Cytological and histopathological correlation of thyroid lesions

Madiha Syed,[1] Noreen Akhtar,[2] Maryam Hameed,[3] Sajid Mushtaq,[4] Asif Loya,[5] Usman Hassan,[6] Muddassar Hussain[7]

Abstract

Objective: To determine accuracy of cytological diagnosis in comparison with the corresponding histopathological diagnosis of thyroid lesions.

Method: The retrospective study was conducted at the Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan, and comprised data from January to December 2017 of all in-patient cases of thyroid cytology with their histopathological diagnosis. Both Haematoxylin and Eosin stain slides and cytological smears were reviewed. True negative, true positive, false negative and false positive cases were marked using the criteria defined in Table-1.

Results: Of the total 36 cases, 5(13.9%) were non-diagnostic or unsatisfactory for cytological assessment. Cytological diagnosis achieved sensitivity of 82.3%, specificity 64.3%, positive predictive value 73.6%, negative predictive value 75%, false positive rate 35.7% and false negative rate 17.6%. The diagnostic accuracy of cytological diagnosis was 63.9%.

Conclusion: There was significant cytological and histopathological concordance of thyroid lesions.

Keywords: FNAC, fine needle aspiration cytology, Bethesda system, Thyroid, Cytology, Histopathology.
(JPMA 72: 300; 2022) **DOI: https://doi.org/10.47391/JPMA.2224**

Introduction

Fine needle aspiration cytology (FNAC) is widely accepted as the most accurate and cost-effective diagnostic technique. It is indicated in all palpable thyroid nodules and non-palpable lesions found suspicious on radiology. Non-palpable thyroid nodules are aspirated with ultrasound assistance. Though ultrasound-guided FNA is relatively expensive, it helps in targeting the area of interest, especially in cystic lesions.

There are two systems used worldwide for cytological classification of thyroid lesions. One is the British Thyroid Association (BTA) or the Thy classification system, and the other is the Bethesda system for reporting thyroid cytopathology (TBSRTC) which has six categories and allows effective reporting of thyroid cytology specimen on which the management of patients with abnormal FNAs can be based Table-2.

However, like every other procedure, FNA has certain pitfalls like inadequate sampling, inappropriate sampling technique, experience of the pathologist interpreting the aspirate, and morphological overlap between certain benign and malignant lesions. The follicular neoplasms and suspicious cytology in particular pose diagnostic challenges, and accuracy is lower in such cases.[1,2] Misinterpretation can have serious consequences on patient management and can end up in lawsuits.

The current study was planned to correlate FNAC of thyroid lesions and the corresponding histopathology in order to determine diagnostic accuracy of thyroid cytology.

Materials and Methods

The retrospective study was conducted at the Shaukat Khanum Memorial Cancer Hospital (SKMCH), Lahore, Pakistan, and comprised data from January to December 2017 of all in-patient cases of thyroid cytology. After approval from the institutional ethics review board, data was retrieved from the hospital's archives. Cases included had data available for both thyroid cytology and along with their histopathological diagnosis. For histological assessment, only total or hemi-thyroidectomies were included. Also included in the study were Haematoxylin and Eosin (H&E) stain slides / blocks sent for review from outside hospitals. Core biopsies, recurrent malignancies and completion thyroidectomies were excluded.

Table-1: Definitions of false negative (FN), true positive (TP), false positive (FP) and true negative (TN).

Definitions	Bethesda Classification	Histological findings
True negative	Category 2	Hyperplastic/inflammatory
False negative	Category 2	Neoplasm(benign or malignant)
True positive	Category 5&6	Malignant neoplasm
	Category 3&4	Malignant or benign follicular neoplasm
False positive	Category5&6	Hyperplastic/inflammatory process
	Category 3&4	Benign non-neoplastic disease

[1,3-7]Department of Histopathology and Cytopathology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan, [2]Department of Histopathology and Cytopathology, Queens Medical Center, Nottingham University Hospital, United Kingdom.
Correspondence: Madiha Syed. Email: dr-madihasyed@hotmail.com

Table-2: The Bethesda system for reporting thyroid cytopathology: implied risk of malignancy and recommended clinical management.

