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A STUDY OF THE CONCORDANCE BETWEEN USG-TIRADS ASSESSMENT AND BETHESDA GRADING IN FNAC OF THYROID SWELLINGS AND ITS CORRELATION WITH HISTOPATHOLOGY

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ABSTRACT

Background

Several studies have explored the correlation between TIRADS grading by ultrasound and Bethesda grading by cytology in the past. Most of them conclude that there is a positive correlation between the two and that using TIRADS scoring for evaluating thyroid lesions proves to be a major breakthrough in diagnostics. This study was conducted to analyse the correlation of radiological findings of thyroid lesions using TIRADS grading with their cytological features using the Bethesda Categorisation.

Methods

FNAC was conducted among 67 cases who had been evaluated radiologically and assigned appropriate TIRADS (Thyroid Imaging Reporting and Data Approach) scores. Cytological analysis using the Bethesda Categorisation was compared with the assigned TIRADS score, with histopathology as the gold standard.

Results

The sensitivity and specificity of TIRADS classification in differentiating benign and malignant neoplasms were 91.2% and 90%, respectively. The sensitivity and specificity of the Bethesda Classification in differentiating benign and malignant neoplasms were 94.7% and 80%, respectively. A positive correlation was achieved on comparing the Bethesda Classification and TIRADS grading with a p-value of 0.001 and the Pearson correlation r-value of 0.726.

Conclusion

The present study presents a highly significant positive correlation between TIRADS and TBSRTC. It highlights the combined use of radiological categorisation along with cytological categorisation as a better means of risk stratification of thyroid lesions.

Keywords: TIRADS Grading, Bethesda Classification, Thyroid Lesions.

INTRODUCTION

Globally, the incidence of thyroid cancer has grown. According to Globocan 2018 statistics, the age-standardized incidence rate per 1 lakh population in India is 89.4, and the incidence of thyroid cancer is 11,57,294.[1] Though histopathology is the gold standard tool in diagnosing thyroid lesions, categorisation by means of cytology and radiology as a screening tool has been gaining importance recently. It provides an option of avoiding surgery in certain cases. Directly diagnosing a lesion includes inter-observer variations, which makes it difficult for surgeons to decide further management. It is easier for them if the lesions are classified under broader terms related to their prognostic potential. In this way, benign-appearing cases can opt to wait rather than immediately undergo surgeries.

The Bethesda approach is now the accepted method for cytology reporting of thyroid nodules, according to the ATA (American Thyroid Association) management guidelines for thyroid malignancies.[2] The Bethesda system of reporting thyroid cytology facilitates effective communication among cytopathologists, endocrinologists, surgeons, radiologists, and other healthcare providers, hence facilitating cytohistologic correlation, allowing easy and reliable sharing of data from different laboratories across the globe. TIRADS (Thyroid Imaging Reporting and Data Approach), a risk stratification approach for categorizing thyroid lesions approved by the American College of Radiology, is used to perform ultrasonographic characterisation of thyroid nodules. Based on sonographic features, the US TIRADS system assists in identifying nodules that warrant further examination for possible cancers.[3] Internal composition, echogenicity, borders, echogenic foci, and nodule shape were among the sonographic characteristics taken into account. All of these factors are taken into account while determining TIRADS scoring. The probability that a thyroid nodule will be cancerous increases with the cumulative TIRADS score.

Several studies have explored the correlation between TIRADS grading by ultrasound and Bethesda grading by cytology in the past. Most of them conclude that there is a positive correlation between the two and that using TIRADS scoring for evaluating thyroid lesions proves to be a major breakthrough in diagnostics. We discovered that there aren't many published articles from India when we reviewed the literature on the comparison of the Bethesda system with final histology and the US TIRADS system. Hence, this study was conducted to analyze the correlation of radiological findings of thyroid lesions using TIRADS grading with their cytological features using the Bethesda Categorisation.

MATERIALS & METHODS

This was a prospective study carried out over a period of 2 years, involving 67 patients who came to the OP section of the Department of Pathology for FNAC of palpable thyroid lesions after being evaluated radiologically and assigned an appropriate TIRADS score. Cytological analysis using the Bethesda Categorisation was compared with the assigned TIRADS score, with histopathology as the gold standard. Pediatric patients with congenital goiter and those not willing to undergo surgery and follow-up were excluded from the study.

For staining with H&E stain and Pap stain, slides were fixed in absolute alcohol. For Diff-Quik staining, slides were air-dried. (The composition of each stain is listed in Annexure IV). After fixation, the slides were stained primarily with H&E stain. Pap stain and Diff-Quik stains were used wherever required. Interpretation of thyroid cytology by various stains is as shown in the table below.

Morphology	H & E stain	Pap stain	Diff-quik stain
Cytoplasm	Pink	Pinkish orange to green	Pink
Nuclei	Purple	Purple to blue	Purple
Colloid	Pink	Pale green to orange	Blue violet

Table 1: Interpretation of Thyroid Cytology by Various Stains

The excised thyroid specimen after surgery was received, and grossing was done. Tissue bits from necessary areas were taken and submitted for routine histopathological processing. Staining was done

with hematoxylin and eosin stain and diagnosed subsequently. The cytology smears were studied, and the adequacy of the sample was evaluated at low power. High magnification was used for detailed analysis of the cytomorphology, characteristics of background cells, and colloid. With the findings obtained, the specimens were classified into six categories as proposed by the Bethesda System of Reporting Thyroid Cytology.

