Radiological-pathological correlation of ACR-TIRADS ultrasound classification of thyroid nodules with fine needle aspiration cytology results at TikurAnbessa Specialized Hospital: Prospective study from April 2023- November 2023

A research thesis submitted to Addis Ababa University, college of Health science, School of Medicine, Department of Radiology; in partial Fulfillment for the Requirements of Post graduate certificate in Radiology

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1. Abbreviations

AAU: Addis Ababa University

ACR: American College of Radiology

CHS: College of Health Sciences

CT: Computed Tomography

FNA: Fine Needle Aspiration

MNG: Multinodular Goiter

MRN: Medical Record Number

MRI: Magnetic Resonance Imaging

TASH: TikurAnbessa Specialized Hospital

TBSRTC: The Bethesda System for Reporting Thyroid Cytology

TIRADS: Thyroid Imaging, Reporting and Data System

US: Ultrasound

2. Summary

2.1 Background

Ultrasound based risk stratification is a widely used method currently helping to guide management in patients with thyroid nodules; which are common and mostly benign. The use of these risk stratification methods has helped reduce unnecessary FNAC rates, therefore, reducing the burden both on patients and the health care system. This study aims to determine the effectiveness of ultrasound-based risk stratification by correlating ultrasound findings and pathologic diagnosis at TikurAnbessa specialized hospital (TASH).

2.2 Methodology

This was a hospital based prospective radiologic pathologic correlation study in patients referred for ultrasound guided FNAC based on their American College of Radiology Thyroid Imaging, Reporting and Data System (ACR-TIRADS) score at TikurAnbessa Specialized Referral and Teaching Hospital, radiology department, during the time period of April-September 2023 to assess accuracy of ACR-TIRADS in ultrasound based thyroid nodule risk stratification in our hospital.

Sixty two patients with thyroid nodules were subjected to ultrasound and USG guided FNAC. Each was assigned a TIRADS and Bethesda category. The outcomes were contrasted in order to assess the ultrasound's sensitivity, specificity, and positive predictive value (PPV) in terms of distinguishing benign from malignant nodules.

RESULT: Twenty-six of the sixty-two nodules that were analyzed classified into TIRADS 3, and thirteen and twenty-three, respectively, into TIRADS 4 and 5. On FNAC, 36 were found to be Bethesda 2 & 5, 7, 1 and 8 to Bethesda 3, 4, 5 and 6 respectively. The sensitivity, specificity and PPV of ultrasound were found to be 93.75, 54.35, and 41.67 % respectively.

Key words: Thyroid nodule, Ultrasound, ACR-TIRADS, FNAC, pathologic diagnosis, effectiveness/accuracy

3. Introduction

3.1 Background

A radiologically distinct lesion within the thyroid gland that is isolated from the surrounding thyroid parenchyma is known as a thyroid nodule. Certain palpable lesions might not be associated with specific abnormalities in radiology. These anomalies do not fit the precise description of thyroid nodules. (1) Thyroid nodules occur in up to 50% of adults while palpable thyroid nodules occur in only 3-7%. In 20%–68% of patients with high-resolution US, 25% with contrast-enhanced CT, and 16%–18% with MRI, they are incidentally found. A common characteristic in the prevalence of thyroid disorders is its female preponderance with a female-to-male ratio at about 4:1 for thyroid nodules and the increasing prevalence with age. (2) (3) (4) (5) (6) (7)

According to a study done on prevalence and associated factors of thyroid incidentaloma among adult people attending Gondar University Hospital, Ethiopia, the frequency of thyroid incidentaloma was found to be 33.4%. It was detected in 42.4% of females and 22.7% of males. (8)

Malignancies occur in 5-7% of all thyroid nodules. And generally the probability of malignancy in a nodule is higher for men and for patients under the age of 15 years and above 45 years. Yet, the incidence of thyroid malignancy is higher in females with ratio of 2-3:1. (9) (10) (11)

Ultrasound is a safe, fast and comfortable method for evaluating the thyroid gland and regional anatomy. High resolution probe between 10-15MHz should be used in thyroid imaging. (4) (5) (12) Specific characteristics, such as microcalcifications, extension beyond the thyroid edge, cervical lymph node metastases, taller than wider form in transverse plane, and marked hypoechogenicity, are utilized by ultrasound for determining suspicious nodules. Lack of halo, ill-defined or irregular margin, solid composition and increased central vascularity are less specific features that may raise suspicion. It has been reported that, as more of these suspicious features are seen in a nodule the probability of it being malignant also increases. (2) (9) (10)

Radiologists who analyze thyroid US images often have a difficult time of reporting nodules, despite their widespread occurrence and high degree of benignity. Systems of risk categorization have been created as a result to address this issue. (13)

One of these risk stratification guidelines is the ACR-TIRADS which we recently started to use in our hospital. The American College of Radiology created the ACR TI-RADS risk stratification system in 2017 with the goal to offer practitioners a simple way to decide management. It is intended to help patients by adopting guidelines that are backed by data and consensus expert opinion, while also enhancing uniformity among practices and institutions. It is predicated on ultrasonic imaging data, which are separated into five categories: composition, shape, margin, echogenicity and echogenic foci. Each feature is given a point value between 0

and 3. The risk level of a nodule is determined by its total point, which varies from TR1 (benign) to TR5 (very suspicious). For TR1 and TR2, the projected risk of nodule malignancy was 2% or less; for TR3, it was 2.1-5%; for TR4, it was 5.1-20%; and for TR5, it was more than 20%. In conjunction with the nodule's maximum diameter, the TR level determines whether to recommend FNA biopsy, follow up US exam, or no further action. For nodules classified as "benign" (TR1) or "not suspicious (TR 2)," ACR TI-RADS does not advise FNAC; however, FNAC is recommended if the largest nodule diameter is >25 mm for "mildly suspicious" (TR3), >15 mm for "moderately suspicious" (TR4), and >10 mm for "highly suspicious" (TR5). (12) (13) (14)

When diagnosing thyroid nodules, fine needle aspiration cytopathology (FNAC) is a crucial test, and the diagnostic yield is increased when FNA is guided by US. In this study we used TBSRTC, which is developed to facilitate communication among profesionals involved in the patient management; facilitate research and allow easy as well as reliable sharing of data for national and international collaborative studies. TBSRTC established a standardized category-based reporting system for thyroid fine-needle aspiration (FNA) specimens. (15)

Six diagnostic categories are available in the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), including: non-diagnostic or unsatisfactory (I), benign (II), follicular lesion of undetermined significance or atypia of undetermined significance (III), follicular neoplasm (IV), suspected for malignancy (V), and malignant (VI). The categories have indicated risk of malignancy, ranging from 0-3% for benign to 97-99% for malignant. The management may be clinical follow up for benign lesions while subtotal thyroidectomy can be done for malignant lesions; but it depends on other factors, including clinical and sonographic features. Those with unsatisfactory results have indicated a risk of malignancy of 1-4%, and ultrasound guided FNA is the recommended procedure. (15) (16)

In this study, we did the sonographic evaluation according to the ACR-TIRADS protocol, and correlated the pathological findings with the cytology results which are reported according to TBSRTC.

