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Diagnostic utility of CK-19 in Thyroid Lesions

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A B S T R A C T

Background: Differentiating benign from malignant thyroid lesions using histology alone can be difficult, particularly in follicular-patterned neoplasms. Cytokeratin 19 (CK19), a low molecular weight cytokeratin, is emerging as a useful immunohistochemical (IHC) marker in the diagnosis of papillary thyroid carcinoma (PTC).
Objective: To evaluate the utility of CK19 in differentiating benign from malignant thyroid lesions.
Materials and Methods: This prospective study was conducted from June 2015 to June 2017 at a tertiary care hospital in Nandyal. A total of 108 thyroidectomy specimens were processed and subjected to hematoxylin and eosin (H&E) staining. CK19 IHC was performed where necessary. CK19 positivity was defined as membranous with or without cytoplasmic staining in ≥10% of cells.
Results: Of 108 thyroid specimens, 85 were benign and 23 were malignant. CK19 was positive in 17/18 (94%) PTCs and 1/2 follicular variant PTCs. All cases of medullary carcinoma and most benign lesions were negative. CK19 had a sensitivity of 94.4%, specificity of 84.2%, and a statistically significant association with malignancy ($p<0.001$).
Conclusion: CK19 is a sensitive and specific marker for PTC and serves as a valuable diagnostic tool to differentiate it from benign mimickers.

Keywords: CK19, Thyroid lesions, Papillary thyroid carcinoma, Immunohistochemistry, Follicular neoplasm.

INTRODUCTION

Thyroid lesions range from non-neoplastic to malignant and are commonly encountered in pathology. Histological differentiation between benign and malignant follicular lesions is sometimes ambiguous. CK19, a cytoskeletal protein typically absent in normal thyroid tissue, is upregulated in malignancies, particularly PTC (1,2).
This study evaluates CK19 expression in benign and malignant thyroid lesions to assess its diagnostic accuracy.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology, Santhiram Medical College and Hospital, Nandyal, between June 2015 and June 2017. Ethical clearance was obtained prior to initiation.
Sample Size: 108 thyroidectomy specimens
Techniques:

- Routine H&E staining for all cases
- IHC staining for CK19 using monoclonal mouse anti-human CK19 (DAKO RCK108)
- CK19 expression was considered positive when ≥10% of cells showed membranous ± cytoplasmic staining
- Staining distribution was graded: focal (10–50%) or diffuse (>50%)

Statistical Analysis: Sensitivity, specificity, PPV, NPV, and chi-square test were used.

RESULTS

Out of 108 cases, 85 were benign and 23 malignant. Female predominance was noted (M: F = 1:13). CK19 expression was present in 89% of malignant lesions and 18% of benign lesions. (Table 1,2).

CK19 positivity was seen in 17/18 (94%) of Papillary Thyroid Carcinoma with moderate to high intensity. (50%) 1 out of 2 cases of follicular variant of papillary thyroid carcinoma showed positive expression with CK19. CK19 expression was not detected in Medullary Thyroid carcinoma. In all the malignant cases 19/19 (100%), adjacent normal thyroid tissue was negative for CK19 staining. (Table 3)

Expression of CK19 was absent in benign thyroid lesions which includes Nodular goiter, Multi nodular goiter, nodular goiter with Hashimoto's thyroiditis, follicular adenoma and Hashimoto's thyroiditis. But it was positive in Nodular goiter with papillary hyperplasia (50% cases), Nodular goiter with adenomatoid nodule (50%) and Adenomatoid nodule (40%). The present study included one case of Hurthle cell adenoma which expressed focal weak CK19 positivity.

In present study the expression of CK19 in malignant conditions are statistically significant ($p < 0.001$). The sensitivity of CK19 in discrimination of malignant from benign thyroid lesion was 94.44% and specificity was 84.21%. positive likelihood ratio 5.98 and negative likelihood ratio of 0.07. The disease prevalence rate was 32.14%. the positive predictive value 73.91%, Negative predictive value was found to be 96.97%. (Table 4).

