Thyroid nodules' evaluation by ultrasound and fine-needle aspiration cytology

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ABSTRACT

The clinical significance of knowing the status of thyroid nodules is the need to exclude thyroid cancer. The purpose of this study is to evaluate ultrasound (U/S) features of thyroid nodules and correlate them with fine-needle aspiration cytology (FNAC). A descriptive prospective study was conducted at the Radiology Department, King Khalid University Hospital, King Saud University (KSU), Riyadh, KSA. The inclusion criteria were adult patients with neck swelling, palpable neck lesion, and/or abnormal thyroid-stimulating hormone (TSH) laboratory test result. Philips IU22, epic, sonosite, and Toshiba-Xerio ultrasound (U/S) systems with 7-MHz transducers were used in this study. All participants underwent a thyroid U/S scan according to standard protocol. FNAC-U/S was conducted for 159 nodules (according to suspicious U/S features) using a 10-ml plastic syringe with conventional (23 to 25) gauge needle. There were 246 participants included in this study (165 females [67%] and 61 males [33%], age range 13 to 88 years). There were 303 types of thyroid nodules noted, as follows: 47.8% were solid nodules, 42.5% were complex, and 9.6% were cystic nodules. Among 159 FNAC samples, 8.2% (n = 13) were positive results for malignancy. Females predominantly had malignant results (P = 0.001). U/S showed a sensitivity of 89.1 and 78.0% and a specificity of 43.0 and 57% for the right and left lobes, respectively. FNAC showed a sensitivity of 10.0% and 21% and a specificity of 56.9% and 42% for the right and left lobes, respectively. In conclusion, nodule malignancy and gender were significantly associated. Mixed and hypoechoic nodules were common features of malignancy. Both U/S and FNAC confirmation were important in thyroid nodule evaluation.

Keywords: Ultrasound, thyroid, nodules, fine needle, aspiration, cytology, Saudi Arabia.

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INTRODUCTION

The clinical significance of knowing the status of thyroid nodules is the need to exclude thyroid cancer, which is present in 4 to 6.5% of all thyroid nodules in nonsurgical series, Ross (2019). Anil et al. (2011) stated that the best tool for thyroid nodule malignancy risk stratification is an ultrasound (U/S) and guided biopsy of nodules with suspicious imaging features. The fine needle aspiration cytology (FNAC) method is commonly used with U/S guidance for diagnostic confirmation in cases where malignancy is suspected. For sensitivity and specificity,

Neagoe (2017) showed that FNAB recorded a sensitivity of 33.3%, specificity of 93.3%, false-negative rate of 50%, and false-positive rate of 12.5%, whereas cervical ultrasound recorded a sensitivity of 92.3%, specificity of 75.3%, false-negative rate of 2.8%, and false-positive rate of 48.9%.

The prevalence of a benign nodule was noted in 72% and malignant nodules were noted in 6% of patients, reported by Ugurluoglu et al. (2015). Saeed et al. (2018) studied thyroid lesions in the western region of Saudi Arabia and concluded that there was a marked female predominance in all types of thyroid nodules. The most common age group affected was 30 to 39 years.

Norman (2019) has shown that thyroid fine-needle aspiration (FNA) biopsy is the only non-surgical method that can differentiate between malignant and benign nodules in most, but not all, cases.

The objective of this current study was to evaluate U/S features of thyroid nodules and correlate them with FNAC. The target population included patients with one of the following: neck swelling, palpable neck lesion, and abnormal thyroid function laboratory test result. The researchers in this descriptive study investigated the following questions: Which of the U/S features correlate with positive FNAC results for malignancy? Which types of thyroid nodules are common? And which of these types are associated with age or gender in the Saudi population?

A few studies discussed the topic of this study; so, the researchers suspect that the results of this study may have a clinical significance.

