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RESEARCH ARTICLE

MODIFIED THYROID IMAGING REPORTING AND DATA SYSTEM OF THYROID NODULES WITH SUSPICIOUS SONOGRAPHIC CRITERIA: PREDICTION OF MALIGNANCY FOR CLINICAL MANAGEMENT.

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Abstract

Objective: To validate the effectiveness of the TIRADS classification in assessment of thyroid nodules with suspicious sonographic criteria and its application in clinical practice.

Materials and Methods: 1266 nodules with suspicious sonographic signs in 750 patients were included in our study. US scans of the thyroid gland and neck regions were performed. Color Doppler and elastography were done for all nodules. Each nodule was analysed according to the size, shape, margin, internal component (solid or mixed), evidence of calcifications, degree of hypoechogenicity, vascularity and stiffness on elastography. Each criterion was assigned a point, and an additional point was added for suspicious cervical lymph nodes. A final score of malignant probability was obtained. US-guided FNAB was performed for each nodule with a 21-gauge needle.

Results: The study included 429 patients with 821 malignant nodules (57.2%) and 321 patients with 445 benign nodules (42.8%). Suspicious sonographic features; including marked hypoechogenicity, irregularity and ill definition of the margins, microcalcification/non-calcification, taller than wider and hard nodules were associated with significant increase in the rate of the pathologically proven malignancy. The US features of each thyroid nodule were characterized and classified into different TIRADS categories which were confronted with the results of pathology. The risk of malignancy was found to increase from TIRADS 4a to 5. No single US criteria is fully predictive of malignancy.

Conclusion: TIRADS is more accurate in assessing thyroid nodules by using numbers of US features and not depending on each criterion separately.

Based on the score assigned and the risk of malignancy of each in category 4aFNAC should be limited to patients having other risk factors of developing malignancy. Higher categories including 4b and 4c must proceed to FNAC except if contra-indicated. Category 5 should undergo surgery.

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Introduction:-

Thyroid nodules (TNs) have a high prevalence among the adult population, with some studies reported prevalence of up to 68% (1).

Thyroid nodules may show highly diverse ultrasound patterns which impair accurate diagnosis (2). Although various US criteria have been proposed to recognize nodules at risk for malignancy, but it is still difficult to determine which lesion for followed up and which lesion necessitates further management because the thyroid nodules may be classified in different ways using different guidelines (3-6).

Therefore, in 2009 Horvath et al. proposed an evaluation system for TNs called TI-RADS (Thyroid Imaging Reporting and Data System) Similar to BI-RADS (Breast Imaging Reporting and Data System) of the American College of Radiology (7). They defined 10 US patterns of thyroid nodules and reported rate of malignancy according to the pattern.

This was a promising way to standardize the reporting of thyroid US that can be easily understood by clinicians and also predict the risk of malignancy (8). However, these US patterns were difficult in application to all thyroid nodules in routine clinical practice.

In 2009, Park *et al*. suggested an equation for anticipation of malignancy in thyroid nodules utilizing 12 US features (9). Although this approach is a simple stratification of nodules into categories, it was difficult to assign every thyroid nodule into the equation in clinical practice.

To achieve a practical tool for assessment of thyroid nodules and to improve communication between radiologists and clinicians, Russ *et al*. (10) proposed a TIRADS classification that was modified after feedback from those who used it.

In 2011, Kwak et al published a new TIRADS classification, adding one subtype using number of suspicious US features to predict the risk of thyroid malignancy and to simplify its practical application (11) as Counting the number of suspicious US features is more sensible than pattern matching in classification of TIRADS 4A, 4B, 4C and 5 (12).

Five suspicious US criteria of solidity, microcalcifications, hypoechogenicity, microlobulated or irregular margins, and taller-than-wide shape were applied for TI-RADS classification. Nodules without any suspicious features were classified as TI-RADS category 3, while nodules with one, two, three or four, or five suspicious sonographic features were classified as categories 4a, 4b, 4c, and 5 (13).

The aim of our study is to validate the effectiveness of the TIRADS classification in assessment of thyroid nodules with suspicious sonographic criteria and its application in clinical practice.

Materials and Methods:-

Our study is a prospective study during the period of March 2012 to March 2014.

Patient selection:-

We included patients had a thyroid nodule(s) with suspicious US criteria. Nodule stratification based on suspicious US criteria using combination from Horvath et. al(8) and Kwak J Y, et. al.(11) was applied.

1266 nodules in 750 patients (121 males and 629 females, mean age 47 years, range 18-76 years) were studied. 231 patients had single nodule and 519 had multiple thyroid nodules. The diameter of the 1266 nodules ranged from 4.0 mm to 65.0 mm (mean, 34.5 mm).

Imaging and Imaging Analysis:-

Thyroid gland and neck regions ultrasound scans were performed using a linear-array transducer (5 - 12 MHz) on a Philips US scanner (iU22 Philips Medical Systems, Bothell, Wash). B-mode, Color Doppler and elastography were done for all nodules. One radiologist with more than ten years of experience performed all thyroid US scans.

Each thyroid nodule with suspicious criteria was analyzed according to the size, shape, margin, internal component (solid or mixed), evidence of calcifications, the degree of hypoechogenicity, vascularity and stiffness on elastography.

