Original Article

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Immunohistochemical Study of MUC1 and MUC5AC Expression in Gall Bladder Lesions

Pathology Section

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ABSTRACT

Introduction: Immunohistochemical (IHC) markers of mucin family are associated with various Gallbladder Lesions (GBLs).

Aim: To study the distribution of GBL with respect to age and sex as well as to analyse the IHC profile of MUC1 and MUC5AC in GBLs and attempt correlation with clinical and histopathological findings.

Materials and Methods: The present study was conducted over a period of six years. A technique of manual tissue array was employed for cases subjected to IHC using MUC1 and MUC5AC. Results were statistically analysed using software program "The Primer of Biostatistics 5.0".

Results: A total of 629 GBL were encountered. Out of 605 of non-neoplastic lesions, 32 (5.29%) expressed MUC1 while 515 (85.12%) cases expressed MUC5AC. Out of 24 cases of neoplastic GBL, 20 cases (83.33%) showed positivity for MUC1 and 9 cases (37.5%) were positive for MUC5AC. The rate of MUC1 expression was significantly higher in Gall Bladder Cancer (GBC) {18GB carcinoma (ca) +3 Carcinoma In Situ (CIS)} (85.71%) than chronic cholecystitis (4.71%). The positive rate of MUC5AC expression was significantly lower in GBC (28.57%) than chronic cholecystitis (87.19%). The percentage of cases showing MUC1 expression increased as the severity of disease progressed from hyperplasia to CIS. The percentage of cases showing MUC5AC expression decreased as the severity of disease progressed from hyperplasia to CIS.

Conclusion: In this study, 96.18% cases were non neoplastic GBL of which chronic cholecystitis (87.77%) was predominant. 3.81% of the GBL constituted for neoplastic lesions of which 75% were GBC. MUC1 showed higher rates of expression in neoplastic GBL. MUC5AC showed higher rates of expression in non neoplastic GBL. Expression of MUC1 and MUC5AC might be closely related to pathogenesis of neoplastic and non neoplastic GBL.

Keywords: Dysplasia, Gall bladder carcinoma, Metaplasia, Mucin markers

INTRODUCTION

Gall Bladder (GB) shows varied histomorphological lesions which include inflammatory, preneoplastic and neoplastic [1]. Amongst these chronic cholecystitis is known to be associated with various premalignant changes which eventually progresses to invasive carcinoma [1]. GBC is a rare disease in India associated with poor prognosis [2]. Early diagnosis is crucial for better patient management. Very few cases can be subjected to complete surgical tumour removal as a result of delayed presentation in majority of the cases [3].

IHC markers of mucin family are known to be associated with various GBLs [4,5]. MUC1 is membrane associated mucin, while MUC5AC is a characteristic secretory mucin [6]. Inflammation of the GB is accompanied by a higher level of MUC5AC expression [4]. Expression of MUC1 and MUC5AC are found closely related to carcinogenesis, clinical, biological behaviour and prognosis of GB adenocarcinoma (adeno ca) [5]. MUC1 expression is considered as a potential marker of malignant transformation and invasion of GB epithelium [7]. It is also known to be associated with invasion, lymph node metastasis and a non papillotubular type of carcinoma (ca). Also in adenomas, dysplasias and ca, the expression of MUC5AC tend to decrease, whereas MUC1 expression tends to increase [8]. The aim of this study was to study the distribution of GBLs with respect to age and sex as well as to analyse the IHC profile of MUC1 and MUC5AC in various GBLs and attempt correlation with clinical and histopathological findings.

