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Diagnostic Accuracy of Ultrasonography Using U Classification of Thyroid Nodules in Detection of Malignant Thyroid

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ABSTRACT Ultrasonography (US) helps diagnose malignant thyroid nodules based on various characteristics, including echogenicity, margins, microcalcifications, size, form, and aberrant neck lymph nodes. The study aimed to determine the diagnostic accuracy of ultrasonography for cancer diagnosis in thyroid nodules, using Histopathology as the gold standard. To minimize morbidity and death from the condition and the number of solely invasive procedures biopsies, the results of our research will give patients and physicians with a noninvasive, cost-effective, and conveniently accessible diagnostic technique for differentiating cancerous from benign nodules. A cross-sectional analytical study was designed to collect data prospectively from July 2022 to October 2022 in the Department of Radiology at Nuclear Medicine, Oncology and Radiotherapy Institute Islamabad. Patients in the age range of 18-60 years, both genders were enrolled. Th data was entered into SPSS 24. The frequencies and percentages of categorical factors such as sex and malignancy in thyroid nodules were determined using descriptive analysis. For numerical variables such as age, the mean and standard deviation were computed. We evaluated the sensitivity, specificity, PPV, and NPV with a 95% confidence interval for the U-classification of malignant thyroid nodules and represented as Two by Two tables. In addition, Histopathology was used to evaluate U's efficacy as a diagnostic tool for finding malignant thyroid nodules. The study sample comprised 34 (68%) female and 16 (32%) male patients. On Biopsy, cancerous nodules were diagnosed in only 19 (38.5%) patients, and the remaining 31 (62%) had benign lesions. The prevalence of thyroid malignancy in our sample was 38%. On ultrasonography, malignancy was diagnosed in 15(30%) lesions, while the remaining 35(70%) patients were diagnosed with benign lesions. Histopathology confirmed malignant thyroid nodules in 15 (true positive) cases, whereas 6 (false positive) had no malignant lesion on Histopathology. In US negative patients, 27 were true negative, while 2 were false negative. The sensitivity of ultrasound U-score in diagnosing malignant thyroid nodules was 88.2%, specificity was 81.8%, PPV was 71.4%, and NPV was 93% Diagnostic accuracy is high when the US is used to detect thyroid problems, making it the preferred noninvasive technique. We recommend that thyroid lesions be routinely assessed clinically, imaged radiographically, and analyzed histo-pathologically. U Classification system for identifying potentially cancerous thyroid nodules is a valuable tool. It allows for a more prudent choice of nodules to undergo FNAC, reducing the number of needless procedures.

INDEX TERMS Pakistan, Diagnostic accuracy, Histopathology, Ultrasound, Thyroid cancer

I. INTRODUCTION

A thyroid nodule (TN) is a mass of solid, fluid-filled, or a combination of the two that develops from aberrant growths of thyroid cells within the thyroid gland. TNs are prevalent, affecting 20% to 76% of the population [1]. The incidence of TNs have been measured at 2-6% by physical examination, 19-35% by imaging, and 8%-65% by autopsy [2]. The incidence increases with age and is more common in women than in men [3]. The need to rule out thyroid cancer, which occurs in 7–15% of people, is what makes TNs assessment so important [4]. Non-modifiable risk variables include female gender, advancing age, and prior neck radiation exposure. Iodine deficiency,

alcoholism, and smoking are risk factors that may be modified[2], [5] Because of its low cost, relative safety, and lack of risk associated with surgery, ultrasonography (US) is often used, especially for examining thyroid nodules. Although many imaging modalities, such as radionuclide thyroid scan, CT, and MRI, are used to identify thyroid disorders, It is common practice to use US to check for thyroid nodules. [6].

The British Thyroid Association ultrasound (U-classification of thyroid nodules) was implemented pertaining to the general guidelines for thyroid cancer therapy, mainly to help determine whether to continue with FNAC [7]–[9]. The degranulation, colloid artifact, outline, and vascularity of nodules are used to assign them to one of five different categories (U1-U5). Normal thyroid parenchyma (U1), benign nodules (U2), indeterminate/equivocal nodules (U3), concerning nodules (U4), and malignant nodules (U5) are all classifications used to describe thyroid nodules. FNAC is advised for nodules classed as U3, U4, and U5[10]. "Thyroid Imaging Reporting and Data System'' (TIRADS) and 'BTA U classification' systems aid radiologists and doctors in defining the type of nodules and choosing patients for histo-pathology. The gold standard for distinguishing TNs is the histological examination after FNA biopsy. Cytology by FNA is suggested for nodules larger than 10 mm. FNA biopsies have a miss rate of 1-3% for nodules less than 4 cm and a rate of 10-15% for those greater than 4 cm. [11].