The patient was then admitted to the ward for surgical management. After surgery, the excised specimen was received in the Department of Pathology in 10% neutral buffered formalin for histopathological analysis. Careful gross examination was done, and tissue bits from necessary areas were taken and submitted for routine histopathological processing. Staining was done with hematoxylin and eosin stains and examined.

Both radiological interpretation in the form of TIRADS classification and cytological interpretation as per the Bethesda system of reporting were correlated statistically. Histopathology was used as the gold standard test for comparison. Microsoft Excel 2010 was used to enter the data obtained from the study. Statistical interpretation and analysis were done using SPSS software.

RESULTS

Among the 67 cases studied, the majority (47.8%) of the cases were in the age group of 30-44, with a total mean of 42.58 years. In the benign category, the mean age of the patients was 42.47 years, and the mean age of the patients in the malignant group was 43.2 years.

	No. of Cases	**Mean + Standard Deviation**	**Median IQR (in years)**
Benign	57	42.47 + 13.55	40 (35-54)
Malignant	10	43.2 + 11.12	39 (34-55.5)
Total	67	42.58 + 13.15	40 (35-54)

Table 2: Age Distribution

Among the 67 patients, 60 were females, accounting for 89.6% of the total cases, and the remaining 7 cases were males, accounting for 10.4%. Of the 60 female patients, 52 of them had benign lesions and 8 of them had malignant lesions. 2 of the male patients had malignant lesions, and 7 of them had benign lesions.

The majority (32) of the cases presented as multinodular swelling (47.8%). 42% of patients came with a solitary nodule in the thyroid, and the remaining 10.4% of the patients had a diffuse enlargement of the thyroid gland.

Of the total 67 cases, nodular colloid goiter was diagnosed in 24 cases. Hashimoto thyroiditis is the second major category, with 11 cases. Among the malignant conditions, papillary carcinoma is the predominant diagnosis, accounting for 9% of the total number of cases. Medullary carcinoma is the second most commonly seen malignancy, with 2 cases out of the total 67 cases. No metastatic carcinoma was observed in the cases studied.

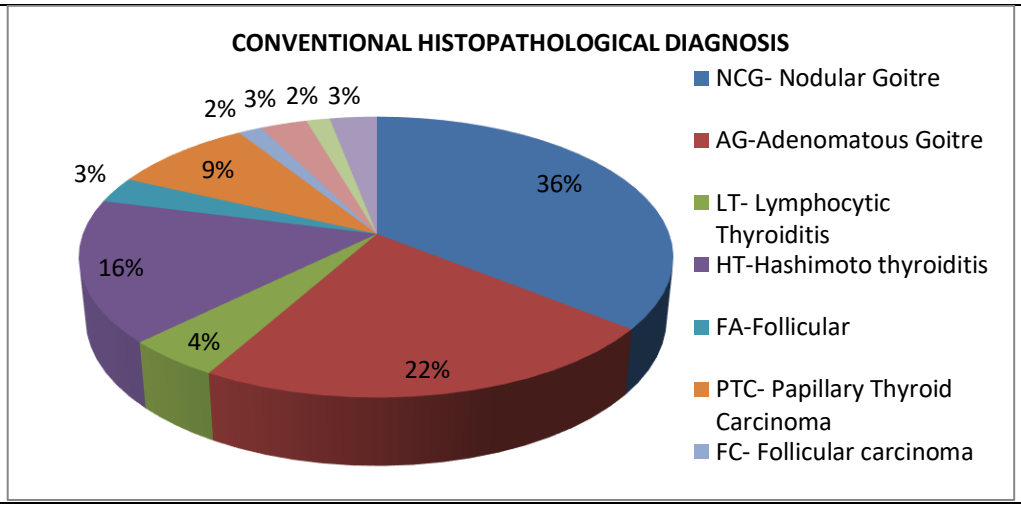

Figure 1: Distribution of Cases by Final Histopathological Diagnosis

In TI-RADS classification, the overall majority was in TR2—42 (62.7%). The overall distribution of the cases is as shown in Figure 2.