MATERIALS AND METHODS

The present cross-sectional study was conducted over a period of six years from 2007 to 2012 in the Department of Pathology, Shrimati Kashibai Navale Medical College and General Hospital, Pune, Maharashtra, India. Ethical clearance was obtained from the Institute's Ethical Committee. All cases of cholecystectomies received for histopathological examination were included. The relevant clinical details, investigation findings, histomorphological features and final diagnosis were noted. One section each from body, fundus and neck of the GB and additional section from grossly abnormal appearing areas was taken. Section from the cystic duct and lymph node was taken if the GB contained the tumour. Lymph nodes were searched along the GB neck. Sections were further processed as routine surgical specimen. They were then stained with Haematoxylin and Eosin (H&E) and representative slides were studied. All the lesions in the surrounding mucosal lining epithelium of non neoplastic and neoplastic GB were documented.

IHC

A technique of manual tissue array confirming sufficient representation of different areas in the cores was used for IHC [9]. The primary antibodies used were MUC1 (Clone Ma 695, Novocastra) and MUC5AC (Clone CLH2, Novocastra). Sections from lung and muscle tissue were used as positive and negative controls respectively for MUC1. Sections from gastric mucosa and tonsils were used as positive and negative controls respectively for MUC5AC. MUC1 was expressed in the luminal border and cytoplasm of cancer cells. MUC5AC was mainly expressed in the cytoplasm of cancer cells.

Staining results were estimated semi quantitatively by agreement of two pathologists on the basis of the percentage of positive cells: negative-<10%, 1-10%–25%, 2-26%–50%, 3->50%. For statistical analysis, cases with staining in 10% or more of the cells were considered.

STATISTICAL ANALYSIS

A correlation was attempted between clinical, immunohistopathological findings using Pearson's Chi-square test and Fisher-exact test. Software program "The Primer of Biostatistics 5.0" (manufactured by McGraw-Hill) was used for analysis of MUC1 or MUC5AC expression. The results were considered to be significant when the $p<0.05$.

RESULTS

Out of 16072 histopathological specimens received, 629 (3.91%) were GBLs. Percentage of calculous cholecystectomies (71.45%) was higher than acalculous cholecystectomies (28.64%). Gall stones were present more commonly in females (63%) in the age group of 41-50 years.

Age and sex distribution of non neoplastic and neoplastic GBLs is given in [Table/Fig-1].

Mucin Expression in Non neoplastic GBLs

Out of 605 of non neoplastic GBLs, 32 (5.29%) expressed MUC1 while 515 (85.12%) cases expressed MUC5AC [Table/Fig-2]. All cases of Acalculous Cholecystitis (ACC) (160) were negative for MUC1 [Table/Fig-3]. Expression rate for MUC5AC was significantly lower in ACC (73.12%, 117/160) as compared to calculous cholecystitis (93.26%, 346/371) (χ^2=38.811; $p<0.001$) [Table/Fig-3].

Mucin Expression in Neoplastic GBLs

Out of 24 cases of neoplastic GBLs, 20 cases (83.33%) showed positivity for MUC1 and nine cases (37.5%) were positive for MUC5AC [Table/Fig-4].

Type of Gallbladder lesion		Cases	Males (%)	Females (%)	Peak age
Acute Cholecystitis		7	3 (42.8)	4 (57.2)	61-80
Acute on chronic cholecystitis		8	6 (75)	2 (25)	51-60
Chronic cholecystitis of usual morphology		531	207 (39)	324 (61)	41-50
Chronic cholecystitis other than usual morphologic variant	Chronic follicular Cholecystitis	5	4 (80)	1 (20)	41-60
	Atrophic	2	1 (50)	1 (50)	11-70
	Eosinophilic Cholecystitis	1	1 (100)	0	65
	Xanthogranulomatous Cholecystitis	4	0	4 (100)	41-50
	Adenomatous hyperplasia	8	3 (37.5)	5 (62.5)	41-50
	Glandularis proliferans	1	0	1 (100)	25
	Cholesterosis	10	3 (30)	7 (70)	31-40
Primary papillary hyperplasia		2	1 (50)	1 (50)	31-40
Polyp		3	1 (33.3)	2 (66.7)	21-40
Developmental anomaly	Biliary atresia	1	1 (100)	0	3 mths
	Choledochal cyst	7	3 (42.8)	4(57.2)	<1
	GI Heterotopia	1	0	1 (100)	52
Miscellaneous	Ascariasis of GB	1	0	1 (100)	35
	Cholecystic granuloma	2	0	2 (100)	21-50
	Gangrenous GB	4	3 (75)	1 (25)	65
	Empyema of GB	2	1 (50)	1 (50)	31-50
	Ischemic GB	1	0	1 (100)	40
	Inflammatory adhesion	4	2 (50)	2 (50)	61-70
Neoplasm	Adenoma	3	1 (33.3)	2 (66.7)	21-60
	Adenocarcinoma	15	8 (53.3)	7 (46.7)	51-70
	Papillary adenocarcinoma	2	0	2 (100)	61-70
	carcinosarcoma	1	1 (100)	0	55
	Carcinoma in situ (Bil IN)	3	1 (33.3)	2 (66.7)	41-60
	Total	629	251	378	