We aimed to assess the diagnostic efficacy of the U categorization scheme, using Histopathology as the reference standard. Our research aimed to determine how well ultrasonography utilizes the U" classification of thyroid nodules compared to histology for diagnosing malignant thyroid nodules. The contribution of this study is as follows:
1) The study will fill the research gap on the subject.
2) Reducing disease-related mortality and the need for invasive diagnostic biopsies, the findings of the current study will provide patients and doctors with a noninvasive, inexpensive, and convenient imaging method for determining if thyroid nodules are benign or cancerous.

II. METHODOLOGY

A cross-sectional analytical study was designed to collect data prospectively from July 2022 to October 2022 in the Department of Radiology at Nuclear Medicine, Oncology and Radiotherapy Institute Islamabad.

A. STUDY POPULATION

Patients in the age range of 18-60 years, both genders were enrolled. Only Patients presenting with both solitary and multinodular solid nodules thyroids were included.

Patients with known thyroid disease with neck abscesses were diagnosed with ultrasonography, and proven histopathology reports were excluded. Using the reported sensitivity of ultrasonography in detecting thyroid cancer at 81.2%[12] and assuming a 95% confidence interval and a margin of error of 5%, a sample size of 50 was necessary for the study. All eligible patients referred to the radiology department at NOORI Hospital were enrolled. Patients had been suffering from thyroid nodules for more than six months, and their presentations varied from solitary to multinodular. Patients considered for inclusion had a comprehensive history and physical examination in addition to standard hospital investigations.

B. DATA ACQUISITION

Patients had ultrasonography carried out by a technician in the watchful eye of a radiologist at the hospital's Radiology department. All of the readily accessible ultrasound scans of the gland and cervical regions were acquired with an optimal gain utilizing a linear-array transducer (7.5 MHz and curvilinear 3.5 MHz) on an ultrasonic scanner by Phillips Medical Systems (HD11, HD11 XE, iU22) or Toshiba (Xario200). Every ultrasound was done with the patient lying supine in a relaxed environment. The Radiologist examined each picture on either the Osirix workstation or Medweb.

C. DATA PROCESSING

The characteristics of each thyroid nodule were determined by analyzing their size, composition, echogenicity, edges, evidence of calcifications, height about width, halo, color flow, and lymphadenopathy. Using the criteria outlined in the BTA Guidelines, nodules are classified as either usual (U1), benign (U2), indeterminate (U3), worrisome/suspected (U4), or cancerous/malignant (U5)[13]. If one or more of the following sonographic characteristics were present in an ultrasound examination of a thyroid nodule, it was determined that the nodule was cancerous. In microcalcification, tiny hyperechoic, ghon tubercles are diagnostic. A nodule was characterized as micro-lobulated with a surface covered in tiny lobules or with ragged edges. Extremely low echogenicity compared to the surrounding neck muscle is known as "marked hypo-echogenicity." Nodules are determined by their vertical rather than horizontal dimensions. If the sonographer did not find any of the characteristics above in the thyroid nodule, it was considered benign [14]. When the tissue sample showed atypical enlarged, crowded pleomorphic cells with overlapping nuclei, the nodule was classified as True positive (TP) or malignancy detected; otherwise, the nodule was categorized as malignancy not established or True negative (TN) [15], [16].

Thyroid nodules were classified as false positives when ultrasonography results hinted at cancer (FP). However, there were no cytologically abnormal cells in the sample. Similarly, ultrasonography results of benignity for a thyroid nodule that later proved to have malignant histology constituted a false negative (FN). Positive predictive values (PPV) were calculated to ascertain the chance that a subject had cancer if an ultrasonographic finding of a malignant nodule was made. Ultrasound's negative predictive value (NPV) was also computed to determine what percentage of patients did not have malignancy.

Correctly categorized participants (those with thyroid cancer and those with benign thyroid nodules, (TP+TN) were divided by all patients (True positive+ True negative+ False positive+ False negative) to determine the percentage of correct classifications.

Thyroid nodule size was not a criterion because it has been demonstrated that US measurements of nodule size do not correlate with their malignancy risk. One consultant radiologist with over 8 years of experience performed FNAC after all ultrasounds. To avoid bias, a histopathologist with 5 years of experience analyzed the FNAC samples without knowing that the patient had been diagnosed in the US with a thyroid nodule.. Thyroid nodule FNAC cancer diagnoses were gathered from the electronic medical records and used as a comparison group. The conceptual framework of the study methodology is shown in FIGURE 1.

