Original Research Article

# Study of ultrasonic thyroid nodules calcifications in detection of malignancy at a tertiary care hospital

Bhavesh P Popat[1], Avinash D Kurdukar[2*]

[1]Professor, [2]Assistant Professor, Department of Radiology, B.K.L. Walawalkar Rural Medical College, Kasarwadi, Sawarda, Chiplun, Ratnagiri, Maharashtra, INDIA.

**Email:** dradkurdukar@yahoo.com, drbhaveshpopat@gmail.com

## Abstract

**Background:** FNAC and HPE are considered gold standard for study of thyroid nodules but ultrasonography is best for initial evaluation. Calcifications are common findings within thyroid nodules, and various calcification types may be seen at various rates4. Punctate microcalcifications on ultrasonography have been reported as an important characteristic for differentiating between malignant and benign nodules5,6. The purpose of present study is to assess accuracy of ultrasonic thyroid nodules calcifications in detection of malignancy. **Material and Methods:** This Prospective, observational study was done in department of radiodiagnosis, in patients who were referred to our department for assessment of thyroid nodules and later during follow up had conclusive pathological work up report (fine needle aspiration cytology- FNAC report and/or histopathological report -HPE) were included. **Results:** Total 135 patients were considered for present study. The average age of patients was 36.4±9.6 years. Most common age group was 21-30 years (31 %), followed by age group 31-40 years (21 %). Female patients were 83 %, male to female ratio was 1:4.86 in present study. HPE/FNAC report was considered as final cyto-pathological diagnosis. According to final cyto-pathological diagnosis 118 (87 %) cases were benign and 17 (13 %) were malignant. In benign cases colloid nodule 86 (73 %) was most common. In 17 malignant cases most common malignancies were papillary carcinoma 12(71%) followed by follicular carcinoma 3(18%), medullary carcinoma 1(6%), anaplastic carcinoma 1(6%). We noted microcalcification in 53 % cases of malignancy and only 3 % of benign cases. Similarly macrocalcification was seen in 29 % cases of malignancy as compared to 3 % of benign cases. Other features such as rim calcification and equivocal echogenic foci were noted in 18 % and 12 % of malignant cases while 6 % and 4 % respectively in benign cases. No calcification was noted in2 (18 %) cases of malignancy and only 101 (86 %) of benign cases. Statistically we compared diagnostic efficacy of USG diagnosed calcification and FNAC/HPE for evaluation of thyroid nodule. USG diagnosed calcification when compared with final cyto-diagnosis report had sensitivity (88 %), specificity (91 %), PPV (76 %), NPV (92 %), accuracy (93 %). **Conclusion:** USG diagnosed calcification can guides for diagnosis of throid malignancy. USG-thyroid should be considered as a first step and as an investigation of choice in evaluation of thyroid nodule.

**Key Words:** Thyroid malignancy, micro calcification, sensitivity, specificity.

***Address for Correspondence:**

Dr. Avinash D Kurdukar Professor, Department of Radiology, B.K.L. Walawalkar Rural Medical College, Kasarwadi, Sawarda, Chiplun, Ratnagiri, Maharashtra, INDIA.

**Email:** drbhaveshpopat@gmail.com

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## INTRODUCTION

Thyroid nodules are frequently seen in OPDs and it is estimated that 4–7% of adults have palpable enlargement of thyroid and ten times more have impalpable nodules[1]. Thyroid nodules are more frequent among females, elderly people, history of irradiation to the head and neck, and a diet containing high amount of goitrogenes. Most of the thyroid nodules are benign and fewer than 5% of them are actually malignant[2]. The possibility of incidence of thyroid cancer increases with age (more likely for people with age more than 50 years). Women are twice more likely to be affected by thyroid cancer than men. But once affected, its prognosis is worse for men compared to women[3]. Generally, patients with asymptomatic benign thyroid nodules usually need routine follow up, but surgical intervention is for patients with malignant thyroid nodules. Generally, thyroid cancer manifests as a