[Table/Fig-1]: Age and sex distribution in non neoplastic and neoplastic gall bladder lesions.
Bil IN- Biliary intraepithelial neoplasm

Type of non neoplastic lesions (no. of cases)			MUC1				MUC5AC			
605			0	1+	2+	3+	0	1+	2+	3+
Acute Cholecystitis		5	5	-	-	-	-	5	-	-
Acute cholecystitis in background of Xanthogranulomatous cholecystitis		2	2	-	-	-	-	-	2	-
Acute on chronic cholecystitis		8	7	-	1	-	-	6	2	-
Chronic cholecystitis of usual morphologic variant	Calculous	371	346	25	-	-	25	136	148	62
	Acalculous	160	160	-	-	-	43	37	48	32
Chronic cholecystitis other than usual morphologic variant	Chronic follicular Cholecystitis	5	5	-	-	-	1	4	-	-
	Atrophic	2	2	-	-	-	1	1	-	-
	Eosinophilic Cholecystitis	1	1	-	-	-	-	-	-	1
	Xanthogranulomatous Cholecystitis	4	4	-	-	-	2	2	-	-
	Adenomyomatosis	8	6	2	-	-	-	-	3	5
	Glandularis proliferans	1	1	-	-	-	-	-	-	1
	Cholesterosis	10	10	-	-	-	7	3	-	-
Primary papillary hyperplasia		2	2	-	-	-	2	-	-	-
Polyp		3	1	2	-	-	-	-	1	2
Developmental anomaly	Biliary atresia	1	1	-	-	-	1	-	-	-
	Choledochal cyst	7	7	-	-	-	3	4	-	-
	GI Heterotopia	1	1	-	-	-	-	1	-	-
Miscellaneous	Ascariasis of GB	1	1	-	-	-	-	1	-	-
	Cholecystic granuloma	2	2	-	-	-	-	1	1	-
	Gangrenous GB	4	4	-	-	-	3	1	-	-
	Empyema of GB	2	2	-	-	-	1	1	-	-
	Ischemic GB	1	1	-	-	-	-	1	-	-
	Adhesion	4	2	1	1	-	1	1	-	2

[Table/Fig-2]: Expression of MUC1 and MUC5AC in non neoplastic lesions.

Comparison of Mucin Expression between Non-neoplastic and Neoplastic GBLs

a) MUC1

Positive expression rate of MUC1 was significantly higher in neoplastic lesions (83.33%, 20/24) as compared to non neoplastic GBLs (5.29%, 32/605) (χ^2=175.255; p<0.001). The rate of MUC1 expression was significantly higher in GBC (18GBC+3CIS) (85.71%, 18/21) than chronic cholecystitis (4.71%, 25/531) (χ^2=173.440; p<0.001). Expression rate for MUC1 was significantly lower in calculous chronic cholecystitis (CCC) (6.47%, 24/371) as compared to GBC (18GBC+3 CIS) (85.71%, 18/21) (χ^2=122.357; p<0.001)