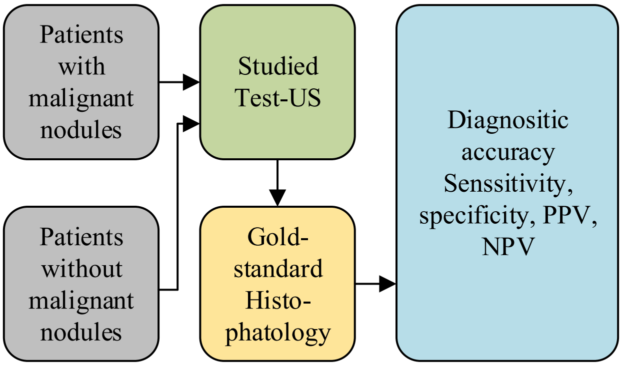

FIGURE 1. The conceptual framework

D. DATA ANALYSIS

The latest version of SPSS (V. 26) was used to analyse the data. Thyroid nodule sex and malignancy were two of the categorical variables that were analysed using descriptive statistics to calculate frequency and percentage. For numerical variables, like age, we can get the mean and standard deviation. With regards to the U-classification of thyroid nodule malignancy, we analysed sensitivity, specificity, PPV, and NPV with 95% confidence interval. In addition, Histopathology was used to establish U's performance as a means of determining whether or not thyroid nodules are cancerous.

III. RESULT

50 patients who'd been diagnosed with thyroid nodules were included in the current research. 44 (or 68%) of the patients were female, whereas just 16 (or 32%) were male. Patients' ages ranged from 22 to 59, with a mean of 42.48 (±9.145) years. The demographic characteristics of the study sample are shown in TABLE 1.

TABLE 1
Demographic characteristics of patients

Parameter	n	%	Mean ± SD
Age	50	100	42.24 ± 9.482
BMI			24.34 ±4.65
Male	16	32.0	-
Female	34	68.0	-
Family H/O Thyroid disease			-
Yes	29	58.0	
No	21	42.0	

After a BTA U classification nodule evaluation, the Radiologist classified thyroid nodules as U2 represents benign nodules, U3 represents indeterminate/equivocal nodules, U4 represents worrisome nodules, and U5 represents cancer nodules. TABLE 2 shows the Thyroid nodule prevalence by U categorization category.

TABLE 2
Thyroid nodule prevalence by U categorization category

U Score	N	%
U2	26	52.0%
U3	8	16.0%
U4	7	14.0%
U5	9	18.0%

TABLE 3
Histopathology Findings

Histopathology	N	(%)
Benign	**31**	**62%**
Nodular hyperplasia	13	41.9%
Follicular adenoma	8	25.8%
Hashimoto's thyroiditis	7	22.6%
Hurthle cell adenoma	2	6.5%
Riedel's thyroiditis	1	3.2%
Malignant	**19**	**38%**
Papillary carcinoma	7	36.8%
Follicular carcinoma	6	31.6%
Hurtle cell carcinoma	2	10.5%
Follicular variant PTC	2	10.5%
Microscopic PTC	2	10.5%

On Histopathology, cancerous lesions were diagnosed in 19 (38.5%) subjects, and the remaining 31 (62%) had benign lesions. The prevalence of thyroid malignancy in our sample was 38%. On ultrasonography, malignancy was diagnosed in 15(30%) lesions, while other 35(70%) patients were diagnosed with benign lesions as shown in TABLE 3. Histopathology confirmed malignant thyroid nodules in 15 (true positive) cases, whereas 6 (false positive) had no malignant lesion on Histopathology. In US negative patients, 27 were true negative while 2 were false negative. The sensitivity of ultrasound U classification in diagnosing malignant thyroid nodules was 88.2%, specificity was 81.8%, PPV was 71.4%, and NPV was 93% (TABLE 4, TABLE 5).

TABLE 4
Two-by-Two Table: Ultrasound U-Score in the Diagnosis of Malignant Thyroid Nodules vs Histopathology as the Gold Standard

Malignancy on Ultrasound	Malignancy on Histopathology		Total Number
	Yes (U4-U5)	No (U1-U3)	
Yes	15	6	21
No	2	27	29
Total Number	17	33	50

TABLE 5
Diagnostic accuracy of US

Parameter	Percent
Sensitivity	88.2%
Specificity	81.8%
Positive Predictive Value	71.4%
Negative Predictive Value	93.1%

