

Histomorphological Spectrum of Goiter and the Diagnostic Utility of CD56 in Thyroid Lesions: A Cross-Sectional Analysis**Presil Arthy Sneha T.S.¹, Sandilyan A.², Samanth Kumar K.³, Pooja R.⁴, Sumathi S.⁵**¹Assistant Professor, Department of Pathology, Government Medical College, Ramanathapuram, India²Assistant Professor, Department of Pathology, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, India³Assistant Professor, Department of Pathology, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, India⁴Assistant Professor, Department of Pathology, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, India⁵Professor and HOD, Department of Pathology, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research

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Abstract**Background:** Thyroid lesions are among the most prevalent endocrine disorders, often presenting as goiter. Their etiology spans a spectrum from physiological hypertrophy to neoplastic processes, necessitating precise histopathological differentiation to guide therapeutic interventions.**Objectives:** This study evaluates the histomorphological characteristics of various thyroid lesions and investigates the diagnostic efficacy of CD56 immunohistochemical expression in distinguishing benign from malignant thyroid pathologies.**Materials and Methods:** A cross-sectional study was conducted in the Department of Pathology, MAPIMS, Melmaruvathur, over a two-year period. Thirty-five thyroidectomy specimens were analyzed, comprising 18 benign and 17 malignant lesions. Histopathological evaluation was performed alongside CD56 immunohistochemical staining. Statistical analysis assessed the discriminative value of CD56 in thyroid lesion classification.**Results:** A female predominance (85.7%) was observed, with the highest incidence in the 31-40-year age group. CD56 was strongly expressed in 94.4% of benign lesions, except for a single follicular adenoma (5.5%) that was negative. In contrast, all cases of classic papillary thyroid carcinoma (PTC) (100%) and 57.1% of follicular variant PTC (FVPTC) lacked CD56 expression, demonstrating statistical significance ($P=0.02$). The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of CD56 in differentiating benign from malignant lesions were 82.3%, 94.4%, 93.3%, 85.0%, and 88.6%, respectively.**Conclusion:** CD56 is a robust negative marker for PTC and provides a valuable adjunct in differentiating malignancies from benign thyroid lesions, thereby enhancing diagnostic precision and mitigating the risk of over diagnosis.**Keywords:** CD56, Thyroid lesions, papillary thyroid carcinoma, Immunohistochemistry.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Thyroid nodules represent a significant clinical challenge in endocrine pathology, with a reported palpability rate of 4-7% in the general population [1,2]. These lesions encompass a broad spectrum of pathological entities, ranging from hyperplastic and inflammatory conditions to benign and malignant neoplasms.

Papillary thyroid carcinoma (PTC) constitutes approximately 80% of thyroid malignancies, necessitating accurate histopathological assessment

for definitive diagnosis [3]. The diagnostic landscape is complicated by significant histopathological overlap between PTC and benign thyroid lesions—such as follicular adenoma, nodular hyperplasia, and Hashimoto's thyroiditis.

This overlap often creates diagnostic challenges that can impact treatment decisions. Immunohistochemical (IHC) markers have emerged as valuable adjuncts in refining diagnostic accuracy. CD56, a neural cell adhesion molecule, is

typically expressed in normal thyroid follicular cells but is frequently absent in malignant transformation, particularly in PTC [4,5]. This differential expression pattern suggests potential utility in diagnostic applications.

Materials and Methods

This cross-sectional study was conducted in the Department of Pathology, MAPIMS, from January 2021 to October 2022. The study included 35 thyroidectomy specimens that were processed

according to standard histopathological protocols. Each specimen underwent careful gross examination followed by tissue processing and hematoxylin & eosin (H&E) staining.

Immunohistochemical analysis was performed using monoclonal antibodies against CD56 (PATHNSITU).

To ensure reliability, positive controls using normal thyroid tissue and negative controls omitting the primary antibody were included in each batch.

Table 1: CD56 Expression Scoring System

Score	Positive Cell Percentage
0	Negative
1	<10%
2	10-25%
3	25-50%
4	50-75%
5	>75%

Table 2: Staining Intensity Grading

Grade	Description
0	Negative
1	Pale brown
2	Golden brown
3	Dark brown

Table 3: Final Interpretation Criteria

Score Range	Interpretation
0-2	Negative
3-4	Weak Positive (1+)
5-6	Moderate Positive (2+)
7-8	Strong Positive (3+)

Results: The demographic and histopathological analysis revealed distinctive patterns in the study population. The distribution of cases is summarized in the following tables:

