CORRELATION BETWEEN THE THYROID IMAGE AND REPORTING DATA SYSTEM (TIRADS) AND THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY IN PATIENTS WITH THYROID NODULES

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ABSTRACT

Objective: To determine the correlation between the thyroid image and reporting data system (TIRADS) and the Bethesda system for reporting thyroid cytopathology in patients presenting with thyroid nodules.

Methods: This cross-sectional study was performed at the histopathology department of Allama Iqbal teaching hospital DG Khan, over six months. A total of 87 patients aged 18 to 60 years referred to the pathology department for FNAC of thyroid nodules were included. Exclusion criteria were prior thyroid cancer diagnosis, ongoing chemo / radiotherapy or recurrence. Demographic details laterality and TIRADS grading were recorded. Samples were stained with hematoxylin and eosin and assessed microscopically. Histopathology reporting followed the Bethesda system. Data were analyzed using SPSS version 23. Spearman's correlation was used to evaluate TIRADS and Bethesda grades.

Results: The mean participant age was 36.3 ± 10.7 years. Gender distribution was almost equal. Unilateral thyroid nodules were noted in 51.7% of the cases. TIRADS grading showed most nodules as grade 3 (40.2%) or grade 4 (39.1%). FNAC reported benign cytology (grade 2) in 72.4% and malignant (grade 6) in 11.5%. Malignancy was suspected in 48.3% by TIRADS and confirmed in 22.9% on histopathology. A weak but significant positive correlation existed between TIRADS and Bethesda grade ($r_s = 0.245$, $p = 0.022$).

Conclusion: TIRADS showed a weak correlation to cytopathologic grading.

Keywords: Thyroid nodule, Fine needle aspiration biopsy, TIRADS scoring, Bethesda system

INTRODUCTION

A distinct lesion in the thyroid gland that is different from the surrounding thyroid tissue on radiological grounds, is called a thyroid nodule. It can manifest as solid, mixed solid-cystic, or cystic, and it can arise in one or more types.[1] Ultrasound significantly increases the rate of thyroid nodule detection to 70%.[2] Although there is a 5% chance of thyroid malignancy in a thyroid lesion, the risk of cancer is the primary concern when evaluating the thyroid nodule.[3]

A lot of work was done on evaluation and treatment of thyroid nodules after Horvath et al introduced the Thyroid Image and Reporting Data System (TIRADS) in 2009.[4]

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The thyroid nodule undergoes additional testing in accordance with TIRADS classification in order to ascertain its histological condition and rule out thyroid cancer.[5] Depending on the grey-scale feature of the thyroid nodule, it divides characteristics into six subcategories: normal thyroid, benign lesion, presumably benign lesion, suspicious thyroid lesion, probably malignant type, and biopsy-proven malignant thyroid lesion.[6]

After an ultrasound thyroid assessment, fine needle aspiration cytology (FNAC) is considered as the gold standard for evaluating thyroid nodules.[7] A minimally invasive technique for evaluating the thyroid nodule is FNAC. Thyroid FNAC is classified into 6 categories (I–VI, non-diagnostic, benign, AUS/FLUS, follicular or suspicious of follicular malignancy, suspected of malignancy, and malignant, respectively) by the Bethesda system, which was introduced in 2007. The chance of malignancy is 1–4%, 0–3%, 5–15%, 15–30%, 60–75%, and 97–99%, respectively, for each category.[8]

Many international research studies have demonstrated that the TIRADS system can be used to direct clinical practice and has a strong association with the Bethesda system.[9] In order to standardise international nomenclature and classify the lesion according to the risk of malignancy, the Bethesda system for reporting thyroid cytopathology was created in 2007.[10]

The goal of this study was to evaluate the correlation between the two scoring systems in

patients presenting with thyroid nodule in our local setting.

