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Correlation of FNAC diagnosis with histopathological diagnosis of thyroid lesions: a five-year retrospective study

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Abstract

Introduction: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) provides a standardized reporting framework that facilitates clinical management. This study aimed to determine the correlation between fine-needle aspiration cytology (FNAC) diagnosis (as per TBSRTC) with final histopathological diagnoses in a surgical cohort.

Method: A retrospective cross-sectional analysis was conducted on 152 thyroidectomy cases with a history of prior FNAC, over five years' duration. FNAC diagnoses were categorized as per TBSRTC, and correlated with final histopathological findings. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and kappa statistics were calculated. The risk of malignancy (ROM) was calculated for each category based on its corresponding final histopathological results.

Result: The study showed a female predominance (86.18%) with a peak incidence in the fifth decade. Bethesda category II was the most common cytological diagnosis (44.08%), followed by category VI (32.24%). Histopathological evaluation revealed 57.24% malignant lesions, with papillary thyroid carcinoma being the most frequent malignancy. FNAC demonstrated a sensitivity of 78.50%, specificity of 98.00%, PPV of 98.40%, and NPV of 74.60%. The cyto-histopathological concordance was substantial, with a kappa-value of 0.724. The ROM for Bethesda-II, Bethesda-VI, Bethesda-V and Bethesda-IV were 23.88%, 97.96%, 92.86% and 35.71%, respectively.

Conclusion: FNAC is a reliable diagnostic tool for triaging thyroid lesions, demonstrating high specificity and a strong PPV, with significant cyto-histological concordance, especially for category V lesions. However, relatively higher risk of malignancy in the benign category in this specific study highlights the limitation of FNAC in isolation. Clinico-radiological correlation is essential in minimizing diagnostic discrepancies.

Keywords: Correlation, FNAC, Histopathology, Nepal, Thyroid

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Introduction

Fine needle aspiration cytology (FNAC) is a minimally invasive diagnostic modality for the evaluation of abnormal lumps/ swellings of body parts. FNAC is one of the first lines of investigation for thyroid lesions, as it is relatively affordable and differentiates benign from malignant lesions in a relatively short period of time.[1] The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), introduced in 2010, has six (I-VI) categories under TBSRTC, each with its recommended clinical management, and implied risk of malignancy.[2] Lobectomy/thyroidectomy is recommended for categories IV (Follicular neoplasm), V (Suspicious for malignancy), and VI (malignant).[2] Occasional cases of categories I (non-diagnostic) and II (benign) also undergo surgical excision when there is compelling clinical and radiological suspicion of malignancy, or if the thyroid swelling is large enough to create significant clinical symptoms.[3]

Studies demonstrate that FNAC, when reported using the Bethesda system, maintains high diagnostic accuracy, typically ranging from 75.9% to 97.5%.[4–6]

A study conducted in Nepal identified specificity of 69.56% for conventional (non USG-guided) FNAC and 66.7% for USG-guided FNAC, and accuracy of 67.5% for conventional FNAC and 82.5% for USG guided FNAC.[7]

The risk of malignancy (ROM) for each Bethesda category can differ significantly from international pooled data, and across institutes. It is, hence, vital for tertiary care centers like Patan Hospital to establish their own local ROM rates, which will serve to develop local benchmarks. This study was conducted to determine the degree of concordance between FNAC and final histopathological findings in our institute.

Method

This was a single-center, retrospective cross-sectional study using data collected over a five-year period, conducted at a tertiary care center of Nepal. All cases of thyroidectomy following FNAC evaluation, diagnosed as per The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), at a tertiary care center of Nepal, were included in the study. Neoplastic lesions in histopathology were classified according to the WHO classification of tumors of endocrine organs. Diagnostic interpretation was done by consultant pathologists. Exclusion criteria included: non-diagnostic samples, cases for whom TBSRTC was not used. Prior FNAC diagnoses and final histopathological diagnoses were evaluated for their correlation (concordance versus discordance). All data were entered in Microsoft Office Excel, and statistical analysis was carried out in EZR software. Descriptive statistics were used for numerical and categorical variables. Kappa statistics were employed to analyze the level of agreement between FNAC and histopathological diagnosis. Sensitivity, specificity, positive predictive value, and negative predictive value of FNAC were evaluated.

The study was initiated after approval from the "Institutional Review committee" (Ref: drs2509162120).