MATERIALS AND METHODS

This descriptive prospective study was conducted at the radiology department at King Khalid University Hospital, King Saud University (KSU), Riyadh, KSA. The inclusion criteria were adult patients who exhibited one or more of the following: neck swelling, palpable neck lesion, and abnormal thyroid-stimulating hormone (TSH) laboratory test result (the normal value of TSH ranges from 0.4 to 4.0 milliunit per liter (mU/L)). Patients with known thyroid cancer were excluded. The participants were selected through convenience sample selection. Philips IU 22, epic, sonosite California, USA and Toshiba-Xerio, California, USA ultrasound (U/S) systems with 7-MHz transducers were used in the study. All participants underwent a thyroid U/S scanning in the supine position with a pillow under their shoulders for optimal viewing of the thyroid. Both right and left thyroid lobes with the isthmus were scanned in sagittal and transverse views. U/S-guided FNAC was conducted for 159 of 303 nodules (52%), according to the nodules' suspicious features based on the U/S findings. The needle size or number of passes used in the U/S–FNAC procedure was performed according to the U/S features of the thyroid nodule. A parallel technique was applied to obtain the biopsy samples (the needle location was parallel to the U/S probe). The patient's anterior neck was locally sterilized with chloroprep and was numbed with Xylocaine 1%. A 10-ml plastic syringe with a conventional 23–25-gauge needle was used. The needle tip and thyroid nodule were visualized using real-time U/S during the procedure. The needle was targeted to areas that were assumed to contain the most cellular material, such as the solid or non-central parts of a vascular nodule or cyst. Continuous low suction pressure was applied simultaneously with forward-and-back movements of the needle within the lesion until the material was seen in the needle hub. Suction was slowly released before the needle was removed from the incision. After the procedure, manual compression was applied for 10 minutes at the biopsy site. All patients were observed for 30 minutes after the biopsy and they were informed of the possible signs and symptoms of a hematoma. All collected samples were labeled and sent for histopathological assessment, and the results were correlated with the nodules' U/S features.

Data collection

A datasheet was used to collect and organize the study variables, which included patient demographic data, FNAC results, and U/S findings. The American Thyroid Association Management Guidelines, Haugen (2016) were considered when evaluating the nodules. Nodules' U/S features that had a high risk of being malignant in the study were: hypoechoic, mixed echogenicity, intranodular hypervascularity, and irregular outlines nodules. To ensure patient confidentiality and anonymity, patients were given a number instead of writing his/her name on the data collection sheet. Identifying information was also removed from the selected images. Verbal consent was obtained from the participants. Ethics approval (16/0241/IRB) was obtained from the institutional review board (IRB) of King Saud University (KSU) College of Medicine.

Data analysis

The software Statistical Package for Social Sciences (SPSS) 16.0 (LAS VEGAS – USA) was used to analyze the data. Pearson's correlation and Chi-square tests were used for statistical analysis of the associations between the study variables. The statistical association was considered to be significant when $P < 0.05$.

RESULTS

There were 246 participants included in this study, among whom 165 were female (67%) and 61 were male (33%), with an age range of 13 to 88 years. Table 1 summarizes the types of thyroid nodules detected. There were 303 types of nodules detected (some participants had multiple nodules): 47.8% were solid nodules, 42.5% were complex, and 9.6% were cystic nodules. There was no statistical association of the nodule type with age or gender (p = 0.97 and 0.16, r = −0.0 and −0.08, respectively). The nodule means sizes were 1.4 ± 1.0 and 1.6 ± 1.3 cm for the right and left lobes, respectively. A Pearson's correlation between nodule size and FNAB results revealed no statistical association for the right and left lobes (p = 0.129 and 0.078, r = 0.151 and 0.183).

Tables 2 and 3 present the U/S features of the detected thyroid nodules and correlations between the U/S features with positive FNAC results. The most common nodule features were a peripheral halo of low echogenicity, which was detected in 43.8 % nodules, followed by perinodular blood flow, which was detected in 37.9% nodules. All the malignant nodules matched the suspicious U/S features, and among 13 malignant nodules, seven nodules showed mixed echogenicity and

Table 1. Frequency of nodule types.

