical lymphadenopathy is common in patients with papillary thyroid carcinoma.[11] Follicular carcinoma tends to spread via blood stream rather than via lymphatics.

Benign lesions

In this study 44 patients (88%) were showing benign lesion. Out of this, 72.72% cases were colloid goiter, 13.63% nodular goiter, 2.27% thyroid cyst, 6.81% follicular adenoma, 4.54% were Hashimoto's thyroiditis. Most common benign lesion was colloid goiter. Similarly, Goellner and Gharib reported colloid goiter (40%) to be the most common histologic diagnosis followed by follicular adenoma (18%) and adenomatous goiter in about 11% cases with a 16% malignancy rate.[12]

Malignant lesions

In this study, 6 patients (12%) were showing malignant lesion. Out of this, 33.33% cases were anaplastic carcinoma, 33.33% squamous cell carcinoma, 16.66% papillary carcinoma, 16.66% cases were medullary carcinoma. According to available literature incidences of papillary carcinoma, follicular carcinoma, anaplastic carcinoma, medullary carcinoma and others are 60-65%, 15-20, 10-15%, 5-10%, 10% respectively.[13]

Diagnostic accuracy

On USG 84% cases found to be benign and 12% cases are malignant. On FNAC 84% cases are benign and 12% cases are malignant. Out of 4% inflammatory lesions only 2% cases were correctly diagnosed on USG. All cases diagnosed benign on USG were proved benign in FNAC, similarly all cases diagnosed malignant on USG were found to be malignant in FNAC. Thus, there was total correlation between the two diagnostic techniques. However inflammatory lesions could not be reliably distinguished on sonographic examination. Similar concern was shown by Yeh et el.[14]

CONCLUSION

The present study concludes that high resolution sonography along with CDFI and pulse Doppler should be used as first line imaging modality in evaluations of thyroid nodules. High resolution sonography along with color Doppler flow imaging and pulse Doppler are very useful in differentiating benign from malignant thyroid nodules. An excellent correlation was seen in diagnosis of thyroid lesions between sonography (Gray scale, CDFI and PD) and histopathology.

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