b) MUC5AC

Rate of MUC5AC expression was significantly higher in non-neoplastic lesions (85.12%, 515/605) as compared to neoplastic lesions of gallbladder (37.5%, 9/24) (χ^2=34.302; p<0.001). The positive rate of MUC5AC expression was significantly lower in GBC (18GBC+3CIS) (28.57%, 6/21) than chronic cholecystitis (463/531) (χ^2=49.850; p<0.001). Positive expression rate of MUC5AC was significantly higher in CCC (93.26, 346/371) as compared to GBC (18GBC+3CIS) (28.57%, 6/21) (χ^2=83.849; p<0.001).

Expressions of MUC1 and MUC5AC and their correlation with clinicopathologic parameters of malignant GB tumours are depicted in [Table/Fig-5].

Meticulous examination of the surrounding mucosal lining epithelia of the non neoplastic and surrounding lining epithelia of the neoplastic gallbladder mucosa showed presence of hyperplasia, metaplasia, dysplasia and CIS [Table/Fig-6]. Combination of various lesions was also noted in some cases [Table/Fig-7]. MUC1 and MUC5AC expression in various GBLs is shown in [Table/Fig-8,9] respectively.

Mucin Expression in Surrounding GB Mucosal Lining [Table/Fig-6]

The positive rate of MUC1 expression was significantly higher in GBC (83.33%, 15/18) than that in hyperplasia (4.35%%, 11/253) (χ^2=111.935, p<0.001). The positive rate of MUC5AC expression was significantly higher in hyperplasia (91.70%, 232/253) than that in GBC (16.67%, 3/18) (χ^2=75.744, p<0.001). Pyloric metaplasia was more common (29.38%, 156/531) type of metaplasia seen in chronic cholecystitis than intestinal metaplasia (13.37%, 71/531). There was significant difference between rate of expression of MUC1 in pyloric metaplasia (33.20%, 84/253) and GBC (83.33%, 15/18) (χ^2=16.117, p<0.001). No case of intestinal metaplasia showed expression for MUC1. Rate of expression for MUC5AC was significantly higher in metaplastic change (83.64%, 276/330) as compared to GBC (16.67%, 3/18) (χ^2=44.037, p<0.001). Both pyloric and intestinal metaplasia showed positivity for MUC5AC with no significant difference in the expression rates between them (χ^2=0.258, p=0.611). Rate of expression for MUC1 was higher in dysplasia (85.71%, 18/21) as compared to GBC (83.33%, 15/18) though not statistically significant (χ^2=0.057, p=0.811). MUC5AC expression was higher in dysplasia (57.14%, 12/21) than that in GBC (16.67%, 3/18) but this was not statistically significant (χ^2=5.108, p=0.024). All cases of CIS showed MUC1 expression. MUC5AC expression was higher in CIS (25%, 3/12) as compared to GBC (16.67%, 3/18) though not statistically significant (χ^2=0.009, *p*=0.926). The percentage of cases showing MUC1 expression increased as the severity of disease progressed from hyperplasia to CIS (χ^2=150.494, p<0.001). The percentage of cases showing MUC5AC expression decreased as the severity of disease progressed from hyperplasia to CIS (χ^2=55.431, p<0.001).

