Original Article

Ultrasonographic Evaluation of Solitary Thyroid Nodule with Histopathological Comparison

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Abstract:
Background: Thyroid gland is the largest gland of the body which secretes thyroid hormones named $T_3$ & $T_4$. Incidence of solitary thyroid nodule is common in Bangladesh.

Objectives: To validate the ultrasonography evaluation of solitary thyroid nodule comparing with histopathological diagnosis.

Methodology: This cross sectional study enrolled 75 patients of age range between 14 to 72 years during July 2016 to June 2018 and the study was carried out in the department of Radiology & Imaging of Ultrasonography evaluation was finally compared with histopathological diagnosis which was considered as gold standard.

Results: Among 75 patients are included in this study the age ranged between 14 to 72 years. Majority of the patients 37 (49.3%) were found between 31 to 40 years. 65 (86.3%) were female & 10 (13.3%) were male. All patients were presents with thyroid swelling. In USG findings Microcalcifications were present 9 (12%) in benign & 5(6.7%) in malignant cases. Presence of Halo were in all benign cases 14 (18.7%). Comet tail sign were in 5 (6.7%) in benign & 3 (4%) in malignant cases. Histological nodular goiter were 57 (76%), Follicular adenoma 8 (10.7%), Thyroiditis 5 (6.7%) and Papillary carcinoma 4 (5.3%), Follicular Carcinoma 1 (1.3%).

Conclusion: This cross sectional study was carried out with an aim to determine the usefulness of ultrasonogram diagnosis of solitary thyroid nodule compared with histopathology findings. As the validity test results are higher, it can be concluded that the ultrasonogram is a useful diagnostic modality in the evaluation of solitary thyroid nodule.

Keywords: Ultrasonography, Solitary thyroid nodule.

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Introduction:
Thyroid is the largest endocrine gland of the body which secretes thyroid hormone named $T_3$ and $T_4$. This hormone is one of the important hormones of the body and have an essential role in metabolism. Without proper functioning of this hormone, there is disruption of this rhythm and cause dysfunction of organs and organ systems.¹

The gland is affected by pathological lesion of varied morphology, which can be divided into two types which shows the diffuse pattern and that produce nodules. Diffuse thyroid lesions are mostly associated with non-neoplastic lesions affecting the gland.
Nodular lesions comprise disorders that consist of non-neoplastic nodules as well as benign and malignant.\(^2\)

Thyroid nodules (TN) are common in general population and one of the commonly encountered problem in day-to-day clinical practice though it is more commonly found in women.\(^3\) According to the American Thyroid Association (ATA) Guidelines, a thyroid nodule (TN) is a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma. Nonpalpable nodules are often found when patients undergo diagnostic imaging such as ultrasonography and computed tomography of the chest and neck. For these incidentalomas, current guidelines recommend the same diagnostic strategy that is recommended for palpable nodules.\(^4,5\) Although the risk of malignancy in any given solitary nodule (less than 1 cm) is small, thyroid cancer must be considered in the differential diagnosis. But despite benign in nature of this nodule it is stressful for the patients being diagnosed as a case of solitary thyroid nodule.\(^6,7\)

Statistics evidence showed that palpable thyroid nodules occur in 4–8% of the population and in 13-67% nodules found incidentally during ultrasound (US).\(^8\) And about 5% of the clinically apparent thyroid nodules are malignant, while nonpalpable nodules have the same risk of malignancy as palpable nodules of the same size.\(^9\) In Whickham survey from England palpable thyroid nodule noted in 0.8% of male and 3% of female.\(^10\) These figures present only tip iceberg, because when ultrasonography is done in patients with clinically apparent normal thyroid, nodule is detected 30-50% of adult gland. In the Framingham study, the lifetime risk of developing a thyroid nodule was estimated to be 5-10%. The author found that more than two thirds of the nodules are solitary.\(^11\) Actually, the proportion of malignant nodules becomes higher which reaches 5–15%.\(^12,13\) Some of this increase may be due to advances in diagnostic tools, including high-resolution ultrasonography and computed tomography, allowing for greater detection of thyroid nodules, which may not have been detected before. However, important changes in the intrinsic characteristics of the general population are also assumed to be involved.\(^14,15\)

