



“HISTOPATHOLOGICAL STUDY OF THYROID NEOPLASMS WITH SPECIAL REFERENCE TO EXPRESSION OF GALECTIN-3 IN THYROID NEOPLASMS IN A TERTIARY CARE CENTRE”

Pathology

Dr. Manjula Choudhury

Professor And Head Of The Department Of Pathology

Dr. Shrutilekha Sharma*

Post Graduate Trainee, Department Of Pathology, Gauhati Medical College And Hospital

*Corresponding Author.

ABSTRACT

Background: Globally, the number of thyroid cancer cases was estimated to be 586,000, ranking it 9th in 2020 and the incidence rate in women is 10.1 per 100,000 which is 3-fold higher than that in men (1). Benign neoplasms outnumber thyroid carcinomas, commonly occurring during 3rd to 6th decades of life. Despite histopathology being the mainstay for diagnosis, immunohistochemical markers have been invariably used in the recent years to aid in cases posing morphological diagnostic dilemma. **Aims and objectives:** To study the histopathological spectrum of thyroid neoplasms and expression of Galectin-3 in thyroid neoplasms. **Methodology:** This is a one-year cross-sectional study (2021-2022) carried out in a tertiary care hospital of North East India. A total of histopathologically diagnosed 70 cases were studied and evaluated for immunohistochemical expression of Galectin-3. **Results:** Majority (58.50%) of thyroid neoplasms were found to be benign, mostly affecting the age group of (31-40) years with female: male ratio being 7.75:1. Amongst the benign cases, all were diagnosed as follicular adenoma and amongst the malignancies, conventional papillary thyroid carcinoma constituted majority of the cases (58.62%). Galectin-3 was expressed significantly in the malignant cases and the maximum expression was noted in 15 out of 17 cases (88.23%) of conventional papillary thyroid carcinoma. **Conclusion:** Thyroid neoplasms are highly curable with early detection and appropriate management. Hence, in diagnostically challenging cases, the utility of immunohistochemical markers along with the histomorphological interpretation becomes important.

KEYWORDS

Galectin 3, Histopathology, Immunohistochemistry, Papillary Thyroid Carcinoma, Thyroid Neoplasms.

INTRODUCTION:

Thyroid neoplasms constitute the most common endocrine neoplasms⁽²⁾. In India, over a decade, the incidence rate of thyroid cancer in women has increased from 2.4 to 3.9 and in men from 0.9 to 1.3, a relative increase of 62% and 48% respectively⁽³⁾. Thyroid neoplasms can be benign as thyroid adenoma or malignant as papillary, follicular, anaplastic or medullary carcinoma. Papillary thyroid carcinoma is the most common form of thyroid malignancy representing almost 90% of all diagnosed cancers.

Definite histopathological analysis of haematoxylin and eosin-stained sections of thyroid neoplasms can be diagnostically challenging due to overlapping morphological similarities between primary thyroid malignancies and metastatic secondaries as well as observer variations during interpretation. In such situations, the role of immunohistochemical markers needs to be considered.

Galectin-3 is a lectin protein and plays role in inflammation and neoplastic transformation. It aids in distinguishing papillary and follicular variant of papillary thyroid carcinoma from other follicular patterned nodules⁽⁴⁾.

AIMS AND OBJECTIVES:

- 1) To study the histopathological spectrum of thyroid neoplasms.
- 2) To study the expression of Galectin-3 in thyroid neoplasms.

MATERIALS AND METHODOLOGY:

A one-year cross-sectional study was conducted from July 2021 to June 2022 in the Department of Pathology, Gauhati Medical College and Hospital after receiving approval from the Institutional ethics committee. Tumours occurring in all age groups and both sexes were included in the study. Specimens were collected in 10% Neutral Buffered Formalin, then grossed, processed and stained as per standard protocols⁽⁵⁾. A total of histopathologically confirmed 70 cases of thyroid neoplasms were taken into account and further evaluated for Galectin-3 immunostaining on the representative blocks of paraffin embedded tissue.