Type of lesion	Total	MUC1 + (%)	p-Value*	MUC5AC+ (%)	p-Value*
GB neoplasm	24	20 (83.33%)	<0.001	9 (37.5%)	<0.001
Calculous cholecystitis	371	24 (6.47%)		346 (93.26%)	
Acalculous cholecystitis	160	0 (0%)		117 (73.12%)	

[Table/Fig-3]: Correlation between expression of MUC1 and MUC5AC in calculous and acalculous chronic cholecystitis with gallbladder neoplasm.
Chi square test used

Type of neoplastic lesions		No. of cases (24)	MUC1				MUC5AC			
			-ve	1+	2+	3+	-ve	1+	2+	3+
Neoplasm	Adenoma	3	1	2	-	-	-	2	1	-
	Adenocarcinoma	15	1	2	1	11	12	1	2	-
	Papillary adenocarcinoma	2	2	-	-	-	2	-	-	-
	Carcinosarcoma	1	-	-	-	1	1	-	-	-
	Carcinoma in situ	3	-	3	-	-	-	1	2	-

[Table/Fig-4]: Expression of MUC1 and MUC5AC in neoplastic gallbladder lesions.

Clinicopathologic features		No. of cases	MUC1 +ve	p-value*	MUC5AC +ve	p-value*
Sex	Male	8	7(87.5%)	0.832	1 (12.5%)	0.832
	Female	10	8 (80%)		2 (20%)	
Age	<65 yrs	16	14 (87.5%)	0.737	2 (12.5%)	0.737
	>65 yrs	2	1 (50%)		1 (50%)	
Differentiation	WD	9	7(77.78%)	0.910	3 (33.33%)	
	MD	8	7 (87.5%)		0	
	PD	1	1(100%)		0	
T-Stage	T1	6	4 (66.67%)	0.853	0	
	T2	5	4 (80%)		2 (40%)	0.735
	T3	7	7 (100%)		1 (14.28%)	
LN metastasis	Negative	16	15(93.75%)		2 (12.5%)	0.737
	Positive	2	2 (100%)		1 (50%)	
Gallstones	No	12	10 (83.33%)	0.502	1 (8.33%)	0.502
	Yes	6	5 (83.33%)		2 (33.33%)	

[Table/Fig-5]: Expressions of MUC1 and MUC5AC and their correlation with clinicopathologic parameters of malignant GB tumours.
LN- Lymph node, WD- Well differentiated, MD- Moderately differentiated, PD-poorly differentiated
*p-value deduced after applying Fisher Exact Test.

Type of lesion	Total	MUC1 + (%)	MUC5AC+ (%)
Secondary Hyperplasia	194	9 (4.64%)	178 (91.75%)
Adenomatous Hyperplasia	59	2 (3.39%)	54 (91.52%)
Pyloric metaplasia	253	84 (33.20%)	209 (82.60%)
Intestinal metaplasia	77	0 (0%)	67 (87.01%)
Dysplasia	21	18 (85.71%)	12 (57.14%)
Carcinoma in situ	12	12 (100%)	3 (25%)
GB carcinoma	18	15 (83.33%)	3 (16.67%)

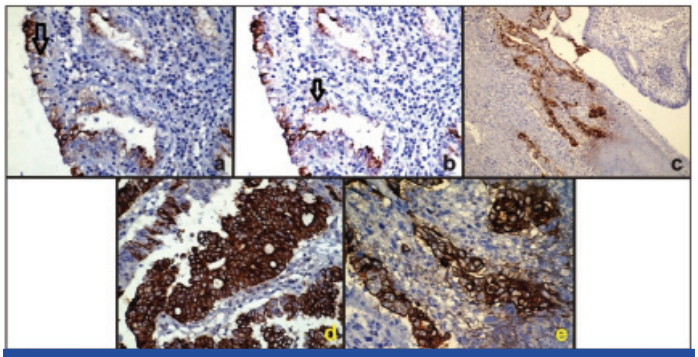
[Table/Fig-6]: Expression of MUC1 and MUC5AC in surrounding mucosal lining in GB lesions.