MATERIALS AND METHODS

This **cross sectional** study was conducted at Histopathology department of Allama Iqbal teaching hospital DG Khan. The study duration was six months from 1st June 2024 to 30th November 2024. The study was approved by the institutional ethics review committee (ERC# 0011/66/MED/DGKMC, dated:30th May 2024). Patients 18 – 60 years of age, either male or female gender referred to pathology department for FNAC of the thyroid nodules were consecutively enrolled in the study after informed consent. Patients with a prior diagnosis of thyroid cancer, those undergoing chemotherapy or radiotherapy, and those with recurrent disease were excluded from the study. Age, gender, laterality (unilateral / bilateral) of the thyroid nodule and TIRADS grade on ultrasonography were recorded. All FNAC were performed as per hospital protocol and specimens were plated on glass slides, air dried and fixed with 95% alcohol. The slides were stained with hematoxylin and eosin. Microscopy was done by 4x lens followed by 10x and then 40x to look for nuclear features. The cytopathology was done by consultant histopathologist with ≥5years post fellowship **experience and not aware of TIRADS grading.** The cytopathology reports were generated using Bethesda system of reporting. A minimum sample size of 87 patients was calculated through one sample correlation formula using online calculator http://sample-size.net/correlation-sample-size/ and assuming a correlation (r) of 0.34 between TIRADS and Bethesda system at 80% power and 5% significance level.[11] The data analysis was done through SPSS version 23. Normality of numerical data was determined through the Shapiro-Wilk test. Mean and standard deviation **was** calculated for age and frequency and percentages for categorical data. Correlation between TIRADS and Bethesda grades was assessed through Spearman's correlation (rs) and p-value ≤0.05 was considered significant. Grades 4,5 and 6 were suspected malignant lesions on TIRADS and confirmed on Bethesda grades of 4,5 and 6 on cytopathology.

RESULTS

The mean age of the participants was 36.3 ± 10.7 years. Male and female distribution was equal (50.6% vs. 49.4%). In 51.7% of the cases thyroid nodules were unilateral **[Table 1].**

Table 1: Patient characteristics with thyroid nodules referred for FNAC (N=87)

Characteristics	Frequency	Percentage
Age (years)	36.3 ± 10.7	
Gender – Male	44	50.6
Female	43	49.4
Laterality – Unilateral	45	51.7
Bilateral	42	48.3

Using TIRADS on thyroid nodule ultrasound the most common grades were 3 (40.2%) and 4 (39.1%). After fine needle aspiration cytology (FNAC) the most common grade was 2 (72.4% - **benign cytology**) followed by 6 (11.5%, malignant cytology). Malignant nodules were labelled in 48.3% on TIRADS and in 22.9% on cytopathology **[Table 2].**

Table 2: TIRADS and Bethesda Grading of thyroid nodules (N=87)

TIRADS Grade – 2	10	11.5
3	35	40.2
4	34	39.1
5	08	9.2
Bethesda Grade – 2	63	72.4
3	4	4.6
4	5	5.7
5	5	5.7
6	10	11.5
Malignant nodules on TIRADS	42	48.3
Malignant nodules on Bethesda	20	22.9

Table 3: Correlation between TIRADS and Bethesda grades in patients with thyroid nodules (N=87)

TIRADS Grade	Bethesda Grade				
	2	3	4	5	6
2	10	0	0	0	0
3	25	4	0	0	6
4	26	0	4	2	2
5	2	0	1	3	2
Spearman Correlation		0.245	**p-value**	0.022	

A positive but weak correlation was observed between TIRADS and Bethesda grades for thyroid nodules (ρ / r_s = 0.245, p-value 0.022) **[Table 3].**

DISCUSSION

This study used the TIRADS and Bethesda systems, to examine the radio-pathological correlations between the thyroid's cytopathological evaluation and ultrasound assessment. The quadruple test comprises of nodular examination, thyroid hormone levels, ultrasonographic findings, and fine needle aspiration which is used to evaluate the thyroid nodule. Even though the incidence of malignancy in persons with thyroid nodules is less (3–7%), these evaluations are carried out to reduce the possibility of overlooking the presence of cancer.[12] The thyroid nodule's sonographic characteristics and the cytopathological grading have demonstrated strong radio-pathological associations in a few investigations.[13]

In our study, the Spearman's correlation coefficient between TIRADS and Bethesda grades was rs = 0.245, indicating a weak but statistically significant positive correlation (p = 0.022). Over the course of six months, 87 patients who had both thyroid ultrasonography and fine needle aspiration of the thyroid nodule were examined in a study. The average patient age at the Lady Reading Hospital in Peshawar was 42.56 ± 11.60 years, and the female-to-male ratio was 2.28:1.[14] The age range and mean age are like our findings, even though their study found a higher frequency among females. The age demographics generally fall during the third to fifth decades of life, despite variations in the gender distribution across studies. This emphasises the significance of closely monitoring thyroid nodules in this age group. Gender proportions may be impacted by random variation owing to the small sample size of 87 patients during a six-month period. Gender trends at the population level are typically better reflected by larger sample sizes. TIRADS and Bethesda grades for thyroid nodules showed a weak but positive connection in our investigation.

