Original Research Article

To evaluate the immunohistochemical expression of galectin-3 and ck-19 in thyroid neoplasms

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Abstract

Aim: The aim of the present investigation to study the immunohistochemical expression of Galectin-3 and CK- 19 marker in relation to histological types of epithelial thyroid neoplasms. **Methodolgy:** Present study is a prospective study carried over a period of 24 months (September 2017 to August 2019) in the Upgraded Department Of Pathology, Osmania General Hospital, Afzalgunj, Hyderabad. A total of 100 cases were studied. The age range was 19-80 years with mean age being 46.26 years. Female preponderance was noted with a male: female= 1:1.7. Majority of cases were seen in 4^{th} and 5^{th} decades. Routine H&E along with immunostaining with Gal-3 and CK-19 was performed. **Results:** Out of 100 cases- 36 were benign, 8 were encapsulated lesions and 56 were malignant lesions. Positive staining with Gal-3 was noted in 27% of benign lesions, 62.5% of encapsulated lesions and 85.71% of malignant lesions with 85%sensitivity and 72.7% specificity in discriminating malignant from benign lesions. Positive staining with CK-19 was noted in 22.2% of benign lesions, 75% of encapsulated and 75% of malignant lesions with 75% sensitivity and 77% specificity in differentiating malignant and benign lesions. Combined expression of Gal-3 and CK-19 showed an increase in sensitivity to 90% and specificity to 82.14%. Although focal CK19 and galectin-3 staining may be found in benign lesions, diffuse positivity is characteristic of malignancy. Expression of Gal-3 and CK-19 showed a statistically significant correlation with many studies. **Conclusion:** We concluded that combined use of CK-19 and Gal-3 increases the sensitivity and specificity in differentiating malignant and benign lesions. Further studies are required to establish the role of CK-19 and Gal-3 in encapsulated thyroid lesions as a diagnostic and prognostic tool in thyroid neoplasms.

Keywords: CK19, Galectin -3, Thyroid lesions, Malignancy, Encapsulated lesions, Immunohistochemical.

Introduction

The thyroid gland is affected by a variety of pathological lesions that are manifested as various morphologies including developmental, inflammatory,hyperplastic and neoplastic pathology.Lesions of thyroid presents as diffuse enlargement or solitary or multiple nodules. As the Incidence of malignancy presenting as solitary thyroid nodules is quiet high, emphasis is placed upon to find diagnostic modalities that may improve the ability to differentiate between non neoplastic and neoplastic lesions and differentiation of benign and malignant lesions[1].

Thyroid cancer is the most common endocrine malignancy of the human body, accounting for approximately 2% of the cancers worldwide. Incidence of thyroid cancer in women is about three times higher than the incidence of thyroid cancer in men (21.0 vs. 7.1 per 100,000 per year), although the mortality rate does not differ by sex (0.5 per 100,000 per year for both)[2].

Thyroid cancer is most frequently diagnosed in people aged 45 to 54 years, although it is the most frequently diagnosed cancer in women aged 20 to 34 years[3].

The majority of clinically apparent thyroid neoplasms are primary and epithelial. Traditionally, they have been divided into adenomas and carcinomas, the latter group incorporating the medullary carcinomas together with the more common lesions composed of follicular cells.

Over the past years, there has been a steep increase in the incidence of thyroid cancers, notably papillary thyroid cancer[4].

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The rise in incidence seems to be attributable both to the growing use of diagnostic imaging and fine-needle aspiration biopsy, which has led to enhanced detection and diagnosis of subclinical thyroid cancers, and environmental factors[5].Ancillary techniques, including immunohistochemistry and molecular diagnostics, may help resolve these difficult cases. The decision favouring benign or malignant lesion has clinical consequence and implies different modalities of further treatment and management[6].In this regard, the diagnostic approach to these tumours should include IHC markers that can aid in better assessment of morphologic details.Galectin-3 is proposed to modulate cell adhesion and cell growth through its influence on the cell cycle. It acts as an adhesion molecule in tumor progression and loosen the connection between tumor cells to promote cancer cell metastasis[7,8].

CK19 is a malignant tumor marker that is released from viable epithelial tumor cells and expression profiling of CK19 is the commonest marker that is used for tracing of disseminated tumor cells. Several investigations publicized that CK19 express in most often of papillary thyroid carcinoma (PTC) and follicular variant of papillary thyroid carcinoma[9,10]

Aims and Objectives

1. To study the immunohistochemical expression of Galectin-3 and CK- 19 marker in relation to histological types of epithelial thyroid neoplasms.
2. To differentiate thyroid lesions into benign and malignant using a panel of Galectin-3 and CK-19
3. To compare the present study with literature

Study Design

Prospective study.

Period of Study

24 months (September 2017 – August 2019)

Place of Study

Osmania General Hospital, Afzalgunj, Hyderabad.

Sample Size

A total of 100 cases are taken up for the study.

Inclusion criteria

1.All histomorphologically and cytologically diagnosed cases of thyroid epithelial neoplasms.

2.All Thyroidectomy specimens including lobectomy, total and sub total thyroidectomy, neoplastic lesions are included.

3.Patients of all ages and both male and females are included

Exclusion criteria

1. Cases of non epithelial thyroid tumors, metastatic tumors and patients who have received prior radiotherapy for any thyroid lesion have been excluded.

Total of 100 cases are collected, which are reported according to WHO classification as Benign- 36

Encapsulated lesions - 8 and Malignant - 56 cases.

Methods

One micro section of 5µm thickness is prepared from the corresponding paraffin blocks, taken on an albumin coated slide for H&E staining.

The kits for Galectin-3 & CK-19 Immunohistochemical staining are obtained from Pathinsitu Company. Staining is done according to manufacturer's protocol. The prostrate is used as positive control & endothelial cells in these samples are used as internal positive controls. Two micro sections of 4µm thickness are prepared from each of the tissue paraffin blocks and taken on poly-L-lysine coated slides for immunostaining of Galectin-3 & CK-19.