TABLES AND FIGURES

Table 1. Age- and sex-wise distribution of benign thyroid lesions (n=85)

Lesion	10–20	20–30	30–40	40–50	50–60	>60	Total
Nodular Goiter	–	8F	3F	6F 1M	2F	–	19
Multinodular Goiter	1F	6F	4F	4F	–	–	15
Adenomatoid Nodule	1F	5F	2F	1M	3F	–	12
NG with Papillary Hyperplasia	–	7F	5F 1M	1F	–	–	13
Follicular Adenoma	–	3F	4F 1M	5F	–	–	12
Hashimoto's Thyroiditis	–	2F	5F	2F	–	1F	10
Hurthle Cell Adenoma	1F	–	1M	–	–	–	2

Table 2. Age- and sex-wise distribution of malignant thyroid lesions (n=23)

Lesion	10–20	20–30	30–40	40–50	50–60	>60	Total
Classical PTC	1F	4F	5 (2M, 3F)	3 (1M, 2F)	3F	1F	18
FVPTC	–	1F	1F	–	–	–	2
MNG with PTC	–	1F	–	–	–	–	1
Medullary Carcinoma	–	–	1F	–	–	–	1

NG: nodular goiter; MNG: multinodular goiter; NGHT: nodular goiter with hashimotos thyroiditis: NGPH: nodular goiter with papillary hyperplasia; NGAN: nodular goiter with adenomatoid nodule; AN: adenomatoid nodule. FA: follicular adenoma; HT: hashimotos tyroiditis; HA: hurthle cell adenoma; PTC: papillary thyroid carcinoma; MTC: medullary carcinoma thyroid. M: Male; F: Female.

Table 3. CK19 expression in thyroid lesions

Diagnosis	N	CK19 Positive (%)	Diffuse	Focal	Negative (%)
Nodular Goiter	8	0 (0%)	–	–	8 (100%)
Multinodular Goiter	5	0 (0%)	–	–	5 (100%)
NG + Hashimoto's	6	0 (0%)	–	–	6 (100%)
NG + Papillary Hyperplasia	6	3 (50%)	2	1	3 (50%)
NG + Adenomatoid Nodule	2	1 (50%)	1	–	1 (50%)
Adenomatoid Nodule	5	2 (40%)	–	2	3 (60%)
Follicular Adenoma	4	0 (0%)	–	–	4 (100%)
Hashimoto's Thyroiditis	2	0 (0%)	–	–	2 (100%)
Hurthle Cell Adenoma	1	1 (100%)	–	1	–
PTC	18	17 (94%)	17	–	1 (6%)
FVPTC	2	1 (50%)	–	1	1 (50%)
Medullary Carcinoma	1	0 (0%)	–	–	1 (100%)

Table 4. Diagnostic performance of CK19

Parameter	Value
Sensitivity	94.44%
Specificity	84.21%
Positive Likelihood Ratio	5.98
Negative Likelihood Ratio	0.07
Positive Predictive Value	73.91%
Negative Predictive Value	96.97%
p-value	<0.001

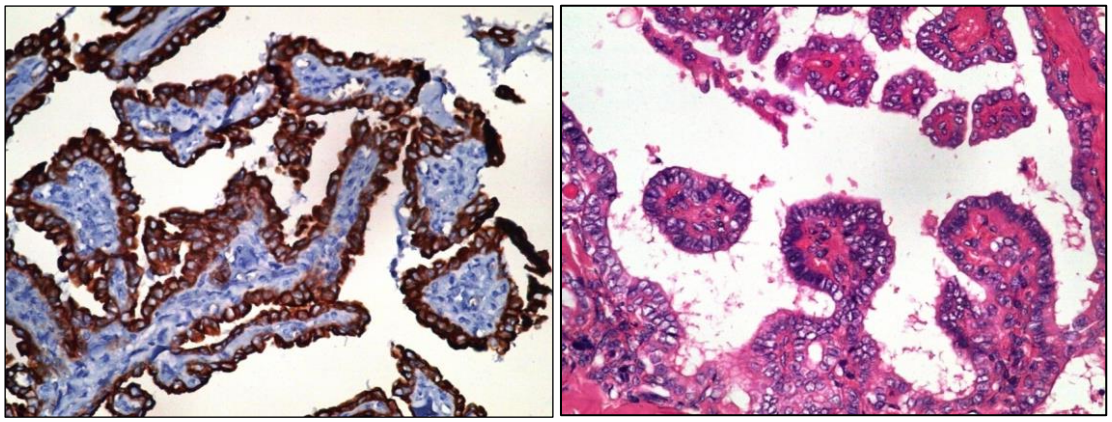

Figure 1. Papillary thyroid carcinoma: H&E section showing characteristic nuclear features; CK19 positive with strong diffuse membranous staining.