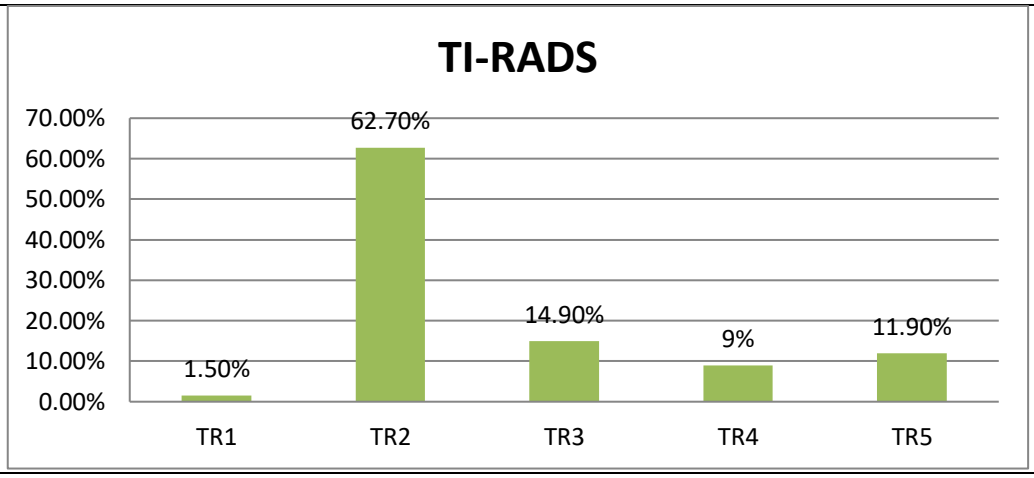

Figure 2: Distribution of Cases According to TIRADS Classification

The sensitivity and specificity of TIRADS classification in differentiating benign and malignant lesions were 91.2% and 90.0%, respectively. The positive predictive value was 98.1% and the negative predictive value was 64.3%.

			Histopathological Diagnosis		Total		
			Benign	**Malignant**			
TIRADS	**Benign**	Count	52	1	53		
		% within TIRADS	98.1%	1.9%	100.0%	**Sensitivity**	91.2%
		% within HPE	91.2%	10.0%	79.1%	**Specificity**	90.0%
	Malignant	Count	5	9	14	**PPV**	98.1%
		% within TIRADS	35.7%	64.3%	100.0%	**NPV**	64.3%
		% within HPE	8.8%	90.0%	20.9%		
Total		Count	57	10	67		
		% within TIRADS	85.1%	14.9%	100.0%		
		% within HPE	100.0%	100.0%	100.0%		

Table 3: Accuracy of TIRADS Classification in Differentiating Benign and Malignant Thyroid Lesions

AUC (Area under the Curve) in comparing the TIRADS classification and histopathological findings was 0.043. The lower bound was 0.000, and the upper bound was 0.089, both of which were statistically highly significant.

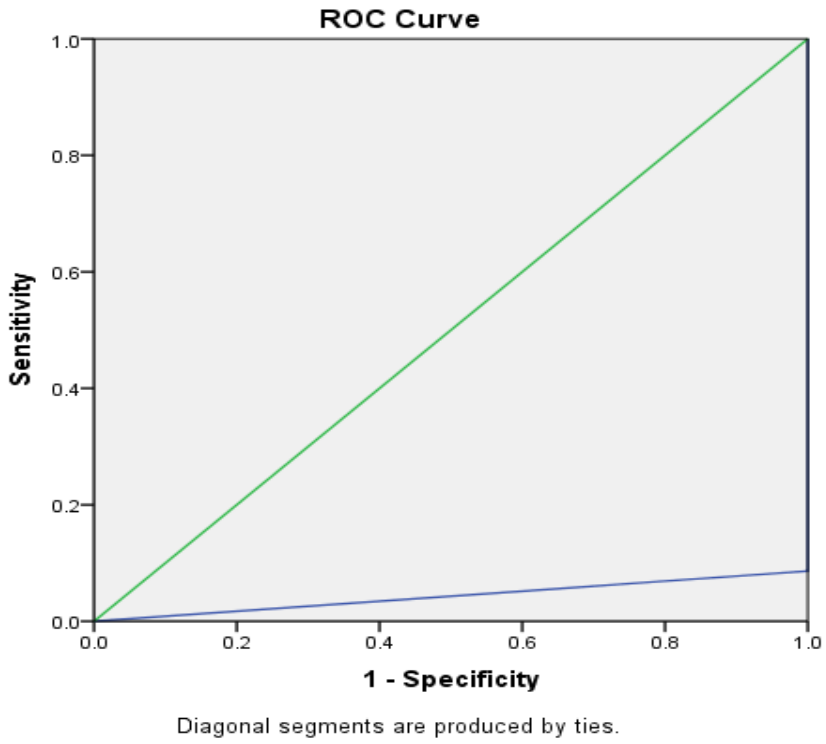

Figure 3: ROC Curve to Predict the Cut Off Value for the TIRADS Classification with Histopathological Findings

Among 67 fine needle aspiration cases categorized under Bethesda classification, the overall majority belonged to category II with 44 cases (65.7%). The distribution of the cases is as shown in Figure 4.