Working definition:

- Thyroidectomy: Surgical removal of all or part of the thyroid gland.
- Cytologically positive: Cases classified as Bethesda categories V (suspicious for malignancy) and VI (malignant).
- Cytologically negative: Cases classified as Bethesda category II (benign).
- Positive cases: Cases classified as Bethesda V (suspicious for malignancy) and VI (malignant) on FNAC.
- True positive: Cases classified as Bethesda V (suspicious for malignancy) and VI (malignant) on FNAC, which on histopathological evaluation confirmed to be malignant or a low-risk neoplasm, such as tumors of low malignant potential (NIFTP).
- False positive: Cases categorized as Bethesda V (suspicious) or Bethesda VI (malignant) on initial FNAC that proved benign or non-neoplastic on histopathological examination.
- Negative: Cases rendered as Bethesda II (Benign) on initial FNAC.
- True negative: Cases rendered as Bethesda II (Benign) on FNAC which subsequently confirmed to be a benign or non-neoplastic lesion by final histopathological evaluation.
- False negative: Cases rendered as Bethesda II on FNAC, which prove to be malignant on histopathological evaluation.

For the purposes of this study, Bethesda category I (non-diagnostic), III (AUS), and IV (FN) were excluded from statistical inferential analysis and were evaluated separately, because of unsatisfactory to indeterminate natures of these categories.

Result

A total of 152 cases of thyroidectomy were included in the study. The demographic distribution showed a predominance of female patients, 131(86.18%) compared to male patients, 21(13.82%), with a Female to male ratio of 6.2:1. The patients spanned various age groups, with the highest frequency of cases occurring in the 5th decade (25.66%), while patients of 8th decade and 3rd decade, 5(3.29%) and 6(3.95%) respectively represented the smallest cohorts, Table 1. The majority of cases of malignancy were identified

Table 1. Age-wise distribution of histological diagnoses of thyroidectomy (total and hemi-thyroidectomy) specimens

Age Group	Benign – Non – neoplastic, n (%)	Benign – Neoplastic, n (%)	Low-risk follicular cell-derived thyroid neoplasms, n (%)	Malignant, n (%)	Total
<20 years	-	-	-	6 (100%)	6
21-30 years	3 (11.54%)	4 (15.38%)	1 (3.85%)	18 (69.23%)	26
30-40 years	3 (11.54%)	3 (11.54%)	-	21 (77.78%)	27
41-50 years	16 (61.54%)	4 (15.38%)	1 (2.56%)	18 (46.15%)	39
51-60 years	11 (42.31%)	4 (15.38%)	1 (3.45%)	13 (44.83%)	29
61-70 years	10 (38.46%)	1 (3.85%)	-	9 (45.00%)	20
71-80 years	2 (7.69%)	1 (3.85%)	-	2 (40.00%)	5
Total (152)	45 (29.61%)	17 (11.18%)	3 (1.97%)	87 (57.24%)	152

Table 2. Comparison between various FNAC diagnoses and their subsequent histopathological results

FNAC diagnostic categories	Histopathological Diagnoses				Total n (%)	Risk of malignancy (%)
	Benign n (%)	Benign neoplasm n (%)	Low-risk follicular cell derived neoplasm n (%)	Malignant n (%)		
I	1 (33.33%)	-	-	2 (66.67%)	3 (1.97%)	66.67%
II	40 (59.70%)	10 (14.93%)	1 (1.49%)	16 (23.88%)	67 (44.08%)	23.88%
III	1 (20.00%)	-	1 (20.00%)	3 (60.00%)	5 (3.29%)	60%
IV	2 (14.29%)	7 (50.00%)	-	5 (35.71%)	14 (9.21%)	35.71%
V	1 (7.14%)	-	-	13 (92.86%)	14 (9.21%)	92.86%
VI	-	-	1 (2.04%)	48 (97.96%)	49 (32.24%)	97.96%
Total:	**45 (29.61%)**	**17 (11.18%)**	**3 (1.97%)**	**87 (57.24%)**	**152**	

Table 3. Frequency of various Histopathological diagnoses

Diagnosis	*f* (%)
Non-neoplastic	**45 (29.61%)**
Follicular nodular disease	34 (22.37%)
Hashimoto thyroiditis	9 (5.92%)
de Quervain's thyroiditis	1 (0.66%)
Calcified nodule	1 (0.66%)
Benign Neoplasm	**17 (11.18%)**
Follicular adenoma	12 (7.89%)
Oncocytic adenoma	5 (3.29%)
Low-risk follicular cell-derived thyroid neoplasms	**3 (1.97%)**
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features	3 (1.97%)
Malignant	**87 (57.24%)**
Papillary thyroid carcinoma	77 (50.66%)
Follicular carcinoma	1 (0.66%)
Medullary thyroid carcinoma	3 (1.97%)
Hurthle cell carcinoma	1 (0.66%)
Anaplastic thyroid carcinoma	2 (1.32%)
Angiosarcoma	1 (0.66%)
Encapsulated angioinvasive follicular variant of papillary thyroid carcinoma	1 (0.66%)
Lymphoma	1 (0.66%)
Total	**152**

Table 4. Comparison between FNAC diagnostic categories and their subsequent Histopathological results