Table 4: Histopathological Distribution of Thyroid Lesions

Diagnosis	Cases (n)	Percentage (%)
Papillary carcinoma (classic)	10	29
Nodular hyperplasia	7	20
Follicular adenoma	7	20
Follicular variant PTC	7	20
Hashimoto's thyroiditis	3	8.6
Hurthle cell adenoma	1	2.9

Table 5: CD56 Expression in Thyroid Lesions

Marker	Expression	Benign (n=18)	Malignant (n=17)	P-value
CD56	Positive	17 (94.4%)	3 (17.6%)	0.001
	Negative	1 (5.6%)	14 (82.4%)	

Table 6: Diagnostic Performance of CD56

Parameter	Value (%)
Sensitivity	82.3
Specificity	94.4
PPV	93.3
NPV	85.0
Accuracy	88.6

Our study analyzed 35 thyroidectomy specimens, revealing a marked female predominance with 85.7% of cases occurring in women. Age distribution analysis showed the highest incidence in the 31-40 years age group, accounting for 40% of all cases. The histopathological examination revealed a diverse spectrum of thyroid lesions, with classic papillary carcinoma being the most prevalent, comprising 29% of cases (10 specimens). Nodular hyperplasia, follicular adenoma, and follicular variant PTC each accounted for 20% of cases (7 specimens each), while Hashimoto's thyroiditis and Hurthle cell adenoma were less common, representing 8.6% (3 cases) and 2.9% (1 case) respectively. The immunohistochemical analysis of CD56 expression demonstrated distinct staining patterns between benign and malignant lesions. Among benign lesions (n=18), 17 cases (94.4%) showed positive CD56 expression, with most exhibiting strong membranous staining. Only one case of follicular adenoma (5.6%) showed negative CD56 expression. In contrast, among malignant lesions

(n=17), 14 cases (82.4%) demonstrated negative CD56 expression, while only 3 cases (17.6%) showed positive staining. This differential expression pattern was statistically significant ($P=0.001$), highlighting the potential diagnostic value of CD56 in distinguishing between benign and malignant thyroid lesions.

The diagnostic performance analysis of CD56 revealed promising results. The marker demonstrated high specificity (94.4%) and good sensitivity (82.3%) in differentiating between benign and malignant thyroid lesions. The positive predictive value was 93.3%, indicating a high probability of malignancy when CD56 expression is negative. The negative predictive value was 85.0%, suggesting a good likelihood of benign pathology when CD56 expression is positive. The overall diagnostic accuracy was 88.6%, demonstrating the robust performance of CD56 as a diagnostic marker in thyroid lesions.

Histopathological and Immunohistochemical Findings

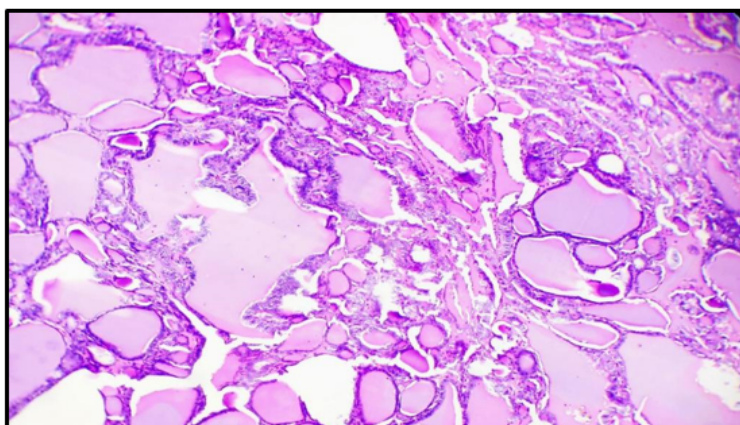


Figure 1: Nodular hyperplasia (H&E stain x100) showing irregular follicles of varying sizes.

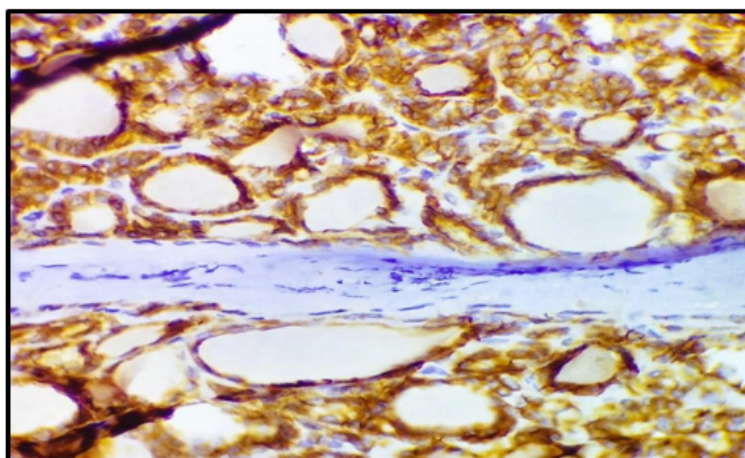


Figure 2: Nodular hyperplasia demonstrating strong membranous 3+ positivity (IHC-CD56 marker x400).