3.2 Statement of the problem

Thyroid nodules are common findings, and also thyroid enlargement is a common presenting symptom in our set up. (8) At TASH ultrasound based risk stratification according to the TIRADS lexicon has been guiding the need for FNAC from the thyroid nodules recently, but the accuracy of this approach has not been tested. Even though it might have been possible to correlate the radiological classification with pathologic results of the patients, since the FNA was being done without imaging guidance at the pathology department of our hospital, it is impossible to assure the nodule imaged and the nodule sampled are the same, making any correlations invalid. In this study we did the correlation based on ultrasound guided FNAC

results, ensuring the nodules that are stratified based on the TIRADS lexicon are the same as those subjected to pathologic evaluation. The aim of this study was to assess the ACR-TIRADS's accuracy in predicting thyroid nodules cancer risk as well as the system's applicability at TASH.

4. Literature review and significance of the study

4.1 Literature review

A study done by Middleton, et.al showed that the risk of malignancy was closely associated with the composition, echogenicity, margins and echogenic foci in the nodules. An increased aggregate risk of nodule malignancy was noted as the TIRADS point level increased from 0-10. They showed that the TIRADS category (TR1-TR5) and the cumulative risk of malignancy for nodules associated with each individual TIRADS point level (0-10) fit within the TIRADS risk categorization limits. (17)

In another research done by Hoang J.K et al., a retrospective study that compared the biopsy rate and precision of diagnosis both before and following TIRADS application; the results showed that TIRADS had significantly improved specificity and accuracy in identification of malignant nodules, and reduced rate of recommendation for biopsy while having comparable sensitivity. (12)

Leni, D. et al. conducted a study comparing ACR-TIRADS risk stratification with cytology results reported based on the five-tiered reporting system for thyroid cytopathology established by the Italian Society for Anatomia Patologica e Citologia Diagnostica (SIAPEC), which is comparable to the Bethesda system. The results showed that ACR TIRADS has an excellent 'rule out' role in ACR-TIRADS 1 and 2 nodules. Extension of FNA indications to those nodules with TIRADS score of ≥3, independent of dimensional criteria, reduced rate of false negatives and increased sensitivity and negative predictive value with significant decrement in specificity. The researchers recommended conducting follow up ultrasound on nodules that had a TIRADS of at least 3 but were too small for a FNA. (18)

In a study conducted in Iraq to determine the association between ACR-TIRADS and TBSRTC by Zainab et al., the risk of malignancy was 0, 0, 2.9, 38, and 80%, for TI-RADS 1, 2, 3, 4, and 5 respectively. There was no a statistically significant difference between men and women. There was a significant agreement ($p<0.0001$) between USG and FNA using the TIRADS and TBSRTC. Therefore, it was possible to lessen the need for invasive, more expensive procedures without increasing the danger of cancer going undetected by employing TI-RADS as the first step in the stratification of all thyroid nodules and as the only step in TI-RADS 1 and TIRADS2 nodules, such that only suspicious lesions are subjected to FNA. They concluded that there is a significant degree of agreement between the diagnosis determined by TBSRTC on FNA and TIRADS on ultrasonography. (19)

In a different prospective study conducted in India by Richa et al., 200 patients with thyroid nodules underwent USG-guided FNAC and ultrasonography. Hundred and sixteen (116) of the 200 nodules that were analyzed belonged to TIRADS 2, whereas the remaining 44, 13, and 27 belonged to TIRADS 3, 4, and 5, in that order. On FNAC, 162 patients belonged to Bethesda 2 & 12, 7, 15 and 4 to Bethesda 3, 4, 5 and 6 respectively. It was discovered that the ultrasound's specificity, sensitivity, PPV, and NPV were, respectively, 90.8, 92.3, 60, and 98.75 percent. They concluded that ACR TIRADS is an effective risk stratification system which should be routinely used in their clinical practice as it can predict the possibility of a particular nodule for being malignant to a great extent. (20)

Among the 184 individuals in an Indian study on the correlation between ACR-TIRADS and TBSRTC, 117 had TIRADS 2 nodules; none of these nodules met the criteria for Bethesda IV or above, meaning they were not malignant. For TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5, the corresponding cancer risk was 0, 2.2, 38.5, and 77.8%. They concluded that the probability of a particular nodule being malignant can be effectively inferred from the ultrasound-based TIRADS system with a certain level of confidence. (21)

Faiz N.G. et al. did a research to see the correlation between the ACR-TIRADS and TBSRTC in Malaysian subjects. Majority of their patients were females (82.7%) and have multiple nodules (74.2%). TIRADS 3 and 4 nodules comprised 102 (34.6%) and 132 (44.7%) of the 295 nodules they evaluated with ultrasound. Regarding the cytopathology reports, most patients belonged to the Bethesda II category (78.3%), followed by the Bethesda IV (10.5), VI (5.1), V (4.1) and III (2.0) categories. They found a good correlation between the ACR-TIRADS and TBSRTC ($p < 0.001$). The malignancy risks for TIRADS 2, 3, 4 and 5 were 0%, 2.9%, 18.2% and 93.1%, respectively. (22)

Isse H.M. et al. did a research on correlation of the ACR-TIRADS with TBSRTC in Uganda with 132 study participants. Majority of their participants were female (90%). TI-RADS 3 was the most common at 42.9% ($n = 69$). TI-RADS 4 and TI-RADS 5 had malignancy proportions of 73.3% and 85.7%, respectively. The sensitivity, specificity and positive predictive values were 90.9%, 98.5% and 90%, respectively. (23)

4.2 Significance of the study

Due to the high prevalence of thyroid nodules, it is obvious doing FNACs or following nodules without prior screening will create a significant burden in a country with limited resources like our country. The limitation on health care budget, human resource and well equipped hospitals is evident. Additionally, researches have shown that the vast majority of the thyroid nodules are benign; and only about 5-7% of thyroid nodules are malignant. Therefore it is important to

identify nodules that are suspicious and manage accordingly; while avoiding unnecessary burden created by the benign nodules.