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painless nodule in the thyroid region of the neck. Other possible signs are enlarged lymph node, pain in the anterior region of the neck and voice change due to involvement of recur-rent laryngeal nerve. FNAC and HPE are considered gold standard for study of thyroid nodules but ultrasonography is best for initial evaluation. Ultrasonography can detect small, multiple nodules and also isolate central or lateral neck lymphadenopathies. It provides accurate clarity in dimensions. It also characterizes nodules if suggestive of malignancy by highlighting irregular margins, absence of halo, micro calcifications. The presence of malignancy can be attributed to ultrasonography imaging features that highlight irregular margins, consistency of a solid nature, texture which is hypoechoic, absence of halo sign, presence of calcifications, and presence of cervical lymphadenopathy. Calcifications are common findings within thyroid nodules, and various calcification types may be seen at various rates[4]. Punctate microcalcifications on ultrasonography have been reported as an important characteristic for differentiating between malignant and benign nodules[5,6]. The purpose of present study is to assess accuracy of ultrasonic thyroid nodules calcifications in detection of malignancy.

## MATERIAL AND METHODS

This prospective, observational study was done in department of radiodiagnosis, Department of Radiology, B.K.L. Walawalkar Rural Medical College, for a period of one year. Institutional ethical committee approval was taken for present study.

**Inclusion criteria:** Patients who were referred to our department for assessment of thyroid nodules and later during follow up had conclusive pathological work up report (fine needle aspiration cytology- FNAC report and/or histopathological report -HPE) were included.

**Exclusion criteria:** Thyroid nodules that were not evaluated further or not having follow up were excluded from the study.

Written informed consent for participation was obtained from the patient. Detailed history, clinical findings, laboratory reports and if underwent surgery then operative findings were noted in pre-designed pro-forma. The nodules were assessed on the basis of echogenicity, calcification, internal vascularity, cystic areas, lymphadenopathy and background thyroid changes. All scans were performed on (Name of USG machine) Ultrasound equipment using a high frequency 5–12 MHz probe. Patients who underwent surgical excision, HPE reports were collected from pathology. FNAC was done as an OPD procedure by pathologist. The nodules were classified as hypoechoic when they were of lower echogenicity when compared to the thyroid gland, hyperechoic when nodule was more echogenic when compared to background thyroid parenchyma. The calcification was classified into microcalcification (for tiny calcification without shadowing and measuring about 1mm) and macrocalcification (calcification with shadowing measuring more than 1mm, including coarse and curvilinear calcification). Presence of internal vascularity on Doppler, and cystic areas was documented. Lymphadenopathy was diagnosed when nodes were enlarged by more than 1 cm in their short axis or had microcalcification or cystic areas (irrespective of size) and architectural distortion. The architecture of rest of the thyroid was assessed for presence of adenomatous hyperplasia, colloid nodules and Hashimoto's thyroiditis. The final ultrasound diagnosis based on these findings was correlated with FNAC and histologic assessment on post thyroidectomy specimen when available. Descriptive statistics was used to infer results. Microsoft excel was used to generate tables. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of various ultrasound parameters were assessed with FNAC/HPE findings.

## RESULTS

During study period we conducted thyroid USG examination in 315 patients. After applying inclusion and exclusion criteria, total 135 patients were considered for present study. The average age of patients was 36.4±9.6 years. Most common age group was 21-30 years (31 %), followed by age group 31-40 years (21 %). Female patients were 83 %, male to female ratio was 1:4.86 in present study.

**TABLE 1:** Distribution of patients by age and gender

| AGE (years) | Male | Female | Total no. of patients (percentage) |
|---|---|---|---|
| Less than 20 | 1 | 8 | 9 (7%) |
| 21-30 | 3 | 39 | 42 (31%) |
| 31-40 | 7 | 22 | 29 (21%) |
| 41-50 | 6 | 17 | 23 (17%) |
| 51-60 | 4 | 13 | 17 (13%) |
| 61-70 | 2 | 9 | 11 (8%) |
| More than 70 | 0 | 4 | 4 (3%) |
| **Total** | **23 (17%)** | **112 (83%)** | **135** |

HPE/FNAC report was considered as final cyto-pathological diagnosis. According to final cyto-pathological diagnosis 118 (87 %) cases were benign and 17 (13 %) were malignant. In benign cases colloid nodule 86 (73 %) was most common, others were follicular adenoma 15(13%), thyroid cyst 8 (7%), Hashimoto's thyroiditis 6 (5%) and subacute thyroiditis 3 (3%).

