



A STUDY OF IMMUNOHISTOCHEMICAL EXPRESSION OF GALECTIN-3 IN NON-NEOPLASTIC AND NEOPLASTIC LESIONS OF THYROID

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ABSTRACT

Introduction: Thyroid lesions are fairly common and have a wide spectrum of diseases ranging from functional, immune mediated to neoplastic lesions. Malignancy of thyroid constitutes approximately 1% of all cancers. These malignant tumors of thyroid gland exhibit a variety of histopathologies and clinical behavior. Immune markers are gaining more and more importance in diagnostic pathology, especially in the differential diagnostics and in the grading of thyroid gland tumors. In the recent times Galectin-3 has received notable recognition for its usefulness as a diagnostic marker for thyroid cancer. **Aims and objectives:** To evaluate the diagnostic role of galectin-3 (Gal-3) in differentiating malignant from benign thyroid neoplasm. **Material and method:** In this observational study, we evaluated Gal-3 expression in a spectrum of all non-neoplastic and neoplastic lesions including benign and malignant lesions of thyroid gland. All types of thyroidectomy specimens were fixed in 10% formal saline and subjected to histopathological examination. Sections were stained with H&E stain. Gal-3 immunoperoxidase reaction was carried out in histological sections from all the cases and descriptive analysis was done. **Result:** In the study of 100 cases of thyroid swelling were included and evaluated by histopathological and by using Gal-3 immunoperoxidase marker. Out of 100 cases, majority of thyroid lesions were seen in females with 76 cases (76%) while only 24 cases (24%) were seen in male. Among 66 non-neoplastic cases, only 6 cases (9.1%) and among 34 neoplastic lesions, 28 cases (82.4%) were positive for galectin-3 marker. Statistical significance of galectin-3 expression between non-neoplastic and neoplastic thyroid lesions found to be statistically significant (P value <0000.1). The sensitivity and specificity of galectin-3 detection of malignant lesions were found to be 82.4% and 91% respectively with 82.4% positive predictive value and 90.9% negative predictive value. **Conclusion:** We suggest that Galectin-3 expression is helpful in enabling better diagnosis and patient care by guiding appropriate therapeutic decisions.

KEYWORDS :

INTRODUCTION:

Thyroid carcinoma is the most common endocrine malignancy and more than 95% of thyroid carcinoma originates from follicular epithelial cells¹. In many cases especially in follicular patterned thyroid lesions, even with histological analysis the diagnosis of neoplasm and distinction between benign and malignant neoplasm can be difficult.^{2,3,4}

The introduction of borderline tumors into thyroid tumor classification significantly impacts pathology practice. As encapsulated non-invasive follicular pattern tumor with papillary thyroid carcinoma (PTC) type nuclear features (PTC-N) were downgraded from carcinoma to borderline tumors in 4th edition WHO classification. Risk stratification of thyroid carcinoma for both PTCs and follicular thyroid carcinoma is one of the most important elements in the diagnosis of thyroid tumors, which aims to reduce over diagnosis and overtreatment of thyroid carcinomas⁵. Furthermore, differentiation between follicular adenoma and follicular carcinoma may be difficult in cases of minimally invasive carcinoma.⁶

in distinguishing between benign and malignant follicular patterned lesions of the thyroid. Among them, the most promising is a beta-galactosidase binding protein galectin-3⁸. Galectin-3 is a polypeptide expressed in many tissues and cell type, where it is localized in the nucleus and/or the cytoplasm, on the cell surface or in the extracellular environment⁷. In the mean time, some benign thyroid lesions (adenoma and multinodular goiter) also expressed galectin-3 as demonstrated by immunohistochemical and RT-PCR studies. Thus the use of galectin-3 as a molecular marker for thyroid carcinoma still needs further investigation, particularly in the differentiation between thyroid follicular lesions. We aimed to evaluate the diagnostic significance of galectin-3 immunostaining in differentiating in non-neoplastic, benign and malignant thyroid nodules in histopathological samples.⁸ Galectin-3 has been suggested to play a role in different physiological and pathological process, including pre-mRNA splicing, cell-cell and cell matrix adhesion, cell growth, neoplastic transformation, metastasis and immune response and it is increased in several human and murine tumor cell lines.⁷

