Predictive Value of Fine Needle Aspiration Cytology Versus Ultrasound TI-RADS In Solitary Thyroid Nodule Comparing With Gold Standard Histopathology Report

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ABSTRACT

Objective

To find the predictive value of fine needle aspiration cytology (FNAC) versus ultrasound TI-RAD in solitary thyroid nodules keeping histopathology report as the gold standard.

Study design

Cross sectional study.

Place & Duration of study

Department of General Surgery, Jinnah Postgraduate Medical Center (JPMC) Karachi, from February 2023 to December 2023.

Methods

A prospective observational cross sectional study was conducted on patients with solitary thyroid nodule. Patients' aged 18 years and above with normal TSH (euthyroid) and free T4 levels, were included. The study incorporated TI-RADS scores based on radiological findings and Bethesda classification for cytopathology examination. Clinical, radiological, cytological, and histopathological features were analyzed. The comparison between FNAC, TI-RADS, and biopsy results was carried out to find diagnostic accuracy.

Results

A total of 360 patients with the mean age of 41.69±9.41 years were enrolled. Most of the patients were between 40 to 60 years (59.4%) of age and predominantly females (68.9%). TI-RADS 4 (45.3%) and TI-RADS 3 (30.3%) were the predominant categories in radiological findings. Bethesda 2 (60.3%) dominated cytopathology results. FNAC showed high sensitivity (98.51%) but lower specificity (27.17%), while TI-RADS exhibited slightly better specificity (44.57%). The prevalence rates of benign cases were significantly higher for both FNAC and TI-RADS.

Conclusion

The association between FNAC versus ultrasound TI-RAD in solitary thyroid nodules compared with final biopsy results emphasizes the importance of this combined diagnostic strategy for timely clinical decision-making.

Key words

Solitary thyroid nodule, TI-RAD ultrasound, FNAC, Thyroid malignancy, Goiter

INTRODUCTION:

Ultrasound is used to describe the characteristics of thyroid nodules so that further steps in the management or investigation may be taken. When deemed necessary fine needle aspiration cytology is carried out for the diagnosis.[1] Thyroid carcinoma is rare, though it is the most common endocrine malignancy. It is expected to become the fourth leading tumor in the United States by 2030. The annual incidence in the United States has increased 500%.[2] According to the American Cancer Society there are 43,800 new cases of thyroid cancer in 2022 and as per the Cancer Statistics Centre the incidence rate is 14.1 per 100,000 in the United States. There has been a rise in the incidence of thyroid cancer globally as well, the cause of which remains undetermined.

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The incidence of thyroid cancer varies significantly based upon the geography. It is more frequently reported in females.[3-5] Within Pakistan the increase in incidence of thyroid cancers has been reported.[6] Since epidemiologic studies and population-based surveys are infrequently done, it is difficult to quantify the current incidence of thyroid cancers in Pakistan. According to a study the female to male ratio was 4.7:1.[7] No epidemiologic studies are done in recent times in Pakistan.

Thyroid Imaging, Reporting and Data System (TI-RADS) defines vocabulary for description of thyroid nodules and recommends a management plan based on the specific qualities of the lesion identified. Reporting ultrasound based on TI-RADS reduces unnecessary FNAC procedures.[8] In this study the predictive value of fine needle aspiration cytology versus ultrasound TI-RAD in solitary thyroid nodules keeping histopathology as the gold standard was planned.

METHODS:

Study design, place & duration: This observational cross sectional study was conducted in the Department of General Surgery, Jinnah Postgraduate Medical Center Karachi, from February 2023 to December 2023.

Ethical considerations: The study was approved by the Institutional Review board, dated 13-02-2023 by letter no.F.2-81/2023-GENL/13/JPMC. Informed consent was taken from the study participants.

Inclusion & exclusion criteria: Patients aged 18 years and above, presenting with thyroid nodules were included. Children and adolescent age group patients were not enrolled as they are managed by the pediatric surgeons.

Sample size estimation: A sample size of 360 was calculated using an online sample size calculator, by keeping the prevalence of solitary thyroid nodules as 0.18, with a 95% confidence level, and a precision of 0.10.[9]

Sampling technique: A non-probability convenience sampling technique was used.

Study protocol: Demographic information, such as residence, gender, age, comorbid along with clinical data including history of thyroid disease, were recorded on a predesigned form. Participants with clinically detected thyroid nodules underwent thyroid function tests, including serum TSH and free T4 estimation by chemiluminescence technique (CLIA) using Siemens Diagnostics kits with an Immulite-1000 analyzer. Only those patients who had normal TSH (euthyroid) and free T4 levels were included.