Ultrasound is the modality of choice in examining the thyroid gland; its high resolution capacity and advanced features give detailed information regarding myriads of thyroid pathologies. Due to interpersonal interpretation variation based on experience and preference of different approaches; it is important to have a standardized image interpretation and reporting system. In our set up we are using the ACR TIRADS, which has proven to be effective in reducing the biopsy rates and guiding management as tested in other institutions. But its level of effectiveness and accuracy has not been tested in our hospital; which is significantly different from the set ups where these studies were done. Some of the differences include the experience of the practitioners doing the ultrasound characterization, and the practice of US guided FNAC and data entry and keeping methods which can significantly affect the results concerning the effectiveness of ACR-TIRADS in our Hospital as compared to those institutions. Also, the demographic factors and the epidemiology of different diseases, including pathologies of the thyroid disease may have significant impact on the outcome of such studies. Therefore, this study aimed to validate the effectiveness of ACR TIRADS; and if effective to justify its use and to recommend its use in other institutions in our country.

5.Objectives

5.1 General objective

- To evaluate the accuracy of the ultrasound based thyroid nodule risk stratification according to the ACR-TIRADS by correlating the US findings with pathologic diagnosis at TASH.

5.2 Specific objectives

- To assess the accuracy of the ACR-TIRADS in assessment of thyroid nodule risk stratification.

- To isolate ultrasound features that has high predictive value in assessment of risk of malignancy

6. Research Methodology

6.1 Study setting

The study was conducted at TikurAnbessa specialized referral and teaching hospital, radiology department, A.A, Ethiopia. TASH is under the college of health sciences campus of AAU, which is one of the pioneer universities in the country. The hospital is a tertiary level referral and teaching hospital providing service to people from all corners of the country in its various departments. The study was conducted in the radiology department in collaboration with the TASH pathology department. Both departments are equipped with qualified human resources, including consultant radiologists and pathologists that are involved in conducting and guiding the research; and the important equipment and materials, including high resolution ultrasound, FNAC sets and microscopes used in pathological analysis; which were required for conduction of this study.

6.2 Study design

Institution based, prospective cross sectional study was conducted in patients referred to Radiology department of TASH for ultrasound evaluation of thyroid nodules and ultrasound guided FNAC, during the time period of April 2023-September 2023.

6.3 Study duration

The study was conducted during the time period of April 2023-November 2023.

6.4 Population

Source population

All patients referred to TASH radiology department for evaluation of thyroid nodule or ultrasound guided FNAC from thyroid nodule during the study period of April 2023-September 2023.

Study population

All patients with thyroid nodule/s evaluated with high resolution ultrasound and have US guided FNAC and have pathology results at TASH department of radiology and pathology respectively, during the study period of April 2023-September 2023 were included in the study.

6.5 Sample size and sampling technique

Since the number of ultrasound guided FNACs for thyroid nodules done at the radiology department of TASH is small, we used a non-probability sampling technique; and all patients for whom ultrasound guided FNAC is done were included in our study.

6.6 Data collection procedure

All thyroid nodules were evaluated using high resolution Mindray ultrasound linear probe (7-13 MHz) by third year radiology residents working at breast and neck ultrasound unit. Patients that are candidates for ultrasound guided FNAC were subsequently re-evaluated by the principal investigator and body imaging follow working the guided FNAC, prior to the procedure. Data concerning the ultrasound features of thyroid nodules was collected by using a structured questionnaire (annex-1) at the procedure room. The questioner included the arbitrarily given identification number and demographic data (the age and sex) of the patient, the number nodules to be sampled and the characteristics of the thyroid nodule for which FNAC is done, the TIRADS score and the TIRADS category. This questioner is filled during the FNAC procedure to ensure the nodule from which FNAC is done and the nodule characterized are the same. The structured questionnaire was filled by third year radiology residents that are attending the procedure. Subsequently the pathologic results were filled by the involved pathologist or 3rd year pathology resident (Annex-2).

6.7 Study variables

Dependent variables

- TIRADS score, TIRADS category and Pathologic diagnosis (Bethesda category)

Independent variables

- Demographic data
  - Age
  - Sex
- Number of thyroid nodules (solitary or multiple)
- Characteristics of the target nodule
  - ✓ Nodule size
  - ✓ Nodule Composition
  - ✓ Nodule Echogenicity
  - ✓ Nodule Shape

- ✓ Nodule Margin
- ✓ Echogenic foci in the nodule

6.8 Eligibility criteria, inclusion criteria, exclusion criteria

6.8.1 Eligibility criteria

All thyroid nodules for which ultrasound guided FNAC is done at TASH, radiology department were included in this study.

6.8.2 Inclusion criteria

All thyroid nodules for which complete ultrasound characterization was done based on the ACR-TIRAD system, have ultrasound guided FNAC with conclusive pathologic results, and complete data is provided on the questioner.

If FNAC is done in more than 1 thyroid nodules of the same patient; the nodules were included as a separate data set; provided that the pathological samples were properly labeled and separately analyzed.

6.8.3 Exclusion criteria

- All thyroid nodules with incomplete data provided.
- All thyroid nodules for which FNA is not done using ultrasound guidance.
- All thyroid nodules for which pathologic results could not be produced.
- All nodules in a patient with known thyroid malignancy.

6.9 Data processing and analysis

All the nodules for which complete US characterization was done based on the ACR-TIRADS classification and pathologic results were obtained were included in the study. The nodules were classified into the different categories of TIRADS based on their TIRADS score. Of those nodules that are grouped into the same category, we calculated how many were benign and how many were malignant based on their pathologic diagnosis. And subsequently the risk of malignancy for each category was calculated based on our data. Finally the risk level associated with each category was compared with that, which is provided by the ACR-TIRADS. (Annex-3)

Data was entered into Ms Excel and exported to SPSS version 27 for analysis. When examining the correlation between variables, the Pearson Chi-Square test is utilized, and a p-value of less than 0.05 is considered statistically significant.

The sensitivity, specificity, accuracy, and positive predictive values with corresponding 95% confidence levels were calculated using the Bethesda system of thyroid classification as a gold standard.

Sensitivity = [True Positive / (True Positive + False Negative)] x 100%

Specificity = [True Negative / (True Negative + False Positive)] x 100%

Positive Predictive Value = [True Positive / (True Positive + False Positive)] x 100%

Accuracy = [(True Positive + True Negative) / (Positive + Negative)] x 100%

7. Results

A total of 62 patients who underwent a thyroid ultrasound scan and ultrasound-guided thyroid FNAC were enrolled in the study. The mean (SD) age was 52.34 (12.66) years, and the range 55 (minimum 25 and maximum 80 years). (Fig. 1) Thirty seven (59.7%) of our patients were in their 5th-6th decade of life and 53 (85.5%) were female.