MATERIAL & METHODS:

All resected thyroid specimens of Lobectomy,

Several molecular markers have been reported to be helpful

hemithyroidectomy, subtotal and total thyroidectomy received in the department of Pathology, B.R.D medical College, Gorakhpur for histopathological examination during a period from July 2021 to June 2022. All samples of patients of thyroid were selected on the basis of inclusion and exclusion criteria. Thyroidectomy specimen were fixed in 10% formal saline and subjected to histopathological examination using paraffin embedding technique. Histopathological diagnosis was made and then freshly cut sections were also used for immunostaining. The sections stained by IHC were examined alongside H&E stained specimens. A P value <0.5 cm will be considered to be statistically significant.

RESULT:

In the present study, a total of 100 specimen of thyroid lesions were studied during one year examination. All the non-neoplastic and neoplastic lesions were analysed for galectin-3 immunostaining. Galectin-3 stained the majority of neoplastic lesions (28/34 cases, 82.4%) in comparison to non-neoplastic lesions (6/66 cases, 9.1%) and the difference was statistically significant (P value <0.0001).

Table -1 Distribution Of Cases On The Basis Of Nature Of Thyroid Lesions

Nature	No. of cases	Percentage
1.Non-neoplastic lesions	66	66%
2.Neoplastic lesions		
A)Benign lesions	07	07%
B)Malignant lesions	27	27%
Total	100	100%

Out of 34 neoplastic cases, 27 cases were malignant and 07 cases were benign. Among malignant lesions, in 8 cases of follicular carcinoma, galectin-3 positivity was seen in 7 cases (87.5%) while 1 case (12.5%) had galectin-3 negativity. In 16 cases of papillary carcinoma, all 16 cases (100%) showed galectin-3 positivity. In 2 cases of follicular variant of papillary carcinoma, both cases (100%) showed galectin-3 positivity, 1 case (100%) of medullary carcinoma showed galectin-3 positivity. Among benign lesions, 1 case (20%) of follicular adenoma was galectin-3 positive while 4 cases (80%) were galectin-3 negative. 1 case (50%) of hurthle cell adenoma showed galectin-3 positivity while 1 case (50%) was galectin-3 negative.

The staining intensity of Galectin-3 expression was interpreted in 100 cases of thyroid neoplasms. among malignant lesions, galectin-3 marker showed strong intensity in 4 cases (50%) of follicular carcinoma while 2 case (25%) had moderate intensity and 1 cases (12.5%) showed mild intensity while 1 case (12.5%) was galectin-3 negative. In 16 cases of papillary carcinoma, 14 cases (87.5%) showed strong intensity while 2 cases (12.5%) had moderate intensity. In 2 cases of follicular variant of papillary carcinoma, 1 case (50%) showed strong intensity while 1 case (50%) had moderate intensity. 1 cases (100%) of medullary carcinoma showed moderate intensity. Among benign neoplastic lesions, 1 case of follicular adenoma showed mild intensity while 4 cases (80%) were galectin-3 negative. 1 case (50%) of hurthle cell adenoma showed mild intensity while 1 case was galectin-3 negative. Among non-neoplastic lesions, in 33 cases of colloid goiter, only 2 cases (6%) showed mild intensity while 33 cases (94%) were galectin-3 negative. In 22 cases of multinodular goiter, 1 case (4.5%) showed moderate intensity and 2 cases (9.1%) showed mild intensity while 19 cases (86.4%) were galectin-3 negative. In 2 cases of thyroglossal duct cyst, both cases (100%) were galectin-3 negative. In 7 cases of hashimoto's thyroiditis, 1 case (14.3%) showed mild intensity while 6 cases (85.7%) were galectin-3 negative.