Thyroid nodule is also common in Bangladesh. The retrospective study done among the thyroid patients attending the thyroid clinic running jointly by the Institute of Nuclear Medicine (INM) and Institute of Post-Graduate Medicine and Research (IPG&M&R), shows that about 32.67% of thyroid patients present with solitary thyroid.\(^16\) Solitary nodules consists of a heterogeneous group of disorders such as colloid nodules, adenomas, thyroiditis and simple cysts. More recent studies have indicated that majority of the thyroid nodules are truly tumors and of clonal origin.\(^17\) Solitary Thyroid Nodules (STN) are common but malignancy is rare, only 5-6% of STN are malignant. However thyroid carcinoma is common malignancy of the endocrine system. Thyroid cancer accounts for 1.5% of all cancers, Malignancy may arise from follicular epithelial cells as papillary (70-80%), follicular (10%) and anaplastic carcinoma (5%), from parafollicular (C-cell) as medullary carcinoma of thyroid (5-10%) and others as lymphoma and secondary from kidneys, breast, lungs, upper gastro intestinal tract and larynx (5%). All are common in females, except medullary carcinoma which occur equally in both sexes.\(^18\)

The critical issue is to determine whether it is benign or malignant. The presence of malignant nodule would necessitate primary surgical therapies whereas a benign nodule can be managed conservatively. For that, thyroid nodule always present diagnostic problems in all age groups as because when all palpable nodules are resected, cancers
are diagnosed only in 10% cases\(^9\). Although a significant amount of patients suffering from thyroid.

**Methods:**
This cross-sectional study was carried out in the department of Radiology and Imaging of Sir Salimullah Medical College and Mitford Hospital, Dhaka total 75 patients who were referred to Radiology and Imaging department by E.N.T department of Sir Salimullah Medical College and Mitford Hospital, Dhaka as a clinically suspected solitary thyroid nodule for USG of neck, during the period July 2016 to June 2018. Prior to the commencement of this study, the research protocol was approved by the Institutional Review Board of SSMC, Dhaka. It was assured that all information and records would be kept confidential and the procedure would be helpful for both the pathologist and the patients in the making rational approach of the case management.

**Results:**
Among 75 patients included in this study the age ranged between 14-72 years. Mean age was 37.02±10.67 (mean±SD) years. Majority of the patients (49.3%) were found between 31-40 years. Six (8%) patients were found below 20 years of age. There were male 10 (13.3%) and female 65 (86.7%)

**Table I :**

| Age in years | Frequency | Percentage (%) | Mean±SD |
|--------------|-----------|----------------|---------|
| <20          | 6         | 8.0            |         |
| 21-30        | 10        | 13.33          |         |
| 31-40        | 37        | 49.34          | 37.02±10.67 |
| 41-50        | 15        | 20             |         |
| 51-60        | 6         | 8.0            |         |
| >60          | 1         | 1.33           |         |
| Total        | 75        | 100.0          |         |

Maximum (49.3%) participants of this study belonged to age group 31 to 40 years followed by 20.0% belonged to 41 to 50 years, 13.3% within 21 to 30 years, 8% within 51 to 60 years and below 20 years. Only 1.3% of each was belonged to extreme age group that is more than 60 years. Mean (±SD) age of the participants was 37.02±10.67 and all participants were within 14 to 72 years age range.

**Table II :**

| Sex       | Frequency | Percentage (%) |
|-----------|-----------|----------------|
| Male      | 10        | 13.3           |
| Female    | 65        | 86.7           |
| Total     | 75        | 100.0          |

Out of all participants, 13.3% were male and 86.7% were female. Male and female ratio was 1:6.5.

**Table III :**

| Presenting Complaints | Frequency | Percent |
|-----------------------|-----------|---------|
| Thyroid swelling      | 75        | 100     |
| Pain*                 | 09        | 12      |
| Dysphagia*            | 06        | 08      |
| Hoarseness of voice*  | 05        | 6.7     |

*multiple response or features along with thyroid swelling

Table shows the different presenting complaints of the participants and all the participants had complaint of thyroid swelling.
(100%) followed by in decreasing order by pain (12%), dysphagia (8%) and hoarseness of voice (6.7%).