Nodule types	Right lobe	Left lobe	Total
Solid	87	58	145
Cystic	16	13	29
Complex/Mixed	85	44	129
Total	188	115	303

Table 2. U/S features for the detected nodules.

Nodule features	Frequency in the right lobe	Frequency in the left lobe	Total
Peripheral halo of low echogenicity	70	63	133
Posterior shadowing	7	7	14
Calcifications	23	24	47
Septations	12	8	20
Intranodular flow	6	4	10
Perinodular flow	75	40	115
Both Intra and Perinodular flow	33	32	65
Nodular irregular outline (contour)	6	7	13
Associated lymphadenopathy	22	24	46

Table 3. Correlations of nodule U/S features with positive FNAC results.

Nodule U/S features	Frequency in the right lobe	Frequency in the left lobe	Total	Percentage (%)	P-value
Hypoechoic nodules	0	6	6	46.15	< 0.001
Mixed nodules	4	3	7	53.8	< 0.001
Irregularity	4	2	6	46.15	< 0.001
Ill-defined margins	3	2	5	38.46	< 0.001
Calcifications	2	4	6	46.15	< 0.001
Associated lymph nodes	2	4	6	46.15	< 0.001

six were hypoechoic nodules. All suspicious U/S features were statistically associated with the FNAC positive results P < 0.001.

Tables 4 and 5 show the FNAC results in crosstabulation with the study gender, and FNACs were 159 samples, with 86 nodules from the right lobe and 73 nodules from the left lobe. Positive FNAC results for malignancy were noted in 8.2% (13 of 159) of lobes (nine in the left lobe and four in the right lobe). Additionally, 76.9% of the malignant nodules were detected in females (P = 0.001). For FNAC results and according to the nodule malignancy diagnosis, the U/S had a sensitivity of 89.1% and 78.0% and a specificity of 43.0% and 57% for the right and left lobes, respectively. The FNAC had a sensitivity of 10.0 and 21% and a specificity of 56.9 and 42% for the right and left lobes, respectively. The Chi-square test revealed a positive association between the FNAC results and the nodule's echogenicity (P < 0.001). Pearson's correlation showed no significant statistical association between the types of nodules or the echogenicity of the nodules and age (P = 0.9 and 0.09,

respectively), and no statistical association between the age and a positive FNAC result (P = 0.06).

Figure 1 presents the frequency of nodules according to their site, and 27% of the participants had right lobe nodules only, 22% had left lobe nodules only, and 47% had bilateral nodules. Figure 2 shows the multiplicity of the nodules, 71% of the participants had multiple nodules, and 29% had solitary nodules. Figures 3, 4 and 5 show representative sample images: a mixed nodule is shown in Figure 3, a solid nodule with intra-nodular vascularity is shown in Figure 4, and a well-defined hypoechoic nodule with complete peripheral halo is shown in Figure 5.

DISCUSSION

The clinical significance of knowing the status of thyroid nodules is the need to exclude thyroid cancer. The current study findings showed 303 nodules, where 47.8% were solid nodules, 42.5% were complex nodules, and

**Table 4.** Patient gender and FNAB results in the right lobe crosstabulation.

Patient gender	FNAB results in right lobe				Total
	None	Negative for malignancy	Positive for malignancy	Equivocal	
Male	50	10	1	0	61
Female	110	60	3	12	185
Total	160	70	4	12	246

Table 5. Patient gender and FNAC results in the left lobe crosstabulation.