Table-2 Statistical Analysis Of Galectin-3 In Follicular/Hurthle Cell Adenoma And Follicular Carcinoma

Histological diagnosis	Galectin-3 +ve	Galectin-3 -ve	Total no. of cases	P- value (two sided)
	No.(%)	No. (%)		
Follicular adenoma	02 (28.6%)	05 (71.4%)	07	Chi square test-5.4 (P value <0.05)
Follicular carcinoma	07 (87.5%)	01 (12.5%)	08	
Total	09	06	15	

On applying Fisher Exact test, the difference of GALECTIN-3 expression between follicular adenoma and follicular carcinoma was found to be statistically significant.(p value <0.05).

Table-3 Statistical Analysis Of Galectin-3 In Nodular Goiter With Papillary Hyperplasia And Papillary Carcinoma

Histological diagnosis	Galectin-3 +ve	Galectin-3 -ve	Total no. of cases	P- value (two sided)
	No. (%)	No. (%)		
Nodular goiter with papillary hyperplasia	00 (00%)	02 (100%)	02	Chi square test- 18 (P value <0.00002)
Papillary carcinoma	16 (100%)	00 (00%)	16	
Total	16	2	18	

On applying Fisher Exact test, the difference of GALECTIN-3 expression between follicular adenoma and follicular carcinoma was found to be statistically significant.(p value <0.05).

Table -4 Sensitivity/specificity/ Positive Predictive Value & Negative Predictive Value Of Galectin-3 In Non-neoplastic And Neoplastic Thyroid Lesions

Histological diagnosis	Galectin-3 +ve	Galectin-3 -ve	Total no. of cases	P- value (two sided)
	No. (%)	No. (%)		
Non-neoplastic lesions	06 (9.1%)	60 (90.9%)	66	(P value <0.00001)
Neoplastic lesions	28 (82.4%)	06 (17.6%)	34	
Total	34	66	100	

Galectin-3 expression in neoplastic thyroid lesions was found to have a sensitivity of 82.6%, specificity of 91%, positive predictive value of 82.4% and negative predictive value of 90.9%.

DISCUSSION:

The current standard in the diagnosis of thyroid lesions is by histological examination of routine H&E stained sections. However it is widely known that the interpretation of follicular patterned lesions can be quite difficult and many other challenging situations are encountered where and malignant⁹. So the benefit of using Galectin-3 as a diagnostic marker for thyroid cancer has recently attracted considerable attention and it has been the most investigated molecule to diagnosing thyroid cancer.

Galectin-3, a protein which bonds to β galactosidase residues of glycoproteins on the cell surface, is also defined in cytoplasmic and nuclear compartment. Galectin-3 expression has been reported to be a valuable marker for distinguishing between benign and malignant thyroid nodule.10

In our study- Total of 100 cases of thyroid lesions were studied and found majority of 66 (66%) were non-neoplastic while rest of 34 (34%) were neoplastic. Among neoplastic lesions malignant lesions were more common than benign neoplastic lesions. This is similar to studies by K.F. Magdalene et al

(2017)11, Dr. Shreedevi et al (2018)12 and Dr. Biren parikh et al (2022)13. According to present study, majority of non-neoplastic lesions were of colloid goiter(33%). Among benign non-neoplastic lesions, follicular adenoma is most common and among malignant lesions, papillary carcinoma is most common thyroid lesion. Above these findings of our study are similar to studied done by K.F Magdalene et al (2017)11, Dr. Shreedevi et al (2018)12 and Ayesha Fatima et al (2018)14.

In our prospective study, most of the non-neoplastic conditions were galectin-3 negative 60/66 (82.4%) however 06/66 (9.1%) were galectin-3 positive. Out of benign neoplastic lesions, 2 case of adenomas were positive as also reported by others including Jakubiak-Wielganowicz et al (8/42 cases)15, kawachi et al (2/34 cases)16 and Aratake et al(2/14 cases)17.