Table IV:
Distribution of local examination findings of the participants (n=75)

| Local Examination                  | Frequency (n) | Percent (%) |
|------------------------------------|---------------|-------------|
| Size of the thyroid gland          |               |             |
| • Enlarged                         | 75            | 100.0       |
| Consistency                        |               |             |
| • Soft                             | 22            | 29.3        |
| • Firm                             | 45            | 60.0        |
| • Hard                             | 8             | 10.7        |
| Tenderness                         |               |             |
| • Tender                           | 09            | 12.0        |
| • Non-tender                       | 66            | 88.0        |
| Move with deglutition              | 75            | 100.0       |
| Any palpable cervical lymph nodes  | 8             | 10.7        |

Table V:
Distribution of the ultrasound findings of the thyroid gland (n=75)

| Ultrasound finding                | Frequency (n) | Percent (%) |
|-----------------------------------|---------------|-------------|
| Position of the nodule            |               |             |
| • Right lobe                      | 46 (61.3)     | 5 (6.6)     |
| • Left lobe                       | 22 (29.3)     | 2 (2.6)     |
| Margins of nodule                 |               |             |
| • Regular                         | 65 (86.7)     | 3 (4.0)     |
| • Irregular                       | 3 (4.0)       | 4 (5.3)     |
| Microcalcification                | 9 (12.0)      | 5 (6.7)     |
| Presence of Halo                  | 14 (18.7)     | 0 (0)       |
| Comet tail sign                   | 5 (6.7)       | 3 (4.0)     |

Table VI:
USG findings of benign and malignant solitary thyroid nodule (n=75)

| Ultrasound findings | Benign (n=68) | Malignant (n=7) | Total (n=75) |
|---------------------|---------------|----------------|--------------|
| Position of the nodule |               |                |              |
| • Right lobe        | 46 (61.3)     | 5 (6.6)        | 51 (68.0)    |
| • Left lobe         | 22 (29.3)     | 2 (2.6)        | 24 (32.0)    |
| Margins of nodule   |               |                |              |
| • Regular           | 65 (86.7)     | 3 (4.0)        | 68 (90.7)    |
| • Irregular         | 3 (4.0)       | 4 (5.3)        | 7 (9.3)      |
| Microcalcification  | 9 (12.0)      | 5 (6.7)        | 14 (18.7)    |
| Presence of Halo    | 14 (18.7)     | 0 (0)          | 14 (18.7)    |
| Comet tail sign     | 5 (6.7)       | 3 (4.0)        | 8 (10.7)     |

Table VII:
Distribution of the respondents by histopathological findings (n=75)

| Histopathological findings | Frequency (n) | Percent (%) |
|----------------------------|---------------|-------------|
| Benign                     | 70            | 93.3        |
| • Nodular goiter           | 57            | 76          |
| • Thyroiditis              | 5             | 6.7         |
| • Follicular adenoma       | 8             | 10.7        |
| Malignant                  | 5             | 6.7         |
| • Papillary                | 4             | 5.3         |
| • Follicular               | 1             | 1.3         |

Table VIII:
Comparison of ultrasound evaluation with histopathological diagnosis of thyroid nodule (n=75)

| USG findings | Histopathological diagnosis | Total |
|--------------|-----------------------------|-------|
|              | Benign | Malignant |      |
| Benign       | 67 (TP)| 1 (FP)    | 68    |
| Malignant    | 3 (FN) | 4 (TN)    | 7     |
| Total        | 70     | 5         | 75    |

TP = True positive; FP = False positive; FN = False negative; TN = True negative
Among 67 cases, were diagnosed as having benign nodule by USG and confirmed by histopathological evaluation. They were true positive. One case was diagnosed as having benign by USG which came out to be malignant in histopathological examination. They were false positive. USG diagnosed 7 cases as malignant. Histopathology revealed 3 of them as benign and 4 of them as malignant. They were false negative and true negative respectively.

Sensitivity of USG in differentiation of thyroid nodule was 95.71%, specificity 80%, positive predictive value (PPV) 98.52%, negative predictive value (NPV) 57.14% and accuracy 94.7%.

Discussion:
Total 75 patients of thyroid enlargement were included in the study. Mean age of the study participants was 37.02 ± 10.67 years ranging from 14–72 years. Majority patients (49.34%) belonged to age group 31 – 40 years. This is concordant with the findings of other studies involving solitary thyroid nodule done in Bangladesh by Khan et al.\(^2\) and Akhter et al.\(^2\) in their study found that out of 118 patients 54 were aged between 30 – 40 years. Akhtar et al.\(^2\) and her team found 42% patients belonging to age group 31 – 40 years.

Majority patients were female in this study constituting 86.7% of the study population. The ratio between male and female of the study group was 1: 6.5. Similarly, Akhter et al.\(^2\) found a male-female ratio of 1: 7.3 in their study and Khan et al.\(^2\) found a male-female ratio of 1:3.15 in the 30 -40 year age group in their study. Other age group also had more than double females than males in the study by Khan et al.\(^2\) and colleagues.