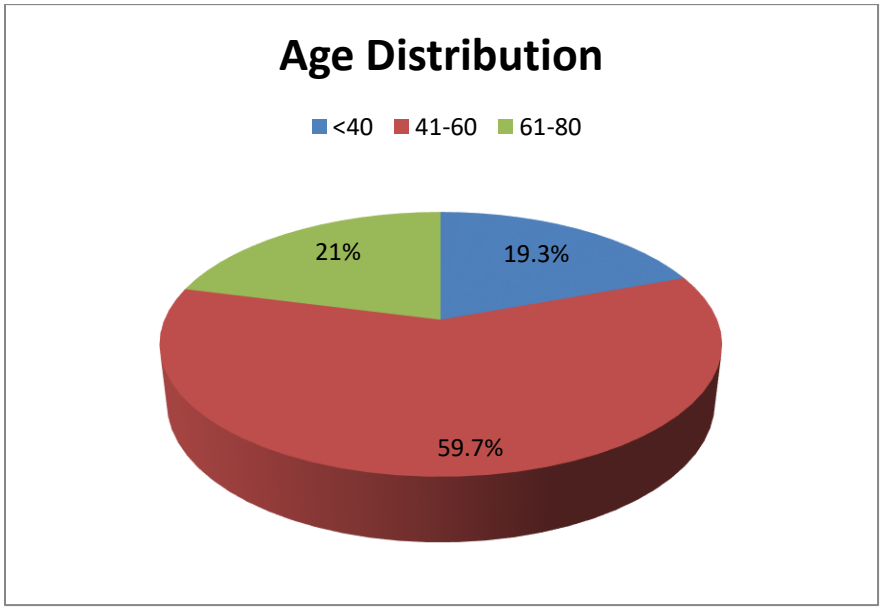

Fig.1:- Study subjects according to their age distribution

On ultrasonography (USG), the mean size of the nodules was 3.46 cm (range 1.5–6.6cm). Regarding the size of the nodules 89.3% of them were <4.3cm in maximum dimension. Multiple thyroid nodules were seen in 54 (87.1%) patients.

Regarding the specific sonographic features of the nodules 46 (74.2%) were solid in composition. The echogenicity of the nodules were hyperechoic or isoechoic in 32 (51.6%) of

the cases followed by 24 (38.7%) hypoechoic nodules. Only 6 (9.7%) were found to be very hypoechoic. Fifty five (88.7%) of the nodules were wider than tall in shape and the rest taller than wide. Smooth margin of the nodules were seen in 57 (91.9%) of the cases and only 2 (3.22%) nodules have lobulated/irregular margin. Considering the sonographic characteristics of echogenic foci 28 (45.2%) of the nodules have macrocalcifications followed by none or come tail artifact in 24 (38.7%) nodules. (Table 1)

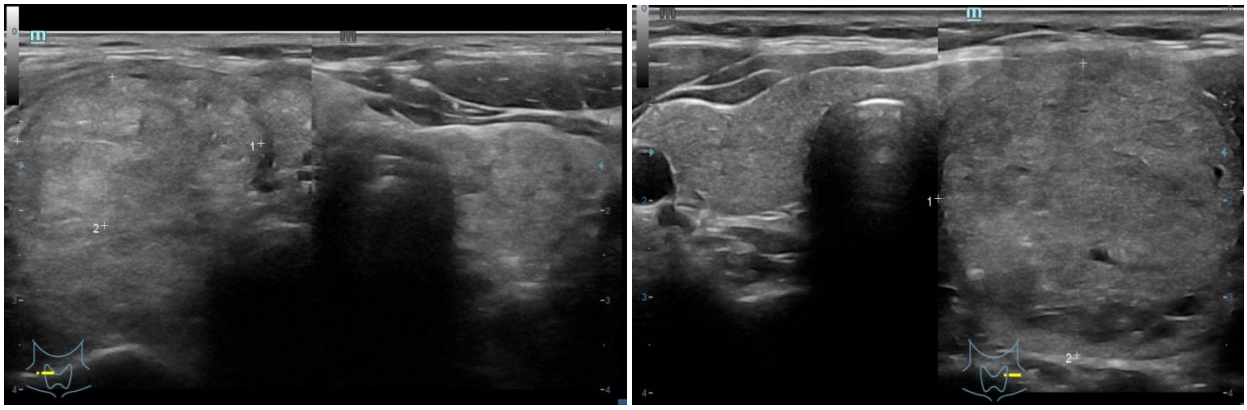

Fig. 2:-**Left image**: - Right thyroid lobe 2.7cm*1.7cm solid, hyperechoic, wider than tall nodule with smooth margin and no echogenic foci. According to ACR-TIRADS the score is 3 and the category is TIRADS 3. Upon cytology by TBSRTC it turned out to be Bethesda 2 (colloid goiter). **Right image**: - Left thyroid lobe 3.5cm*3cm solid, isoechoic, wider than tall nodule with smooth margin and punctate echogenic foci. According to ACR-TIRADS the score is 6 and the category is TIRADS 4. Upon cytology by TBSRTC it turned out to be Bethesda 4 (follicular neoplasm).

USG feature		Number of case	Frequency (%)
Composition	Mixed solid-cystic	16	25.8%
	Solid or predominately solid	46	74.2%
Echogenicity	Hyperechoic or isoechoic	32	51.6%
	Hypoechoic	24	38.7%
	Very hypoechoic	6	9.7%
Shape	Wider than tall	55	88.7%
	Taller than wide	7	11.3%
Margins	Smooth	57	91.94%
	Ill-defined	3	4.84%
	Lobulated/irregular	2	3.22%
Echogenic foci	None/Comet tail artifact	24	38.7%
	Macrocalcifications	28	45.2%
	Peripheral rim calcifications	4	6.5%
	Punctate echogenic foci	6	9.75

Table 1: Frequency of different ultrasound characteristics of the thyroid nodules

Forty nine (79%) of the thyroid nodules come under TIRADS 3 and TIRADS 4 classifications on ultrasound imaging. The thyroid ultrasound reports for ACR TI-RADS groups 3, 4, and 5 were 26 (41.90%), 23 (37.1%), and 13 (21.0%), respectively.