Scoring and evaluation

Galectin-3 Positive – Brown cytoplasmic staining, nuclear localization was also sometimes observed.

CK-19 Positive-- Brown cytoplasmic membrane staining, sometimes cytoplasmic staining seen.

Table 1: Intensity Grade of staining

Score	Pattern
0	No staining
1+	Light/weak staining
2+	Moderate staining
3+	Intense staining

Table 2: Proportion of staining

Score	Pattern
+++	>60% of neoplastic cells in cytoplasm/nucleus
++	30-60% of neoplastic cells in cytoplasm/nucleus
+	< 30% of neoplastic cells in cytoplasm/nucleus
-	No reaction

Statistical analysis

Correlation between Galectin-3 & CK-19 expression in benign and malignant lesions was evaluated using Chi square test. p-values <0.05 were considered to be statistically significant. Analysis was done using SPSS(Statistical Package for Social Sciences) statistical Analysis software.

Results and observations

- 100 cases of Thyroid neoplasms are included in the present study.
- It included 63 females and 37 males in the ratio of 1.7:1
- Age of patients ranged from 19 to 80 years.
- Overall, the mean age is 46 and median is 44 years.
- Mean age among men is 47.35 and median is 48.
- Mean age among women is 45.61 and median is 44.

Majority of cases are seen in the 3rd to 4th decades. Among males, most of the cases are seen in 4th decade and in in females in 3rd and 4th decades.

Case distribution according to WHO Classification is

- Benign -36
- Encapsulated lesions(Borderline) - 8
- Malignant -56

Table 3: Gender distribution, mean and median age in patients of Thyroidneoplasms

	Male	Female
No. of cases	37	63
Mean age	47.35	45.61
Median age	48	44

Table 4: Age distribution of all cases

Age group(years)	No.of cases(%)
0-20	1(1%)
21-30	15(15%)
31-40	19(19%)
41-50	31(31%)
51-60	17(17%)
>60	17(17%)
Total	**100**

Table 5: Age distribution in neoplastic lesions

Age group(years)	Benign neoplasms	Encapsulated neoplasms	Malignant neoplasms
0-20	**0**	**0**	**1**
21-30	**10**	**1**	**4**
31-40	**11**	**1**	**9**
41-50	**12**	**3**	**16**
51-60	**3**	**3**	**12**
>60	**0**	**0**	**14**
Total	**36**	**8**	**56**

Table 6 : Distriution of Thyroid lesions

Thyroid lesions	No.of cases	Mean Age group	% of cases
Benign	**36**	**39.2**	**36%**
Encapsulated	**8**	**46**	**8%**
Malignant	**56**	**50.6**	**56%**

Table 7: Distribution of Histopathological Diagnosis In Benign Lesions

HPE diagnosis	No .of cases	Mean Age Group	% of cases
Follicular adenoma	20	41.85	55.55%
Hurthle cell adenoma	6	36.5	16.6%
Hyalinizing Trabecular adenoma	10	35.8	27.7%
Total	36	39.2	100%

Table 8: Distribution of Encapsulated thyroid neoplasms

Histopathology diagnosis	No.of cases(%)	Mean Age Group
WDT-UMP	**2(25%)**	**56**
NIFTP	**6(75%)**	**42.6**
Total	**8(100%)**	**46**

Table 9: Distribution of malignant thyroid neoplasms

HPE diagnosis	No. of cases	Mean Age Group	% of cases
PTC	30	46.8	53.5%
FVPTC	11	46.4	19.6%
Papillary microcarcinoma	3	40	5.3%
PTC-columnar variant	1	58	1.7%
Follicular Carcinoma	4	67	7.1%
Anaplastic carcinoma	3	72.6	5.3%
Medullary carcinoma	4	66.75	7.1%
Total	**56**	**50.6**	**100%**

Immunohistochemical scoring of Galectin-3

Galectin-3 expression was interpreted in terms of intensity grade(I) and proportion of stained cells(P). Out of 100 cases, it was observed that malignant cases showed higher scores than benign and encapsulated lesions.

Table 10: IHC scoring of Gal-3 in benign lesions-

Benign neoplasms	No. of cases	Galectin 3 staining		Interpretation
		Intensity Grade	Proportion Score	
Follicular adenomas	2	2+	++	Positive
	3	1+	++ 0	Positive
	15	0		Negative
Hurthle cell adenomas	2	1+	++	Positive
	4	0	0	Negative
HTT	3	1+	++	Positive
	7	0	0	Negative
Total	**36**	**10(27.7%)**		**Positive**

Table 11: IHC scoring of Gal-3 in Encapsulated lesions

Hpe diagnosis	No.of cases	Galectin 3 scoring		Interpretation
		I grade	P score	
NIFTP	1	2+	+++	Positive
	2	1+	++	Positive
	3	0	0	Negative
WDT-UMP	2	2+	++	Positive
Total	**8**	**5(62.5%)**		**Positive**

Table 12: IHC scoring of Gal-3 in Malignant lesions

Histologic diagnosis	Number of cases	Galectin 3 staining		Interpretation
		I Grade	P score	
Papillary thyroid carcinoma- classical	5	3+	+++	Positive
	18	2+	++	Positive
	5	1+	++ 0	Positive
	2	0		Negative
Follicular variant ofPTC	3	3+	+++	Positive
	5	2+	++	Positive
	3	1+	+	Positive
Papillary microcarcinoma	3	2+	+++	Positive
PTC-Columnar variant	1	3+	+++	Positive
Follicular carcinoma	2	3+	+++	Positive
	1	2+	++ 0	Positive
	1	0		Negative
Medullary carcinoma	2	2+	++	Positive
	2	0	0	Negative
Anaplastic carcinoma	3	0	0	Negative
Total	**56**	**48(85.7%)**		**Positive**