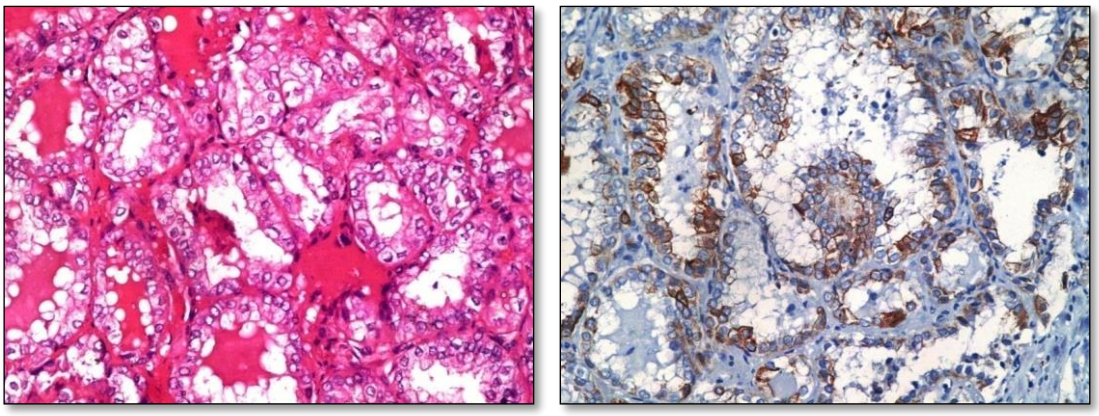

Figure 2. Follicular variant of PTC: H&E shows follicular architecture; CK19 shows focal positivity.

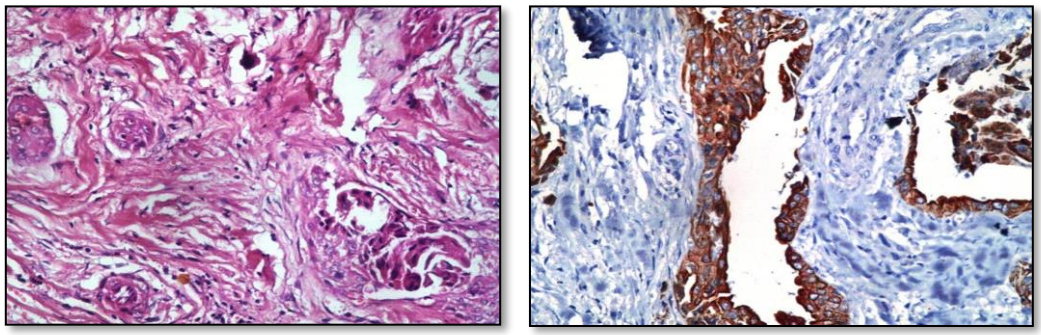

Figure 3. Sclerosing variant of PTC: H&E reveals fibrosis and psammoma bodies; CK19 diffusely positive.

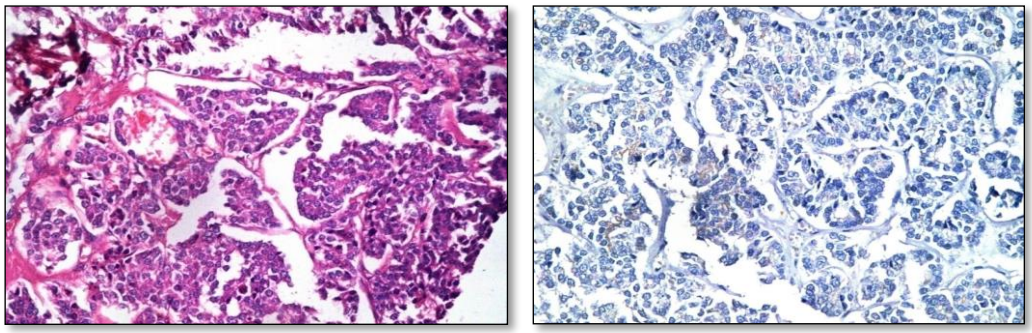

Figure 4. Medullary thyroid carcinoma: H&E shows neuroendocrine pattern; CK19 negative.

