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Comparison Between Combined Scoring of Bethesda Cytology and TIRADS Ultrasound with Post- operative Histopathology in Thyroid Nodule

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Abstract

Introduction: A thyroid nodule is a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma. Thyroid ultrasonography is useful for risk stratification of nodules, and American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) classification provides recommendations for fine-needle aspiration cytology (FNAC) based on objective ultrasonography features of these nodule.

Methods: It is a prospective observational study conducted among 42 patients with the aim of comparing Bethesda cytology scoring and TIRADS ultrasound with post-operative histopathology in thyroid nodule.

Results: Histopathology reports following surgery showed more than half of the nodules as benign nodules. The sensitivity, specificity, positive predictive value, and negative predictive value with Bethesda scoring for malignancy was 76.19%, 71.42%, 72.72% and 75% respectively while it was 65%, 68.18%, 65%, 68.18% respectively for TIRADS. Spearman correlation coefficient between TIRADS and Bethesda was ρ = 0.532 (P < 0.01) and between preoperative Bethesda and postoperative HPE was ρ = 0.547 (P < 0.01). Correlation between preoperative TIRADS and post-operative HPE was found to be ρ = 0.387 (P < 0.05). The sensitivity of the combined test Bethesda and TIRADs is calculated to be 91.67%.

Conclusions: There is parallel testing model reflecting enhanced detection of malignant cases when either tests (Bethesda or TIRADS) indicate a positive result. It suggests combining both investigation Bethesda and TIRADS would certainly aid in improvement in management of thyroid nodules as combining both increase the sensitivity of nodules.

INTRODUCTION

According to American Thyroid Association, "A thyroid nodule is a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma." Most thyroid nodules are benign with only 10% to 15% harboring potential to be malignant.[1] American Thyroid Association recommends that thyroid sonography with survey of the cervical lymph nodes should be performed in all patients with known or suspected thyroid nodules.[1] Thyroid ultrasonography is useful for risk stratification of nodules, and American College of Radiology Thyroid Imaging Reporting and Data System

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(ACR TI-RADS) classification provides recommendations for fine-needle aspiration cytology (FNAC).[2] To maintain uniformity in reporting system FNAC sample are categorized according to the Bethesda system.[3] Unfortunately, 15% - 30% of biopsied nodules exhibit indeterminate cytology.[4] Current guidelines recommend surgical resection for these nodules to permit adequate pathological evaluation, but only 15% - 30% of these nodules prove to be malignant, while 70% - 85% prove benign.[4]

Tan et al studied the value of ACR TI-RADS classification and Bethesda classification for the qualitative diagnosis of benign and malignant thyroid nodules and found improvement in the accuracy of malignant thyroid nodules diagnosis.[5] Lee et al performed similar study and concluded that the combination of the categorical reporting systems between cytology and USG results could be useful to suggest indications of repeat US-guided FNAC.[6]

In country like Nepal there is need of diagnostic system which can help clinician in the management of thyroid patient. At present patient is treated based on Bethesda system. Incorporating the TIRADS scoring system in the same classification as of Bethesda system, can aid clinicians with different options for management of the thyroid nodule based on the USG findings. As Bethesda system and TIRADS both stratify risk of malignancy in thyroid nodule individually so the combined scoring of Bethesda and TIRADS help to increase the diagnostic accuracy. The main aim of the study was to evaluate the usefulness of combined scoring of TIRAD and Bethesda to stratify malignancy risk and compare it with the pathological finding.

METHODS

It is a prospective observational study conducted in ENT-Head and Neck Surgery Department, Shree Birendra Hospital, Chhauni, Kathmandu, Nepal. The study period was from June 2022 to November 2022. The study was commenced after obtaining an ethical clearance from the IRC (Institutional Research Committee) of the institute, vide letter no 628. A non-probability purposive sampling technique was used for the study. All patients who presented with thyroid nodules undergoing hemithyroidectomy or total thyroidectomy were included. Patients with already known case of thyroid malignancies proven by histopathological reports were excluded from the study. Patient unable to give informed consent were also excluded from the study. All individuals who were included in the study had undergone USG Neck and reported by ACR-TIRAD system by the certified radiologist. FNAC was conducted in all the thyroid nodules samples and reported by the certified pathologist in Bethesda system. Thereafter

surgery was performed with either total thyroidectomy or hemi-thyroidectomy on the basis of Bethesda system by the ENT specialists. Specimen collected from surgery were sent to pathologist for histopathological examination. Data was entered into a Microsoft Excel sheet and IBM SPSS version 22 was used for analysis. Descriptive statistics were presented as frequencies and percentages for categorical variables. Point estimate with a 95% confidence interval was calculated, along with frequency and percentage for binary data.