Interpretation Of Galectin 3 Immunostaining:

Distribution and intensity of Galectin-3 cytoplasmic signal interpretation was based on the guidelines followed by Weber KB et al.(6), and Hermann ME et al.(7):-

- Cases that showed specific cytoplasmic staining of more than 5% of the tumour cells, regardless of the intensity, were scored as positive for Galectin-3(6).
- The staining intensity was graded on a scale of 0 to 3 as(6,7):

- 0: no staining
- 1+: weak/slight staining
- 2+: moderate staining
- 3+: intense staining.
- The proportion of stained cells are interpreted as(6,7):
- 1+: <5% of cells
- 2+: 5% to 50% of cells
- 3+: >50% of cells

RESULTS AND OBSERVATIONS:

Table 1: Distribution of cases as per nature of the lesions-

Cases	No. of cases	Percentage (%)
Benign	41	58.5
Malignant	29	41.5

In our study of 70 cases of thyroid neoplasms, 41 cases (58.5%) were of benign nature and 29 cases (41.5%) were malignant.

Table 2: Age-wise distribution of cases-

Age (years)	No. of benign cases	Percentage of benign cases (%)	No. of malignant cases	Percentage of malignant cases (%)
21-30	10	24.3	3	10.3
31-40	17	41.5	6	20.7
41-50	8	19.5	10	34.5
51-60	6	14.7	10	34.5

DISTRIBUTION OF CASES BASED ON AGE

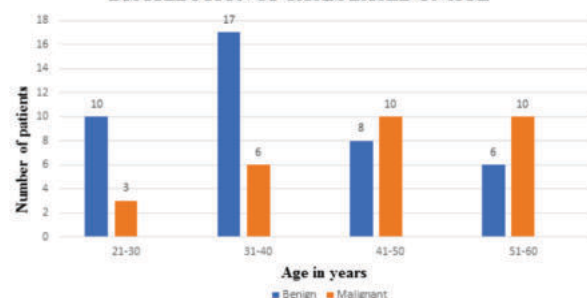


Fig 1: Age-wise distribution of cases

Out of total 70 cases, maximum number of the patients (23 cases, 32.85%) having thyroid neoplasm belonged to the age group of (31-

40) years. In this age group, 17 cases were benign (73.91%) and 6 cases were malignant (26.08%). While majority of the elderly patients aged 40 to 60 years (20 cases, 68.96%) were diagnosed with thyroid malignancies.

Table 3: Distribution of cases based on gender-

Gender	No. of cases	Percentage (%)
Males	8	11.5
Females	62	88.5

In this study, 62 cases (88.5%) were females and 8 cases (11.5%) were males. Male to female ratio was 1:7.75.

Table 4: Distribution based on histological variant-

Histological diagnosis	No. of cases	Percentage (%)
1.Follicular adenoma	41	58.6
2.Conventional PTC	17	24.3
3.FV PTC	6	8.6
4.Follicular carcinoma	5	7.1
5.Medullary carcinoma	1	1.4

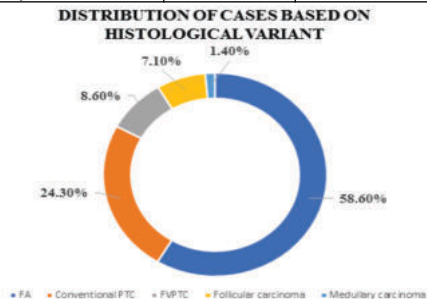


Fig 2: Distribution of cases as per histological variant

Out of 70 cases, majority of the cases were found to be follicular adenoma (41 cases, 58.60%). Amongst the malignant cases, conventional papillary carcinoma constituted the highest number with 17 cases (58.62%) followed by the follicular variant of papillary carcinoma with 6 cases (20.68%).

Table 5: Expression of Galectin 3 in benign and malignant thyroid neoplasms-

Cases	Galectin-3 expression	
	Number	Percentage
Benign	9	21.95 %
Malignant	22	75.86%

This study showed Galectin-3 expression in 9 cases (21.90%) of benign neoplasms and 22 cases (75.86%) of malignant neoplasms.