Local examination of 75 patients showed that all of the patients had thyroid swelling (100%) which moves with deglutition, 12% had pain, 8% had dysphagia and 6.7% had hoarseness of voice. Khan et al.\(^2\) found swelling in the neck 100% cases, dysphagia in 1.69% cases and hoarseness of voice in 0.85% cases, which is similar to this study.

Consistency of the nodules was firm in majority cases (60%), soft 29.3% cases, and hard 10.7% cases. Similarly Rahimi et al.\(^2\) found 63.8% benign nodules as soft and cystic and 36.2% of them being solid (hard).

In the present study 68% nodules were in the right lobe and 32% were in the left lobe. Khan et al.\(^2\) also found right lobe to be the prominent site (55%) cases along with left lobe in 50% cases.

Margin of the nodules were regular in 90.7% cases and irregular in 9.3% cases. Rahimi et al.\(^2\) enlisted a similar picture where 96.9% of the benign nodules were regular and 3.1% were irregular.

Ultrasound findings were consistent with benign nodule in 90.7% cases and with malignant nodule in 9.3% cases. In comparison Teja et al.\(^2\) found 68.3% benign and 31.7% malignant nodule in ultrasonography of thyroid nodules.
Out of 75 cases of present study, 95.6% benign tumor had regular and 4.4% had irregular margin and 42.9% malignant nodule had regular and 57.1% had irregular margin. Thapa,24 showed that 95% benign nodule had with well-defined margin and 90% of malignant nodule had poorly defined margin. Result of this study is lower than Thapa’s24 findings in case of malignancy but higher than Rahimi’s22 findings. Rahimi, et al.22 found 57.1% malignant nodules having regular and 42.9% having irregular margin.

In this study revealed 12.0% benign and 6.7% malignant nodule had microcalcification. Cappelli et al.25 In a study we found that the microcalcifications were significantly more frequent in malignant lesions than in benign nodules (72.2 vs 28.7%). This is similar to the findings of this study. Thapa,24 showed that among the various sonographic features microcalcification had the highest accuracy (76.0%) for the diagnosis of malignant lesion. Out of 82 benign lesions, calcification was present in 20 cases in their study and among them 65.0% were microcalcification.

In the present study out of all, 93.3% had benign and 6.7% had malignant lesion on histopathologic evaluation. In. Martínek et al.26 series 77.0% were benign and 23.0% were malignant in the histopathology of the resected thyroid nodules, which is comparable with findings of this study. Nggada et al.27 also found 73.9% benign cases and 26.1% malignant cases in their series and Teja et al.23 found 68.3% benign and 31.7% malignant cases. Compared to other studies the present study found more benign cases.

In the present study out of all benign nodule 10.7% were follicular adenoma, 6.7% thyroiditis, and 76 nodular goiter in histopathology and among malignant lesions 6.7% were papillary carcinoma and 1.3% were follicular carcinoma. In comparison Akhtar et al.21 Khan et al.20 found 24% cases of follicular adenoma and 12% cases of papillary carcinoma. Khan et al.20 found 44% colloid nodule, 2.54% thyroiditis and 12.71% papillary carcinoma.

Out of 75 patients halo sign was present in 18.7% cases and all of this nodules were benign. In Thapa,24 series all found 25.8% of benign cases had thin peripheral halo.

In the present study the sensitivity of USG to diagnose benign thyroid nodule was 95.71%, specificity 80%, positive predictive value 98.2% negative predictive value 57.14% and accuracy 94.7%. In a study Stacul et al.28 correlated the diagnosis of thyroid nodules with histopathological findings and found the similar results our study sensitivity, specificity and PPV, NPV and overall accuracy values of the grey scale ultrasound of their series were 46%,73%, 34%, 82% and 67% respectively, for solitary thyroid nodules. One hundred twenty patients undergone thyroid surgery for thyroid nodules or goiter were examined by preoperative ultrasound and fine needle aspiration cytology by Watters et al.29 In their study they found in the determination of type of lesion ultrasound had sensitively, specificity, and PPV of 74%, 83% and 51% respectively, that is also consistent with our study.

Conclusion: This cross sectional study was carried out with an aim to determine the usefulness of ultrasonogram diagnosis of solitary thyroid nodule was compared with histopathology findings. As the validity test results are higher,
thus it is evident that the USG useful diagnostic modality in the evaluation of solitary thyroid nodule.

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