Ghazi FN et al, in 2023, examined two hundred and ninety-five patients who had thyroid nodule ultrasound examinations and FNAC. Between TIRADS and Bethesda, the linear-weighted kappa was 0.20 (95% CI: 0.15–0.25) and the Spearman's correlation value (ρ) was 0.464 (p <0.001). The diagnostic accuracy of both systems was good (area under the curve [AUC]: 85.8% and 85.6%, respectively).[11]

Eleven hundred cases with ages from 7 to 85 years were enrolled by Dhar L et al, in 2023. For 1036 cases, the TIRADS scoring was achieved. With a considerable Kappa agreement of 0.688 and a p-value of 0.00, there was a significant connection between the TIRADS and Bethesda systems.[15] Similarly, Al Shaikh R et al, in 2022, discovered a strong positive association between the TIRADS and Bethesda scores (r = 0.338, p ≤0.001) after enrolling 189 cases.[16]

The TIRADS and Bethesda systems were found to be significantly associated in a prospective study carried out in India by Periakaruppan G, in 2018. The sensitivity, specificity, positive and negative predictive values were 92.3%, 94%, 54.5%, and 99.8%, respectively.[17] As surgical histopathology was not available, diagnostic accuracy was not assessed in this study.

In a study with 397 patients, Atar et al, in 2024, discovered a weak but substantial connection (r = 0.33, p <0.001) between the Bethesda categories and ACR TIRADS. TIRADS's sensitivity and specificity in identifying malignancy were 80.3% and 60.8%, respectively, which closely matched with the findings of our investigation.[18] According to George et al, in 2022, there was a 69.8% overall concordance between TIRADS, Bethesda, and final histology, with a sensitivity of 72.3% and specificity of 66.7% for TIRADS.[19]

Another study conducted by Huang EY et al, in 2023, that examined 630 thyroid nodules discovered that ACR TIRADS scores of 4 and 5 had stronger predictive values when connected with histology but lower positive predictive

values when compared to Bethesda scores.[20] In particular, there was a moderate association between TIRADS and Bethesda systems. The cancer rates for TIRADS 4 and 5 nodules following thyroidectomies were 10.9% and 71.4%, respectively.[20] The TIRADS and Bethesda systems showed a strong connection ($p = 0.464$; $p = 0.464$; $p < 0.001$) in a study by Ghazi FN et al, in 2023. With an AUC of 85.8%, the total sensitivity and specificity were 81% and 90.6%, respectively. With a kappa value of 0.203.[11] The reported agreement using the linear weight was 62.3%.

Similarly, 83% concordance rate with overall sensitivity and specificity of 70.6% and 90.4%, respectively, were obtained from a Singaporean study conducted by Singaporewalla RM et al, in 2017 that included one hundred thyroid nodules.[21] The TIRADS system's high diagnostic accuracy suggests that it can be utilised in clinical practice to help determine whether surgery or a biopsy is necessary.

Numerous research studies have looked into the Bethesda system's validity.[22] The Bethesda system demonstrated an accuracy of 68.8% in a meta-analysis of 25,445 patients of FNAC. The system's reported sensitivity, specificity, PPV, and NPV were 97%, 50.7%, 98.6%, and 96.3%, respectively. Additionally, the false-negative and false-positive rates were 3% and 0.5%, respectively.[23]

Together, these studies support the idea that although TIRADS is a useful tool for thyroid nodule risk stratification, its diagnostic accuracy is only modest and that it performs better when combined with cytological evaluations such as the Bethesda system. This study's primary limitations were its small sample size and the fact that it only included patients from one institution; as a result, the findings cannot be applied to the whole population. Second, as biopsy is considered the gold standard for diagnosing benign and malignant lesions, the absence of histopathological confirmation limits our ability to determine the true diagnostic accuracy of TIRADS and Bethesda classifications.

CONCLUSION

TIRADS demonstrated a positive but weak correlation with Bethesda grading in the assessment of thyroid lesions. TIRADS may serve as a useful non-invasive screening tool but should be complemented by FNAC and surgical histopathology for definitive diagnosis. The results of our study will help doctors and patients to make wise decisions during process of investigating and managing the thyroid nodule. The study will help in reducing patient anxiety and invasive procedures by better identifying low-risk nodules that do not need FNA or surgery. This will optimize resource allocation in busy radiology and pathology departments. More prospective research with more institutions and a bigger sample size is recommended.

Author contributions

SS: Idea conception, data collection, manuscript writing
US: Proof reading, draft making, data analysis, Final approval
SH: Critical analysis, data analysis, methodology writing
MU: Critical analysis, Data analysis, manuscript writing
NQ: Manuscript writing, proof reading

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Declaration:

- The manuscript has been read and approved by all the authors, that the requirements for authorship as stated below in this document have been met, and that each author agrees to be accountable for all aspects of the work.
- This study has not been submitted or presented elsewhere.

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