RESULTS

The study population consisted of 42 participants. There were 33 (78.6%) were female patients and nine (21.4%) male patients with mean age of 44.17 + 12.66 years with minimum age of 20 years and maximum 66 years. Participants categorized under TIRADS (Percentage distribution) and Bethesda scoring (frequency distribution) are shown in Figure 1 and Figure 2 respectively. All of the study population underwent surgery of which 16 (38.1%) underwent left hemithyroidectomy, 12 (28.6%) right hemithroidectomy, 13 (31%) total thyroidectomy, and one (2.4%) total thyroidectomy with central compartment neck dissection. Various pathological findings with population distribution as per histopathological examination are illustrated in Figure 3.

Among 42 participants, 20 were considered benign among which they were categorized as Bethesda 1 (N = 1), Bethesda 2 (N = 15) and Bethesda 3 (N = 4). Remaining 22 nodules classified as Bethesda 4 - 6 were considered malignant of which 16 nodules turned out to be malignant according to HPE report while remaining six were reported to be benign. Meanwhile 15 out of 20 nodules within Bethesda 1 - 3 showed HPE report of being truly benign, and five of the nodules under Bethesda 1 - 3 turned out to be malignant. This resulted in Bethesda categorization to have 76.19%, 71.42%, 72.72%, 75% of sensitivity, specificity, positive predictive value, and negative predictive value respectively for malignancy.

Out of 42 participants, 22 were considered benign among which they were classified as TIRADS I (N = 1), TIRADS II (N = 11) and TIRADS III (N = 10). Remaining 20 nodules classified as TIRADS IV - V were considered malignant of which 13 nodules turned out to be malignant on HPE while remaining seven nodules were reported as benign. Meanwhile 15 out of 22 nodules within TIRADs I - III showed HPE report of being truly benign, and seven of the nodules turned out to be malignant on HPE reports. This resulted in TIRADS categorization to have 65%, 68.18%, 65%, 68.18% of sensitivity, specificity, positive predictive value, and negative predictive value respectively for malignancy.

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Using Spearman's correlation, our study showed a strong correlation between Bethesda and postoperative HPE ($\rho = 0.547$; $P < 0.01$). There was also a strong correlation between TIRADS and Bethesda ($\rho = 0.532$; $P < 0.01$), while moderate correlation was found between TIRADS and post-operative HPE ($\rho = 0.387$; $P < 0.05$). The sensitivity of the combined test Bethesda and TIRADs is calculated to be 91.67% in parallel testing model reflecting enhanced detection of malignant cases when either test (Bethesda or TIRADS) indicate a positive result.
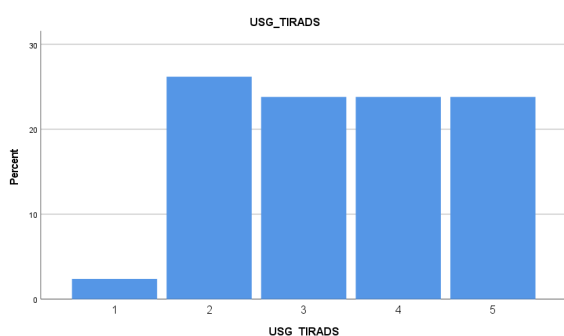

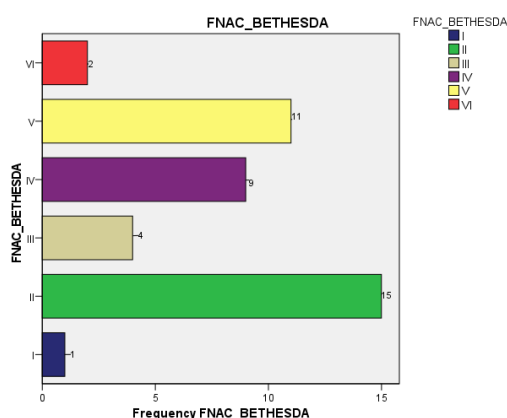**Fig 1:** Percentage of population as per TIRADS Classification.

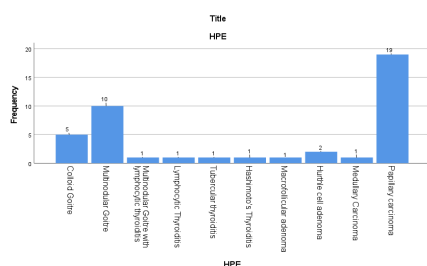**Fig 2:** Frequency of population as per Bethesda classification

Fig 3: Frequency of population as per histopathological classification.