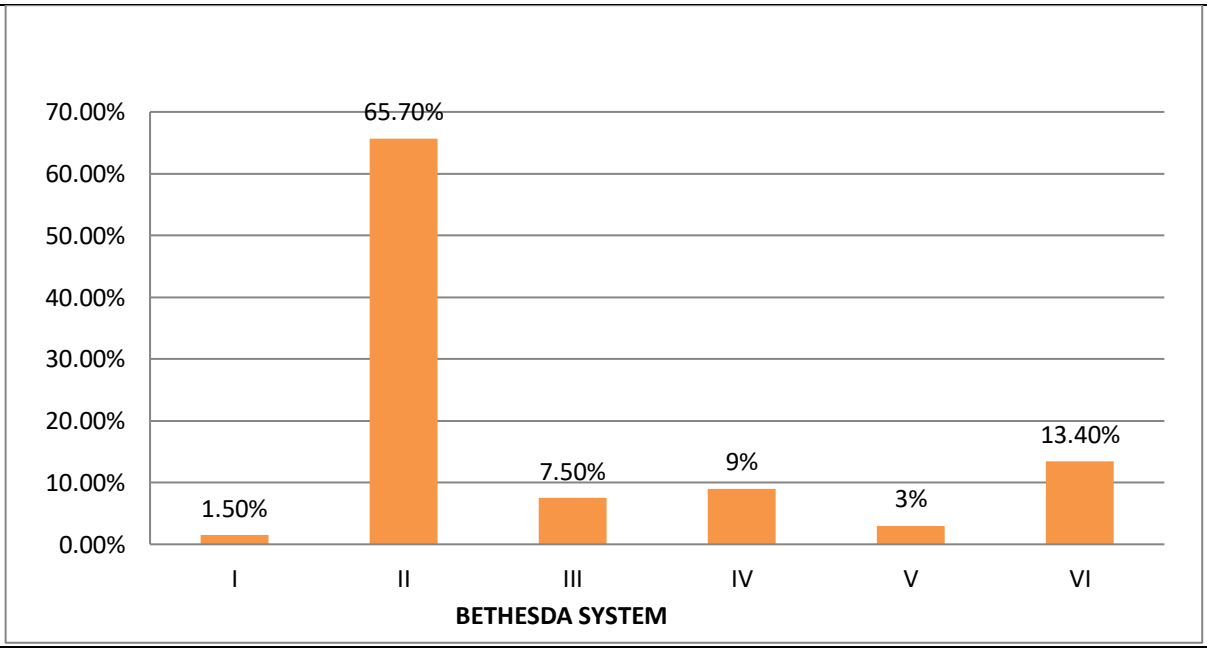

Figure 4: Distribution of Cases According to TBSRTC Categorisation

Accuracy of Bethesda system classification in differentiating benign and malignant thyroid lesions is as shown in the table below.

			Histopathological Diagnosis		Total
			Benign	Malignant	
TBSRTC	Benign	Count	54	2	56
		% within TBSRTC	96.4%	3.6%	100.0%
		% within HPE	94.7%	20.0%	83.6%
	Malignant	Count	3	8	11
		% within TBSRTC	27.3%	72.7%	100.0%
		% within HPE	5.3%	80.0%	16.4%
Total		Count	57	10	67
		% within TBSRTC	85.1%	14.9%	100.0%
		% within HPE	100.0%	100.0%	100.0%

Table 4: Accuracy of Bethesda System Classification in Differentiating Benign and Malignant Thyroid Lesions

The sensitivity and specificity of TBSRTC in differentiating benign and malignant lesions were 94.7% and 80.0%, respectively. The positive predictive value was 96.4% and the negative predictive value was 72.7%.

AUC between Bethesda classification and histopathological findings was 0.081. The lower bound was 0.000 and the upper bound was 0.206, both of which were statistically highly significant.

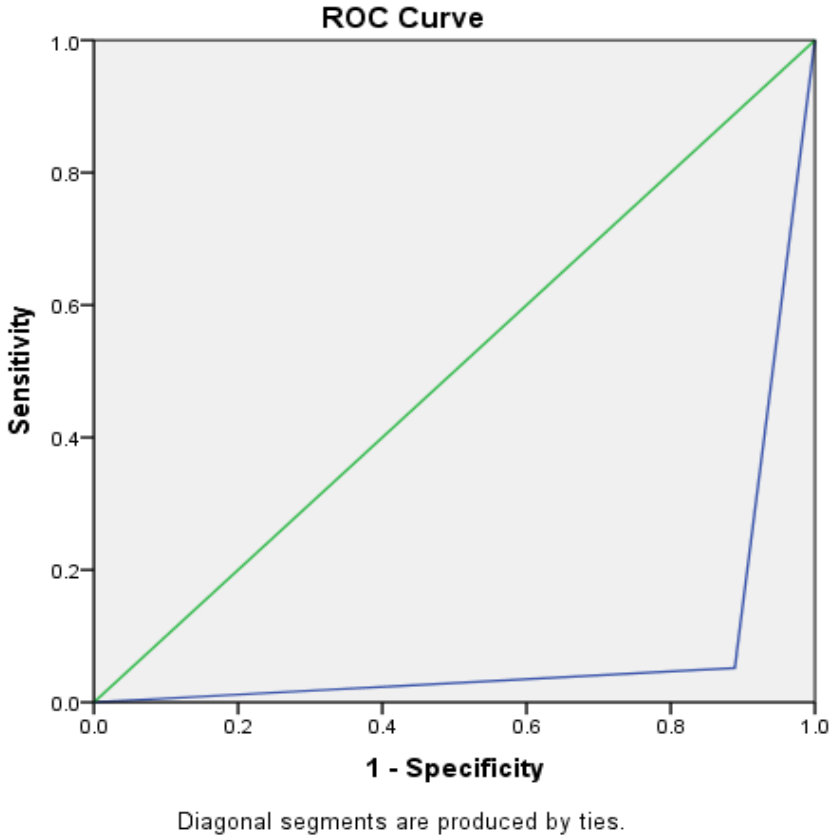

Figure 5: ROC Curve to Predict the Cut Off Value for the Bethesda System Classification with Histopathological Findings

The mean and standard deviation of radiological evaluation by using TIRADS was 2.672 ± 1.078, and FNAC by Bethesda classification was 2.866 ± 1.465. This shows a positive correlation. The Pearson correlation r-value was 0.726, and the p-value was p = 0.001, both of which were highly significant.