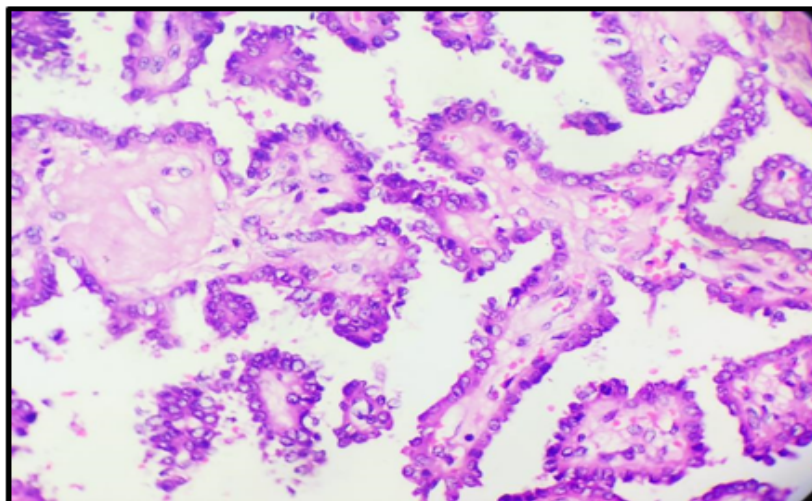


Figure 3: Papillary carcinoma classic variant (H&E stain x100) exhibiting characteristic nuclear features.

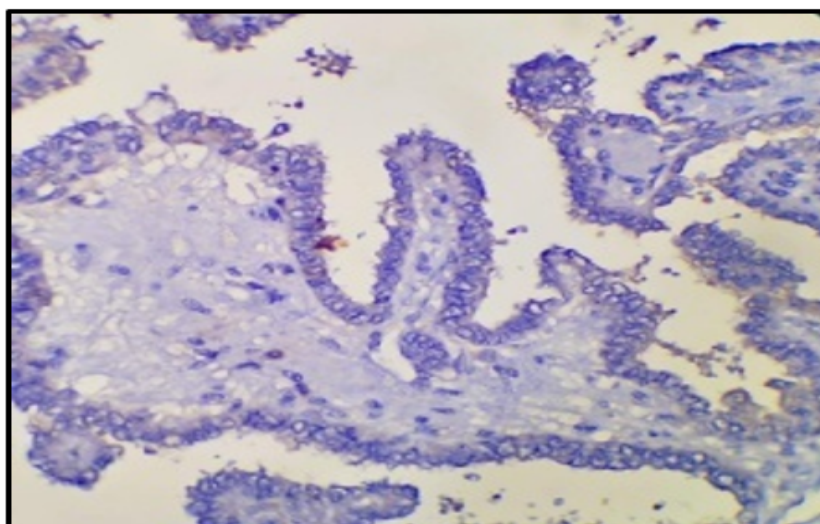


Figure 4: Papillary carcinoma classical variant showing negative staining expression (IHC-CD56 marker x400).

Discussion

The accurate diagnosis of thyroid lesions remains a critical challenge in surgical pathology, particularly in distinguishing PTC from its benign mimics. Our findings demonstrate the significant utility of CD56 as a diagnostic marker, aligning with previous studies in this field [6-9]. The high rate of CD56 positivity (94.4%) in benign lesions observed in our study corroborates the findings of Abd El Atti et al. (93%) and Shahebrahimi et al. (92.4%) [10,11]. The consistent absence of CD56 expression in classic PTC cases (100%) and its reduced expression in FVPTC cases (57.1%) align with observations by Park et al. (92.5%) and Golu et al. (100%) [12,13]. This pattern of expression supports the role of CD56 as a negative marker for PTC. The diagnostic efficacy demonstrated in our study, with specificity at 94.4% and overall accuracy at 88.6%, parallels the findings of Erdogan-Durmus et al. ($P < 0.001$) [14].

Conclusion

CD56 is a highly specific marker for distinguishing PTC from benign thyroid lesions. The consistent absence of CD56 expression in classic PTC and its reduced expression in FVPTC underscore its utility as a diagnostic tool. These findings reinforce the value of CD56 Immunohistochemistry in routine evaluation of thyroid lesions, particularly in cases where conventional histopathological features are equivocal.

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