**Table 2:** Final cyto-pathological diagnosis in benign cases

| Final Diagnosis (FNAC/ HPE) | No. of Cases (Percentage) |
|---|---|
| Colloid nodule | 86 (73%) |
| Follicular adenoma | 15 (13%) |
| Cyst | 8 (7%) |
| Hashimoto's thyroiditis | 6 (5%) |
| Subacute thyroiditis | 3 (3%) |
| **Total** | **118** |

In 17 malignant cases most common malignancies were papillary carcinoma 12(71%) followed by follicular carcinoma 3(18%), medullary carcinoma 1(6%), anaplastic carcinoma 1(6%).

**Table 3:** Final cyto-pathological diagnosis in malignant cases

| Final Diagnosis (FNAC/ HPE) | No. of Cases (Percentage) |
|---|---|
| Papillary carcinoma | 12 (71%) |
| Follicular carcinoma | 3 (18%) |
| Medullary carcinoma | 1 (6%) |
| Anaplastic carcinoma | 1 (6%) |
| **Total** | **17** |

Radiologically, calcification features were compared with cyto-pathological diagnosis. Calcifications can be classified as microcalcifications, macrocalcifications, rim calcifications, equivocal echogenic foci and absence of any calcification. The size of the calcium deposit is 1 mm or less in diameter in micro calcifications, while in macrocalcifications, it is greater than 1 mm. Calcification present around the nodule is called rim calcification. Equivocal echogenic foci (present tiny bright reflectors with a clear-cut comet-tail artefact at conventional ultra-sonography) finding was also considered. We noted microcalcification in 53 % cases of malignancy and only 3 % of benign cases. Similarly macrocalcification was seen in 29 % cases of malignancy as compared to 3 % of benign cases. Other features such as rim calcification and equivocal echogenic foci were noted in 18 % and 12 % of malignant cases while 6 % and 4 % respectively in benign cases. No calcification was noted in2 (18 %) cases of malignancy and only 101 (86 %) of benign cases.

| Characteristic | Malignant nodules | Benign nodules |
|---|---|---|
| Total | 17 | 118 |
| Microcalcification | 9 (53%) | 4 (3%) |
| Macrocalcification | 5 ( 29%) | 3 (3%) |
| Rim calcification | 3 (18%) | 7 (6%) |
| Equivocal echogenic foci | 2 (12%) | 5 (4%) |
| None | 2 (12%) | 101 ( 86%) |

Statistically we compared diagnostic efficacy of USG diagnosed calcification and FNAC/HPE for evaluation of thyroid nodule. USG diagnosed calcification when compared with final cyto-diagnosis report had sensitivity (88 %), specificity (91 %), PPV (76 %), NPV (92 %), accuracy (93 %).

**Table 4:** Diagnostic Test Statistics of USG and FNAC for evaluation of thyroid nodule

| Diagnostic Statistics | USG diagnosed calcification |
|---|---|
| Sensitivity | 88 |
| Specificity | 91 |
| PPV | 76 |
| NPV | 92 |
| Accuracy | 93 |

## DISCUSSION

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is distinguishable from the adjacent parenchyma at USG. Basic use of sonography in the thyroid nodule evaluation is to determine the location of palpable neck mass, characterize nodule as benign or malignant, know about extent of thyroid malignancy, and guide fine needle aspiration of the thyroid nodule or cervical lymph node. The categorization of thyroid nodules into benign and malignant nodules by USG is very important as it helps in the further management of the patients with nodular thyroid disease. Ultrasound has become the first-line imaging modality for the evaluation of the thyroid gland due to excellent visualization of the