Diagnostic Category	Risk of malignancy	Usual management
1 Non-diagnostic or unsatisfactory	1-4	Repeat FNA with utrasound guidance.
2 Benign	0-3	Clinical follow up
3 Atypia of undetermined significance or follicular lesion of undetermined significance	~5-15	Repeat FNA
4 Follicular neoplasm or suspicious for a follicular neoplasm	15-30	Surgical lobectomy
5 Suspicious for malignancy	60-75	Near total thyroidectomy or surgical lobectomy
6 Malignant	97-99	Near total throidectomy

FNA: Fine needle aspiration.

Cytological smears with inadequate material were also excluded.

The FNA was performed either by the palpation method or with ultrasound assistance. The cytological smears included both wet-fixed and air-dried smears. Air-dried smears were stained by Diff-Quick/haemacolour. For wet-fixed smears, 95% ethyl alcohol was used as fixative, while staining was done using the papanicolaou stain.

The thyroid excision specimen received in 10% formalin were sliced after 24-hour fixation. H&E slides were prepared from paraffin-embedded sections after due processing.

All cytological smears along with H&E slides were reviewed by two consultant pathologists with significant experience in the relevant field. SKMCH uses the TBSRTC.[1,2] Table-2 The results of cytological diagnosis were compared with their corresponding histopathological diagnosis, and diagnostic discrepancies were noted.

As there were no widely accepted definitions of false positive (FP), false negative (FN), true positive (TP) and true negative (TN), these were set in the light of literature[3-5] (Table-1). The data was analysed using the following compositions:

Sensitivity = TP/ TP + FN; Specificity = TN / TN + FP; Positive predictive value (PPV) = TP / TP + FN; Negative predictive value (NPV) = TN / TN + FN; False positive rate (FPR) = FP / FP + TN; False negative rate (FNR) = FN / FN + TP; and Total accuracy = TP + TN / Total number of cases.

Results

Of the total 36 cases, 7(19.4%) were males and 29(80.6%) were females. The overall mean age was 39±15 years (range: 7-71 years). Out of 36 cases, 12(33.3%) turned out to be benign on cytology, 2 (5.6%) were follicular lesion of undetermined significance, 9(25%) were interpreted as suspicious for follicular neoplasm, 2(5.6%) were suspicious for malignancy, and 6(16.7%) were malignant on cytology. The remaining 5(13.9%) cases were non-diagnostic or unsatisfactory for cytological assessment.

Table-3: Relationship between cytologic and final diagnosis.

Cytolgic diagnosis	Final diagnosis Benign	Final diagnosis Neoplastic	Total
Benign (Bethesda 2)	9(TN)	3(FN)	12
Follicular neoplasm (Bethesda 3&4)	5(FP)	6(TP)	11
Suspicious and malignant (Bethesda 5&6)	0(FP)	8(TP)	8
Total	14	17	31

FP: False positive, FN: False negative, TP: True positive, TN: True negative.

Table-4: Comparison of study results with other studies.

Study	Year	No. of cases	Sensitivity	Specificity	Accuracy
Venu Anand[14]	2017	225	99%	100%	99%
Disha J. Ramteke[15]	2017	385	92.31%	97.01%	96.25%
Shrish S Nandekar[16]	2018	606	85.7%	98.6%	97.7%
Tazeen Jeelani[17]	2018	400	92.2%	72.5%	83.5%
Md Iqbal Karim[18]	2019	160	90.2%	98.2%	97.1%
Our Study	2021	36	82.3%	64.3%	63.9%

Table-5: FNA classification by Bethesda category.