Many previous researchers have reported that the immuno histochemical expression of Galectin-3 increases in thyroid malignancies. In our study we got similar findings like galectin-3 expression was seen maximally in malignant lesions, in all cases (100%) of papillary carcinoma, 87.5% of follicular carcinoma, 100% in follicular variant of papillary carcinoma and medullary carcinoma. This study in accordance with Hayam A Aiad et al (2008)18, Hussain A Saleh et al (2010)19 and BS sumana et al (2015)20.

In our study, maximum intensity of galectin-3 expression was seen in papillary carcinoma (87.5%) followed by follicular variant of papillary carcinoma (50%) and follicular carcinoma (50%). This is in accordance with study done by BS sumana et al (2015)20. In our study there is strong relationship between galectin-3 expression and malignancy as which is statistically significant (P<0.00001). We found statistically significant (P value < 0.00001) difference of galectin-3 expression between follicular adenoma and follicular carcinoma and between nodular goiter with papillary hyperplasia and papillary carcinoma respectively.

These findings of our study and others lead us to the assumption that galectin-3 positive adenoma may represent an incipient malignant transformation but for confirmation further studies are required. Results from this study reported a sensitivity, specificity, positive predictive value and negative predictive value are 82.6%, 91%, 82.4% and 90.9%. These findings are similar to study done by B.S. Sumana et al (2015)20 Hayam A Aiad et al (2008)18 and Husain A Saleh et al (2010)19

Table-5 Expression Of Galectin-3 Positivity In Various Non-neoplastic And Neoplastic Lesion

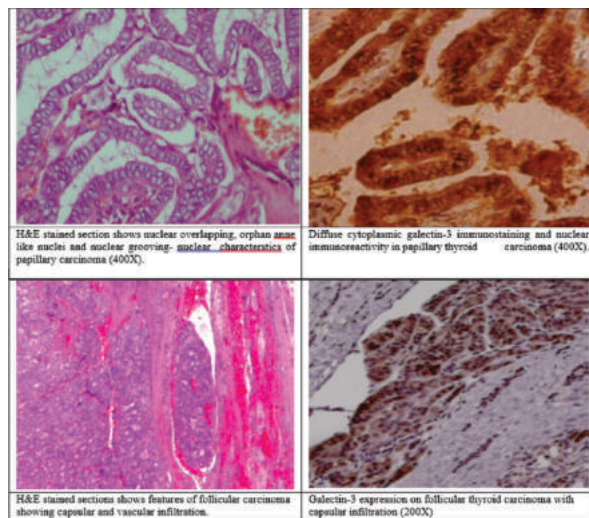
Thyroid lesions	Presnt study (100 cases)	B.S. Sumana et al (50 cases)	Fabio oriandi et al (64 cases)	Hayam A Aiad et al (79 cases)	Husain A saleh et al(152 cases)
Neoplastic lesions	82.4%	87%	91.4%	93%	85.1%
Non-neoplastic lesions	9.1%	15%	10.3%	10.5%	15.3%

Table-6 Comparison Of Sensitivity And Specificity Of Galectin-3 In Various Thyroid Lesion

Authors	Sensitivity	Specificity	PPV	NPV
B.S.Sumanaet al (50 cases)	86.7%	85%	89.66%	80.9%
Hayam A Aiad et al (79 cases)	93%	89.5%	90.5%	92%
Husain A saleh et al (152 cases)	85.2%	72.4%	63%	89.9%
Present study (100 cases)	82.6%	91%	82.4%	90.9%

CONCLUSION:

The result of our study implicates that galectin-3 expression is low in non-neoplastic thyroid lesions, intermediate in benign of thyroid lesions. Thus, we concluded that Galectin-3 expression is helpful in enabling better diagnosis and patient care by guiding appropriate therapeutic decisions.



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