Table 13: Comparison of Gal-3 scoring in Benign, Encapsulated &MalignantLesions

Galectin-3 interpretation	BenignLesions N= 36	Malignantlesions N=56	Encapsulatedlesions N=8	P value
Positive	10	48	5	<0.001
Negative	26	8	3	

Table 14: IHC scoring of CK-19 in Benign lesions

Benign neoplasms	No.ofcases	CK-19 staining		Interpretation
		Intensity Grade	Proportion Score	
Follicular adenomas	5	1+	++0	Positive
	15	0		Negative
Hurthle cell adenomas	6	0	0	Negative
HTT	3	1+	++	Positive
	7	0	0	Negative
Total	**36**	**8(22.2%)**		**Positive**

Table 15: IHC scoring of CK-19 in Encapsulated lesions

Hpe diagnosis	No.of cases	CK-19 scoring		Interpretation
		I grade	P score	
NIFTP	2	2+	+++0	Positive
	4	0		Negative
WDT-UMP	1	2+	++	Positive
	1	1+	+	Positive
Total	**8**	**5(62.5%)**		**Positive**

Table 16: IHC scoring of CK-19 in Malignant lesions

Histologic diagnosis	Number of cases	CK-19 staining		Interpretation
		I Grade	P score	
Papillary thyroid carcinoma- classical	14	3+	+++	Positive
	12	2+	++	Positive
	2	1+	++	Positive
	2	0	0	Negative
Follicular variant of PTC	7	3+	+++	Positive
	2	2+	++	Positive
	2	0	0	Negative
Papillary microcarcinoma	2	3+	+++	Positive

	1	0	0	Negative
PTC-Columnar variant	1	3+	+++	Positive
Follicular carcinoma	4	0	0	Negative
Medullary carcinoma	4	0	0	Negative
Anaplastic carcinoma	2	2+	++	Positive
	1	0	0	Negative
Total	**56**	**42(75%)**		**Positive**

Table 17: Comparision of CK-19 scoring in Benign, Encapsulated &MalignantLesions

CK-19 interpretation	Benign LesionsN= 36	Malignantlesions N=56	Encapsulated lesions N=8	P value
Positive	8	42	6	<0.001
Negative	28	14	2	

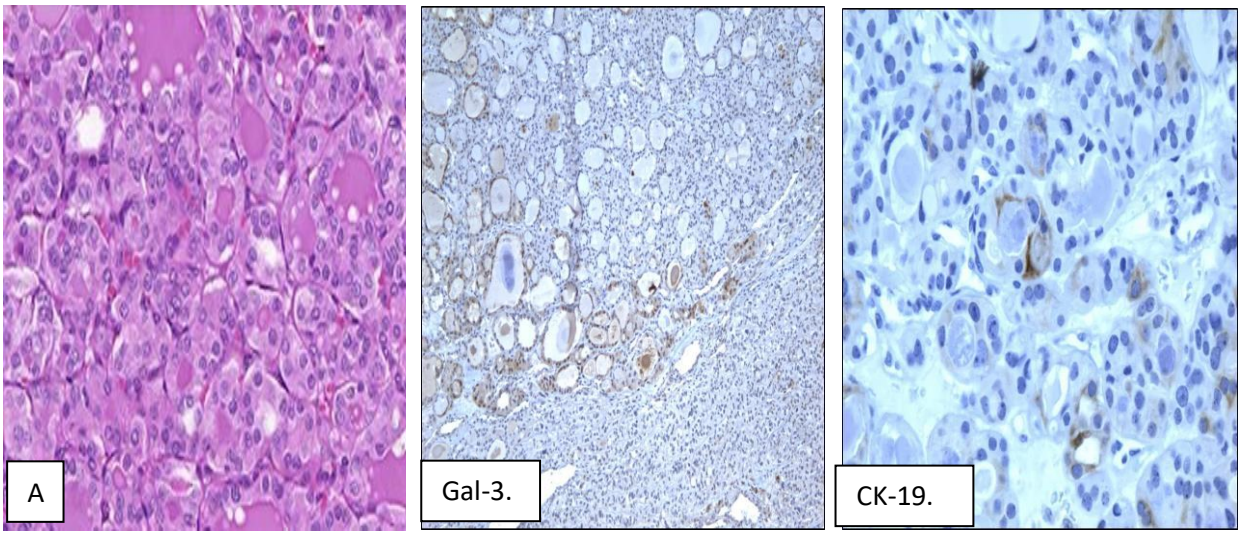


Fig 1: A case of Follicular adenoma on H&E showing Gal-3 weak cytoplasmicpositivity & Ck-19 Negative

Fig. 2: Gross specimen of total thyroidectomy with cut section showing grey whitetumor tissue(PTC)

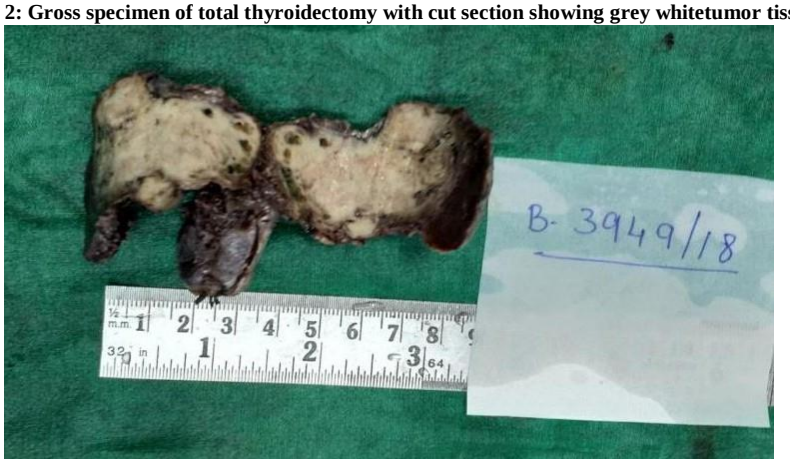


Fig. 3: A case of Hurthle cell adenoma on H&E showing Gal-3 cytoplasmic positivity.CK-19 Focal membranous positivity

