ASSOCIATION OF ULTRASONOGRAPHY AND ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF THYROID NODULES

Binit Dev*, Ajay Kumar Yadav, Sushil Taparia, Roshana Khadka, Shripad J. Walavalkar

ABSTRACT

Introduction
Ultrasound (USG) is the most commonly used imaging method to evaluate thyroid nodules. The sonographic features of thyroid nodules are very important to determine whether the nodule is benign or malignant. Fine Needle Aspiration Cytology (FNAC) is the gold standard to determine whether the nodule is benign or malignant.

Objective
The purpose of this study was to compare ultrasound and color Doppler features of thyroid nodules with ultrasound-guided FNAC results to determine the relative importance of these features in predicting the risk of malignancy.

Methodology
This prospective cross-sectional study was conducted in Birat medical college teaching hospital in Tankasinuwari, Morang, Nepal. The study was conducted from September 2019 to April 2021. In total sixty-one patients with thyroid nodules were evaluated for sonographic characteristics. Finally, USG guided FNA for cytopathological examination was performed. Both descriptive and inferential statistics were used to analyze the result.

Result
Out of the 61 patients, 34 (55.7%) were females and 27 (44.2%) were males. Majority of the malignant nodules were solid (91.6%), whereas cystic and mixed nodules were predominantly seen in benign nodules (36.7%) and (61.2%) respectively. In malignant nodules 10 (83.3%) were heterogeneous and 2 (16.6%) were isoechoic. In benign nodules 29 (59.1%) were heterogeneous and 15 (30.6%) were anechoic with comet-tail artifact and 5 (10.2%) were isoechoic. Among 12 malignant cases, internal and peripheral vascularity were equally present in six cases each. Benign nodules showed peripheral vascularity in 48 (97.9%) and internal vascularity was noted in only one nodule. All of the malignant nodules showed calcification. None of the benign nodules showed micro-calcification. In malignant cases, cervical lymph nodes were present in 7 (58.3%) and absent in 5 (41.6%). In benign cases, cervical lymph nodes were present in 4 (8.1%) and absent in 45 (91.83%).

Conclusion
The ultrasound features associated with malignancy in thyroid nodules are predominantly solid component, presence of micro-calcifications and internal vascularity. Enlarged cervical lymph nodes are good predictors for malignancy. USG guided FNAC confirms the suspicious features of thyroid nodules seen on USG.

KEY WORDS
Diagnosis, Thyroid nodule, Ultrasonography
INTRODUCTION
Thyroid gland is the largest endocrine gland in the human body. Nodules and diseases in the thyroid are common findings and are found mainly in the iodine-deficient areas of the world. According to Surveillance, Epidemiology, and End Results (SEER) data, thyroid cancer constitutes 3.0% of all newly diagnosed cancers.1

The extensive use of thyroid ultrasound has led to an increased diagnosis of low-risk thyroid cancer. Therefore, we should pay more attention to risk evaluation and result prediction to minimize morbidity and unnecessary treatment.2

Ultrasound (USG) is a reliable and simple diagnostic method with high sensitivity (90%) and specificity (85%) for thyroid nodules.3 It is suggested that the ultrasonic features of malignant thyroid nodules include hypoechoic, solid structure, irregular margin, micro-calcification, and regional lymph node metastasis.4-7 Intranodular hypervascularity and nodule size ≥ 2 cm are also consider as indicators of thyroid cancer.8-10

Majority of thyroid nodules are due to hyperplasia of glands containing solid and cystic components, in the later stage calcification (micro/macro) occur.11,12 Lesions that are initially isoechoic may become hyperechoic as the size of the mass increases due to various pathological changes. The approximate prevalence of malignant nodules are Papillary carcinoma 75-90%, Follicular carcinoma 5-15%, Medullary carcinoma 5%, Lymphoma 4%, and Anaplastic carcinoma <2%.13

Ultrasound being non-ionizing, fast, easy to perform, cheaper and widely available, and therefore easy to assess the thyroid nodule, and its acceptability to evaluate the thyroid disease has increased day by day. USG is helpful in differentiating solid and cystic lesions, solitary from multinodular lesions, and also from diffuse enlargement of the gland. It is therefore an ideal investigation of choice for evaluating thyroid nodules.14 Fine Needle Aspiration Cytology (FNAC) is a simple, quick, and well-established first-line diagnostic tool for the evaluation of thyroid disease.15 USG guided FNAC has much higher sensitivity, specificity, and positive predictive value than palpation guided FNAC.16 The purpose of this study was to assess the sonographic characteristics in thyroid nodule and predict the risk of malignancy and also compare sonography findings with USG guided FNAC findings.