Patient gender	FNAC results in left lobe				Total
	None	Negative for malignancy	Positive for malignancy	Equivocal	
Male	46	11	2	2	61
Female	127	42	7	9	185
Total	173	53	9	11	246
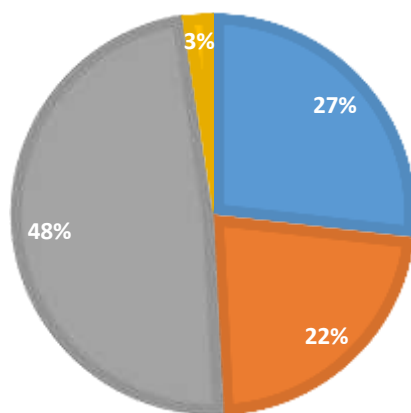
Figure 1. Nodule site frequency.
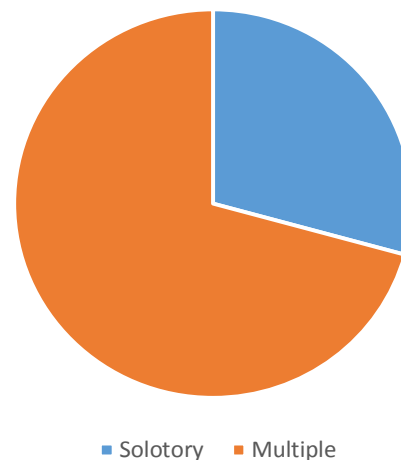
Figure 2. Nodule multiplicity according to the participants.

9.6% were cystic nodules.

Regarding the sensitivity and specificity of U/S in diagnosing nodule malignancy, this study agrees with Neagoe (2017) who suggested that cervical ultrasound has a sensitivity of 92.3% and specificity of 75.3%. These results also agree with Li et al. (2016) who stated that the U/S diagnosis of thyroid nodules had an overall sensitivity of 86.0% and a specificity of 81.9%. Neagoe (2017) showed that FNAC had a sensitivity of 33.3% and specificity of 93.3%. Conversely, these results disagree with the current study, which showed that the FNAC had a sensitivity of 10.0% and 21% and a specificity of 56.9% and 42% for the right and left lobes, respectively.

In the current study, among 159 FNAC samples that were selected according to U/S suspicious features, only 8.2% of these samples were confirmed to have malignant nodules; these results are in agreement with Remonti et al. (2015) who concluded that U/S features in isolation do not provide reliable information to select nodules that should be assessed using FNAC. Additionally, the results were not in agreement with Park et al. (2016) who reported that 28.8% of the selected thyroid FNAC samples showed a positive result for malignancy.