The nodules were divided into seven groups according to their size and the ***numbers of nodules*** of in each group were listed; as follows: < 1cm, 1-<2cm, 2-<3 cm, 3-<4cm, 4-<5 cm, 5-<6 cm and 6 cm and more.

Echogenicity was classified as hyperechogenicity, iso-echogenicity, hypoechogenicity/marked hypoechogenicity. Iso-echogenicity was defined if the nodule is similar to the surrounding healthy thyroid parenchyma. Marked hypoechogenicity was identified if the echogenicity was less than of the surrounding strap muscles.

The ***shape*** of the nodule was categorized as taller-than-wide (anteroposterior dimension greater than its transverse dimension) and wider-than-tall.

Margins were defined as well circumscribed, lobulated or irregular.
Calcifications were categorized as microcalcifications (< 3 mm) and macrocalcifications (> 3 mm with acoustic shadowing).

Nodular vascularity was assessed by Color Doppler and classified as central intranodular or peripheral.
Qualitative assessment of strain elastography was done by using visual scoring of colors within and around the nodules. The elastic image was superimposed on the B-mode image, and tissue stiffness was displayed as a range of colors from red (soft tissue) to blue (hard tissue). The nodules with ***high stiffness*** are added as a suspicious criterion according to Russ review of article (14).

Each criterion was assigned a point plus an additional point if suspicious cervical lymph nodes were noted. Thus, a final score of malignant probability of a TN was obtained Table 1 shows the sonographic features used to identify suspicious nodules.

Then the selected suspected nodules were classified into ***TIRADS*** categories according the number of suspicious US features proposed by Kwak J Y, et. al.(11) as shown in Table (2).

US-Guided FNAB:-
US-guided FNAB was performed by another radiologist than who performed the US scan. US-guided FNAB was performed with a 21-gauge needle attached to a 10ml disposable plastic syringe. Tissues obtained were smeared on glass slides and sent to the pathology laboratory.
FNAB was taken from each suspicious nodule; more than on nodule in 519 patients.

Data Collection and Analysis:-
A standardized form was used for data collection. Sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV) and accuracy were calculated for each suspicious US criterion. The risk of malignancy of each category was estimated using chi-square test. Statistical analysis was performed using IBM SPSS 20.0 software (SPSS Inc, Chicago, USA).

Results:-
The study included 429 patients with malignant nodules (57.2%) with 821 nodules and 321 patients with benign nodules (42.8%) with 445 nodules. The average size of the thyroid nodules was 34.5 mm (range 4 to 65 mm). Table (3) shows the patient demographics and nodular size in relation to pathologically proven malignant nodules. The malignant nodules were generally larger than the benign nodules. A relevant statistical significant association was found between size of nodules categories and the rate of malignancy ($p<0.001$). Malignant nodules were slightly more common in older age (45.1±11.1 versus 42.4±16.2). This difference was statistically significant, $p=0.008$. Gender did not differ significantly between the malignant and benign nodules ($P=0.657$).

In the present study, suspicious sonographic features; including marked hypoechogenicity, irregularity and ill definition of the margins, microcalcification/non-calcification, taller than wider and hard nodules were associated with significant increase in the rate of the pathologically proven malignancy as seen in the table (4).

The sensitivity, specificity, positive, negative predictive values, and accuracy of each US suspicious criterion were calculated as seen in (table 5). The highest sensitivity percentages were reported with taller than wider (88.1%) and hard (87.8%) nodules. Specificity was highest with Iso/hyper echogenecity (95.1%), wider than taller (86.7%) and non-calcification (83.8%). Positive predictive value was highest with elastography hard nodules (82%), non-circumscribed (81%), non-calcified (80.7%), marked hypoechogenic (80%) and predominantly central vascularized nodules (80%). Negative predictive values were highest with soft (74.2%) and circumscribed (72.8%) nodules. The highest accuracy percentages were reported with marked hypoechogenic (73.9%) and (71.7%) circumscribed nodules.

The US features of each thyroid nodule were characterized and classified into different TIRADS categories, as shown in Figure 1. The TIRADS 3 category was dominant, accounting for 226 cases (52.6%).

The different TIRADS categories were confronted with the results of pathology and the risk of malignancy was calculated (Table 6). The risk of malignancy was increased from TIRADS 4a (Figure 2) to 5. Benign and malignant cytology results were significantly associated with the different TIRADS categories ($p < 0.001$).