Table 6: Scoring of Galectin-3 expression in benign thyroid neoplasms-

Benign neoplasms	Gal-3 scoring			
	0	1+	2+	3+
Follicular adenoma (n= 9)		8	1	

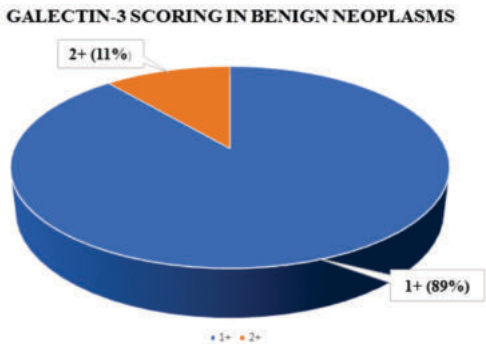


Fig 3: Galectin-3 scoring in benign thyroid neoplasms

Amongst the 41 cases of follicular adenoma, 9 cases (21.95%) showed galectin-3 expression. On interpretation of staining intensity, 8 cases (89%) showed score of 1+ (mild) and 1 case (11%) showed score of 2+ (moderate).

Table 7: Scoring of Galectin-3 in malignant thyroid neoplasms-

Malignant neoplasms	Gal-3 scoring			
	0	1+	2+	3+
Conventional PTC	2		5	10
FVPTC	2		2	2
Follicular carcinoma	2			3
Medullary carcinoma	1			

GALECTIN-3 SCORING IN MALIGNANT NEOPLASMS

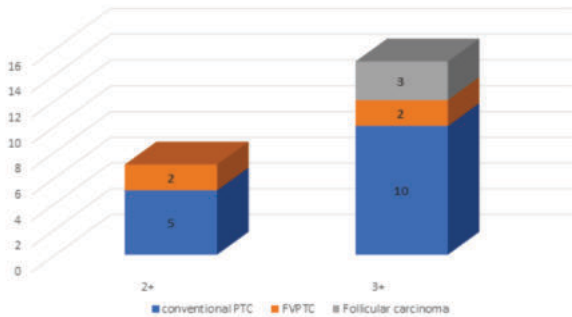


Fig 4: Galectin-3 scoring in malignant thyroid neoplasms

In this study, 22 cases of the 29 malignant cases showed Galectin-3 expression. Maximum number of conventional papillary thyroid carcinomas (15/17 cases, 88.23%) had shown Galectin-3 expression in different intensities: 10 cases (58.82%) showed intense staining with a score of 3+ and 5 cases (29.41%) showed moderate staining with a score of 2+. Also, 4/6 cases (66.67%) cases of FVPTC showed Galectin-3 positivity with variable scores of intensities and 3/5 cases (60%) of follicular carcinoma showed Galectin-3 expression with a score of 3+.

Statistical Analysis:

The statistical analysis of the data collected was done using SSPS software V21. The association between histopathological diagnosis and the immunohistochemical marker was calculated using Pearson chi-square test and p-value less than 0.05 was considered statistically significant.

	GALECTIN-3
Sensitivity	96.55%
Specificity	65.85%
Positive Predictive Value (PPV)	66.67%
Negative Predictive Value (NPV)	96.43%
PEARSON correlation coefficient	27.56
p-value	<0.001

Case Photographs:

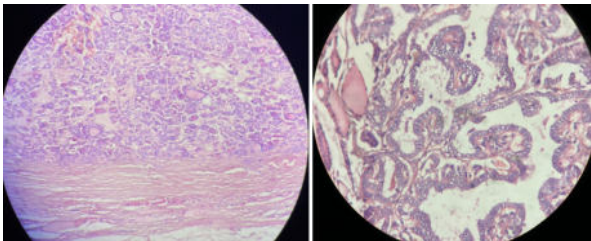


Fig 5: Hpe Of Thyroid Follicular Adenoma (h&e 10x)

Fig 6: Hpe Of Papillary Thyroid Carcinoma (h&e 40x)

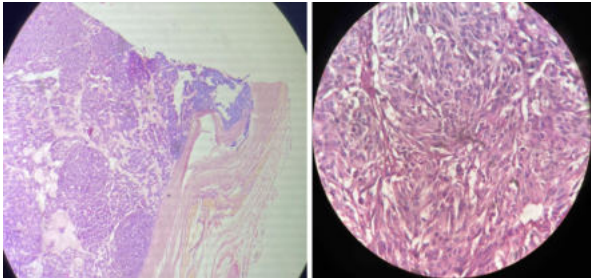


Fig 7: Hpe Of Follicular Thyroid Carcinoma (h&e 10x)

Fig 8: Hpe Of Medullary Thyroid Carcinoma (h&e 40x)