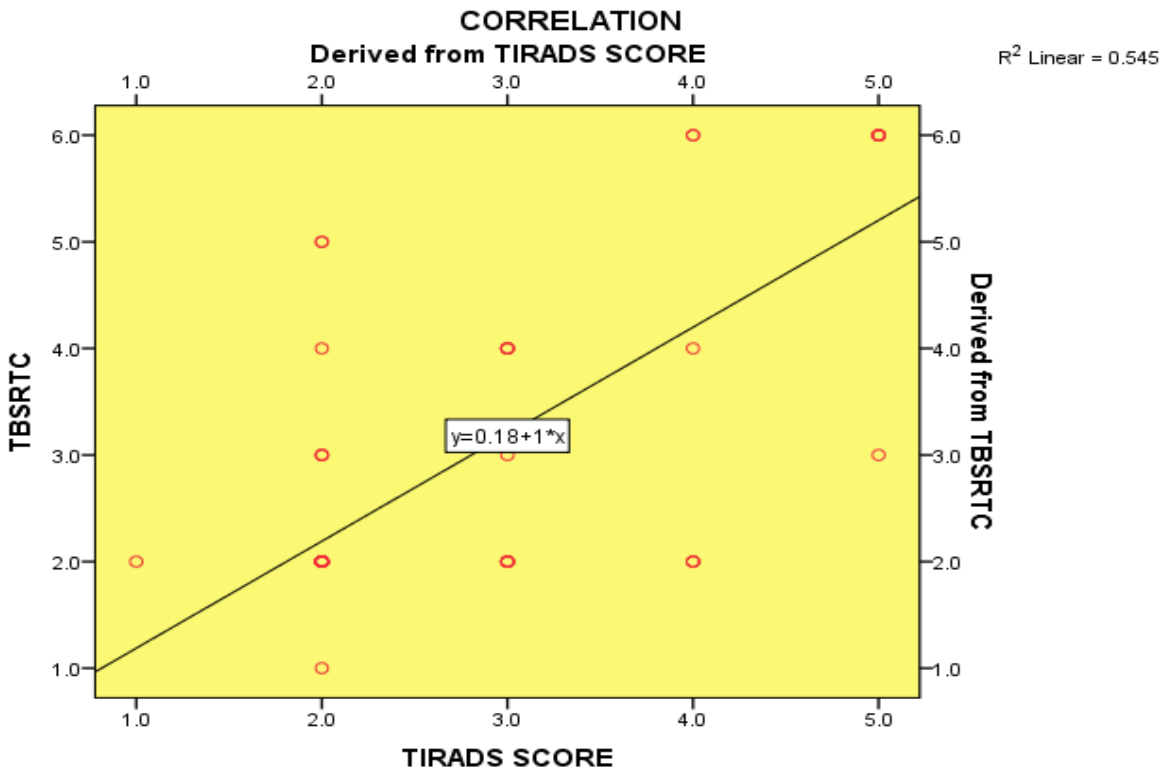

Figure 6: Correlation between the Radiological Gradings of Thyroid Lesions with FNAC Gradings Using Bethesda Classification

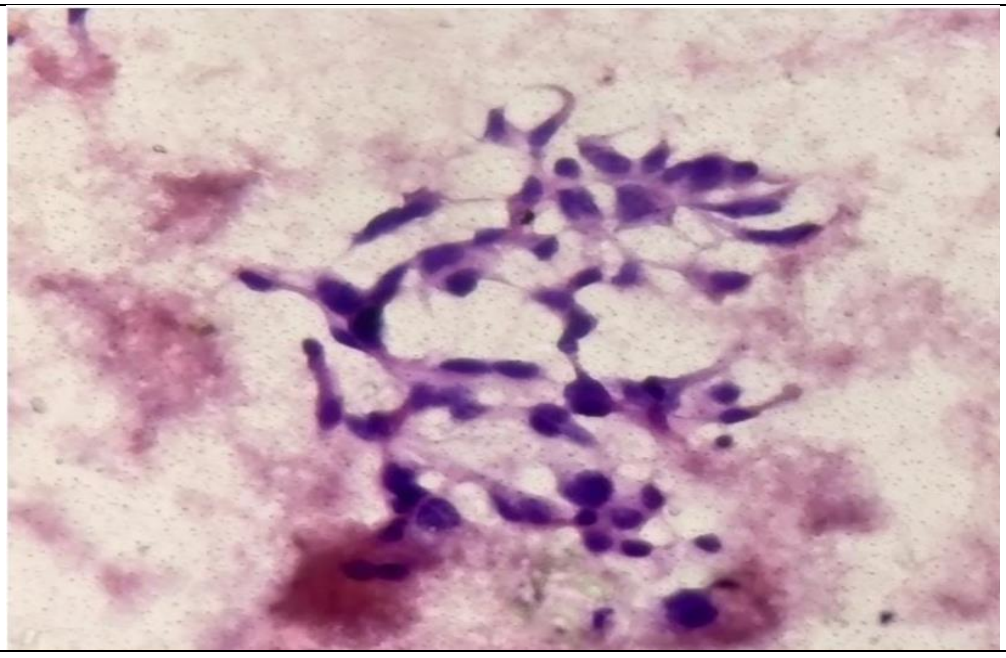

Figure 1 showing Spindle shaped malignant cells of Medullary carcinoma-TBSTC VI (40x view, H&E)