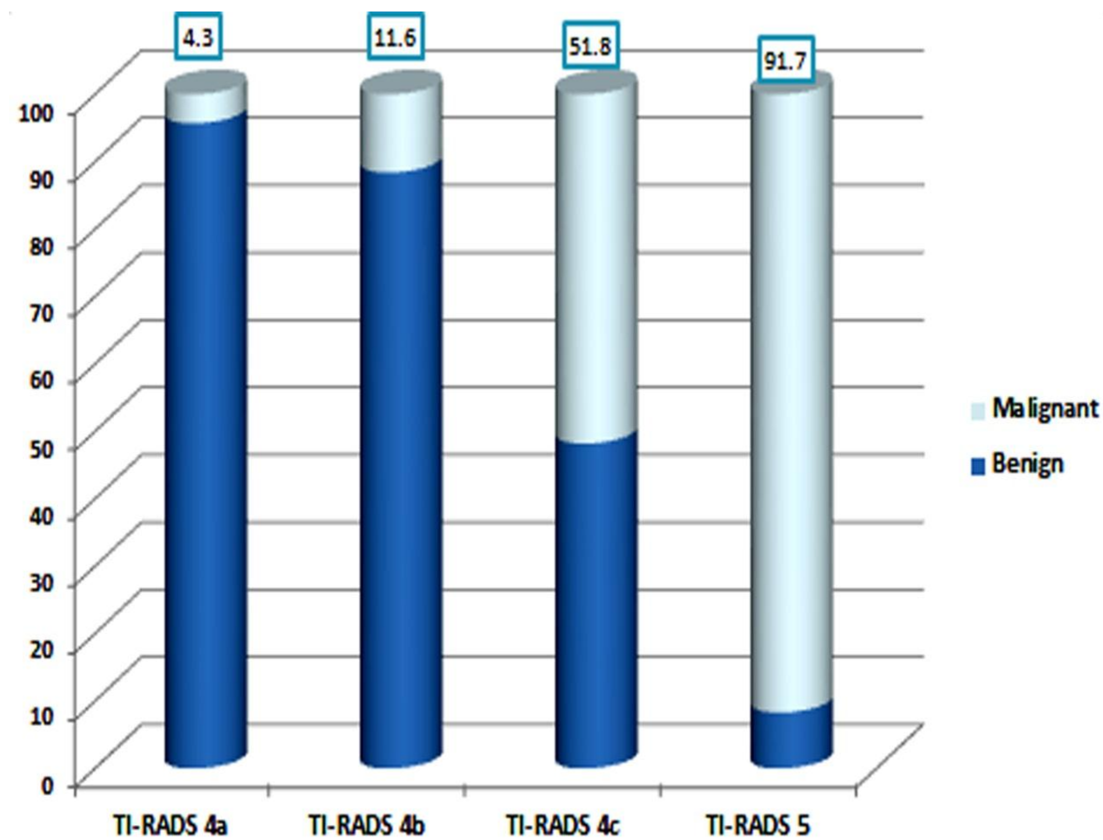

Figure 1:- Distribution of malignancy among various TIRADS subgroups.

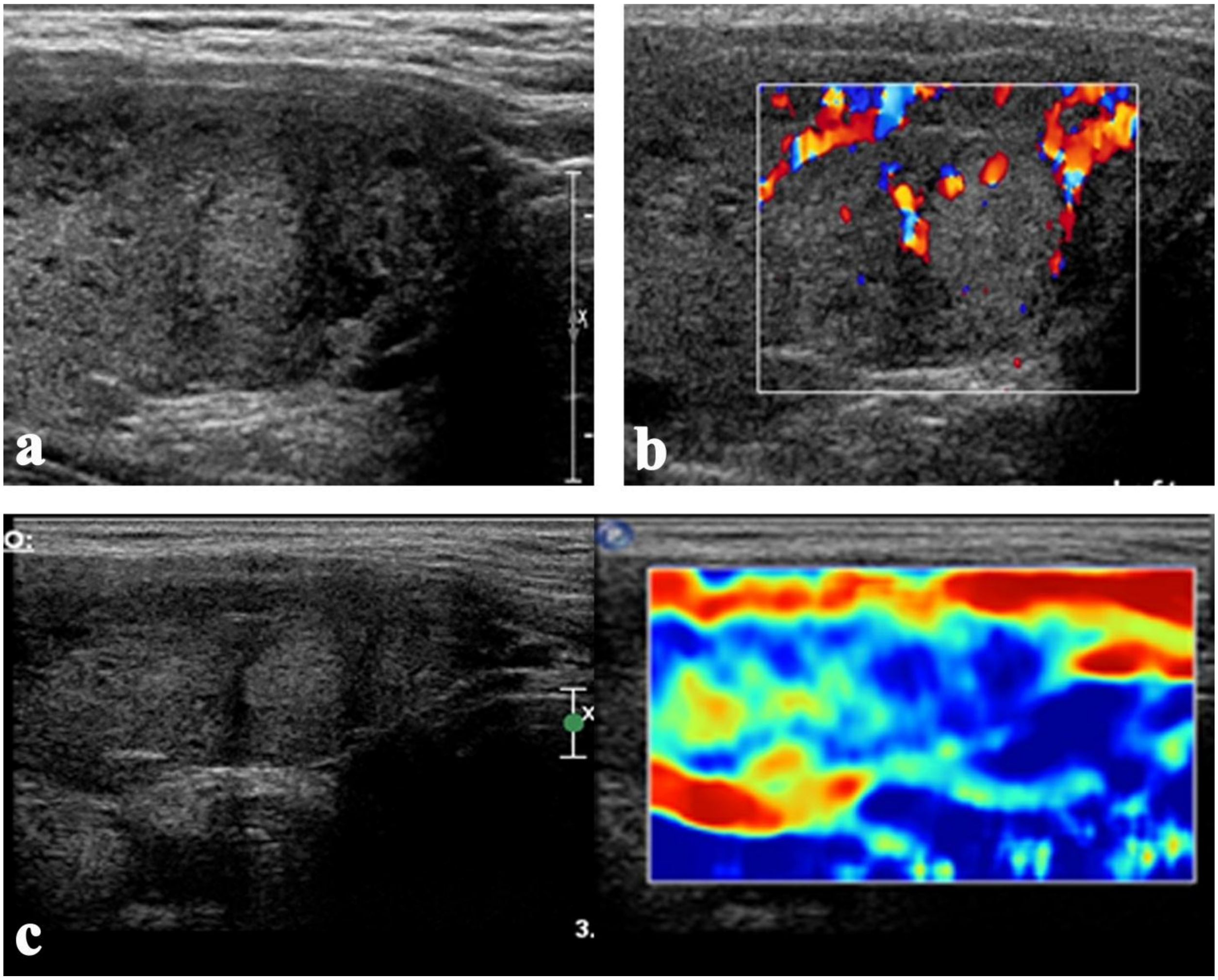

Figure 2 TI-RADS 4a:- A large well defined isoechogenic nodule (a), with low central vascularity (b) and hard on elastography (c). **Score 1**. Pathologically proven colloid nodule.