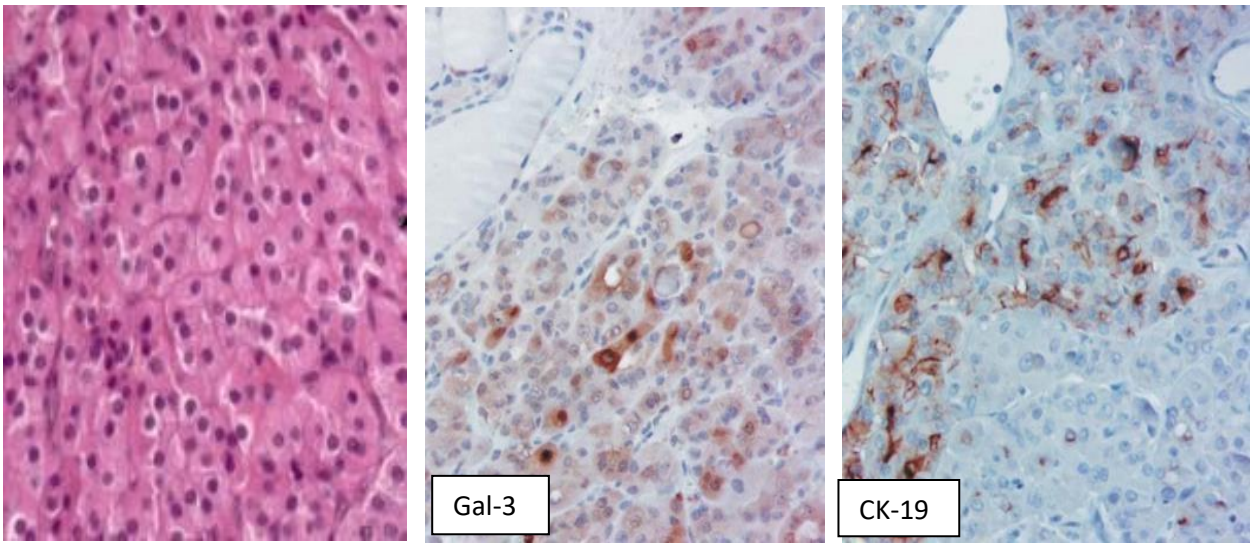


Fig. 4: A case of HTT on H & E showing diffuse cytoplasmic positivity for Gal-3

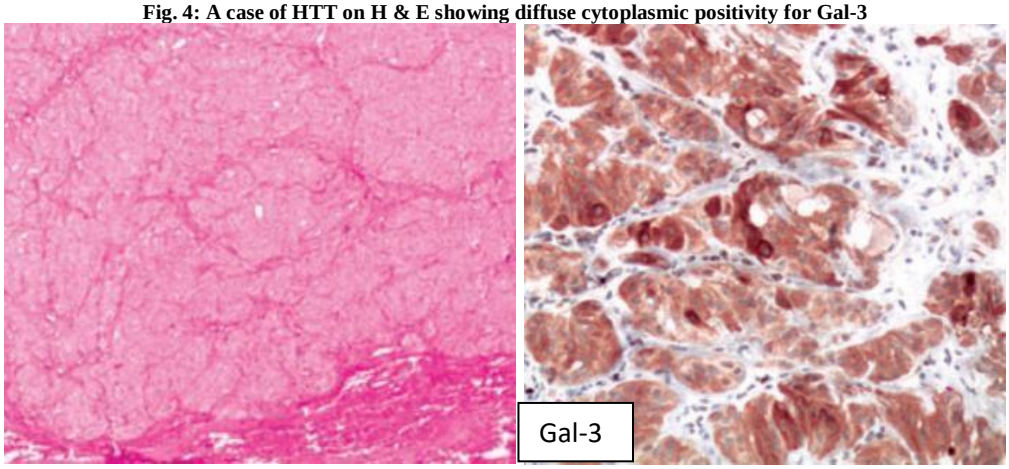


Fig. 5: A case of WDT-UMP on H&E showing Gal-3 Cytoplasmic positivity & CK-19membranous positivity