FNAC diagnosis	Histopathology positive (Malignant)	Histopathology Negative (Benign)	Total
Positive (V-VI)	62	1	63
Negative (II)	17	50	67
Total	79	51	130

Table 5. Implied risk of malignancy with expected ranges, as per The Bethesda System for Reporting Thyroid Cytopathology[2]

Diagnostic ategory	Risk of malignancy Mean% (range)	Present study (%)
Non-diagnostic	13 (5-20)	66.67
Benign	4 (2-7)	23.88
Atypia of Undetermined Significance	22 (13-30)	60
Follicular Neoplasm	30 (23-34)	35.71
Suspicious for Malignancy	74 (67-83)	92.86
Malignant	97 (97-100)	97.96

in the patients at their 3rd to 5th decades of life, with a peak at the 4th decade, Table 2. The tendency of malignancy decreased beyond the 5th decade of life.

FNAC specimens were categorized according to The Bethesda System for Reporting Thyroid Cytopathology (categories I-VI). Category II (Benign) was the most frequent cytological diagnosis, accounting to 44.08% (n=67) of the total cases. Category VI (malignant) was the second most common, comprising 32.24% (n=49) of the overall cases. Categories IV, V, III, and I comprised 14(9.21%), 14(9.21%), 5(3.29%), and 3(1.97%) respectively, Table 2.

Following lobectomy/ thyroidectomy of 152 cases, histopathological examination confirmed the majority of the cases to be malignant 87(57.24%). Benign non-neoplastic lesions were identified in 45(29.61%) of patients, while benign neoplasms (including follicular adenomas, oncocytic adenomas) and follicular cell derived tumors of low malignant potential [Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)] accounted for 3(1.97%)

of cases. Malignancy was identified in 87(57.24%). Among the malignant cases, Papillary thyroid carcinoma (PTC) was the most prevalent, with various subtypes such as classic, follicular, hobnail, tall cell, and clear cell features noted. Other malignancies included Medullary thyroid carcinoma, Anaplastic thyroid carcinoma, and Hurthle cell carcinoma in this cohort, Table 3.

For evaluation of diagnostic accuracy (sensitivity, specificity, positive and negative predictive values), Bethesda categories V and VI were considered cytologically positive, and category II was considered cytologically negative. Non-diagnostic (category I), atypia of undetermined significance (category III), and follicular neoplasm (category IV) were excluded from this evaluation. Out of 130 eligible cases, FNAC yielded 62 true positives, 50 true negatives, 1 false positive, and 17 false negatives (Table 4). The FNAC showed a sensitivity of 78.48%, specificity of 98.04%, positive predictive value (PPV) of 98.41%, and negative predictive value (NPV) of 74.63%. The agreement between FNAC and histopathology was substantial, with a kappa value of 0.724. The risk of malignancy observed in each Bethesda category in this study showed some variation compared to the standard Bethesda estimates (Table 5).

Discussion

In this study, thyroid lesions showed a marked female predominance with a female-to-male ratio of 6.2:1, which is comparable to previously published studies by Mishra et al.[8], Kunwar et al.[9], and Acharya et al.[10], which also report a higher incidence of thyroid nodules and malignancies in females. The peak incidence of malignancy was observed between the third and the fifth decades of life, consistent with findings from other regional studies that demonstrate similar age distribution patterns.[9,11]

Bethesda category II (benign), 67(44.08%), was the most frequent FNAC diagnosis in this study, followed by category VI (malignant), 49(32.24%). This distribution is comparable to other studies that also used the Bethesda system, such as studies by Doley et al.[1] Mishra et al.[8] where benign lesions typically constituted the largest proportion of cases with 91.30% and 84.20%, respectively. On histopathological examination in the present study, malignant lesions accounted for 87(57.24%) of cases, with papillary thyroid carcinoma (PTC) being the most common malignancy. Predominance of malignant histopathological diagnoses can be explained may be attributed to selective excision of benign lesions, which are typically removed only when associated with pressure related clinical symptom. This predominance of PTC is consistent with global and regional literature, where PTC constitutes the majority of thyroid cancer.[3]

The calculated sensitivity (78.48%) and specificity (98.04%) of FNAC in this study fall within the ranges reported in previous studies, where sensitivity typically ranges from approximately 62.00% to 78.00%, and specificity from 90.00% to 100.00%.[1,8,10,11] Some studies have noted higher sensitivity when FNAC was done under ultrasonography guidance.[7] In the present study, such segregation was not done; both palpation and USG-guided FNAC were included. The high specificity and positive predictive value (98.41%) observed in this study indicate that FNAC is highly reliable in confirming malignancy in an adequate sample. Similar findings have been reported in other studies conducted in Nepal and elsewhere, supporting the role of FNAC as an effective screening tool for thyroid malignancies.[9,12] The kappa coefficient of 0.724 observed in this study indicates substantial agreement between FNAC and histopathological diagnoses, further reinforcing the diagnostic reliability of FNAC in triaging patients with thyroid nodules. In other studies, Bhatta S et al.[13], Gupta N et al.[14], Gupta M et al.[12] found the kappa coefficient to be 0.69, 0.786 and 0.607, respectively.