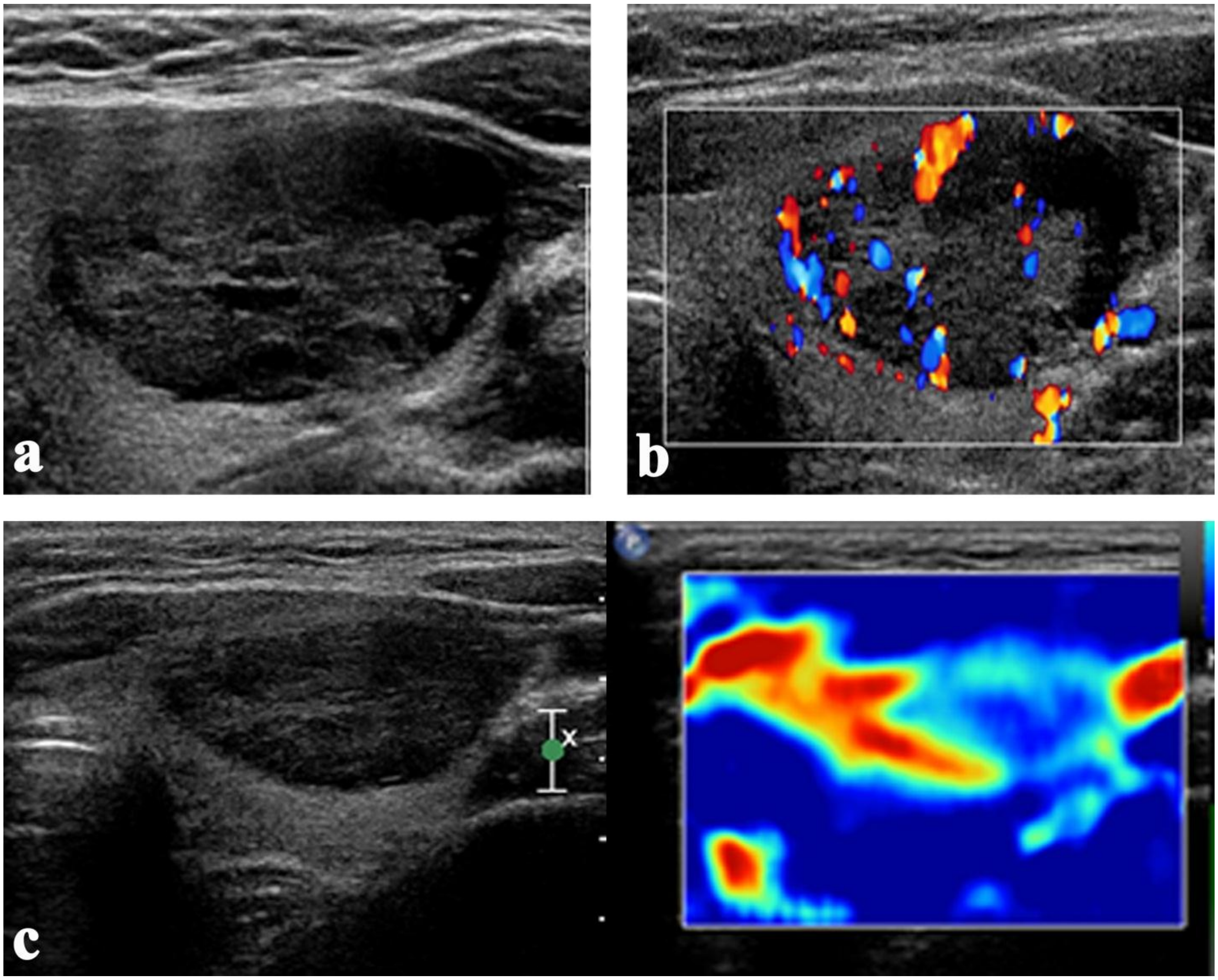

Figure 3 TI-RADS 4b:- A well defined hypoechogenic nodule (a), low central vascularity (b) and hard on elastography (c). **Score of 2.** Pathologically proven inflammatory nodule.