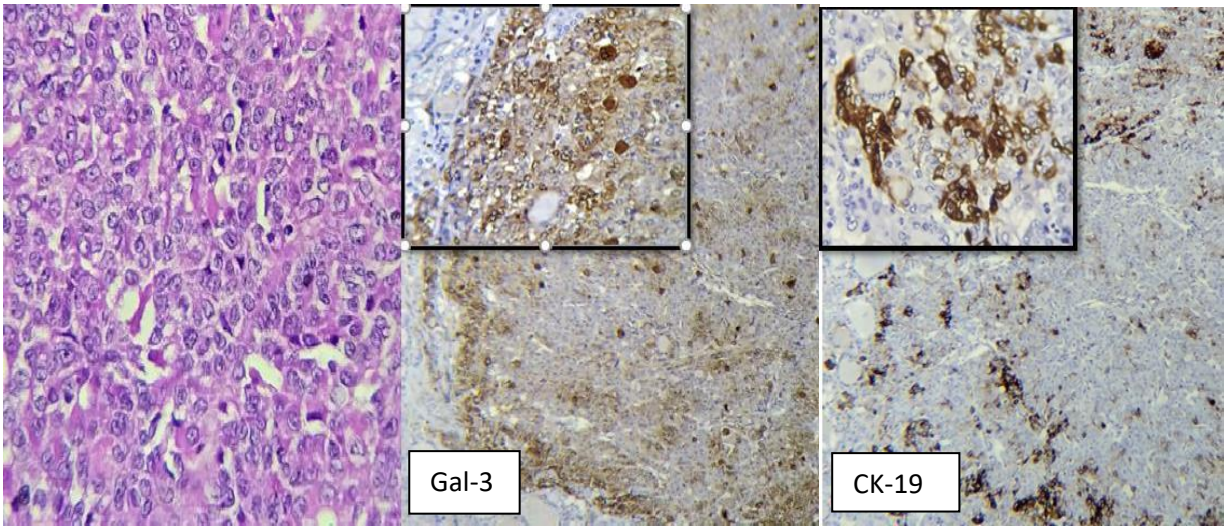


Fig. 6: A case of Conventional PTC with strong & diffuse positivity of Gal-3(cytoplasmic) & CK-19(membranous) C.H&E staining

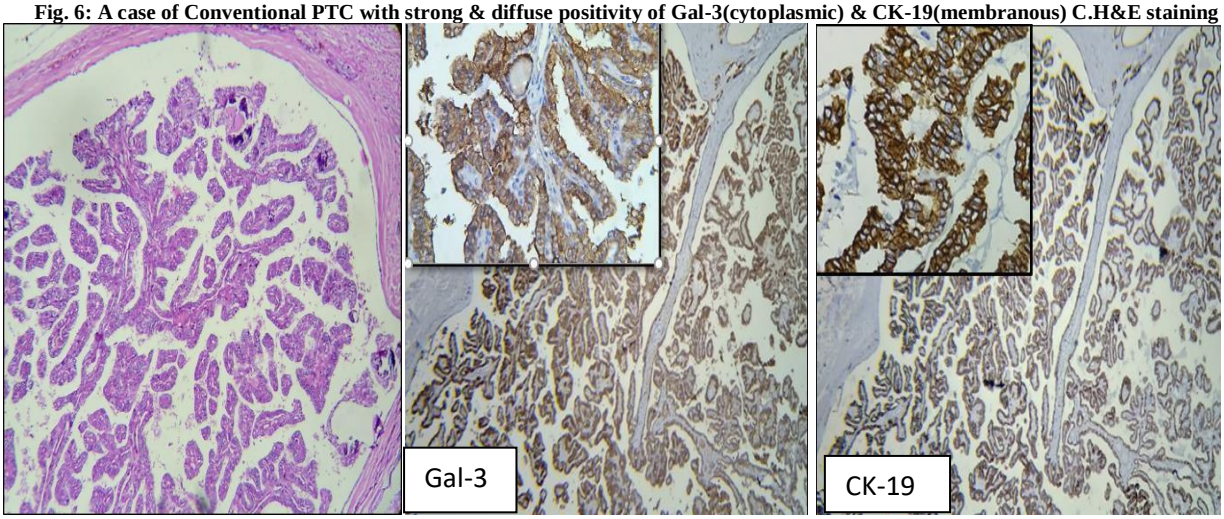


Fig. 7: A case of FVPTC on H&E showing Gal-3 cytoplasmic positivity & CK-19membranous positivity

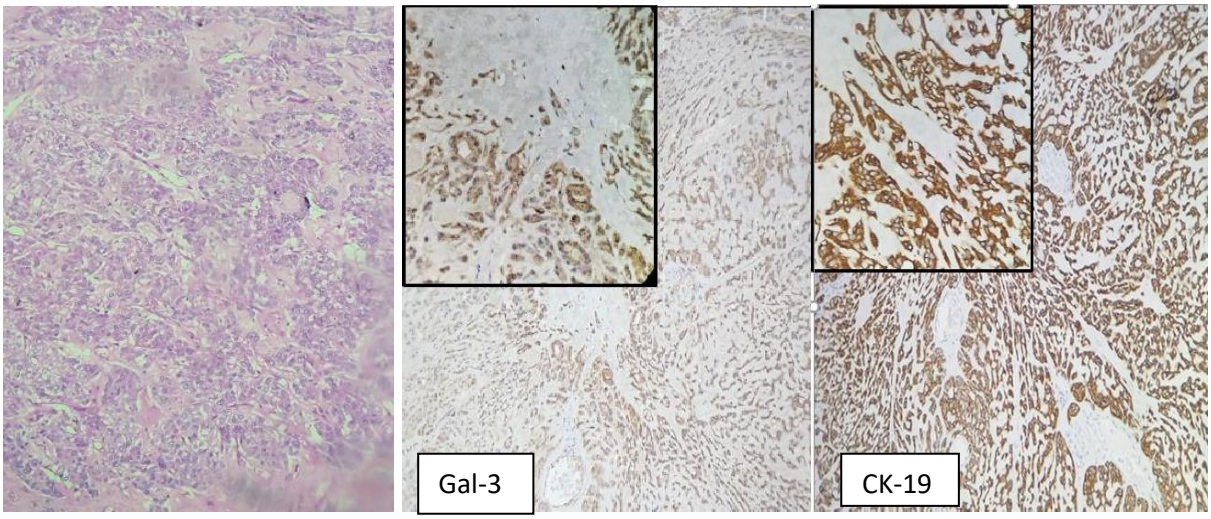


Fig. 8: A case of Papillary microcarcinoma on H&E showing Gal-3 (3+) cytoplasmicpositivity & CK-19 membranous positivity