METHODOLOGY
After getting the approval from institutional ethical committee, this prospective cross-sectional study was conducted from September 2019 to April 2021 in the department of Radiology and Pathology at Birat Medical College Teaching Hospital, Tarsealinwari, Morang, Nepal. During this period, all patients with thyroid nodules referred for ultrasound were considered appropriate for the study. Sample size was calculated using formula \( n = \frac{z^2 \cdot S_e \cdot (100-S_e)}{(d^2 \cdot \text{Prevalence})} \) and obtained 55.

where \( z = 1.96 \) at 95% confidence level, \( S_e = \text{Sensitivity} = 66.7 \) taking coarse macro-calcification as a single parameter to diagnose malignancy, \( d = \text{maximum tolerable error} = 4\% \), prevalence of malignancy in thyroid nodules = 9.6%.

As there could be indefinite cases, we added 10% of the calculated sample size and hence final sample size is 61, which is comparable to sample size taken in various similar published studies.17 USG of the neck was carried out with a linear high-frequency probe. The nodules were interpreted concerning for echotexture, composition, calcification, vascularity, and presence of cervical lymph nodes. Fine needle aspiration was performed under ultrasound guidance by using a 23 G needle with standard technique using suction aspiration and slides were sent to the department of pathology for cytological study. The definitive diagnosis for each case was determined by cytological examinations.

STATISTICAL ANALYSIS
Statistical analysis was performed using SPSS software version 22.0 and data were analyzed using both descriptive and inferential statistics. Frequency tables, sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated. Chi-square test was used to test the level of significance. Data associations were considered statistically significant at \( P<0.05 \).

RESULTS
In this study, patients’ age was ranged from 20 to 70 years. The mean age for malignant lesions was 39.5 years and for benign lesions was 38.4 years. Out of the 61 patients, 34 (55.7%) were females and 27 (44.2%) were males. Gender variation for malignant thyroid nodules showed female preponderance, which was not evident in benign cases as shown in table 1.

<table>
<thead>
<tr>
<th>Table 1: Patient’s Demography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>&lt; 20</td>
</tr>
<tr>
<td>20 – 39</td>
</tr>
<tr>
<td>40 – 59</td>
</tr>
<tr>
<td>&gt; 60</td>
</tr>
<tr>
<td>Gender ratio</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>female</td>
</tr>
<tr>
<td>Location</td>
</tr>
<tr>
<td>Right lobe</td>
</tr>
<tr>
<td>Left lobe</td>
</tr>
<tr>
<td>Isthmus</td>
</tr>
<tr>
<td>Both lobes</td>
</tr>
</tbody>
</table>

Fisher exact test

Majority of the malignant nodules were solid 11 (91.6%), whereas cystic and mixed (solid and cystic) nodules were predominantly seen in benign. In malignant nodules 10