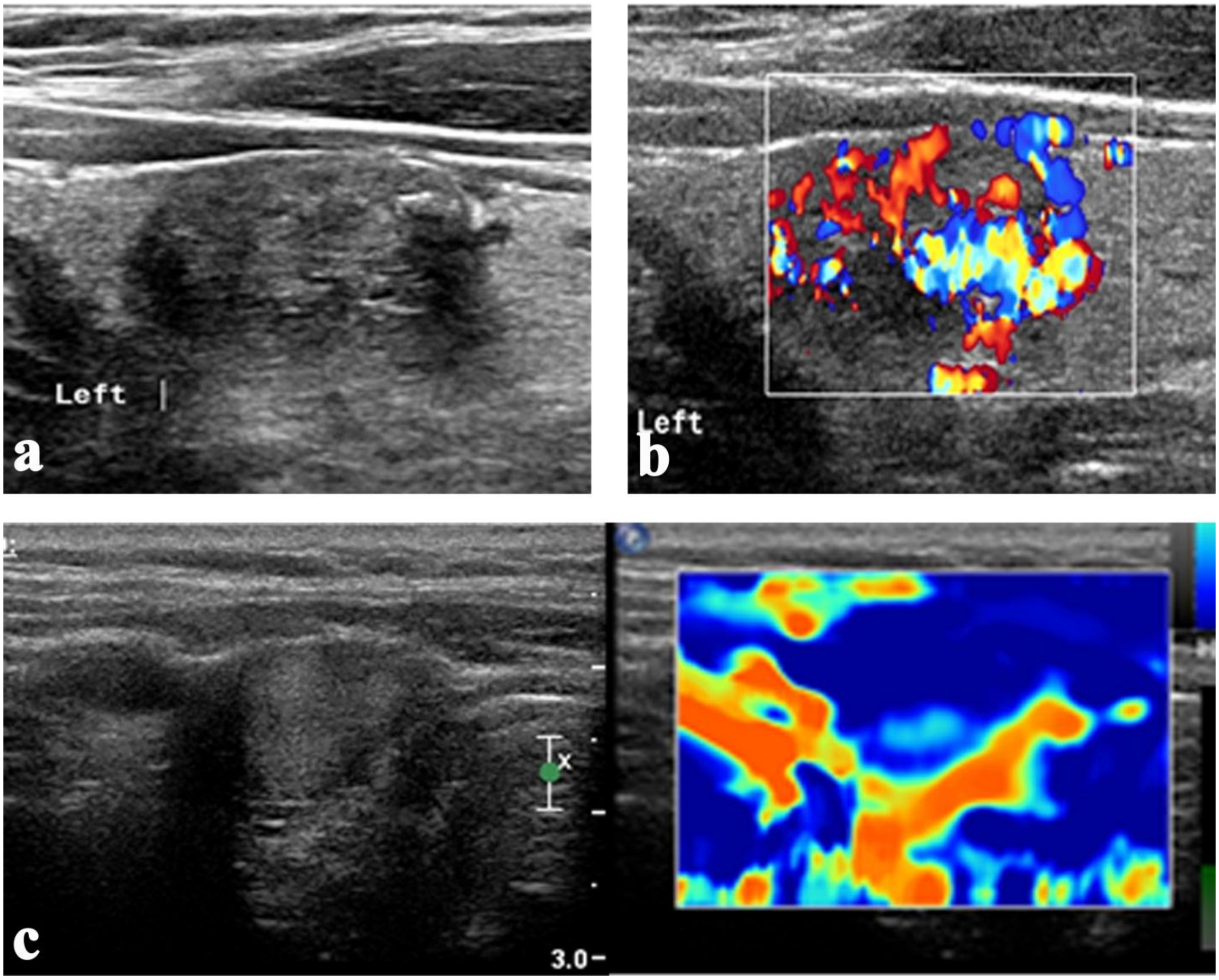

Figure 4 TI-RADS 4c:- An isoechogenic nodule with ill defined deep border (a), marked vascularity (b), and hard on elastography (c). **Score of 3**. pathologically proven papillary carcinoma.