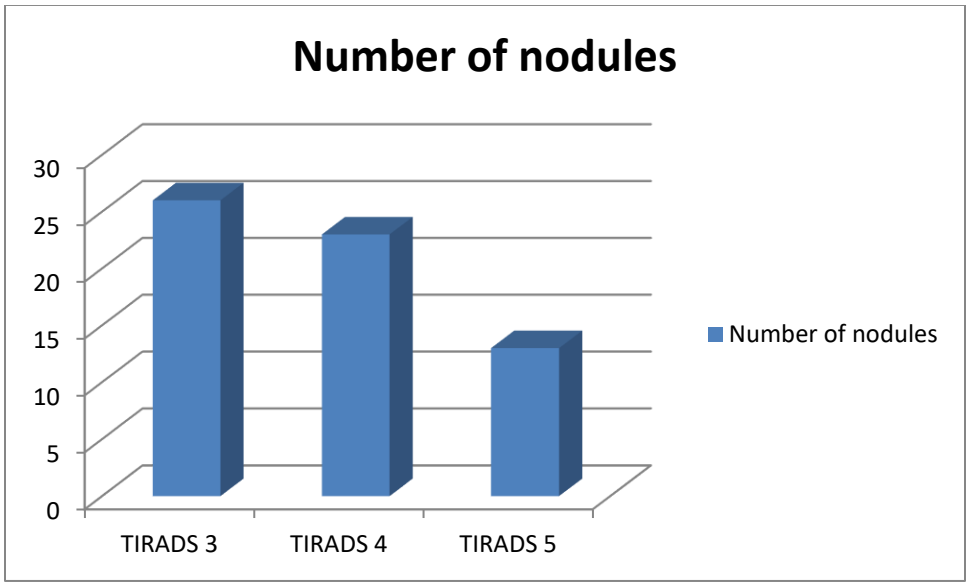

Fig. 3: TIRADS category of the nodules

Similarly, 41 nodules (66.2%) on FNAC prove to be Bethesda I and II. Based on information from the TBSRTC reporting system, the thyroid FNAC results were: non-diagnostic (8.06%), benign (58.06%), atypia of unknown significance (8.06%), follicular neoplasm (11.29%), suspicious for malignancy (1.61%), and malignant (12.90%). Overall 16 (25.8%) of the 62 nodules turn out to be Bethesda category more than 4, malignant category. (Fig. 2)

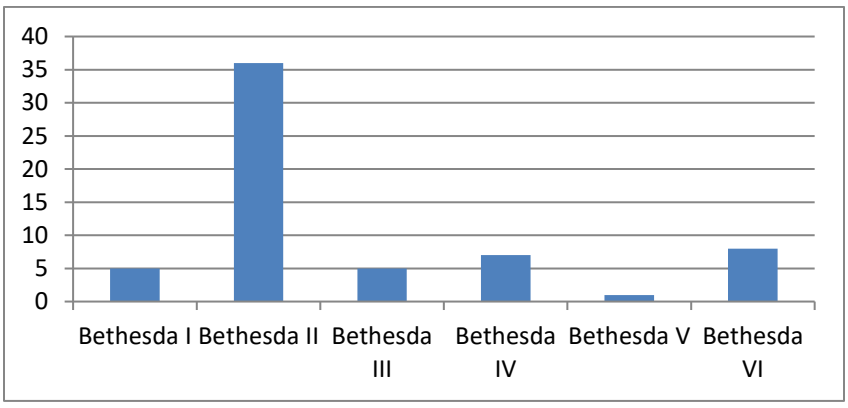

Fig. 4: Bethesda category of the nodules

On FNAC findings, 25 out of 26 (96.2%) ACR TI-RADS 3 nodules showed non-malignant changes: Bethesda I (15.4%) compared to Bethesda II (73.1%). Out of 13 ACRTI-RADS 5 nodules 10 of them (76.9%) revealed signs of malignancy. (Table 2)

		BETHESDA category of a nodule						
		1	2	3	4	5	6	Total
TIRADS category of a nodule	3	4	19	2	1	0	0	26
	4	1	14	3	2	1	2	23
	5	0	3	0	4	0	6	13
	Total	5	36	5	7	1	8	62

Table 2: Thyroid imaging reporting and data system TIRADS and BETHESDA correlation

There were 21(58.3%) out of 36 nodules which appeared suspicious for malignancy on ultrasound to be classified under TIRADS 4 and TIRADS 5 but turned out to be benign in Bethesda classification (BETHESDA category 1-3). Considering all 16 malignant nodules, the proportion of nodules classified as TIRADS 3, TIRADS 4, and TIRADS 5 were 1 (6.25%), 5 (31.25%), and 10 (62.5%), respectively.

On comparing TIRADS results with the Bethesda system of classification, the risk of malignancy for TIRADS 3, TIRADS 4, and TIRADS 5 was 3.8, 21.7, and 76.9%, respectively.

Regarding specific ultrasound features of the nodules and their BETHESDA outcomes, 15 out of 46 solid nodules (32.6%) turned out to be malignant (BETHESDA 4-6) but only 1 out of 16 (6.25) mixed solid and cystic nodules were malignant. As to the echogenicity of the nodules 3 out of 32 (9.4%) isoechoic or hyperechoic nodules and 8 out of 24 (33.3%) hypoechoic nodules were malignant. Five out of 6 (83.3%) very hypoechoic nodules became malignant on cytology. There were 7 nodules with taller than wide appearance from which 6 (85.7%) came out malignant according to their BETHESDA category. From 55 wider than tall nodules 10 (18.2%) were found to be malignant. There was statistically significant correlation between solid composition, very hypoechogenicity and taller than wide appearance with risk of malignancy having P-value of 0.02, < 0.001 and 0.006 respectively using Pearson Chi-Square test. No statistically significant correlation was found between size, margin and echogenic foci of the different nodules.

Colloid nodules, follicular neoplasm, and papillary carcinoma of thyroid contributed 43.5, 11.3, and 9.7%, respectively.

TIRADS and BETHESDA results were cross-tabulated in a 2x2 table (Table 3) with TIRADS 4/ 5 and BETHESDA 4/5/6 considered positive for malignancy and the rest as negative. The accuracy tests results were sensitivity (93.75%), specificity (54.35%), positive predictive value (41.67%), and accuracy value (64.52%). (Table 3)

		FNAC		
		POSITIVE(malignancy positive)	NEGATIVE(malignancy negative)	Total
TIRADS (Screening test)	Positive	15 (a)	21 (b)	36 (a+b)
	Negative	1 (c)	25 (d)	26 (c+d)
	Total	16 (a+c)	46 (b+d)	62 (a+b+c+d)

Table 3: 2 x 2 Table for diagnostic test results

8. Discussion

In this study, using cytology as a gold standard we evaluated the relationship between the ultrasound-based categorization system and cytopathology-based system to determine how reliable the TI-RAD approach was in identifying or ruling out cancer.