Halenka and Frysak (2017) proposed that nodules with suspected malignancy are solid, hypoechoic, and have punctuated calcifications. Park et al. (2016) indicated that the most frequent finding was associated with marked hypoechogenicity and the least frequent finding was a non-circumscribed nodule's margin. The current study showed that besides these suspicious features that were identified using U/S, mixed nodule echogenicity, and irregular and ill-defined margin are also associated with
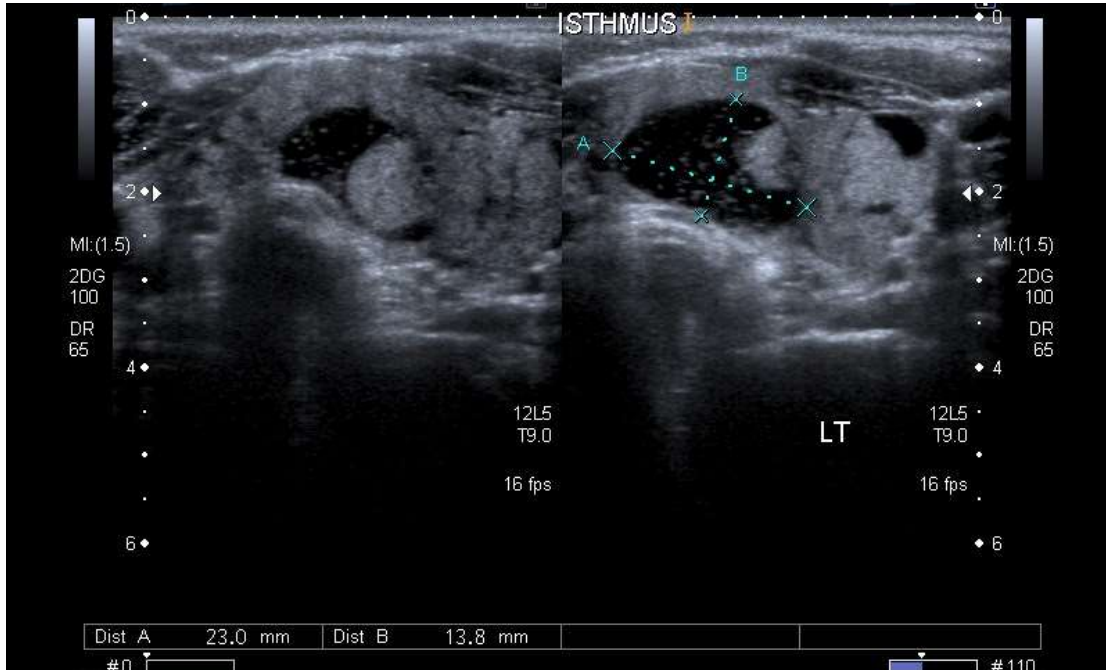
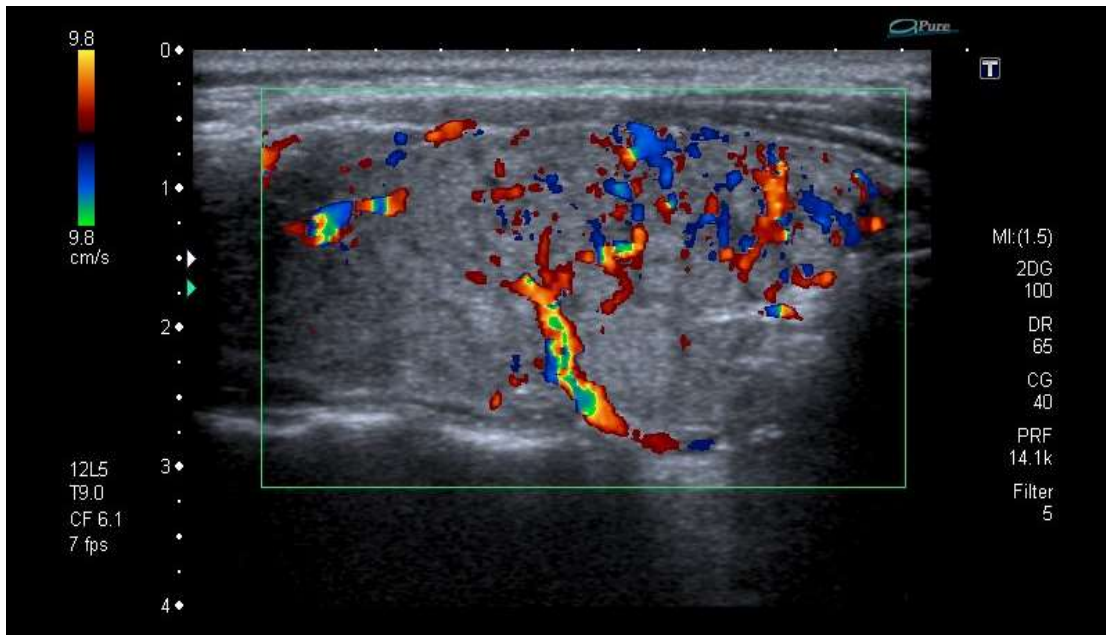**Figure 3.** A mixed nodule measuring 2.3 × 1.3 mm was noted in the left thyroid lobe.

Figure 4. Intra-nodular vascularity was noted in a 44-year-old female in the left thyroid lobe.

malignancy. Additionally, associated lymph nodes are noted in 46% of the confirmed malignant cases.

This study showed that there was no association between positive FNAC results and nodule size. These findings are in agreement with Norman (2019) who concluded that the size of the nodules is not a reliable indicator of their malignant potential.

The current study indicated that 76.9% (which is 10 cases) out of the 13 malignant nodules were detected in females, which is a statistically significant association. These results agree with Saeed et al. (2018) who showed a marked female predominance in all types of thyroid nodules.