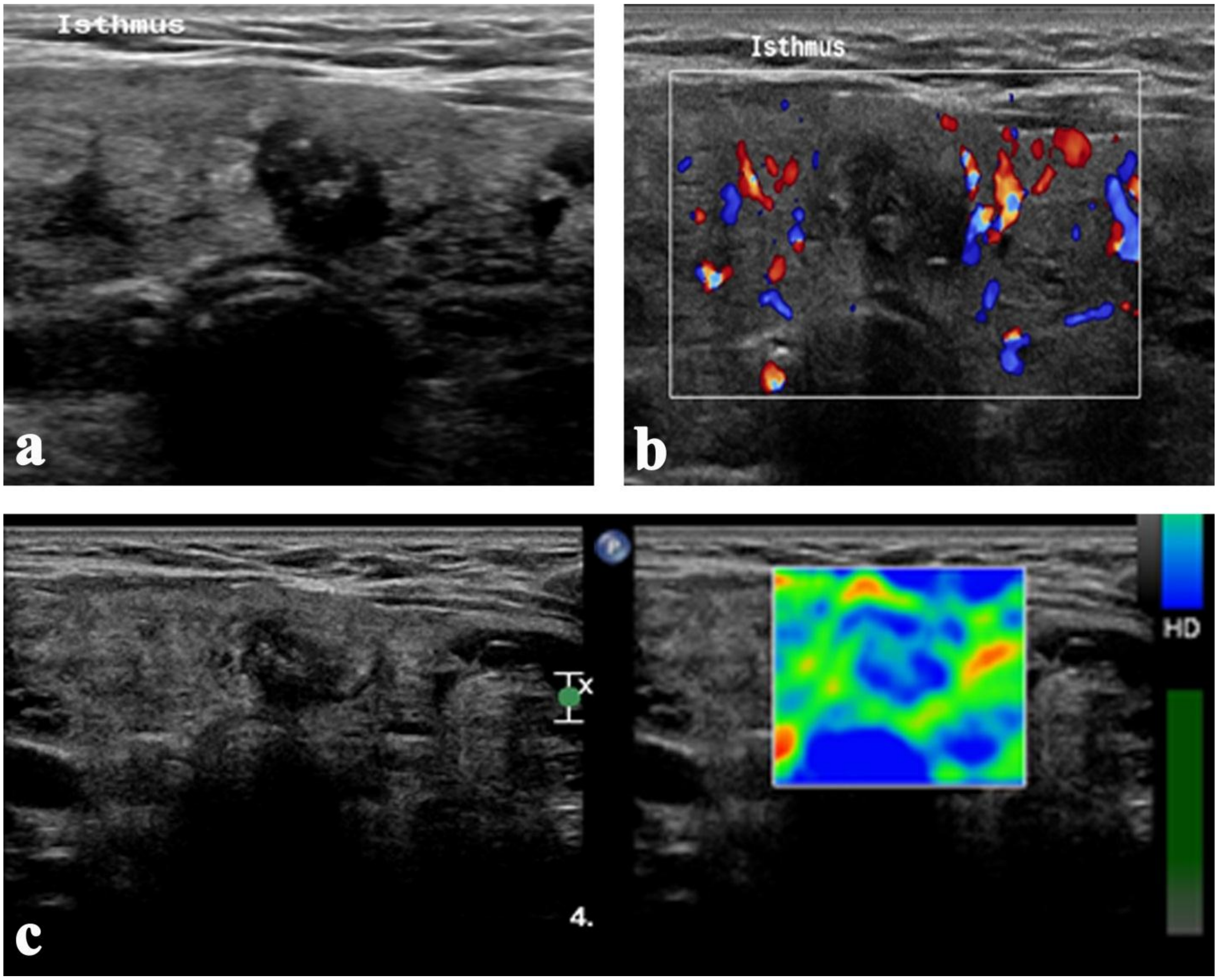

Figure 5 TI-RADS 5:- A markedly hypoechogenic nodule, non circumscribed borders taller than wide shape (a), mild central vascularity (b) and hard on elastography (c). **Score of 4**. Pathologically proven papillary carcinoma.