Despite its overall diagnostic accuracy, false-negative and false-positive cases were encountered. False-negative cases were primarily observed in Bethesda category II lesions that were later diagnosed as malignant on histopathology. Such discrepancies have been observed by other authors as well.[10] They may arise due to sampling error, particularly in heterogeneous nodules, primarily when there is extensive cystic degeneration.[15] Extensive cystic degeneration can result in aspiration of predominantly colloid or cyst fluid, thereby missing potentially malignant lesions that tend to be solid in nature. This limitation may be reduced by encouraging FNAC under ultrasound guidance. Follicular-patterned lesions and follicular variants of papillary thyroid carcinoma are known to present diagnostic challenges on cytology. This is because capsular and vascular invasion cannot be assessed on FNAC, and also the follicular patterns on cytology may not be prominent enough in low-grade neoplasms like NIFTP which are known to carry partial nuclear features of PTC.

There are certain overlapping cytological features such as nuclear atypia which can be seen in benign conditions, including thyroiditis or hyperplastic nodules, as well as in malignant conditions. However, false-positive cases were rare in this study, reflecting the high specificity and positive predictive value of FNAC. The low false-positive rate observed in this study is consistent with previous reports and supports the reliability of FNAC in avoiding unnecessary surgeries. On the similar lines, Choudhury S et al.[16], Mishra H et al.[8], Singh P et al.[6] also observed no false-positive cases in their studies.

The risk of malignancy observed in each Bethesda category in this study showed some variation compared to the standard Bethesda estimates (Table 5).[2] In the present study, notable discrepancies were observed for ROMs of categories I, II, and III. One out of three cytologically non-diagnostic (category I) cases was identified to be malignant on histopathology. Similarly, category II lesions also demonstrated a higher risk of malignancy (23.88%) than the implied risk as per TBSRTC and other studies. This discrepancy may be attributed to selection bias, as only cases that underwent thyroidectomy were included in the study. Category III (AUS) showed ROM of 60.00%. Surgical excision for cytologically benign, non-diagnostic and also AUS cases was typically reserved for patients showing compelling clinical and radiological findings of those with significant clinical symptoms. Low cellular yield in extensive cystic changes that can happen even in malignant lesions may be a cause of false-negative interpretations. This low cellular yield with accompanying abundant background colloid can at times direct a pathologist into considering these lesions as benign, especially when cellularity is technically just adequate (six clusters of benign follicular epithelial cells). Similar observations have been reported in other institution-based studies where only surgically excised cases were analyzed, resulting in an overestimation of malignancy risk.[10] These discrepancies stress the need of multi-disciplinary approach in the management of thyroid lesions.

Bethesda categories V and VI demonstrated high risks of malignancy in this study, demonstrating a high accuracy and positive predictive value of these categories.

Limitation of the study: Being a retrospective single-center study, it may be subject to selection bias. Additionally, only cases that underwent surgery were included, which may have resulted in an overrepresentation of malignant lesions and an overestimation of malignancy risk in certain Bethesda categories.

Conclusion

The findings of this study support the role of FNAC as a reliable diagnostic tool for thyroid lesions. While high ROM in the benign category of this specific study highlights the limitation of FNAC in isolation, the overall system provides high specificity and a strong positive predictive value. Careful evaluation of cytological features and clinico-radiological correlation is essential in minimizing diagnostic discrepancies, highlighting the role of multidisciplinary approach. Present study included only categories II, V, VI for statistical interpretation, because of inherently indeterminate nature of categories I, III and IV. Clinical management of categories I, III, IV require individualized approach with strong radiological correlation, acknowledging the fact that extensive cystic changes can yield non-diagnostic to indeterminate findings even in malignant lesions. Category IV lesions can represent variable histological outcomes, from benign hyperplastic lesions, low-grade neoplasms to even malignancies. Hence, these lesions (categories I, III, IV) may require either repeat sampling, close follow-up, or even surgical excision for definite diagnosis.

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Conflict of Interest

None

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Author Contribution

Concept, design, planning: GS, PS, AR; Literature review: GS; Data collection: GS, SKC, DG, MS, PS, AR, DY; Data analysis: GS, SKC; Draft manuscript: GS; Revision of draft: GS, SKC, DG, MS, PS, AR, DY; Final manuscript: GS, SKC, DG, MS, PS, AR, DY; Accountability of the work: GS, SKC, DG, MS, PS, AR, DY; Guarantor: GS, SKC.

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