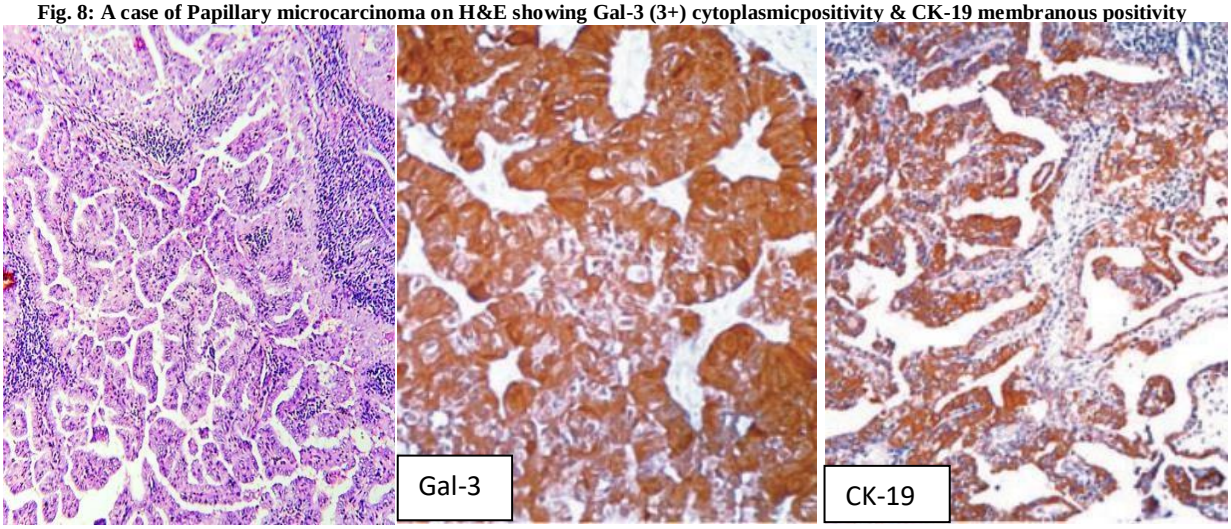
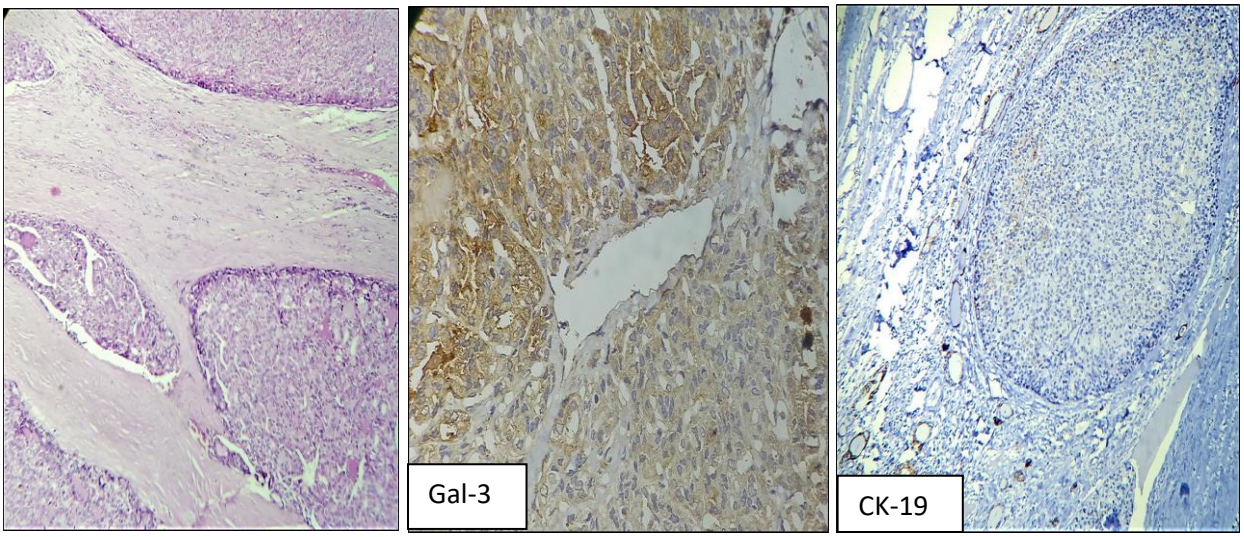


Fig. 9: A case of Follcular carcinoma on H&E showing Gal-3 cytoplasmic positivity& CK-19 Negative



Discussion

The present study is carried over in the Upgraded Department of Pathology, Osmania general hospital, Afzalgunj. Staining patterns of Gal-3 and CK-19 are evaluated in thyroid neoplasms.Thyroid cancer is the most common endocrine malignancy of the human body, accounting for approximately 2% of the cancers worldwide. Thyroid cancer is the sixth most common cancer in women. It is the most common cancer in women 20 to 34years[2,3]. About 2% of cases occur in children and teens.Women are 3 times more likely to have thyroid cancer than men, but women and men die at similar rates. This suggests that men have a worse prognosis than women when there is a diagnosis of thyroid cancer.

Over the past years, there has been a steep increase in the incidence of thyroid cancers, notably papillary thyroid cancer. The The decision favouring benign or malignant lesion has clinical consequence and implies different modalities of further treatment and management . Many IHC markers are studied and found useful in thyroid neoplasms, some of them being HBME-1, CD56, Galectin-3, Ret oncopreotein etc,. Among these Galectin-3 & CK-19 are useful markers in differentiating benign from malignant thyroid lesions.

In the present study, 100 cases of thyroid lesions included benign, encapsulated and malignant neoplasms.The range of the ages is comparable to the studies done by Pallavi Vijay Borkar et al[14]. and H.A.Alshenawy et al[15]. The ages in various studies ranged from 13-80 years. The median ages are also comparable to these studies. There is no statistical significance between the age, mean age, median age and expression of Gal-3 and CK-19. Even in the studies comparing the ages of patients, no statistical significance was established between the age and expression of Gal-3 and CK-19.

rise in incidence seems to be attributable both to the growing use of diagnostic imaging and fine-needle aspiration biopsy, which has led to enhanced detection and diagnosis of subclinical thyroid cancers, and environmental factors[11].Most follicular cell derived carcinomas are well differentiated malignancies which can be treated effectively by surgical resection 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. Exclusive follicular pattern in adenomatoid nodules and disruption of capsule in adenomas create difficulties in diagnosis by histopathology. However, papillary carcinomas are also prone to diagnostic discrepancies among pathologists[12].