thyroid parenchyma[7]. It is highly sensitive in detective small nodules, calcification, septations, and cysts as well as in guiding fine needle aspiration biopsies. Thyroid nodules are very common and may be observed at USG in 50% of the adult population[8].Sonographically the thyroid nodule was evaluated for size, shape, location, echotexture, margins, presence of halo, calcification, accessory nodules and associated cervical lymphadenopathy. In a study by Bumiya and Roopa[9], benign pathology was observed in 90% cases, amongst which the commonest was goitre (66%) patients. We noted similar findings. National Comprehensive Cancer Network (NCCN) suggests all thyroid nodules be evaluated with thyrotropin and USG of thyroid and neck as a first step and prefers FNA (with or without sono-guidance) as an investigation of choice in only suspicious lesions[10]. The size of the calcium deposit is 1 mm or less in diameter in micro calcifications, while in macrocalcifications, it is greater than 1 mm. Calcification present around the nodule is called rim calcification. Equivocal echogenic foci (present tiny bright reflectors with a clear-cut comet-tail artifact at conventional ultra-sonography) finding was also considered. Kwak *et al.*[11] regarded it as having microcalcification that a nodule had both types of calcifications, Park *et al.*[12] defined microcalcifications as calcifications that were equal to or less than 0.5 mm in diameter. 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. 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 Microcalcifications are also common in malignant nodules. Coarse calcifications are thought to represent dystrophic calcifications in fibrous or necrotic nodules[13] and often seen in the nodules of multinodular goiter. Some investigators consider it a feature of benignity[14]. However, coarse calcifications are significantly associated with the false negativity of ultrasound-guided fine-needle aspiration (UGFNA) in a study and they recommended microcalcification or coarse calcification should be considered an indication for FNAC[15]. We noted that USG diagnosed calcification when compared with final cyto-diagnosis report had sensitivity (88 %), specificity (91 %), PPV (76 %), NPV (92 %), accuracy (93 %). In a recent study, results showed small nodular size, taller-than-wide shape, well-defined margin, microcalcification and coarse calcification were related to the false-negativity of UGFNA, among which the maximum diameter and calcifications were identified as independent predictors of the false-negativity of UGFNA by multivariate logistic regression analysis[15]. Frates MC *et al*[16] noted sensitivity of any type of calcification to predict malignancy was 64%, the specificity was 65.6 % and the accuracy was 64.9%. they also noted in their study that malignancy was associated with 70% of patients with micro calcifications and 60% of patients with macro calcifications. The sensitivity of microcalcifications in detecting malignancy was 29.1%, specificity was 93.9%, and accuracy was 66.6%. Micro calcification is a feature in papillary carcinoma and is seen due to the psammoma bodies. Coarse calcification is seen in medullary carcinoma and in adenomatous nodules. Micro calcification was seen in 43% of patients, macrocalcifications was seen in17% of patients with papillary carcinoma. John A *et al*[17] noted that fealures like hypoechoic nodule with micro calcification, coarse calcification in a hypoechoic nodule, well marginated oval shape nodule with hypoechoic hallo, irregular solid nodule with hypervascularity with local invasion, distant lymph node metastasis are more specific for malignancy or are potentially malignant and should undergo FNAC. FNA biopsy is recommended for nodules > 1 cm with high suspicion features (solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with either one or more of features: irregular margin or microcalcification or taller than wide shape or rim calcification or evidence of extra thyroidal extension; estimated malignancy risk of 70–90 %) or > 1 cm with intermediate suspicion features (hypoechoic solid nodule with smooth margins without microcalcification, extra thyroidal extension or taller than wide shape; estimated malignancy risk 10–20 %)[18]. The persistent combination of common individual ultrasound characteristics, or, more properly, their absence, is a better alternative to the analysis of individual features for more pattern-oriented approach, advocated by Reading *et al.*[19]. Those authors described eight typical appearances of commonly encountered benign and malignant nodules, allowing them to separate more than one half of thyroid nodules into those that could be observed versus those requiring biopsy. According to their results, the following four classic patterns necessitate biopsy: 1, a hypoechoic nodule with microcalcifications; 2, coarse calcifications in a hypoechoic nodule; 3, well-marginated, ovoid, solid nodules with a thin hypoechoic halo; and 4, a solid mass with refractive shadowing from the edges, which is

believed to occur as a result of fibrosis. The four classic patterns of nodules that did not require biopsy in that series were the following: 1, small (< 1 cm) colloid filled cystic nodules; 2, a nodule with a honeycomb appearance consisting of internal cystic spaces with thin echogenic walls; 3, a large predominantly cystic nodule; and 4, diffuse multiple small hypoechoic nodules with intervening echogenic bands, which are indicative of Hashimoto's thyroiditis. Ying Wang *et al*[20] suggested that solid composition, hypoechogenicity, marked hypoechogenicity, homogeneous echotexure, microlobulated or irregular margin, microcalcification, mixed calcification and taller than-wide shape were independent US features in prediction of thyroid malignancy. Thyroid nodules (TNs) may show highly diverse ultrasound patterns which often impairs an accurate classification regarding malignancy. For this reason, in 2009 Horvath *et al*[21] proposed an evaluation system for TNs called TI-RADS (Thyroid Imaging Reporting and Data System), In 2011, Kwak *et al*[11], complemented this classification adding one subtype.