Majority of the patients in our study were females (85.5%). Other similar studies also reported predominance of the female population presenting with thyroid lesions. (24) (21) (25) Studies have shown that this predominance can be explained by the effect of estrogen and progesterone, as the size of the nodules increased during pregnancy. (20)

The mean age of our patients was 52.34 (12.66) years. This finding is similar to those reported previously by Vargas U.H at el. (mean age, 57 years; SD 14 years) and older than the study done in Uganda (mean age, 41 years; SD 13 years). (26)

A significant proportion of the patients in the current study had multiple thyroid nodules (87.1%), which is comparable with a study done in Malaysia. (22)

The predominant sonographic features of the thyroid nodules, solid or almost completely solid, hyperechoic or isoechoic, wider than tall and smooth margin are similar with the study done in India by Yashraj P.P. et al. (27)

TIRADS 3 and 4 nodules represented the largest group (41.90% and 37.1% respectively), and Bethesda II was the most commonly reported cytopathology grade (58.1%) in the current study. The findings are similar with a study done by Richa et al. in all except for slightly reduced percent of TIRADS 4 nodules. (20) Likewise the study done in Uganda by Isse H.M. et al showed a comparable predominance of TIRADS 3 nodules by 42.9%. (23)

In our analysis, 58.3% of nodules that looked suspicious enough on ultrasonography to be put into TIRADS 4 and TIRADS 5 categories turned out to be benign when placed in the Bethesda

category. A study by Richa et al. revealed a relatively lower result of 40%. (20) This can be due to the exclusion of Bethesda category 1 nodules from their study.

Majority of the nodules in our study were found to be TIRADS 3 amongst which 3.8% are malignant according to BETHESDA classification. This is comparable with the study done by Zainab et al. and lower than a study done in Pakistan (13.6%) by Naushaba et al. (19) (26) The relatively higher risk of malignancy for TIRADS 3 nodules in the study done in Pakistan can be explained by the higher incidence of malignant thyroid nodules (5-15%) in Pakistan.

The FNAC results of our study according to TBSRTC showed that Bethesda category I, II, III, IV, IV and VI were 5 (8.06%), 36 (58.06%), 5 (8.06%), 7 (11.29%), 1 (1.61%) and 8 (12.90%) respectively. The non-diagnostic Bethesda category I results are within the expected range suggested by other authors. (16)

The overall proportion of malignant nodules in our study is 25.8% which is almost comparable with the study done by Richa et al. and higher than the study done by Isse H.M. et al. in Uganda. (20) (23)The lower proportion of malignant nodules in the study done in Uganda can be explained by the fact that they included TIRADS 1 and 2 nodules in their study.

In our study taller than wide shape and very hypoechoic echogenicity were the most vulnerable to malignancy (85.7% and 83.3% respectively) among the suspicious characteristics, accompanied by punctate echogenic foci (66.67%), hypo-echogenicity (33.3%) and solid composition (32.6%) in that order. The study done by Seong N. Goong et al. showed that solid composition, hypoechoic appearance and the presence of punctate calcification were associated with risk of malignancy. (28) In our study the two nodules with lobulated/irregular margin turned out to be malignant on TBSRTC. Since this is small number it is difficult to conclude and compare with other studies.

The sensitivity in our study (93.75%) is comparable with the study done by Richa et al. and the specificity (54.35%) is lower than findings of the mentioned study which is 90.3%. (20) The larger percentage of malignant nodules in our study and the exclusion of TIRADS 2 nodules may be the cause of the decreased specificity. Manoj et al. conducted a study in India and reported findings of 76% accuracy, 44% positive predictive value, 75% specificity, and 80% sensitivity. These results are less than those of our investigation. (29)

	Our study	Richa et al.	Manoj et al.
Sensitivity	93.75%	92.3%	80%
Specificity	54.35%	90.8%	75%
PPV	41.67	60%	44%

Table 4: Comparative evaluation of test characteristics in various studies

The risk of malignancy for TIRADS 3, 4 and 5 were 2.9%, 38% and 80% in a study done by Zainab et al. in Iraqi. (19) These findings are similar with our study where we found a malignancy risk of 3.8%, 21.7% and 76.9% for TIRADS 3, 4 and 5 lesions respectively.

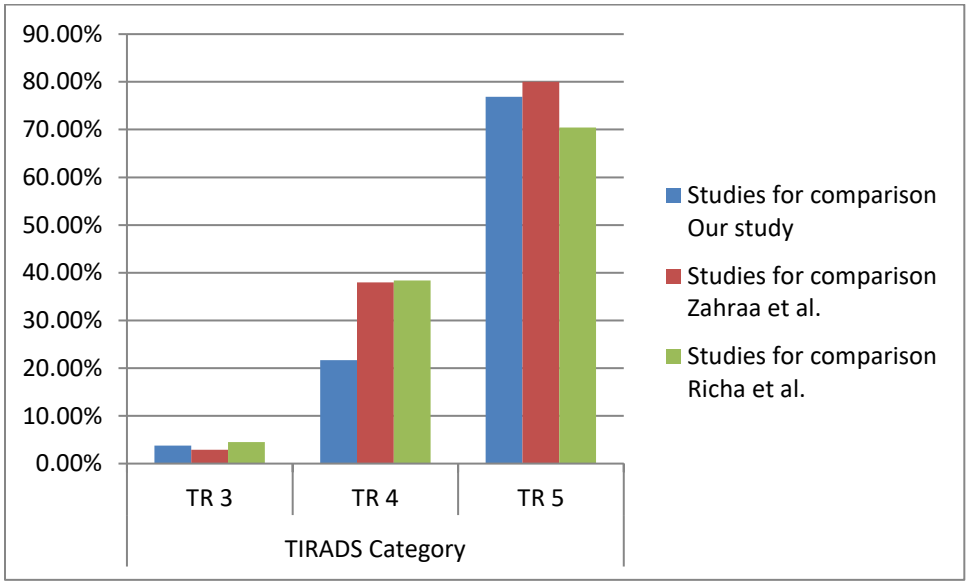

Fig. 5: Study comparison for risk of malignancy

Finally comparison of the risk of malignancy for the different TIRADS categories of our study was done with the one provided by the ACR-TIRADS category and findings were almost comparable as displayed in Table 5. (6)