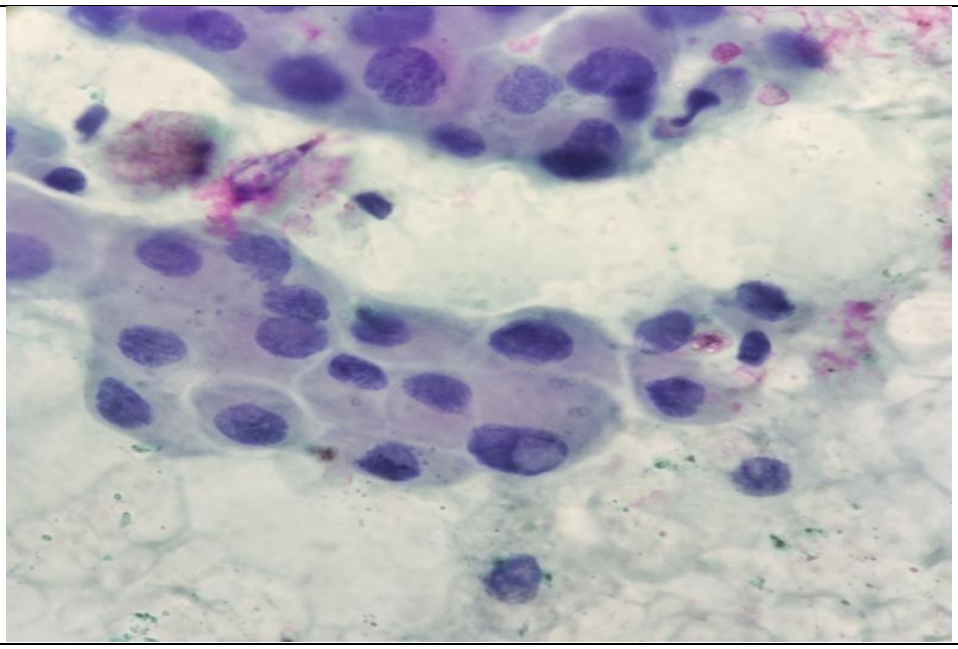

Figure 2: Papillary carcinoma- Intra nuclear cytoplasmic inclusions-TBSRTC VI (40X view, PAP stain)

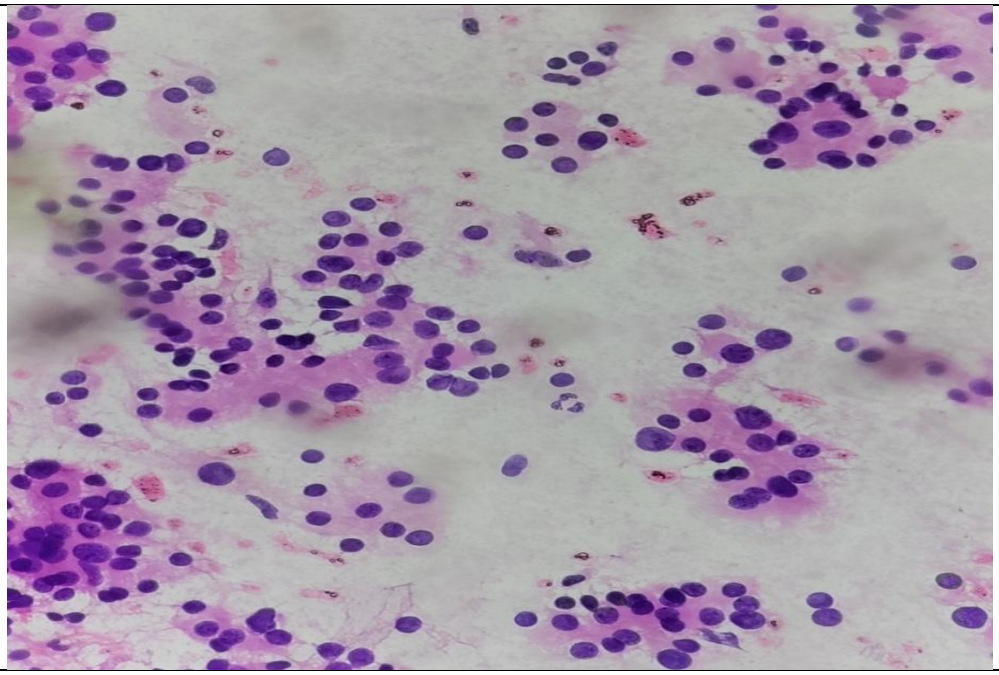

Figure 3 showing follicular cells arranged in repetitive follicular pattern – TBSRTC IV (10X view, H&E)

DISCUSSION

Both FNAC and ultrasound are essential for conclusively diagnosing thyroid nodules prior to surgery. The ATA's recommendations now include the Bethesda system of thyroid cytology;[2] however, they do not yet include the TIRADS classification for ultrasound reporting of thyroid nodules. TIRADS classification is not frequently applied in clinical practice, in contrast to BIRADS classification for breast masses. Nonetheless, the American College of Radiologists has approved US TIRADS, which facilitates thyroid nodule clinico-radiological correlation.