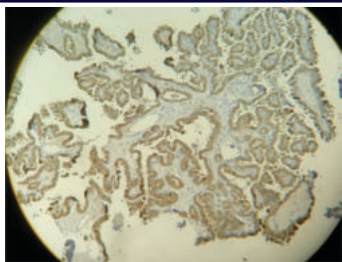


Fig 9: Diffuse Galectin-3 (3+) Positivity Of Papillary Thyroid Carcinoma (h&e 10x)

DISCUSSION:

A. Comparative Analysis Of Age Distribution:

The present study found thyroid malignancy commonly occurring in the age group of (40- 60) years and that is in concordance with the study results of Nabil Al-Zaher et al⁽⁸⁾, R.K.Orosco et al⁽⁹⁾, F.M.Girardi⁽¹⁰⁾ and Lingbin Du⁽¹¹⁾. However, the study by Jayarajah et al⁽¹²⁾ found majority of the malignancies to occur in relatively lesser age.

B. Comparative Analysis Of Sex Distribution:

This study found that 88.50% of the affected patients were female with male: female ratio being 1:7.75 in concordance with the studies of Bose et al⁽¹³⁾, Magdalene et al⁽¹⁴⁾, Pham et al⁽¹⁵⁾ and PA Prasad et al⁽¹⁶⁾.

C. Comparative Analysis Of Histopathological Variants Of Thyroid Malignancies:

The present study found that papillary thyroid carcinoma including both conventional and follicular variants constituted the highest number of malignant cases (23 cases, 79.31%). This result was found to be concordant with those of Magdalene et al⁽¹⁴⁾, Jayarajah et al⁽¹²⁾, Pham et al⁽¹⁵⁾ and Chandana et al⁽¹⁷⁾.

D. Comparative Analysis Of Galectin-3 Expression In Thyroid Neoplasms:

In the present study, 21.95% cases of benign neoplasms (follicular adenoma) and 75.86% cases of malignancies expressed Galectin-3. Amongst the malignant cases, 88.23% cases of conventional type, 66.67% cases of follicular variant of papillary thyroid carcinoma and 60% cases of follicular carcinoma showed Galectin-3 expression. These findings were concordant with the studies conducted by Beesley et al⁽¹⁸⁾, Scognamiglio et al⁽¹⁹⁾, Saleh et al⁽⁵⁾, Huang et al⁽²⁰⁾, Edward et al⁽²¹⁾ and PA Prasad et al⁽¹⁶⁾.

CONCLUSION:

- The following conclusions were made in this study of 70 cases of thyroid neoplasms-
- Majority of the neoplasms were benign in nature.
- Most of the affected cases belonged to the age group of 31 to 40 years with female preponderance (88.5%). With advancing age, malignancy was more common to occur.
- Papillary thyroid carcinoma (79.31%) constituted most of the malignant cases, followed by follicular carcinoma.
- Significant expression of Galectin-3 was found in the malignant cases with diffuse expression mostly in papillary carcinoma.

Histopathological examination of thyroid neoplasms serves as a key tool providing complete morphological assessment of the resected tissue. It enables to look for pattern of arrangement of the tumour cells, capsular as well as vascular invasion, presence or absence of features favouring high grade features of malignancy. But, at times due to overlapping histomorphological features, focal and subjective nuclear features of papillary thyroid carcinoma or in differentiating metastatic thyroid malignancies, diagnostic dilemma may step in. Hence, the use of immunohistochemical markers in adjunct to morphological analysis becomes significant in differentiating the benign and malignant thyroid lesions.

REFERENCES:

- 1) Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021 May 1;71(3):209–49.
- 2) Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995. *Cancer*. 1998;83(12):2638–48.
- 3) Sekkath Veedu J, Wang K, Lei F, Chen Q, Huang B, Mathew A. Trends in thyroid cancer