Category	Number of nodules	Benign	malignant	Calculted risk of malignancy (malignant/total number of nodules)	TIRADS risk estimate
TR-3	26	25	1	3.8%	2.1 - 5%
TR-4	23	18	5	21.7%	5.1-20%
TR-5	13	3	10	76.9%	>20%
Total					

Table 5: The risk level associated with each TIRADS category compared with the one provided by ACR-TIRADS committee

Overall, our study has revealed that there is a good correlation between the ACR-TIRADS sonographic features of thyroid nodules and TBSRTC. Other studies have also shown similar results. (22)

9. Limitations

This study didn’t include the thyroid nodules classified under ACR-TIRADS categories I and II which made evaluation of the NPV of the study impossible. Since the ACR-TIRADS advises against performing FNAC for nodules that fall into these categories (TIRADS 1 "benign" and TIRADS 2 "not suspicious" nodules), these nodules were excluded from our study. (14)

10. Conclusion

The ACR-TIRADS showed an excellent diagnostic sensitivity, reaching 93.75% in identifying malignant thyroid nodules, with relatively lower specificity (54.35%). The risk of malignancy among different TIRADS categories were comparable with the one devised by the ACR-TIRADS committee. We discovered that in ordinary practice, ACR-TIRADS is a suitable and noninvasive approach for evaluating thyroid nodules. Larger-scale research would support these conclusions.

11. Recommendations

We recommend to do further studies with a larger sample size over multiple institutions so as to implement the ACR-TIRADS reporting system nationally.

12. Dissemination of Results

The findings of this study will be submitted to to TASH's department of radiology as part of the dissertation requirement for the postgraduate certificate program. The research will also be presented on a seminar organized by the research committee. It will also be submitted to medical journals in hopes of being published.

13. Compliance with Ethical Standards

The department's research committee's ethical criteria were followed in every procedure carried out for this study.

14. Acknowledgments

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15. Disclosure of Conflict of Interest

The writers say they have no competing interests.

Annex

Annex-1: Questioner

MRN:_____ Date of exam:_____

Demographic data: Age:_____ Sex: _____

Number of thyroid nodules: 1. Solitary 2. Multiple

Target Nodule: Size: _____mm

Composition

Cystic or almost completely cystic (0)

Spongiform (0)

Mixed cystic and solid (1)

Solid or almost completely solid (2)

Echogenicity

Anechoic (0)

Hyperechoic or isoechoic (1)

Hypoechoic (2)

Very hypoechoic (3)

Shape

Wider than taller (0)

Taller than wider (3)

Margin

Smooth (0)

Ill defined (0)

Lobulated or irregular (2)

Extrathyroidal extension (3)

Echogenic foci

None or large comet tail artifacts (0)

Macrocalcifications (1)

Peripheral calcification (2)

Punctate echogenic foci (3)

Total TIRADS score=_____

TIRADS category:

- TR1 (score=0)
- TR2 (score=2)
- TR3 (score=3)
- TR4 (score=4-6)
- TR5(score>/=7)

Annex-2

Pathologic reporting guide

MRN: FNAC number:

Results: according to the TBSRTC

- Bethesda I
- Bethesda II
- Bethesda III
- Bethesda IV
- Bethesda V
- Bethesda VI

References

1. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper, D. S., Doherty, G. M., Haugen, B. R., Kloos, R. T., Lee, S. L., Mandel, S. J., Mazzaferri, E. L., McIver, B., Pacini, F., Schlumberger, M.

2. Russ, G., Leboulleux, S., Leenhardt, L., & Hegedüs, L. (2014). Thyroid incidentalomas: epidemiology, risk stratification with ultrasound and workup. European thyroid journal, 3(3), 154–163. https://doi.org/10.1159/000365289.

3. Guth, S., Theune, U., Aberle, J., Galach, A., & Bamberger, C. M. (2009). Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. European journal of clinical investigation, 39(8), 699–706. https://doi.org/10.111.

4. Fisher, S. B., & Perrier, N. D. (2018). The incidental thyroid nodule. CA: a cancer journal for clinicians, 68(2), 97–105. https://doi.org/10.3322/caac.21447.

5. Xie, C., Cox, P., Taylor, N., & LaPorte, S. (2016). Ultrasonography of thyroid nodules: a pictorial review. Insights into imaging, 7(1), 77–86. https://doi.org/10.1007/s13244-015-0446-5.

6. Tappouni, R.R., Itri, J.N., McQueen, T.S., Lalwani, N., & Ou, J.J. (2019). ACR TI-RADS: Pitfalls, Solutions, and Future Directions. Radiographics : a review publication of the Radiological Society of North America, Inc, 190026 .

7. Kant, R., Davis, A., & Verma, V. (2020). Thyroid Nodules: Advances in Evaluation and Management. American family physician, 102(5), 298–304.

8. Tadesse, T., Hailu, T., Getachew, A., & Abebe, S. M. (2020). Prevalence and Associated Factors of Thyroid Incidentaloma among Adult People Attending Gondar University Hospital, Northwest Ethiopia. Ethiopian journal of health sciences, 30(1), 23–30. https:.

9. Nachiappan, A. C., Metwalli, Z. A., Hailey, B. S., Patel, R. A., Ostrowski, M. L., & Wynne, D. M. (2014). The thyroid: review of imaging features and biopsy techniques with radiologic-pathologic correlation. Radiographics : a review publication of the Rad.

10. *American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations.* . Gharib, H., Papini, E., Paschke, R., Duick, D. S., Valcavi, R., Hegedüs, L., Vitti, P., & AACE/AME/ETA Task Force on Thyroid Nodules (2010). s.l. : Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 16(3), 468–475. https://doi.org/10.4158/EP.16.3.468.

11. *Pattern recognition of benign nodules at ultrasound of the thyroid: which nodules can be left alone?* Bonavita, J. A., Mayo, J., Babb, J., Bennett, G., Oweity, T., Macari, M., & Yee, J. (2009). s.l. : AJR. American journal of roentgenology, 193(1), 207–213. https://doi.org/10.2214/AJR.08.1820.

12. *Reduction in Thyroid Nodule Biopsies and Improved Accuracy with American College of Radiology Thyroid Imaging Reporting and Data System.* Hoang, J. K., Middleton, W. D., Farjat, A. E., Langer, J. E., Reading, C. C., Teefey, S. A., Abinanti, N., Boschini, F. J., Bronner, A. J., Dahiya, N., Hertzberg, B. S., Newman, J. R., Scanga, D., Vogler, R. C., & Tessler, F. N. (2018). s.l. : Radiology, 287(1), 185–193. https://doi.org/10.1148/radiol.2018172572.