IV. DISCUSSION

Ultrasound is usually the very first radiological test recommended for thyroid nodules, particularly in females. It was formerly believed that ultrasound was only helpful in distinguishing solid nodules from cystic nodules; however, with improved resolution, this is no longer the case. Doppler scans and probes have elevated ultrasound to a new level by revealing several advances made possible by the new technology [17]–[20]. Thyroid nodules can be either benign or cancerous, and there is no one sonographic marker that can accurately tell the difference between the two. The British thyroid association classified nodules into five categories based on their knowledge of characteristics associated with recorded instances of cancerous and non-cancerous nodules, with U1 representing normal nodules and U5 indicating characteristics generally linked with malignancy. In 2014, a new categorization system called U was introduced. Given the potential cost and logistical burden of attempting to aspirate every single nodule, this tool will help the Radiologist better direct the need for FNAC on selected patients. In addition to being physically taxing, this can also put an extra financial burden [21]. Therefore, U2 nodules are always safe, and it is sufficient to report them as such merely; no more action is necessary. However, U4 and U5 included features associated with malignancy, whether present alone or in high numbers. As a result, they had to be wiped out. Although U3 was the most common class, it was also the hardest to predict. The reason is that the probability of cancer in this group was low but not zero[22], [23].

Thus, we choose to perform this research to gauge the diagnostic precision of our classification scheme within our infrastructure. Therefore, the study will benefit us by reducing patient anxiety and morbidity. The patients have been split in half, each receiving treatment tailored to one of two U classification categories. Group one consisted of the benign nodules with U-1 through U-3. Nodules that are classified as U4 or U5 were placed in the second group because they were thought to be malignant. In our study ultrasound, U classification for differentiation of non-cancerous from cancerous nodules had an 88.2% sensitivity, 81.0% specificity, 71.4% positive predictive value (PPV), and 93.1% negative predictive value (NPV). Our findings are similar to those of prior research. The results demonstrate a relatively good sensitivity, and the specificity and PPV are also consistent with prior work.[24]–[26] Thyroid cancer was present in 38 percent of our study population. Potentially attributable to the small sample size in the current study. A recent study compared the U classification to TIRAIDS, the study demonstrated that the U classification is more accurate at predicting the presence of thyroid cancer. TIRADS indicated FNA with a sensitivity of 73.3% and specificity of 64.2%. With the TIRADS evaluation of TN, the NPV was 75.5% and the PPV was 61.5%[27]. According to Ghani et al., the ultrasound U score has a PPV of 60% and an NPV of 100% when detecting malignant lesions, and it is also 100% sensitive and 91.3% specific. This study aims to evaluate the accuracy of the new thyroid classification for predicting thyroid cancer by comparing ultrasonography results to those of the gold-standard histological findings [22]

Similar findings were reported by Ahmad et al., who analyzed data from an additional 210 patients with thyroid nodules to determine the diagnostic accuracy of ultrasound U-score. They found that US has a sensitivity of 90.24 percent, a specificity of 94.6 percent, a positive predictive value of 80.4 percent, and a negative predictive value of 97.5 percent [27]. Akhter et al. found that the U-score obtained via ultrasound had a sensitivity of 80%, a specificity of 34%, a positive predictive value of 100%, and a negative predictive value of 90 [28].

Compared to other classification methods, the U classification has been shown to have a relatively less needless FNA. We conclude from our research that U categorization may help minimize the number of needless FNAs performed on Pakistani patients, relieving financial and emotional strain on these individuals and their families. There are some limitations to this study that should be discussed. 1) Unfortunately, scheduling restrictions required that our study only included a small number of participants. Thus the study included a small size. 2) Since 2014, our hospital has followed the BTA recommendations for treating patients with thyroid nodules, not TRIADS. Future investigations will be necessary to compare TIRADS and U classification with a larger sample size and consider potential biases.

IV. CONCLUSION

The current study's aim was to assess the Diagnostic accuracy of U classification in the detection of malignant Thyroid nodules and the findings show that U classification is valuable to detect malignant nodules in patients, making it the preferred noninvasive technique. The sensitivity of ultrasound U classification in diagnosing cancerous thyroid nodules was 88.2%, specificity was 81.8%, positive predictive value was 71.4%, and negative predictive value was 93%. We recommend that thyroid lesions be routinely assessed clinically, imaged radiographically, and analyzed histo-pathologically, just like breast lesions. Further studies should be conducted comparing the two classification systems like U and TIRADS to assess which technique is more accurate in the detection of malignant nodules. The BTA Guidelines' U Classification system for identifying potentially cancerous thyroid nodules is a valuable tool according to our results as it allows for a more judicious choice of nodules to undergo FNAC, reducing the number of needless procedures. Additional research ought to concentrate on the comparison of BTA U classification and TIRADS for discriminating benign from malignant thyroid nodules. These methods have the potential to replace FNAB in a population undergoing unnecessary invasive and cost intensive diagnostic tests. Moreover, the use of the U Classification will provide a shared apprehension of the thyroid nodule among radiologists, and doctors, allowing for more efficient and cost-effective follow-up and improved results.

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