Bethesda category	Bethesda expected incidence	Our study
1 Unsatisfactory	5-11%	13.9%
2 Benign	55-74%	33.3%
3 AUS/ FLUS	5-15%	5.6%
4 Suspicious for follicular neoplasm	2-25%	25%
5 Suspicious for malignancy	1-6%	5.6%
6 Malignant	2-5%	16.7%

FNA: Fine needle aspiration, AUS: Atypia of undetermined significance, /FLUS: Follicular lesion of undetermined significance. N/A: Not applicable.

The results of cytological diagnosis were compared with their corresponding histopathological diagnosis. Of the 12(33.3%) cases diagnosed as benign, 9(75%) with Bethesda category 2 on cytology were TN and turned out to be benign on histopathology, like adenomatous nodule and nodular hyperplasia of thyroid, and 3(25%) cases were FN and were neoplastic on histopathology. Table-3. Of the FN cases, 1(33.3%) turned out to be follicular adenoma and 2(66%) FN cases were diagnosed

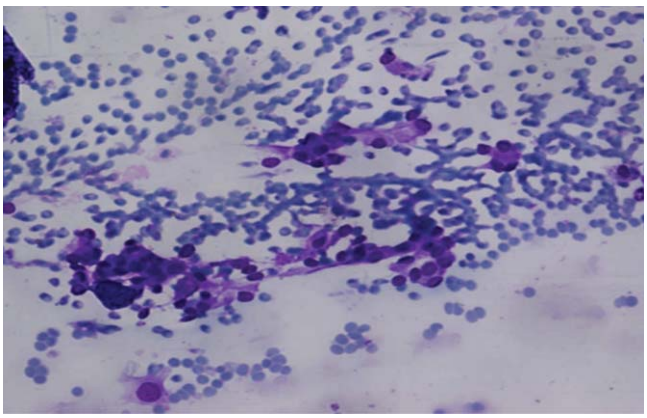

Figure-1A: Bethesda category 2 on cytology. 40x view.

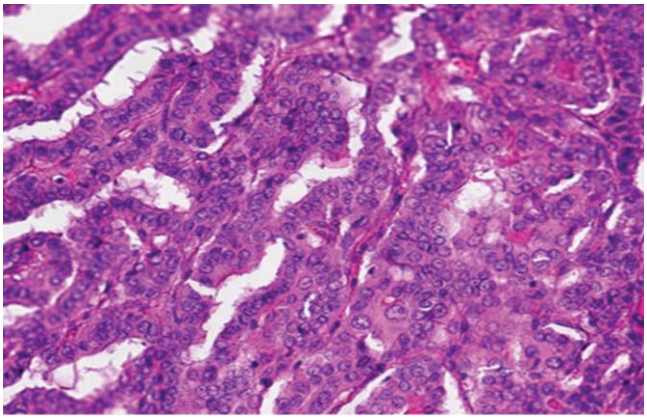

Figure-1B: Classic papillary thyroid carcinoma on histopathology. 40X view.

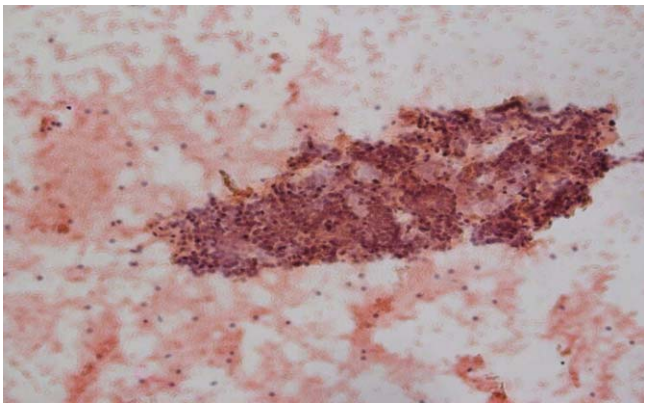

Figure-2A: Bethesda category 4 on cytology. 40X view.

as papillary thyroid carcinoma on histopathology (Figure-1A-B).