The euthyroid patients then underwent high-resolution ultrasound and fine needle aspiration cytology. Ultrasound reports were prepared according to the TI-RADS Score, ranging from TI-RADS 1 (benign) to TI-RADS 5 (highly suspicious). FNAC was performed on indicated thyroid nodules, with cytopathology reports prepared according to the Bethesda classification. Histopathology was conducted for all patients, serving as the gold standard.

Statistical analysis: Statistical analysis was carried out using IBM SPSS version 25, employing methods like Fisher exact test and Chi-square test. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for ultrasound features suggesting malignancy. Odds ratios (OR) were calculated with 95% confidence intervals, determining the risk of malignancy in each TI-RADS and Bethesda category relative to histopathological reports.

RESULTS:

The demographic profile of the studied population reveals a diverse range of characteristics. The mean age of the patients was 41.69±9.41 years. The majority falls within the age group of 40 to 60 years (n=214 - 59.4%), with 248 (68.9%) females. Type 2 diabetes mellitus was found in 269 (74.7%) subjects. Presenting symptoms included neck swelling (n=95 - 26.4%). Details are given in table I.

According to the TI-RADS scores majority were in TI-RADS 4 (45.3%) and TI-RADS 3 (30.3%) categories. In terms of cytopathology, Bethesda 2 was the most prevalent (60.3%), followed by Bethesda 3 (16.4%) and Bethesda 4 (15.3%). The TI-RADS classification showed a predominantly benign pattern (87.8%). Fine-needle aspiration cytology (FNAC) results exhibited a high percentage of benign findings (91.9%). Biopsy results showed a majority of benign cases (74.4%) with a notable proportion being malignant (25.6%). Details are given in table II.

In the comparison between biopsy and FNAC, FNAC demonstrated a significantly higher prevalence of benign cases (73.3%) and a lower prevalence of malignant cases (18.6%) with an odds ratio (OR) of 24.62 (95% CI: 8.28 - 73.17), indicating a substantial difference (p < 0.001). Similarly, the comparison between biopsy and TI-RADS revealed a significantly higher prevalence of benign cases with TI-RADS

Table I: Baseline Characteristics of the Patients		
Demographic Variable	Frequency (n)	Percentage (%)
Age (years)		
18 – 40	136	37.8%
40 – 60	214	59.4%
>50	10	2.8%
Gender		
Male	112	31.1%
Female	248	68.9%
Presenting symptoms		
Neck swelling	95	26.4%
Fever	24	6.7%
Warm skin	20	5.6%
Excessive sweating	57	15.8%
Changes of voice	23	6.4%
Difficulty in swallowing	28	7.8%
Pain neck	39	10.8%

Table II: Clinical, Radiological, Cytological and Histopathological Features		
Clinical Features	Frequency (n)	Percentage (%)
TI-RADS score		
TI-RADS 1	37	10.3%
TI-RADS 2	07	1.9%
TI-RADS 3	109	30.3%
TI-RADS 4	163	45.3%
TI-RADS 5	44	12.2%
TI-RADS		
Benign	316	87.8%
Malignant	44	12.2%
FNAC report		
Benign	331	91.9%
Malignant	29	8.1%
Biopsy report		
Benign	268	74.4%
Malignant	92	25.6%

Table III: FNAC Versus Ultrasound TI-RADS Comparing With Final Histopathology Report						
Comparison		Histopathology Report				P-Value
		Benign	Malignant	OR	95% C. I.	
FNAC (n=360)	Benign	264 (73.3%)	67 (18.6%)	24.62	8.28 - 73.17	0.000
	Malignant	4 (1.1%)	25 (6.9%)			
TI-RADS (n=360)	Benign	265 (73.6%)	51 (14.2%)	71.01	21.17 - 238.13	0.000
	Malignant	3 (0.8%)	41 (11.4%)			

Fisher's Exact tests, Odd Ratio (OR), Confidence Interval (C.I.)