Table 1: Relation between Bethesda and TIRADS

I		USG (TIRADS Grading)				Total
		II	III	IV	V	
FNAC (Bethesda Scoring)	1	0	0	0	1	0	1
	2	1	8	4	2	0	15
	3	0	0	2	1	1	4
	4	0	2	2	2	3	9
	5	0	1	2	2	6	11
	6	0	0	0	2	0	2
Total		1	11	10	10	10	42

DISCUSSION

Thyroid nodule is among the most common endocrinopathies of thyroid gland. Evaluation of thyroid nodules must follow a quadruple assessment. A four-pronged approach begins with history taking and clinical examination, thyroid function tests, Ultrasonography, and cytology.[7] In our study of mean age of participants is 44.17 ± 12.66 years with female preponderance of 78.6% which is comparable with the study performed in 98 study population by Chaudhary AK et al where the mean age was 44.8 ± 16.74 years and 84.7% of the population were females.[8]

Although the prevalence of thyroid nodules is more in females, risk of malignancy is higher in male population. About two-third (66.67%) of the male population with thyroid nodules were proven to have malignancy while only 39.39% of female was diagnosed as malignant. So, we can conclude that although prevalence of the thyroid nodules is higher in females, preponderance for malignancy is higher in males.

In the present study, all of the study population underwent surgery of which 16 (38.1%) underwent left hemithyroidectomy, 12 (28.6%) right hemithroidectomy, 13 (31%) total thyroidectomy, and one (2.4%) total thyroidectomy with central compartment neck dissection. More than half (52.4%) of population were diagnosed with benign nodules among which most common is multinodular goiter. The majority of patients with malignancy were diagnosed with papillary thyroid carcinoma which is similar with findings of the study performed by Ghazi FN et al.[7]

In our study, malignancy rate of Bethesda III, IV, V and VI are 25%, 44.4%, 90.9%, and 100% respectively which is comparable with the study conducted by George et al where risk of malignancy is 33.3% and 100% in Bethesda III and V respectively.[9] Sensitivity and NPV of Bethesda system in our study was comparable to the one in the

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study by Kessler et al,[10] while specificity and PPV were less as compared with Hawkins F et al and Afroz et al as mentioned in Table 2.[11,12] Our study showed lower specificity and PPV as compared with other studies. Potential reasons for this disparity could have been single centric study with relatively small sample size.

Table 2: TIRADS Correlation with final histopathological report

Authors	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV)	Negative predictive value (NPV)
Hawkins F et al	86.30	95.30	85.40	92.30
Kessler et al	79.00	98.50	98.70	76.60
Afroz et al	61.90	99.30	92.80	94.70
Present study	76.19	71.42	70.72	75.00

Risk of malignancy in TIRADS I, II, III, IV, V was found to be 0%, 27.27%, 20%, 60%, and 70% respectively. All the compared article by Moifo et. Al, Horvath et, al and Kwak et.al have same proportion of malignancy in TIRADS I (0%).[13-15] Whereas TIRADS IV and V have similar risk of malignancy as that of Kwak et al.[15]

Table 3: TIRADS correlation with final histopathological report

Authors	Kwak et al	Moifo et al	Horvath et al	Present study
TIRADS I	0%	0%	0%	0%
TIRADS II	0%	0%	0%	27.27%
TIRADS III	1.7%	2.2%	14.1%	20%
TIRADS IV	3.3% – 72.4%	5.9% – 57.9%	45%	60%
TIRADS V	87.5%	100%	89.6%	70%

In our study we found a strong correlation between TIRADS and Bethesda (r = 0.532; P < 0.01) which is similar to the study conducted by Ghazi et al (r = 0.464; P < 0.001).[7]

The present study does have to acknowledge some limitations. Because of small sample size and single centered study design, the result of our study cannot be generalized with complete assurance at the population level of our country. There could a potential bias due to involvement of multiple pathologists and radiologists in the study. We have not followed up with the long term outcome of the study population. However, we expect that the present study would encourage further, larger, multi centric studies on this topic in the future.

CONCLUSIONS

The sensitivity of the combined test Bethesda and TIRADs is calculated to be 91.67% in parallel testing model which predicts the higher rate of detection of malignant cases when either test (Bethesda or TIRADS) indicate a positive result. It suggests combining both investigations of Bethesda and TIRADS would certainly increase the diagnostic accuracy and thus help in improvement in management of thyroid nodules.