Further, 2(5.6%) cases interpreted as follicular lesion of undetermined significance Bethesda category 3 on cytology had benign diagnosis on histopathology, and were considered FP.

There were 9(25%) cases in Bethesda category 4 having

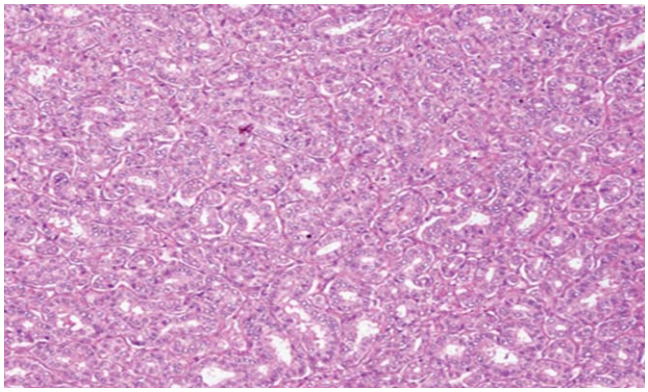

Figure-2B: Follicluar variant of papillary thyroid carcinoma on histopathology. 40X view.

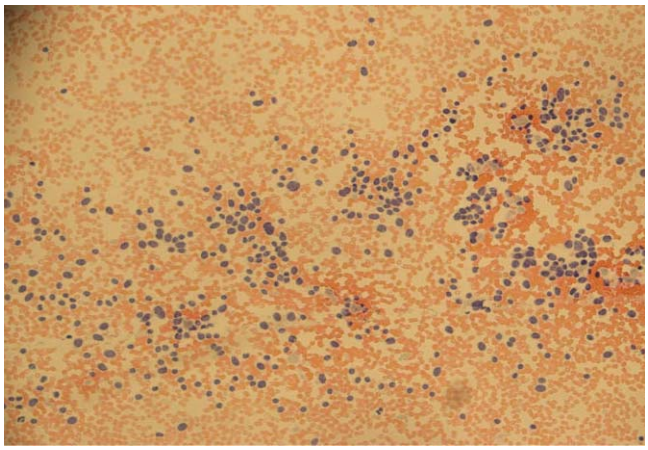

Figure-3A: Bethesda category 4 on referred slides. 40X view.

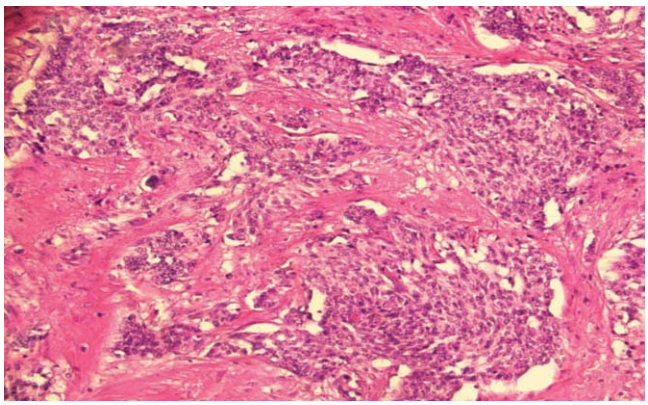

Figure-3B: Medullary thyroid carcinoma on histopathology. 40X view.

follicular neoplasm or were suspicious for follicular neoplasm. Of them, 3(33.3%) were FP and turned out to be adenomatous nodule and nodular hyperplasia on histopathology. Another 3(33.3%) cases were TP and turned to be Hurthle cell and follicular adenomas on histopathology, while the remaining 3(33.3%) cases turned out to be malignant on histopathology and were

considered TP because, from the management point of view, Bethesda category 4 is treated by surgical excision and is not managed conservatively. Table-3. Among the malignant cases, 2(66.6%) were follicular variant of papillary carcinoma (Figure-2A-B) and one was medullary carcinoma on histopathology (Figure-3A-B).