The present study comprised a total of 67 cases that were graded radiologically by TIRADS classification and cytologically by the Bethesda Classification. The diagnosis was further confirmed using histopathological examination of the resected thyroidectomy specimens.

The mean age of presentation in the present study is 42.58 years. The distribution of thyroid lesions in our study shows the majority of cases in the age group of 30-44 years. This was similar to a study done by byPeriakaruppan et al.,[4] in which, out of the total 184 cases studied, the majority of the patients with thyroid lesions were in the age group of 30-50 years. The male-to-female ratio was 8.9:1.1, showing a female preponderance. The worldwide statistics also show that females are more vulnerable to thyroid lesions than males.

The benign lesions outnumbered malignant lesions in our study, with percentages of 85.1% and 14.9%, respectively. The benign: malignancy ratio was 5.7:1. A study conducted by Pepper et al. showed a similar result in a sample size of 102 cases. The percentage of benign cases was 82%, and malignant cases was 18%. The benign: malignancy ratio in the study was 4.8:1.[5]

The incidence of cases according to TIRADS and Bethesda categorisation in the present study and those in similar studies are as shown in the table below.

Sl.No.	Name of the Study	TIRADS 1	TIRADS 2	TIRADS 3	TIRADS 4	TIRADS 5	Name of study	TBSRTC I	TBSRTC II	TBSRTC III	TBSRTC IV	TBSRTC V	TBSRTC VI
1	GokulakrishnanPeriyakaruppan et al [4]	0	117	45	13	9	Mondol et al	1.2%	87.5%	1%	4.2%	1.4%	4.7%
2	Simmi Bhatnagar et al [6]	0	10	29	19	4	JiHye Park et al	13.3%	40.6%	9.1 %	0.4%	19.3 %	17.3 %
3	Singaporewalla[7]	0	53	21	6	20	Bhagat et al	5.6%	87.5%	15%	3.1%	0.6%	3.1%
4	Present study	1	42	10	6	8	Present study	1.5%	65.7%	7.5 %	9%	3%	13.4 %

Table 5: Comparative Studies Showing Distribution of Cases

The sensitivity and specificity of the Bethesda Classification in differentiating benign and malignant neoplasms in our study were 94.7% and 80%, respectively. This could be correlated with a study done by Handa et al., which showed a sensitivity of 97% and a specificity of 100%.[8] The sensitivity and specificity of TIRADS classification in differentiating benign and malignant neoplasms were 91.2% and 90%, respectively. This was higher in comparison to a study conducted by Singaporewalla,[7] which showed a sensitivity and specificity of 70.6% and 90.4%, respectively. 90 of the 105 patients with TIRADS 5 lesions in the George NA et al.[9] study had an FNAC report of malignancy, with a greater diagnostic accuracy of 85.7%. According to Krzysztof et al.[10] 95.8% of patients with a thyroid nodule had their thyroid cancer predicted by FNAC. However, in our investigation, the Bethesda system of FNAC had a malignancy prediction accuracy of about 80%, which was greater than the US TIRADS's 72%. This indicates that the FNAC is a more trustworthy test for predicting thyroid nodule malignancy. While 97.14% of TIRADS 5 nodules were malignant in our investigation, Horvath et al.[11] reported that thyroid cancer was present in 98.85% of these nodules. According to Periakaruppan et al.[4] there was a 77.8% chance of cancer among TIRADS 5 thyroid nodules.

Two studies have validated the use of TIRADS scoring for thyroid nodule classification in the Indian population. In their study, Chandramohan et al.[12] discovered that the PPV for malignancy for TIRADS 4 and TIRADS 5 nodules was 36%–64% and 91%, respectively. The likelihood of malignancy for TIRADS 4 and TIRADS 5 nodules was estimated by Srinivas et al.[13] to be 83.3% and 100%, respectively. The malignancy rates of TIRADS 4 and TIRADS 5 nodules were 57.9% and

100%, respectively, in a different French investigation conducted by Moifo et al.[14] Barbosa et al.[15] had determined that thyroid nodules classified as TIRADS 4 and 5 had a greater chance of being malignant in the final histology. Our findings were similar to those of the aforementioned research.
On comparing the results of TIRADS classification and histopathological diagnosis, the p-value was 0.001, which is highly significant, denoting a highly positive correlation. The same p-value was achieved on comparing TBSRTC and histopathological diagnosis. On comparing the Bethesda Classification and TIRADS grading, the p-value was 0.001 and the Pearson correlation r-value was 0.726. This signified a highly positive correlation. The concordance rates of US TIRADS and FNAC with final histology in predicting malignancy were 75.4% and 95%, respectively, in the Mendes et al. publication.[3]
Efficacies of TIRADS and TBSRTC in distinguishing benign and malignant lesions with final HPE diagnosis were similar to a study conducted by Abdelkadhar et al.,[16] in a study of 100 patients. In both the studies, lesions with Bethesda category VI and TIRADS 5 were likely to be malignant. The overall concordance rate of US TIRADS and FNAC with post-operative HP was 75.4% and 81.8%, respectively, according to Abdelkader et al.[16] however, it was 75% and 83.3% in our study. In their investigation, Vargas-Uricoechea et al.[17] found a good concordance between the Bethesda and US TIRADS systems, with 32 out of 35 TIRADS-5 nodules (91.4%) being Bethesda V and VI. This indicates that TIRADS 5 nodules have a greater malignancy rate. Of the 105 TIRADS 5 thyroid nodules in our investigation, 90 (85.7%) were classified as Bethesda V or VI. In their investigation of ambiguous thyroid nodules classified as Bethesda III and V, Chaigneau et al.[18] found that the final histology showed malignancy rates of 23% and 74%, respectively. The malignancy rates for Bethesda III and V in our study were 33.3% and 100%, respectively.