Table 18: Comparison of age range and the median of present study with other studies

Studies	Age group	Median
Pallavi Vijay Borkar et al	20-70 years	-
H.A.Alshenawy et al	13-78 years	32.5
Vanessa Arcolia et al	9-76 years	42.5
Dunđerović et al	37-65years	53
BS Sumana et al	20-60 years	-
Present Study	**19-80 years**	**44**

Table 19: Comparison of male to female ratio in the present study with otherstudies

Studies	Male female ratio
Pallavi Vijay Borkar et al[14]	1:13
BS Sumana et al[13]	1:1.9
H.A.Alshenawy et al[15]	1:1.8
Vanessa Arcolia et al[16]	1:3.12
Dunđerović et al[17]	1:3.5
Present study	1:1.7

Gender distribution in the present study was having female preponderance with male to female ratio of 1:1.7. This was similar to other studies where maximum number of patients were females.

Table 20: Comparison of number of cases taken up in the present study with other studies

STUDY	NUMBER OF CASES
H.A.Alshenawy et al	70
Vanessa Arcolia et al	132
Dunđerović et al	201
BS Sumana et al	50
Y.J. Park et al	241
Beesley M F et al	69
Present Study	**100**

The number of cases taken in the present study is 50. Comparison of studies can be difficult because of the differences in number of cases taken in the study, age ranges of the patients and the male to female ratio of the study.

Table 21: Galectin –3 and CK-19 expression in benign neoplasms

Study	Gal-3	CK-19
M F Beesley & M K McLaren et al (n=28)	5(17%)	7(25%)
Y.J. Park et al (n=89)	4(4.5%)	15(16.9%)
Sumana et al **(n=20)**	3(15%)	-
H.A.Alshenawy et al (n=20)	4(20%)	7(35%)
Dunđerović et al (n=79)	28(35.4%)	23(29.1%)
Present study (n=36)	**10(27.7%)**	**8(22.2%)**

In the present study, benign lesions constituted 36 cases of which 20 were follicular adenoma and 6 cases were hurthle cell adenoma and 10 Hyalinizing trabecular tumor(HTT).

Galectin-3 expression is positive in 10(27.7%) cases including 5 out of 20(25%) cases of follicular adenomas , 3 out of 10(33.3%) cases of HTT and 2 out of 6(33.3%) cases of Hurthle cell adenoma which is similar to Dunđerović et al[17], H.A.Alshenawy et al.CK-19 expression is positive in 8(22.2%) cases including 5/20(25%) cases of follicular adenomas which is similar with Dunđerović et al[17] & Y.J. Park et al[18].Dunđerović et al Showed Gal-3 positivity in 11/27(40.7%) in follicular adenoma and 5/10(50%) in hurthle cell adenoma which is greater than present study. Expression of Galectin 3 is higher in malignant compared to benign thyroid lesions. Galectin 3 have been found to have higher immunoreactivity in papillary (also follicular variant) carcinoma compared to follicular adenoma.

CK-19 positivity in 6/27(22%) in follicular adenoma and 12/20(60%) in hurthle cell adenoma. It is overe xpressed in papillary thyroid carcinoma, diffusely and intensively in most cases. Over expression of this marker is related not just to PTC, but to malignancy. Discouraging thing, is that serious number of benign cases also expressed CK19, although focally and weakly. Only hyperplastic adenomas were completely negative.H.A.Alshenawy et al Gal-3 expression was observed in only 4/20 cases (20%), in which 2/5 were cases of MNG (40%), and 2/7 were cases of FA (29%) which is in concordance with present study.

CK-19 expression was observed in only 7/20 cases (35%), which consisted of 1/4 cases of Grave's disease (25%), 2/5 cases of MNG (40%,) and 4/7 cases of FA (57%) in contrast to present study. Gasbarri et al[20].Observed that galectin-3 is never expressed in benign thyroid lesions. Saggiorato et al[21] observed only 4/52 FA expressing Gal- 3 immunopositivity, whereas all thyroid cancers that those investigators analyzed were immunopositive for Gal-3.Orlandi et al[22] reported that although all the thyroid cancers that they analyzed were Gal-3 immunopositive, only 3/29 FA exhibited such positivity.

Gal-3 & CK-19 expression in Encapsulated lesions

In Present study out of 8 encapsulated lesions 2 were WDT-UMP and 6 NIFTP cases. Gal-3 positive expression is seen in 3 out of 6 NIFTP(50%) and all WDT-UMP(100%) cases. Ck-19 positive expression is seen in 2 out of 6 NIFTP(33.3%) cases and all WDT-UMP(100%) cases. H.A.Alshenawy et al studies show Gal-3 positive in 5 out 7 WDT-UMP(71%) cases and 4 out of 6 FT-UMP(67%) cases. highest sensitivity for Gal-3 was also observed in distinguishing FVPTC from FC and PTC from WDT-UMP (100% both) but the specifificity was low for both (20% and 29% respectively). Also observed that CK19 can differentiate FVPTC from FC and PTC from both WDT-UMP and FTs-UMP.Present study showed increased expression of both Gal-3 and CK-19 in encapsulated lesions in contrast to benign lesions which is in concordance with H.A.Alshenawy et al.In the present study, malignant neoplasms expressed high Gal-3 positivity than benign lesions which is similar with the above studies.