- incidence in India. *J Clin Oncol*. 2018 May 20;36(15_suppl):e18095–e18095.
- 4) Saleh HA, Feng J, Tabassum F, Al-Zohaili O, Husain M, Giorgadze T. Differential expression of galectin-3, CK19, HBME1, and Ret oncoprotein in the diagnosis of thyroid neoplasms by fine needle aspiration biopsy. *CytoJournal*. 2009 Sep 18;6:18.
- 5) Bancroft's Theory and Practice of Histological Techniques. 2019
- 6) Weber KB, Shroyer KR, Heinz DE, Nawaz S, Said MS, Haugen BR. The Use of a Combination of Galectin-3 and Thyroid Peroxidase for the Diagnosis and Prognosis of Thyroid Cancer. *Am J Clin Pathol*. 2004 Oct 1;122(4):524–31.
- 7) Herrmann ME, LiVolsi VA, Pasha TL, Roberts SA, Wojcik EM, Baloch ZW. Immunohistochemical expression of galectin-3 in benign and malignant thyroid lesions. *Arch Pathol Lab Med*. 2002 Jun;126(6):710–3.
- 8) Al-Zaher N, Al-Salam S, El Teraifi H. Thyroid carcinoma in the United Arab Emirates: perspectives and experience of a tertiary care hospital. *Hematol Oncol Stem Cell Ther*. 2008 Jan 1;1(1):14–21.
- 9) Orosco RK, Hussain T, Brumund KT, Oh DK, Chang DC, Bouvet M. Analysis of Age and Disease Status as Predictors of Thyroid Cancer-Specific Mortality Using the Surveillance, Epidemiology, and End Results Database. *Thyroid*. 2015 Jan 1;25(1):125–32.
- 10) Girardi FM. Thyroid Carcinoma Pattern Presentation According to Age. *Int Arch Otorhinolaryngol*. 2017 Jan;21(1):38–41.
- 11) Jayarajah U, Fernando A, Prabhshani S, Fernando EA, Seneviratne SA. Incidence and histological patterns of thyroid cancer in Sri Lanka 2001-2010: an analysis of national cancer registry data. *BMC Cancer*. 2018 Feb 7;18(1):163.
- 12) Du L, Zhao Z, Zheng R, Li H, Zhang S, Li R, et al. Epidemiology of Thyroid Cancer: Incidence and Mortality in China, 2015. *Front Oncol*. 2020;10.
- 13) Bose D, Das RN, Chatterjee U, Banerjee U. Cytokeratin 19 immunoreactivity in the diagnosis of papillary thyroid carcinoma. *Indian J Med Paediatr Oncol Off J Indian Soc Med Paediatr Oncol*. 2012;33(2):107–11.
- 14) Magdalene DKF, Swetha DJ, O DNN, Sumangala DB. Histopathological study of thyroid lesions in a tertiary care center in coastal belt of South India. *Trop J Pathol Microbiol*. 2017 Mar 31;3(1):77–83.
- 15) Pham DX, Nguyen HD, Phung AHT, Bui TD, Tran TS, Tran BNH, et al. Trends in incidence and histological pattern of thyroid cancer in Ho Chi Minh City, Vietnam (1996–2015): a population-based study. *BMC Cancer*. 2021 Mar 20;21(1):296.
- 16) Pa P, K R. Diagnostic utility of CK19 and galectin-3 in differentiating papillary thyroid carcinoma from nonneoplastic lesions of thyroid. *J Cancer Res Ther*. 2022 Jun;18(3).
- 17) Chandana DA, R DG, S DPS. Epidemiological and histopathological study of thyroid lesions in a tertiary care hospital in south India. *Trop J Pathol Microbiol*. 2020 Aug 31;6(6):381–6.
- 18) Beesley MF, McLaren KM. Cytokeratin 19 and galectin-3 immunohistochemistry in the differential diagnosis of solitary thyroid nodules. *Histopathology*. 2002;41(3):236–43.
- 19) Scognamiglio T, Hyjek E, Kao J, Chen YT. Diagnostic Usefulness of HBME1, Galectin-3, CK19, and CITED1 and Evaluation of Their Expression in Encapsulated Lesions With Questionable Features of Papillary Thyroid Carcinoma. *Am J Clin Pathol*. 2006 Nov;126(5):700–8.
- 20) Huang L, Wang X, Huang X, Gui H, Li Y, Chen Q, et al. Diagnostic significance of CK19, galectin-3, CD56, TPO and Ki67 expression and BRAF mutation in papillary thyroid carcinoma. *Oncol Lett*. 2018 Apr 1;15(4):4269–77.
- 21) Edward MM, T AJ. To evaluate the immunohistochemical expression of galectin-3 and ck-19 in thyroid neoplasms. *Int J Health Clin Res*. 2021 Aug 30;4(15):150–60.