13. *Thyroid Imaging Reporting and Data System (TI-RADS): A User's Guide. Radiology, 287(1), 29–36.* Tessler, F. N., Middleton, W. D., & Grant, E. G. (2018). https://doi.org/10.1148/radiol.2017171240.

14. *Evaluation of the Performance of ACR TI-RADS Also Considering Those Nodules with No Indication of FNAC: A Single-Center Experience.* . Amendola S, Wolde Sellasie S, Pedicini F, et al. s.l. : J Clin Med. 2023;12(2):398. Published 2023 Jan 4. doi:10.3390/jcm12020398.

15. *The 2017 Bethesda System for Reporting Thyroid Cytopathology. Thyroid : official journal of the American Thyroid Association, 27(11), 1341–1346.* Cibas, E. S., & Ali, S. Z. (2017). https://doi.org/10.1089/thy.2017.0500.

16. *Correlation of ultrasound findings with the Bethesda cytopathology classification for thyroid nodule fine-needle aspiration: a primer for radiologists.* Heller, M. T., Gilbert, C., Ohori, N. P., & Tublin, M. E. (2013). s.l. : AJR. American journal of roentgenology, 201(3), W487–W494. https://doi.org/10.2214/AJR.12.9071.

17. *Multiinstitutional Analysis of Thyroid Nodule Risk Stratification Using the American College of Radiology Thyroid Imaging Reporting and Data System.* Middleton, W. D., Teefey, S. A., Reading, C. C., Langer, J. E., Beland, M. D., Szabunio, M. M., & Desser, T. S. (2017). s.l. : AJR. American journal of roentgenology, 208(6), 1331–1341. https://doi.org/10.2214/AJR.16.17613.

18. *Diagnostic Performances of the ACR-TIRADS System in Thyroid Nodules Triage: A Prospective Single Center Study.* Leni D, Seminati D, Fior D, Vacirca F, Capitoli G, Cazzaniga L, Di Bella C, L'Imperio V, Galimberti S, Pagni F. . s.l. : PMID: 34066485; PMCID: PMC8124822. Cancers (Basel). 2021 May 6;13(9):2230. doi: 10.3390/cancers13092230..

19. *Correlation between ultrasound TI-RADS classification system and Bethesda cytology result in assessment of thyroid nodule among a sample of Iraqi patient in wasit province.* Zainab Abbas Hassooni 1, *, Zahraa Qasim Zbun 2, Najwa Abdullaah Mrauah 2 and Faris Lutfi Nussrat 3. s.l. : Magna Scientia Advanced Research and Reviews, 2022, 04(02), 025–032.

20. *Radio Pathological Correlation of Thyroid Nodules Using Tirads Based Ultrasound Classification and Bethesda Classification for FNAC: a Prospective Study.* Richa TIWARI, Ruchi GUPTA, Amit Kumar VERMA, Sanjeev KUMAR, Yogita KATIYAR. s.l. : Modern Medicine | 2020, Vol. 27, No. 3.

21. *Correlation between Ultrasound-based TIRADS and Bethesda System for Reporting Thyroid-cytopathology: 2-year Experience at a Tertiary Care Center in India.* Periakaruppan, G., Seshadri, K. G., Vignesh Krishna, G. M., Mandava, R., Sai, V. P. M., & Rajendiran, S. (2018). s.l. : Indian journal of endocrinology and metabolism, 22(5), 651–655. https://doi.org/10.4103/ijem.IJEM_27_18.

22. *Correlation between the Thyroid Image andReporting Data System (TIRADS) and the BethesdaSystem for Reporting the Thyroid Cytopathology inPatients with Thyroid Nodules.* Faiz Najmuddin Ghazi, Wan Zainira Wan Zain, Maya Mazuwin Yahya, Juhara Haron, Wan Faiziah Wan Abdul Rahman, Zaidi Zakaria, Wan Mokhzani Wan Mokhter, Ahmad Zuhdi Mamat, Mohd Nizam Md Hashim, Rosnelifaizur Ramely, Michael Pak-Kai Wong. s.l. : Research square.

23. *Correlation of the ultrasound thyroid imaging reporting and data system with cytology findings among patients in Uganda.* Isse, H.M., Lukande, R., Sereke, S.G. et al. s.l. : Thyroid Research. Thyroid Res 16, 26 (2023). https://doi.org/10.1186/s13044-023-00169-1.

24. *Thyroid nodule fine-needle aspiration.* Langer, J. E., Baloch, Z. W., McGrath, C., Loevner, L. A., & Mandel, S. J. (2012). . s.l. : Seminars in ultrasound, CT, and MR, 33(2), 158–165. https://doi.org/10.1053/j.sult.2011.12.002.

25. *Comparison of TI-RADS classification with FNAC for the Diagnosis of Thyroid Nodule.* Naushaba Malik, Maryam Rauf, Ghazala Malik. s.l. : Journal of Islamabad Medical & Dental College 9(2):129-133.

26. *Concordance between the TIRADS ultrasound criteria and the BETHESDA cytology criteria on the nontoxic thyroid nodule.* Vargas-Uricoechea H, Meza-Cabrera I, Herrera-Chaparro J. s.l. : Thyroid Res. 2017 Feb 2;10:1. doi: 10.1186/s13044-017-0037-2. PMID: 28184253; PMCID: PMC5289008..

27. Yashraj P. Patil, Rubab Kaur Sekhon, Rajesh S. Kuber, Chirag R. Patel. *Correlation of ACR-TIRADS(thyroid imaging, reporting and data system)-2017 and cytological/ Histopathological (HPE) findings in evaluation of thyroid nodules.* s.l. : International Journal of Health and Clinical Research, 2020;3(11):6-19.

28. *Ultrasonography-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings.* Nam-Goong, I. S., Kim, H. Y., Gong, G., Lee, H. K., Hong, S. J., Kim, W. B., & Shong, Y. K. (2004). s.l. : Clinical endocrinology, 60(1), 21–28. https://doi.org/10.1046/j.1365-2265.2003.01912.x.

29. *Correlation of high-resolution ultrasonography findings of thyroid nodules with ultrasound-guided fine-needle aspiration cytology in detecting malignant nodules: A retrospective study in Malabar region of Kerala, South India.* Manoj PB, Innisai A, Hameed DS, Khader A, Gopanraj M, Ihare NH. . s.l. : J Family Med Prim Care. 2019 May;8(5):1613-1616. doi: 10.4103/jfmpc.jfmpc_163_19. PMID: 31198724; PMCID: PMC6559084..