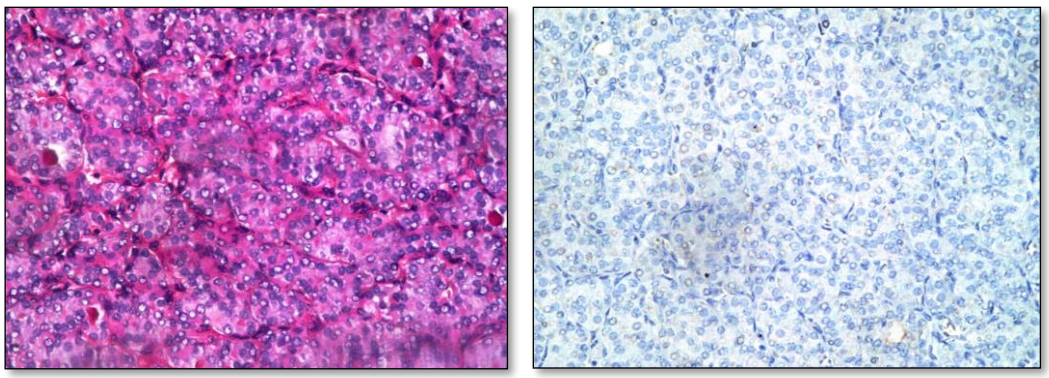

Figure 5. Follicular adenoma: H&E shows encapsulated follicular growth; CK19 negative.

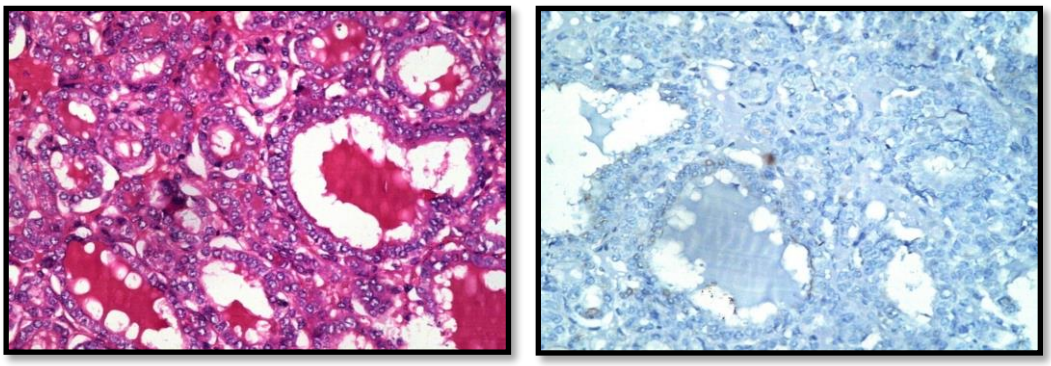

Figure 6. Nodular goiter: H&E shows hyperplastic colloid follicles; CK19 negative.

DISCUSSION

Diagnosing thyroid neoplasms, particularly those exhibiting follicular architecture, remains a significant histopathological challenge. While conventional hematoxylin and eosin (H&E) staining is the gold standard, differentiating follicular adenoma (FA) from the follicular variant of papillary thyroid carcinoma (FVPTC) is often difficult due to overlapping morphological features such as nuclear clearing, grooves, and focal papillary structures. In such scenarios, immunohistochemistry (IHC) serves as a vital ancillary tool.

Cytokeratin 19 (CK19), a low molecular weight cytokeratin, is normally absent in healthy thyroid follicular epithelium but is consistently overexpressed in papillary thyroid carcinoma (PTC). This study aimed to evaluate the diagnostic utility of CK19 in differentiating benign from malignant thyroid lesions using IHC.

In our study of 108 thyroidectomy specimens, 23 cases (21%) were malignant and 85 cases (79%) were benign. CK19 positivity was observed in 89% of malignant lesions, most notably in 94% of classical PTC cases. This is in agreement with the findings of Barroeta et al. (91%) and Park et al. (98%), who also demonstrated high sensitivity of CK19 in diagnosing PTC [4,3]. Song et al. reported 96% positivity in a much larger sample set, further supporting CK19's diagnostic robustness [6].

The focal expression of CK19 in one case (50%) of FVPTC highlights the variability in marker expression within this subtype. FVPTC often mimics benign lesions and lacks classical papillary architecture, making diagnosis especially difficult. Our observation is consistent with Dunderovic et al. who reported 78% positivity in FVPTC cases [7], though some studies like Nechifor et al. reported much lower expression levels (22%) [5]. These discrepancies suggest that CK19 should not be solely relied upon in the diagnosis of FVPTC but may be used in conjunction with other markers such as HBME-1, CD56, and Galectin-3.

All benign lesions in our study—including nodular goiter (NG), multinodular goiter (MNG), Hashimoto's thyroiditis (HT), and FA—were negative for CK19 expression. This aligns with previous studies by Barroeta et al. and Prasad et al., both of whom found no CK19 staining in FA [4,8]. Interestingly, focal CK19 positivity was observed in nodular goiter with papillary hyperplasia (NGPH), nodular goiter with adenomatoid nodules, and Hurthle cell adenoma. This could represent areas of early neoplastic transformation or nonspecific staining, warranting close histological correlation. As observed by Hameed et al., occasional benign lesions may express CK19, particularly when undergoing reactive or hyperplastic changes [1].