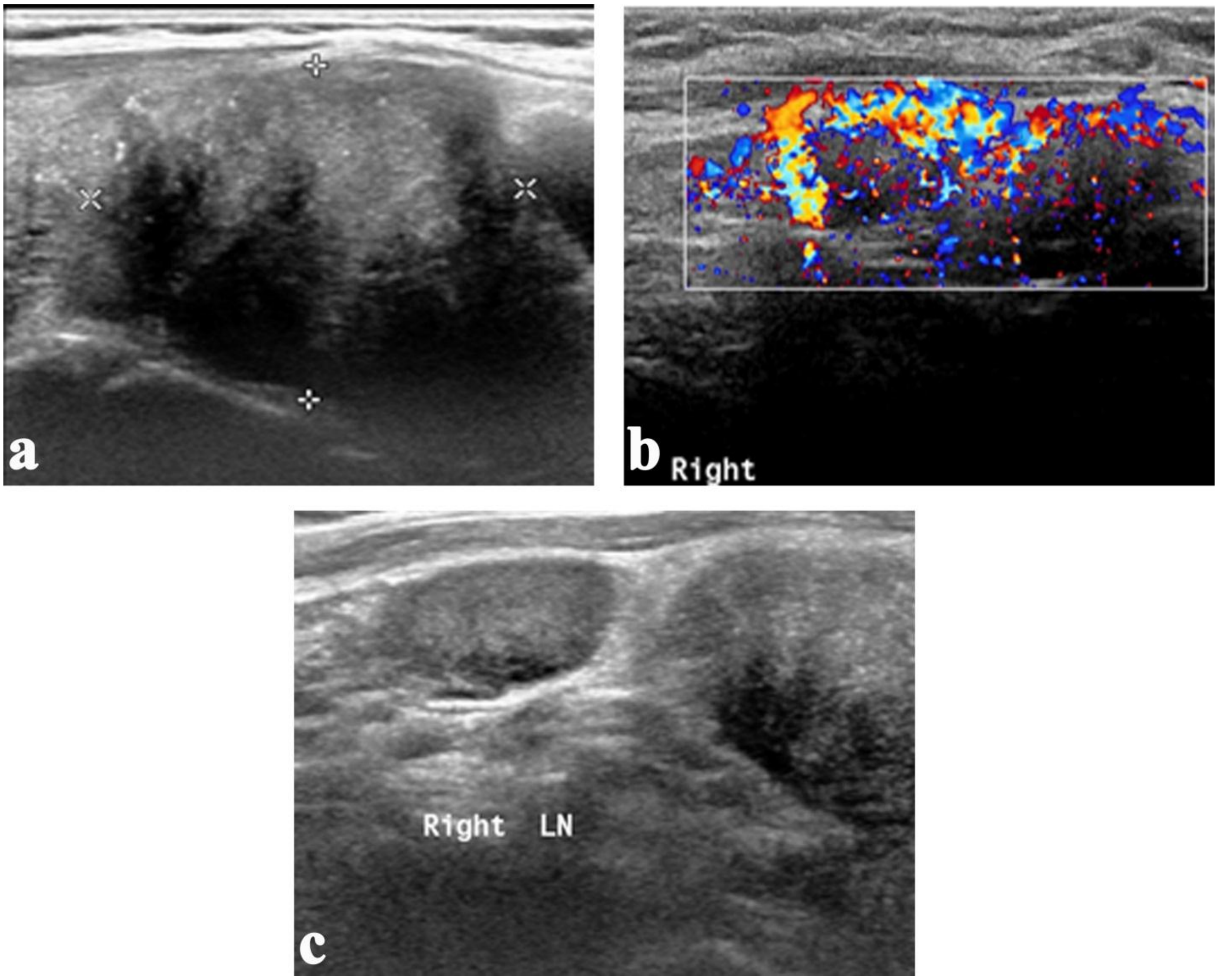

Figure 6 TI-RADS 5:- a nodule of mixed echogenicity with hypoechogenic non circumscribed deep portion and microcalcification (a), high vascularity (b) and suspicious regional LN (c). **Score of 5**. Pathologically proven medullary carcinoma.

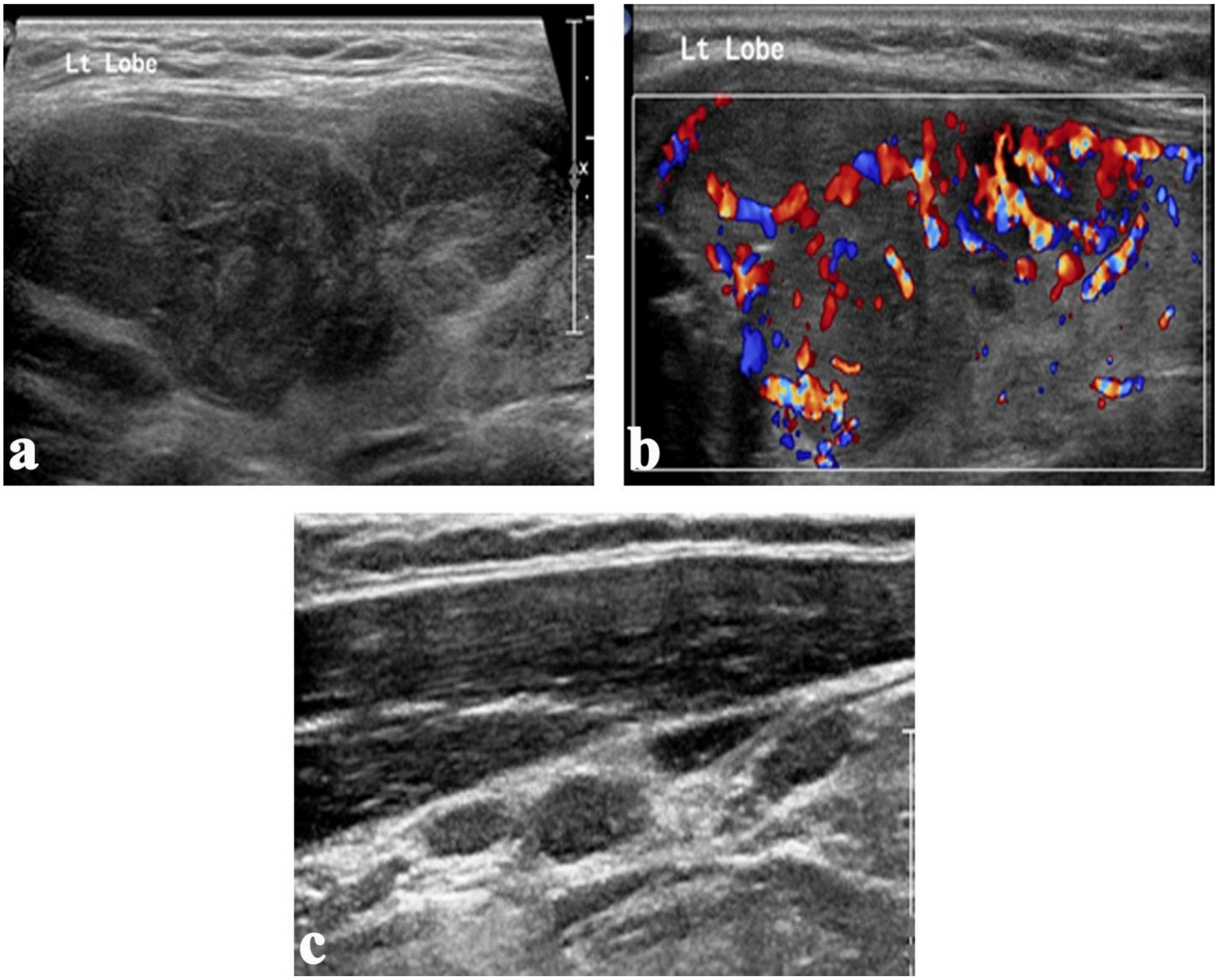

Figure 7 TI-RADS 4c:- A nodule hypoechogenic (a), highly vascular (b) with suspicious regional LN (c). **Score of 3**. pathologically proven papillary carcinoma.

Discussion:-

The technological development of ultrasound equipment, as well as the widespread use of US imaging techniques, lead to an overwhelming increase in the detection of thyroid nodules from 19% to 68% (1).

Among the detected thyroid nodule, thyroid cancer is a relatively rare, with a prevalence of about 5% (15). Therefore, performing FNAB in all detected nodules is not cost effective. Many studies tried to classify thyroid nodules in order to improve the US characterization of each nodule and select which one should be submitted to FNAB according to the risk of malignancy.