1. Surveillance, Epidemiology, and End Results (SEER) data
2. Ultrasound (USG) is a reliable and simple diagnostic method with high sensitivity (90%) and specificity (85%) for thyroid nodules.
3. It is suggested that the ultrasonic features of malignant thyroid nodules include hypoechoic, solid structure, irregular margin, micro-calcification, and regional lymph node metastasis.
4. Intranodular hypervascularity and nodule size ≥ 2 cm are also considered indicators of thyroid cancer.
5. Majority of thyroid nodules are due to hyperplasia of glands containing solid and cystic components, in the later stage calcification (micro/macro) occurs.
6. Lesions that are initially isoechoic may become hyperechoic as the size of the mass increases due to various pathological changes.
7. The approximate prevalence of malignant nodules are Papillary carcinoma 75-90%, Follicular carcinoma 5-15%, Medullary carcinoma 5%, Lymphoma 4%, and Anaplastic carcinoma <2%.
8. Ultrasound being non-ionizing, fast, easy to perform, cheaper and widely available, and therefore easy to assess the thyroid nodule, and its acceptability to evaluate the thyroid disease has increased day by day.
9. USG is helpful in differentiating solid and cystic lesions, solitary from multinodular lesions, and also from diffuse enlargement of the gland.
10. It is therefore an ideal investigation of choice for evaluating thyroid nodules.
11. Fine Needle Aspiration Cytology (FNAC) is a simple, quick, and well-established first-line diagnostic tool for the evaluation of thyroid disease.
12. USG guided FNAC has much higher sensitivity, specificity, and positive predictive value than palpation guided FNAC.
13. The purpose of this study was to assess the sonographic characteristics in thyroid nodule and predict the risk of malignancy and also compare sonography findings with USG guided FNAC findings.
14. Fisher exact test
15. Majority of the malignant nodules were solid (91.6%), whereas cystic and mixed (solid and cystic) nodules were predominantly seen in benign.
(83.3%) were heterogeneous. In benign nodules 29 (59.1%) were heterogeneous (figure 1A), 15 (30.6%) were hypoechoic and 5 (10.2%) were isoechoic. In malignant, all cases showed internal and peripheral vascularity (figure 2B). Whereas maximum benign nodules showed peripheral vascularity. Micro-calciﬁcation was only noted in the malignant cases hence making it a good predictor for malignancy (figure 1A). In malignant cases, cervical lymph nodes were present in 7 (58.3%). In benign cases, cervical lymph nodes were present in only 4 (8.1%), hence the presence of lymphadenopathy is an indicator for malignancy. Sensitivity, speciﬁcity, positive predictive value (PPV), negative predictive value (NPV), the accuracy of USG and FNAC ﬁndings are illustrated in table 3.

Table 2: Characteristics of USG features for benign and malignant thyroid nodules.

<table>
<thead>
<tr>
<th>Composition</th>
<th>Malignant (n=12)</th>
<th>Benign (n=49)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid</td>
<td>11 (91.6%)</td>
<td>1 (2%)</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Cystic</td>
<td>0</td>
<td>18 (36.7%)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>1 (8.3%)</td>
<td>30 (61.2%)</td>
<td></td>
</tr>
<tr>
<td>Echogenicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogenous</td>
<td>10 (83.3%)</td>
<td>29 (59.1%)</td>
<td>0.086</td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>0</td>
<td>15 (30.6%)</td>
<td></td>
</tr>
<tr>
<td>Isoechoic</td>
<td>2 (16.6%)</td>
<td>5 (10.2%)</td>
<td></td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No calcification</td>
<td>0</td>
<td>39 (79.5%)</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Macrocalcification</td>
<td>6 (50%)</td>
<td>10 (20.4%)</td>
<td></td>
</tr>
<tr>
<td>Microcalcification</td>
<td>6 (50%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vascularity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral</td>
<td>6 (50%)</td>
<td>48 (97.9%)</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Intrinsic</td>
<td>6 (50%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Lymph node</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (58.3%)</td>
<td>4 (8.1%)</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>No</td>
<td>5 (41.6%)</td>
<td>45 (91.8%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Sensitivity, speciﬁcity, positive predictive value (PPV), negative predictive value (NPV), accuracy of USG and FNAC ﬁndings for malignant and benign lesions.

<table>
<thead>
<tr>
<th>FNA result</th>
<th>Sensitivity (%)</th>
<th>Speciﬁcity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>71.4</td>
<td>95.9</td>
<td>71.4</td>
<td>87.8</td>
<td>85.0</td>
</tr>
<tr>
<td>Benign</td>
<td>47.0</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Figure 1.A, B. Heterogeneous nodule with a solid and cystic component with absent vascularity. Macrocalcification was also noted. C. Moderately cellular smears with flat sheets showing evenly spaced follicular cells. Nodular goiter was diagnosed by USG and conﬁrmed by ﬁne-needle aspiration cytology (Pap stain X 40).
B)

Figure 2. A, B. Ultrasound image shows a heterogenous nodule with predominantly solid component and micro calcifications with intrinsic vascularity. C. Cells arranged in a papillary pattern and in sheets showing nuclear grooves. Papillary carcinoma was diagnosed by US-guided fine-needle aspiration biopsy (Pap stain X 40)

DISCUSSION

This study was conducted to assess the sonographic characteristics in thyroid nodules and predict the risk of malignancy and also compare sonography findings with FNAC findings.