Biopsy	TI-RADS Score	Cytopathology					P-Value
		Bethesda 2	Bethesda 3	Bethesda 4	Bethesda 5	Bethesda 6	
Benign (n=268)	TI-RADS 1	28 (10.4%)	1 (0.4%)	2 (0.7%)	1 (0.4%)	0 (0.0%)	0.000
	TI-RADS 2	6 (2.2%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	
	TI-RADS 3	71 (26.5%)	6 (2.2%)	13 (4.9%)	1 (0.4%)	1 (0.4%)	
	TI-RADS 4	81 (30.2%)	26 (9.7%)	27 (10.1%)	0 (0.0%)	0 (0.0%)	
	TI-RADS 5	1 (0.4%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.4%)	
Malignant (n=92)	TI-RADS 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	3 (3.3%)	0.000
	TI-RADS 3	6 (6.5%)	0 (0.0%)	0 (0.0%)	3 (3.3%)	8 (8.7%)	
	TI-RADS 4	21 (22.8%)	0 (0.0%)	0 (0.0%)	5 (5.4%)	3 (3.3%)	
	TIRADS 5	3 (3.3%)	26 (28.3%)	11 (12.0%)	1 (1.1%)	0 (0.0%)	

Table IV: Cytopathology Versus TI-RADS Score Comparing With Histopathology

Chi-Square tests, Confidence Interval (C.I.)

Table V: Diagnostic Accuracy of FNAC and TI-RADS Comparing With Histopathology

	Sensitivity	Specificity	Prevalence	PPV	NPV	Accuracy
FNAC	98.51%	27.17%	74.44%	79.76%	86.21%	80.28%
TI-RADS	98.88%	44.57%	74.44%	83.86%	93.18%	85.00%

(73.6%) and a lower prevalence of malignant cases (14.2%) with an odds ratio of 71.01 (95% CI: 21.17 - 238.13), indicating a significant difference (p < 0.001). This is given in table III. The comparison between histopathology and cytopathology results revealed significant associations. Table IV shows a detailed analysis. Diagnostic accuracy of FNAC demonstrated a high sensitivity of 98.51% but a lower specificity of 27.17%. Table V provides further details.

DISCUSSION:
Precise identification of thyroid nodules is essential to prevent unwarranted surgeries and facilitate timely intervention. This study showed how the diagnostic tools can facilitate clinicians as to the management of patients with solitary thyroid nodules, a challenge for the clinicians.[10, 11] FNAC and TI-RADS are widely used diagnostic methods for thyroid nodule investigation. However, their dependability is a matter of discussion.[12,13] This study provided an evidence based data in this regard.

The demographic profile of the study participants was diverse with a range of characteristics. The age groups distribution and gender related statistics of this study are comparable with the reported literature where the prevalence of thyroid nodules among females constituted 86.86% of the total study population.[12]

Following the 2017 ACR TI-RADS criteria the TI-RADS 4 was found most prevalent, followed by TI-RADS 3, portraying a predominantly benign pattern. Cytopathology examination, based on Bethesda classification, revealed that Bethesda 2 was most prevalent. The comparative analysis between FNAC and histopathology report, as well as TI-RADS and histopathology report, revealed significantly higher prevalence rates of benign cases for both FNAC and TI-RADS. The diagnostic accuracy of FNAC demonstrates high sensitivity as evidenced in other studies with lower specificity.[14] This emphasized the efficacy in detecting thyroid nodules but indicating a considerable rate of false positives. TI-RADS, while slightly more specific, showcased a high sensitivity of 98.88%, suggesting its utility in complementing FNAC for a comprehensive diagnostic approach.

This study provides clinicians with an understanding of the association between biopsy results and cytopathology within different TI-RADS categories and emphasizes the importance of an integrative diagnostic strategy for optimal patient care. It suggests that both FNAC and TI-RADS demonstrate high sensitivity in detecting thyroid nodules, with TI-RADS exhibiting slightly better specificity. FNAC, while highly sensitive, has limitations in specificity, leading to a higher rate of false positives. TI-RADS, as a radiological method, complements FNAC, providing additional information on nodules' benign or malignant nature. These findings of the combined diagnostic approach provide valuable insights in informing clinicians to make decisions for further intervention for a thyroid nodule intervention as

reported in literature as well.[15,16]

The issue of dependency on histopathology report as a gold standard for determining the accuracy of other diagnostic methods, specifically FNAC is important to recognize. Different pathologists may interpret the same tissue sample differently.[17,18] The interpretation of cellular features, patterns, and structures can be subjective, leading to variability in diagnoses. Ultrasound TI-RADS is operator-dependent and relies on the sensitivity of the equipment, introducing variability in its application. Accuracy of diagnosis can be influenced by experience of the radiologist.[19] Specific imaging techniques used have has been discussed in literatture.[20]

Limitations of the study: Variations in the interpretation of radiological and cytology specimens can impact the consistency and reliability of staging results.

CONCLUSION:
The ultrasound is a complementary rather than an alternative method to FNAC in euthyroid patients with solitary thyroid nodule. Both FNAC and TI-RADS demonstrated high sensitivity in detecting thyroid nodules, with TI-RADS exhibiting slightly better specificity. A combined diagnostic approach is thus warranted.

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