In our study, we focused on thyroid nodules with suspicious US criteria which all need FNAB. We chose the suspected criteria using a combination from Horvath et. al(8) and Kwak J Y, et. al.(9). We added qualitative stiffness on elastography according to Russ et al (14) and the presence of suspected enlarged cervical LNs according to Sánchez study published at 2013(16).

Malignancy was confirmed histologically in 821 nodules (429 patients) with slight female predominance as shown in the table (3).

According to nodular size, the prevalence of malignancy was more in small nodules (1-3cm), which is similar to the study of McHenry et al. who evaluated 1023 patients, the mean size of benign nodules was larger than malignant nodules ($P<0.05$) (17). Most of published papers show that generally the greater nodular size is less frequently malignant because the small nodular size is more with papillary carcinoma (more common) and less at follicular carcinoma. However, others studies referred the increased incidence of malignancy in small nodules due sampling error at FNAB of large nodule leading to false negative results (18).

Some US features were described in most of the published studies as highly suspicious for malignancy, they include marked hypoechogenicity, taller-than-wide shape, irregular outline and the presence of micro-calcifications (11).

From the calculated indices of each US suspicious criterion in our study, we found that the highest accuracy percentages were reported with marked hypoechogenic (73.9%). This criterion was shown more than 85% of specificity in most of the published studies (about 99.5% at Moifo et al.) (19).

The most sensitive US criterion for malignant risk was the shape of the nodule. Taller than wider nodule (Figure 5) was the most sensitive (88.1%) followed by hardness on elastography (87.8%). Capelli et al retrospectively correlated the histological and US characters of thyroid nodules in 5198 patients and noted that taller than wider >1 had 76% of sensitivity as a criterion of malignancy.

Russ et al noted that combined elastography with grey–scale US increased the sensitivity of malignant detection in thyroid nodules up to 98.5% (21).

Microcalcifications were observed more frequent in malignant lesions (Figure 6) than in benign nodules (69.6 vs 30.4%; P<0.001) coping with Harvorth et al, and Capelli et al studies (8,20).

Other criteria as non- circumscribed contour which is an indicative of extracapsular growth and local extension is also an important criterion to suspect malignancy (PPV 81%) and predominantly central vascularity (PPV 80%) were similar to most of the published studies (5).

By integrating these US features into the classification system, named TIRADS which harmonizes the reporting of thyroid US findings in a very simple way, it can help communication across different specialties. It is also similar to breast BIRADS classification, based on a scoring system which is more practical in evaluating the potential presence of criteria for suspected malignancy.

In our study, the malignant risk increased from TIRADS 4a to 5. It was about 4.3% for TIRADS 4A, 11.6% for TIRADS 4B, 51.8% for TIRADS 4c and 91.7% for TIRADS 5. Our results are

In his work, Horvath suggested a malignant risk greater than 80% for TIRADS 5, 10% to 80% for TIRADS 4B, and 5% to 10% for TIRADS 4A (Figure 7).

Our findings are within the range obtained by Horvath and Kwak et al and similar to that suggested by Russ et al. (8, 11, 10).

By using TIRADS classification in evaluation different thyroid nodules, we don’t rely on specific US features that had been described previously as highly suspicious for malignancy separately.

In our study, these features were found to be highly suspicious for malignancy as we noticed from different calculated indices as sensitivities, specificities, PPV and NPV. However, no single US criterion independently is fully predictive of malignancy and coexistence of 2 or more suspicious criteria significantly increases the risk of thyroid cancer (22).

According to TIRADS classification of suspected US features (from 4a to 5), Sanchez assumed a suitable protocol for management for each category. TI-RADS 4a (Figure 2) needs additional evaluation by FNA, medical history, clinical examination and scintigraphy findings. Based on the result of his study, Sanchez also noted that nodules classified as TI-RADS 4b (Figure 3) and 4c (Figure 4) should always undergo FNA, except if contraindicated and TI-RADS 5 nodules (Figure 7) almost always require histological examination after surgery (16).

The final evaluation of thyroid nodule and therapeutic planning depend on clinical, laboratory, imaging and histopathological assessment. Therefore, TIRADS classification even it is a merely sonographic assessment, it definitely helps in final decision making in an easy and practical way by facilitating communication between different specialties (16)

From this point of view, we agree with Moifo et al argument that TIRADS seems to have come to stay (19).

Conclusion:-

TI-RADS classification of thyroid nodules based on a scoring system according to US criteria suspicious of malignancy can be easier and more applicable in daily practice. As it unifies terminology and codes for classification among physicians of different specialties.

It was also statistically proven that TIRADS is more accurate in assessing thyroid nodules by using numbers of US features and not depending on each criterion separately.

Based on the score assigned in our work and the risk of malignancy of each category, we recommend to clinically re-assess the patient having nodule of category 4a before proceeding to FNAB due to a relatively low risk of malignancy (4.3%), therefore reducing the management cost. The assessment should include the patient's general Clinical condition, family history, neck exposure to radiation and to assess nodule scintigraphy uptake. FNAC should be limited to patients having other risk factors for developing malignancy.

Higher categories including 4b and 4c must proceed to FNAC except if contra-indicated. On the other hand, category 5 should undergo surgery with post-operative pathological study.

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