CONCLUSION

FNAC is a simple, effective, and accurate procedure in diagnosing thyroid lesions. The categorisation of neoplasms under TBSRTC provides a better option for understanding the prognostic potential. In our study, the sensitivity and specificity of TBSRTC were 94.7% and 80%, respectively. This highlights a higher degree of concordance with the final histopathological diagnosis. Similarly, the standard categorisation by means of TIRADS classification using ultrasonography ensures a better approach to management. In our study, the sensitivity and specificity of TIRADS were 91.2% and 90%, respectively. This also shows a good correlation with histopathology. There was a highly positive correlation between the TIRADS and TBSRTC, emphasizing the superiority of the combined approach of TIRADS and TBSRTC in providing a better means of risk stratification rather than using them alone, separately, thus ultimately resulting in the avoidance of unnecessary surgical procedures for patients who do not require them.

REFERENCES

[1] Bray F, Ferlay J, Soerjomataram I. Global cancer statistics: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
[2] Haugen BR, Alexander EK, Bible KC, et al. American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26(1):12-6.
[3] Mendes GF, Garcia MRT, Falsarella PM, et al. Fine needle aspiration biopsy of thyroid nodule smaller than 1.0 cm: accuracy of TIRADS classification system in more than 1000 nodules. Br J Radiol 2018;91:1083.
[4] Periakaruppan G, Seshadri K, Vignesh Krishna G, et al. Correlation between ultrasound-based TIRADS and Bethesda system for reporting thyroid-cytopathology: 2-year experience at a tertiary care center in India. Indian J Endocr Metab 2018;22(5):651.
[5] Pepper GM, Zwickler D. Roseny. Fine needle aspiration biopsy of the thyroid nodule results of a start up project in a general teaching hospital setting Ach Intern Med 1989;149(3):594-6.

[6] Bhatnagar S, Mohi J, Kaur N, et al. Correlation of tirads [Thyroid Imaging Reporting And Data System] and histopathological findings in evaluation of thyroid nodules. IJAR 2017;5(2):159603.
[7] Singaporewalla RM, Hwee J, Lang TU, et al. Clinico-pathological Correlation of Thyroid Nodule Ultrasound and Cytology Using the TIRADS and Bethesda Classifications. World J Surg 2017;41(7):1807–11.
[8] Handa U, Garg S, Mohan H, et al. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: a study on 434 patients. Journal of Cytology 2008;25(1):13.
[9] George NA, Suresh S, Jiji V, et al. Correlation of TIRADS and Bethesda Scoring Systems with final histopathology of thyroid nodules - an institutional experience. Indian J Otolaryngol Head Neck Surg 2022;74(Suppl 3):5753-8.
[10] Krzysztof K, Dorota D, Beata W, et al. Fine-needle aspiration biopsy as a preoperative procedure in patients with malignancy in solitary and multiple thyroid nodules. PLoS One. 2016;11(1):e0146883.
[11] Horvath E, Silva CF, Majlis S, et al. Prospective validation of the ultrasound based TIRADS (thyroid imaging reporting and data system) classification: results in surgically resected thyroid nodules. Eur Radiol 2017;7:2619.
[12] Chandramohan A, Khurana A, Pushpa BT, et al. Is TIRADS a practical and accurate system for use in daily clinical practice? Indian J Radiol Imaging 2016;26:145-52.
[13] Srinivas MN, Amogh VN, Gautam MS, et al. A prospective study to evaluate the reliability of thyroid imaging reporting and data system in differentiation between benign and malignant thyroid lesions. J Clin Imaging Sci 2016;6:5.
[14] Moifo B, Takoeta EO, Tambe J, et al. Reliability of thyroid imaging reporting and data system (TIRADS) classification in differentiating benign from malignant thyroid nodules. Open J Radiol 2013;3:103.
[15] Barbosa TLM, Junior COM, Graf H, et al. ACR TI-RADS and ATA US scores are helpful for the management of thyroid nodules with indeterminate cytology. BMC Endocr Disord 2019;19:112.
[16] Abdelkader AM, Zidan AM, Younis MT, et al. Preoperative evaluation of thyroid nodules: a prospective study comparing the accuracy of ultrasound (TI-RADS) versus the FNAC Bethesda system in relation to the final postoperative histo-pathological diagnosis. Ann Pathol Lab Med 2018;5(10):A801-9.
[17] Vargas-Uricoechea H, Meza-Cabrera I, Herrera-Chaparro J. Concordance between the TIRADS ultrasound criteria and the BETHESDA cytology criteria on the nontoxic thyroid nodule. Thyroid Res 2017;10:1.
[18] Chaigneau E, Russ G, Royer B, et al. TIRADS score is of limited clinical value for risk stratification of indeterminate cytological results. Eur J Endocrinol 2018;179(1):13-20.