REFERENCES

1. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 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;26:1–133 DOI: 10.1089/thy.2015.0020 PMID: 26462967 PMCID: PMC4739132

2. Huang EYF, Kao NH, Lin SY, Jang IJH, Kiong KL, See A, et al. Concordance of the ACR TI-RADS Classification with Bethesda Scoring and Histopathology Risk Stratification of Thyroid Nodules. JAMA Netw Open. 2023;6:E2331612 DOI: 10.1001/jamanetworkopen.2023.31612 PMID: 37703017 PMCID: PMC10500370

3. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2009;132:658–65 DOI: 10.1309/AJCPPHLWMI3JV4LA PMID: 19846805

4. Duick DS, Klopper JP, Diggans JC, Friedman L, Kennedy GC, Lanman RB, et al. The impact of benign gene expression classifier test results on the endocrinologist-patient decision to operate on patients with thyroid nodules with indeterminate fine-needle aspiration cytopathology. Thyroid. 2012;22:996–1001 DOI: 10.1089/thy.2012.0180 PMID: 22873825 PMCID: PMC3464064

5. Tan H, Li Z, Li N, Qian J, Fan F, Zhong H, et al. Thyroid imaging reporting and data system combined with Bethesda classification in qualitative thyroid nodule diagnosis. Med (United States). 2019;98(50) DOI: 10.1097/MD.0000000000018320 PMID: 31852120 PMCID: PMC6984751

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6. Lee SW, Lee HJ, Kim HJ, Lee J, Park JY, Kim SH, et al. Combined categorical reporting systems of US and cytology findings for thyroid nodules: Guidance on repeat fine-needle aspiration cytology. Radiology [Internet]. 2013 Mar 1;266:956-63
    DOI: 10.1148/radiol.12112710
    PMID: 23220892

7. Ghazi FN, Wan Zainira Wan Zain, Yahya MM, Haron J, Wan Abdul Rahman WF, Zakaria Z, et al. Correlation between the Thyroid Image and Reporting Data System (TIRADS) and the Bethesda System for Reporting the Thyroid Cytopathology in Patients with Thyroid Nodules [preprint]. Posted 2025; version 1.
    DOI: 10.21203/rs.3.rs-2502442/v1

8. Chaudhary AK, Khadka S, Dulal S, Thapa NB. Prevalence of thyroid nodules in patients undergoing thyroid ultrasonography at a tertiary care centre. J Kathmandu Med Coll. 2022;11:137-41
    DOI: 10.3126/jkmc.v11i3.50782

9. George NA, Suresh S, Jiji V, Renu S, Thomas S, Janardhan D, et al. Correlation of TIRADS and Bethesda Scoring Systems with Final Histopathology of Thyroid Nodules - An Institutional Experience. Indian J Otolaryngol Head Neck Surg [Internet]. Springer India; 2022;74(January):5753-8
    DOI: 10.1007/s12070-021-02380-8
    PMID: 36742706 PMCID: PMC9895457

10. Kessler A, Gavriel H, Zahav S, Vaiman M, Shlamkovitch N, Segal S et al. Accuracy and consistency of fine-needle aspiration biopsy in the diagnosis and management of solitary thyroid nodules. Israel Medical Association Journal. 2005 Jun;7(6):371-373.

11. Hawkins F, Bellido D, Bernal C, Rigopoulou D, Ruiz Valdepenas MP, Lazaro E, et al. Fine needle aspiration biopsy in the diagnosis of thyroid cancer and thyroid disease. Cancer. 1987 Mar 15;59(6):1206-9.
    DOI: 10.1002/1097-0142(19870315)59:6<1206::AID-CNCR2820590629>3.0.CO;2-7
    PMID: 3815295

12. Afroze N., Kayani N., Hasan S. Role of fine needle aspiration cytology in the diagnosis of palpable thyroid lesions. Indian J Pathol Microbiol. 2002; 45: 241-6.22, PMID: 12785159

13. Horvath E, Silva CF, Majlis S, Rodriguez I, Skoknic V, Castro A Et al. Prospective validation of the ultrasound based TIRADS (Thyroid imaging reporting and data system) classification: results in surgically resected thyroid nodules. Eur Radiol. 2016;27:2619-28
    DOI: 10.1007/s00330-016-4605-y
    PMID: 27718080

14. Moifo B, Takoeta EO, Tambe J, Blanc F, Fotsin JG. Reliability of thyroid imaging reporting and data system (TIRADS) classification in differentiating benign from malignant thyroid nodules. Open J Radiol. 2013;3:10 2009;94:1748-51,
    DOI: 10.4236/ojrad.2013.33016

15. Kwak JY, Han KH, Yoon JH, Moon HJ, Son EJ, Park SH, et al. Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk. Radiology. 2011;260:892-9
    DOI: 10.1148/radiol.11110206
    PMID: 21771959