Medullary thyroid carcinoma (MTC), a neuroendocrine tumor arising from parafollicular C-cells, was negative for CK19 in our study, consistent with its different cellular origin. Similar findings were reported by Liu et al. and Song et al. [9,6]. The diagnostic performance of CK19 in our study was statistically significant with a sensitivity of 94.4% and specificity of 84.2% ($p < 0.001$). These metrics are comparable with those reported by other studies (e.g., Barut et al. – 92% sensitivity; Park et al. – 90%) [10,3]. The high negative predictive value (96.97%) suggests that absence of CK19 strongly favors a benign diagnosis, making it particularly useful in ruling out malignancy.

CONCLUSION

This study demonstrates that Cytokeratin 19 (CK19) is a valuable immunohistochemical marker in the diagnosis of thyroid lesions, particularly papillary thyroid carcinoma (PTC). CK19 showed high sensitivity (94.4%) and specificity (84.2%) in differentiating malignant from benign thyroid neoplasms, with statistically significant correlation. Strong and diffuse CK19 expression was consistently observed in classical PTC, while benign lesions such as nodular goiter, multinodular goiter, follicular adenoma, and Hashimoto's thyroiditis lacked CK19 expression.

Although focal CK19 positivity was seen in certain hyperplastic and adenomatoid nodules, this did not significantly impact its diagnostic reliability when used in conjunction with histopathological features. Its expression in follicular variant PTC was variable, underscoring the importance of using CK19 as part of a panel of markers rather than as a standalone test. Incorporating CK19 into diagnostic protocols can enhance diagnostic accuracy, reduce interobserver variability, and aid in appropriate clinical management of patients with thyroid nodules. Further studies involving larger, multi-center cohorts and complementary markers are recommended to refine its diagnostic role.

REFERENCES

1. Hameed S, Afroze S, Aslam H. Diagnostic Accuracy of CK19 in the Diagnosis of Papillary Thyroid Carcinoma. PJMHS. 2017;11(1):45-8.
2. Rosai J. Papillary thyroid carcinoma: a root-and-branch rethink. Am J Clin Pathol. 2008;130(5):683–6.
3. Park YJ, Kwak SH, Kim DC, Kim H, Choe G, Park DJ, et al. Diagnostic value of galectin-3, HBME-1, cytokeratin 19, high molecular weight cytokeratin, cyclin D1 and p27(kip1) in the differential diagnosis of thyroid nodules. J Korean Med Sci. 2007;22(4):621–8.
4. Barroeta JE, Baloch ZW, Lal P, Pasha TL, Zhang PJ, LiVolsi VA. Diagnostic value of differential expression of CK19, Galectin-3, HBME-1, ERK, RET, and p16 in benign and malignant follicular-derived lesions of the thyroid: an immunohistochemical tissue microarray analysis. Endocr Pathol. 2006;17(3):225–34.
5. Nechifor-Boilă A, Loghin A, Feier DS, Dema A, Borda A, Scurtu R, et al. Utility of IHC markers in differential diagnosis of thyroid nodules. Rom J Morphol Embryol. 2014;55(4):1269–74.
6. Song Q, Wang L, Wu X, Zhang C, Liu Y. Expression of CK19 in thyroid lesions. Int J Clin Exp Pathol. 2011;4(7):639–46.
7. Dunderovic D, Nikolic I, Jotic A, Stanic J, Diklic A, Tatic S. The importance of IHC markers in differential diagnosis of thyroid nodules. Acta Endocrinol (Buchar). 2015;11(1):65–72.
8. Prasad ML, Pellegata NS, Huang Y, Nagaraja HN, De Luca F, Wu CL. Galectin-3, HBME-1, and CK19 expression in thyroid neoplasms. Am J Clin Pathol. 2005;124(3):385–92.
9. Liu YY, Moroz K, Gonzalgo ML, Jackson J, Sharma N, Kowalski J, et al. Diagnostic utility of CK19 in thyroid neoplasms. Mod Pathol. 2008;21(8):1011–20.
10. Barut F, Onak Kandemir N, Baspinar S, Bahadir B, Dogan M, Ozdamar SO. Diagnostic value of cytokeratin 19, galectin-3 and HBME-1 expression in the differential diagnosis of thyroid lesions. Endocr Pathol. 2010;21(4):253–63.