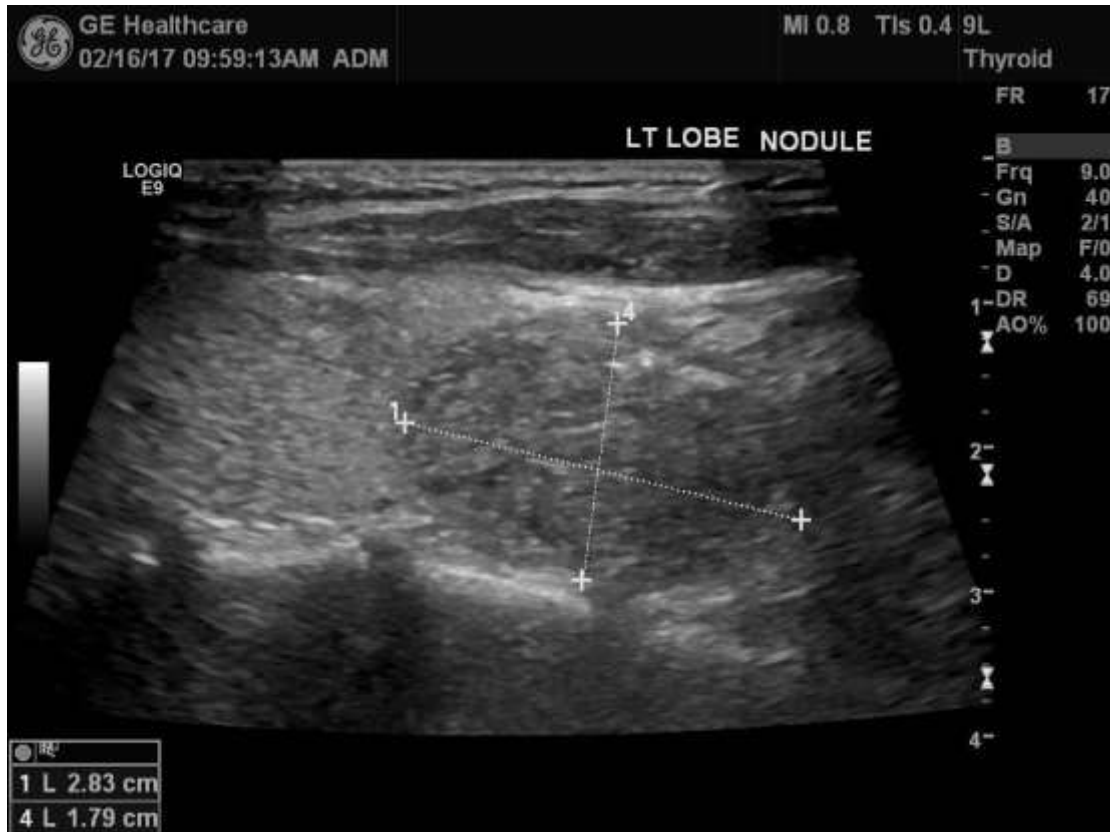These study results revealed no statistical association

Figure 5. A 28 × 17 mm hypoechoic nodule with a complete peripheral halo.

between nodule malignancy and age, pearsn's R was -.049 and P-value was 0.4. Conversely, these findings disagree with Kwong et al. (2015), who suggested that the risk of malignancy in a newly identified nodule decreased with advancing age.

This study is unique because most of the previous studies regarding the same topic in the KSA were retrospective studies.

CONCLUSION

This study concluded that solid nodules are the most common type of nodules and that there is no statistical association between nodule types and age or gender. Not all selected samples with features that were suspicious for FNAC based on U/S were diagnosed as malignant. However, suspicious features on U/S were noted in 100% of nodules that had positive FNAC results. These features include; Ill-defined margins, Hypoechoic, Mixed, and Irregular nodules also, nodules that associated with calcifications and dilated lymph nodes. A significant statistical association was noted between nodule malignancy and gender, with females predominantly showing malignancy. Thus, both U/S features and FNAC confirmation are important in thyroid nodule evaluation.

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