All 8(22.2%) cases in Bethesda categories 5 and 6 were TP and turned out to be malignant on histopathology.

Of the 12(33.3%) cases diagnosed as Bethesda category 2 on cytology, 9(75%) were TN and 3(25%) were FN on histopathology; 2(100%) of the 2(5.6%) cases diagnosed as Bethesda category 3 on cytology turned out to be FP on histopathology. There were 9(25%) in Bethesda category 4, and 7(77.7%) of them were TP and 2(22.2%) were FP on histopathology. All the 8(100%) of the 8(22.2%) cases in Bethesda categories 5 and 6 turned out to be malignant on histopathology.

Cytological diagnosis achieved sensitivity of 82.3%, specificity 64.3%, PPV 73.6%, NPV 75%, FPR 35.7% and FNR 17.6%. The diagnostic accuracy of cytological diagnosis was 63.9%.

Discussion

FNAC is the most reliable, accurate and cost-effective method for the evaluation of thyroid nodules and prevention of unwanted surgeries.[5-7] However, follicular neoplasms and morphological overlap between benign and malignant lesions pose diagnostic challenges for cytopathologists interpreting the aspirate.[8,9] Misinterpretation can have serious implications in terms of patient management. The current retrospective study planned to determine diagnostic accuracy of thyroid cytology and to determine the factors which led to diagnostic errors.

The study took histopathology as the gold standard and compared the cytopathology results with it. For the purpose of calculations and clarifications, it determined TN, TP, FP and FN values based on individual cases.[10-13]

The majority of cases turned out to be benign (41.9%). These included nodular hyperplasia and adenomatous nodule. The Hurthle cell and follicular adenomas constituted 16.1%. Papillary carcinoma was the commonest malignancy (32%) and medullary carcinomas was the second most common malignancy.

The results were compared with 5 studies in literature[14-18] (Table-4).

Two studies[14,15] showed sensitivity, specificity and diagnostic accuracy of 99%, 100%, 99% and 92.3%, 97.01% and 96.25% respectively. The total number of cases in one study[14] was 225 and it was 385 in the other[15] compared to our sample size of 36 cases.

Two other studies[16,17] had samples of 606 and 400 cases respectively. The sensitivity, specificity and diagnostic accuracy in these two studies turned out to be 85.7%, 98.6%, 97.7% and 92.2%, 72.5%, 83.5% respectively.

One study[18] showed 90.2% sensitivity, 98.2% specificity and 97.1% diagnostic accuracy. Compared to these studies[14-18] and Bethesda expected results Table-5, the sensitivity, specificity and diagnostic accuracy of the current study was relatively lower. The difference in results can be attributed to four main reasons. First, the smaller sample size of the current study. This was basically due to the fact that only in-house cases for which histopathological diagnosis was available were included. Second, the current study included outside review cytological smears and blocks for histopathology, leading to lower diagnostic accuracy compared to other studies. Third, cytomorphologic overlap between benign and low grade malignant lesions was a valid reason,[19-21] especially the Bethesda category 4 lesions with high subjectivity in interpretation posed real diagnostic challenge. Fourth, FN FNAC results may occur because of various factors, like sampling error, especially in FNAs performed using the palpation method and coexistence of benign and malignant lesions.

According to literature, the frank thyroid malignancy can easily be picked up on FNAC.[22-24] On the other hand, follicular pattern lesions pose a diagnostic challenge for cytopathologists and should be reported with caution.[25-32]

Conclusion

There was significant correlation between cytological and histopathological diagnosis of thyroid lesions, but the results can be improved further by following the Bethesda system more meticulously. Besides, cases with high subjectivity and difficult interpretation should be subjected to intra-departmental consultation to avoid errors.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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