It is generally accepted that when reliably distinguishing malignant nodules from benign nodules, no ultrasound examination feature has sufficient diagnostic accuracy. It is important to emphasize the recognition of complex patterns rather than a single feature to identify malignant thyroid tumors, otherwise the risk of malignant tumors will be incorrectly assessed. Pattern recognition methods have been applied to distinguish malignant thyroid nodules from benign thyroid nodules on ultrasound images because they can effectively capture the nonlinear relationship that exists in most ultrasound features. Assessment of thyroid nodules by FNA has been the gold standard. The overall accuracy of FNA has been shown to exceed 95%, therefore at present, it is the most precise and cost-effective method for initial evaluation of nodular thyroid disease.

Like Reading et al., we found that the echo pattern method for thyroid nodules is highly sensitive and specific to the presence of benignity. In previous studies, the malignant risk of mixed echogenic nodules ranged from 2.3% to 17.6%. Our malignant rate is within this range.

The incidence rate of malignant tumors is significantly higher in nodules with solid tumors. In the current study, we have noticed that malignant tumors are associated with larger solid components of the nodules. This may be related to the higher degree of angiogenesis associated with solid thyroid nodules and malignant tumors. The sensitivity and specificity of solid nodules were 91.6% and 98%, respectively (P = 0.000). This result is close to that of Enrico Papiniet al., which showed that 87% of malignant nodules were solid hypoechoic.

In this study, the incidence of malignant tumors in patients with calcification was significantly higher. About 70.59% of benign nodules had no calcification or microcalcification. Occurrence of micro-calcification may be a reliable predictor of thyroid cancer which was also demonstrated by Wang et al. that there was a close relationship between micro-calcification detected by ultrasound and thyroid cancer, with a specificity of 96.7%. Chammaset al. reported similar findings, indicating that the presence of microcalcification may be a specific predictor of thyroid cancer.

In present study, all malignant nodules showed vascularity. Nodules with intrinsic vascularity were more likely to be malignant, while nodules with peripheral vascularity were more likely to be benign. A study by Frateset al. analyzed the relationship between the inherent vascular blood flow pattern of color Doppler imaging and the risk of malignant thyroid nodules and concluded that the possibility of malignancy in solid hypervascular nodules is high. A recent study by Papiniet al. showed that hypoechoic combined with the presence of irregular margins, inherent vascular flow patterns, or micro-calcifications had 87% sensitivity in differentiating malignant nodules in the study population.

In this study, most malignant thyroid nodules were associated with the presence of cervical lymph nodes. For the detection of metastatic thyroid cancer lymph nodes, no single ultrasound feature is sensitive enough. In another recent study, sonographic features obtained 4 days before surgery were directly correlated with the histology of 56 cervical lymph nodes. Some of the most specific criteria were cystic areas (100%), hyperechoic spots with colloidal or microcalcifications (100%), and peripheral vessels (82%). Only peripheral blood supply (86%) was sensitive. The sensitivity of all others was less than 60%, which was not enough to be used as a single standard for differentiating malignant tumors. As shown in the early studies of Frasoldati A et al. and Kuna SK et al., the most sensitive feature was the absence of hilum (100%), but the specificity was low (only 29%).
CONCLUSION

USG features suggesting thyroid malignancy include predominantly solid components, presence of micro-calculcations and internal vascularity. Cervical lymphadenopathy with fine calcifications increases the probability of thyroid malignancy metastasis in the setting of suspicious thyroid nodules. USG guided FNAC confirms the suspicious features of thyroid nodules seen on USG.

RECOMMENDATIONS

All palpable and non-palpable thyroid nodules should be recommended for USG examination. The role of USG is very effective in distinguishing benign from malignant nodules recommended for USG examinaion. The role of USG is very effective in distinguishing benign from malignant nodules. The role of USG is very effective in distinguishing benign from malignant nodules.

LIMITATION OF THE STUDY

This study was limited because of its small sample size, a larger sample size would have given us a better understanding. Furthermore, this study was limited to only one hospital. Multi-centered study would have given us better interpretation and a larger sample size.

ACKNOWLEDGEMENTS

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CONFLICTS OF INTEREST

None

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None

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