Xu et al(1995)[23] - For the first time they showed galectin 3 expression was different between normal and malignant thyroid tissues. In their study they showed all papillary and follicular thyroid carcinomas, which were derived from follicular epithelium showed strong and uniform expression of galectin 3. Medullary thyroid carcinomas which originated from parafollicular C cells of neural crest expressed lower levels of galectins and some of these tumors expressed no galectin. They further added that Galectin 3 had a potential role in transformation of thyroid tissue from benign to malignant state, either by increased expression of galectins occurred as a consequence of the neoplastic transformation or whether galectins played a role in acquisition of transformed phenotype. They concluded stating that Galectin 3 may serve as marker for thyroid malignancy and help distinguish between well differentiated thyroid carcinomas and benign adenomas.

Lymph node metastasis

In the present study Galectin 3 & CK-19 showed positive expression in lymphnode metastasis of PTC.According to a review by Takenaka et al[24], it was suggested that galectin-3 plays a role in metastasis through the induction of angiogenesis via its carbohydrate -binding capacity.The study by Kawachi et al[25] reported that a decreased level of galectin-3 may aid the release of cancer cells from the primary lesions form invasion and metastasis. It was explained that decreased galectin-3 may loosen the connection of tumour cells from the primary lesions to the stroma, and this loosening may facilitate extracapsular penetration, vessel invasion and distant metastasis.

In the present study the expression of CK-19 is seen extensively in PTC and its variants which is similar to above studies. 40 out of 45 cases of PTC and its variants showed CK-19 Positivity, out of which 28 were PTC, 9 FVPTC & 3 were papillary microcarcinomas . 24 out of 40 (60%) showed 3+ score , 14 (35%) showed 2+ score & 2(5%) showed +score. All of the follicular thyroid carcinomas were negative for CK-19 expression.

Barut et al[26]

studies showed strong and diffuse CK-19 expression in 28 out of 55(50%) PTC and its variants which is similar to the present study(60%). 2 out 10 Follicular carcinomas showed strong positivity for Ck-19 which is in contrast to the present study. The role of CK-19 in the diagnosis of thyroid carcinoma is controversial. This may be partially due to the subjectivity involved in assessing positive expression. Schelfhout et al[27]have found CK-19 expression in all tumor cells of papillary carcinomas, but it was absent or only focally present in follicular carcinomas and follicular adenomas. The use of monoclonal antibodies for galectin-3, HBME-1, and CK- 19 may provide significant contributions in the differential diagnosis of malignant thyroid tumors. Although focal galectin-3, HBME-1, and

CK-19 expression may be encountered in benign lesions, diffuse positive reactions for these three markers are characteristic for malignant lesions.

Medullary carcinoma

In the present study cases of medullary carcinoma showed negative expression. BS Sumana et al46 showed 50% cases positive. MF Beesley et al[19] showed 1 out of two cases positivity with gal 3. This was in contrast to cvejic et al who found positivity in 16/20 cases. Fernandez and bartolazzi et al showed 50 % positivity. Galectin 3 was not supposed to be not useful for detecting Medullary carcinoma in keeping with their origin from different cell line[13]

Table 24: Sensitivity and specificity of Gal-3 and CK-19 in malignant lesions in the present study.

Marker	Sensitivity	Specificity
Galectin-3	85.7%	54.5%
CK-19	75%	68.1%

The sensitivity and specificity of combined expression of Gal-3 and CK-19 in differentiating malignant from benign lesions are 90% and 82.14% respectively showing parallel increase in the sensitivity and specificity. CK-19 showed 75% sensitivity and 77% specificity in differentiating malignant from benign lesions which are similar to H.A Alshenawy et al and Gal-3 showed 85.7% sensitivity and 72.2% specificity.

H.A. Alshenawy et al[15]

showed 74% sensitivity and 81% specificity for CK-19 and Gal- 3 expression in differentiating malignant from benign lesions. Other studies showed a high sensitivity and specificity of CK19 in PTC. CD56 with HBME-1 were the best to differentiate benign from malignant, CD56, HBME- 1 and Gal-3 were the best in differentiating FVPC from FA, while CD56 and Gal-3 were the best to distinguish FC from FA. CD56 was the most specifific in distinguishing FVPC from FC while the sensitivity was the same as regards the other three markers. To distinguish FC from FT- UMP, the best were CD56 and Gal-3 while to differentiate PTC from WDT-UMP, thebest were Gal-3 and CK19.

Limitations

The histomorphological study of Gal-3 and CK-19 expression if combined with the cytological evaluation of the cases would have provided additional evidence for the diagnostic utility of Gal-3 and CK-19 in thyroid cancer. Even Though our study documented lower Gal-3 expression in FA compared to FTC and FVPTC, the number of cases of FTC and FVPTC are very less to arrive at a significant observation about the follicular patterned thyroid carcinomas.

Conclusion

Present study focuses mainly on the utility of Gal-3 and CK-19 expression in differentiating malignant thyroid lesions from benign neoplasms. Many cases especially in predominantly follicular-patterned adenomatous nodules and disruption of capsule in adenomas create difficulties in diagnosis by histopathology. The decision favouring benign or malignant lesion has clinical consequence and implies different modalities of further treatment and management.In this regard, the diagnostic approach to these tumours should include IHC markers that can aid in better assessment of morphologic details.

Gal-3 and CK-19 showed low expression in benign lesions, although some cases showed positivity, which were mostly focal, a diffuse strong positivity was seen inmajority of the malignant lesions.

Gal-3 is a useful marker for pre-operative diagnosis of thyroid neoplasms into benign and malignant lesions. CK-19 expression is predominantly seen in PTC and its variants aiding in differentiating FVPTC from FC.Combined use of CK-19 and Gal-3 increases the sensitivity and specificity in differentiating malignant and benign lesions. Further studies are required to establish the role of CK-19 and Gal-3 in encapsulated thyroid lesions as a diagnostic and prognostic tool in thyroid neoplasms.

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