## CONCLUSION

Ultrasound evaluation is non-invasive, readily available, relatively inexpensive and with good resolution it helps to detect non-palpable and clinically silent nodules. USG diagnosed calcification can guides for diagnosis of throid malignancy. USG-thyroid should be considered as a first step and as an investigation of choice in evaluation of thyroid nodule.

## REFERENCES


1. W. C. faquin, "Aspiration of the thyroid," in Atlas of Diagnostic Cytopathology, B. F. Atkinson, Ed., pp. 460–470, Saunders, 2004.
2. M. J. Yeung and J. W. Serpell, "Management of the solitary thyroid nodule," Oncologist, vol. 13, no. 2, pp. 105–112, 2008.
3. U. Rajendra Acharya, G. Swapna, S. Vinitha Sree, Filippo Molinari, Savita Gupta, Ricardo H. Bardales, Agnieszka Witkowska, Jasjit S. Suri, A Review on Ultrasound-based Thyroid Cancer Tissue Characterization and Automated Classification, Technology in Cancer Research and Treatment Volume 13, Number 4, August 2014
4. Kakkos SK, Scopa CD, Chalmoukis AK, Karachalios DA, Spiliotis JD, Harkoftakis JG, Karavias DD, Androulakis JA, Vagenakis AG. Relative risk of cancer in sonographically detected thyroid nodules with calcifications. J Clin Ultrasound 2000; 28: 347–352.
5. Haugen BR, Alexander EK, Bible KC, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. The American Thyroid Association (ATA) guidelines taskforce on thyroid nodules and differentiated thyroid cancer. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2016; 26: 1–133
6. Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, Jin C, Kornak J. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: Results of a population-based study. JAMA Intern Med 2013; 173: 1788–1796\
7. Latoo M, Lateef M, Kirmani O. Ultrasonography a useful adjunctive in management of thyroid neoplasms. Indian J Otolaryngol Head Neck Surg 2007;59:13‑4.
8. Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, *et al*. Management of thyroid nodules detected at US: Society of radiologists in ultrasound consensus conference statement Radiology 2005;237:794‑800.
9. Bumiya RG, Roopa. Ultrasonography of the thyroid lesions correlated with FNAC. Int J of Sci Res 2018;7:33‑5.
10. NCCN Clinical Practice Guidelines in Oncology- Thyroid Carcinoma. Version 2.2017-May17, 2017. NCCN.org.
11. Kwak, J. Y. *et al*. Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk. Radiology 260, 892–899 (2011).
12. Park, J. Y. *et al*. A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma. Thyroid 19, 1257–1264 (2009).
13. Anil G, Hegde A and Chong FH. Thyroid nodules: risk stratification for malignancy with ultrasound and guided biopsy. Cancer Imaging 2011; 11: 209-223.
14. Park CS, Kim SH, Jung SL, Kang BJ, Kim JY, Choi JJ, Sung MS, Yim HW and Jeong SH. Observer variability in the sonographic evaluation of thyroid nodules. J Clin Ultrasound 2010; 38: 287-293.
15. Hai-She Mo, Zhi-Xian Li, Si-Da Wang, Xin-Hong Liao, Min Liang, Xiao-Yun Hao, Ultrasonic features of thyroid nodules related to the false negativity in ultrasound-guided fine-needle aspiration for suspicious malignant thyroid nodules Int J Clin Exp Med 2017;10(9):13473-13481
16. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules? J Ultra¬sound Med. 2003;22:127–31.
17. John A *et al* pattern recognition of benign nodules at ultrasound of thyroid: which nodules left alone AJR 2009, 193:1, 207-213
18. Shrikant Tamhane and Hossein Gharib, Thyroid nodule update on diagnosis and management, Clinical Diabetes and Endocrinology (2016) 2:17
19. Reading CC, Charboneau JW, Hay ID, Sebo TJ. Sonography of thyroid nodules: a "classic pattern" diagnostic approach. Ultrasound Q 2005; 21:157–165
20. Ying Wang *et al*, Malignancy risk stratification of thyroid nodules: comparisons of four ultrasound thyroid imaging reporting and data systems in surgically resected nodules, ScIEnTIfIc Reports | 7: 11560 | DOI:10.1038/s41598-017-11863-0
21. Hovarth E, Majlis S, Rossi R, Franco C, Niedmann JP, Castro A, *et al*. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. J Clin Endocrinol Metab. 2009;94:1748---51.