Lesions	No
Hyperplasia +metaplasia	182
Metaplasia +dysplasia +carcinoma in situ	2
dysplasia +carcinoma in situ	1
Dysplasia +carcinoma in situ +GB carcinoma	11
Hyperplasia +dysplasia +carcinoma in situ+ GB carcinoma	6

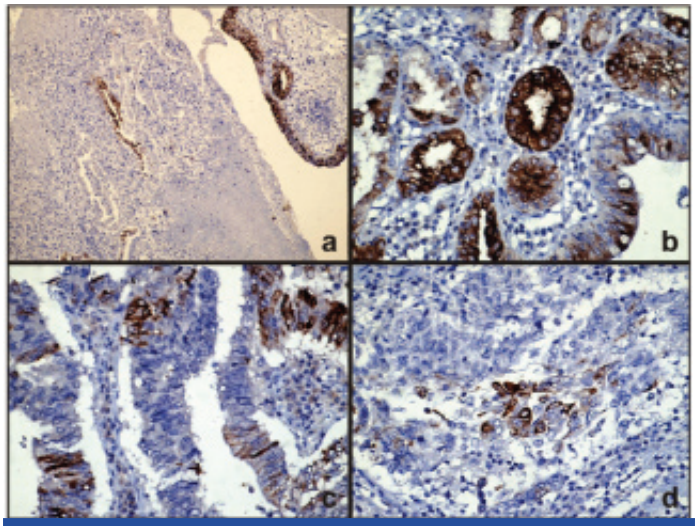
[Table/Fig-7]: Combination of various lesions in surrounding mucosa in GB lesions.

DISCUSSION

Only a small fraction of GBL encountered is neoplastic. However, chronic cholecystitis if left alone may progress through a series of premalignant changes to invasive cancer. This has led to recent studies insisting on the importance of precursor lesions and apomucin expression in cholecystectomy specimens [4,5,10]. Frequently calculous and acalculous cholecystitis present a large range of associated lesions such as hyperplasia, metaplasia, and dysplasia which have cancerous potential [10]. Our study included 84.42% (531/629) cases of chronic cholecystitis.



[Table/Fig-8]: MUC1 expression in GBL: a) Hyperplasia showing +1 positivity (40X); b) Metaplasia showing +1 positivity (40X); c) Dysplasia showing +2 positivity (10X); d) CIS showing +3 positivity (40X); e) Invasive carcinoma showing +3 positivity (40X). Arrow denotes the +1 and +2 positivity in the same photo photomicrograph.



[Table/Fig-9]: MUC5AC expression in GBL: a) Hyperplasia showing +2 positivity (10X); b) Metaplasia showing +3 positivity (40X); c) Dysplasia showing +1 positivity (40X); d) Invasive carcinoma showing +1 positivity (40X).

Gallstones are considered to be the most important risk factor for developing GBC, being reported in 70-98% cases of GBC in literature [11]. However, autopsy studies show that only 1-4% of cholelithiasis cases develop GBC as compared to 0.2% of acalculous cholecystitis [11]. In our study, 3.38% (21/621) of GB lesions showed presence of GBC (18GBC+3CIS). Also, 33.33% (6/18) of GBC cases were associated with gall stones. Recent studies provide quintessential evidence that chronic irritation either due to gall stones or due to changes in the bile owing to the reflux of pancreatic juice into the common bile duct as the basis for gall bladder carcinogenesis [3].

The results of our study strongly suggest that chronic cholecystitis produces a series of mucosal pathological changes which represents the precursor lesions of GBC [12]. We examined the MUC1 and MUC5AC expression in various GBL immunohistochemically. Few studies can be found describing the expressions of MUC1 and MUC5AC and their clinicopathologic significance in GBL in literature [4,13,14]. In our study, the percentage of cases showing MUC1 expression increased and percentage of cases showing MUC5AC expression decreased as the severity of disease progressed from hyperplasia to CIS [5]. Our study gives some evidence to support the pathogenesis of malignant GB lesions which progresses through epithelial hyperplasia, dysplasia, CIS and invasive cancer as seen in literature [5]. The positive expression rate of MUC1 was significantly higher and that of MUC5AC was significantly lower in GB adenoca than chronic cholecystitis in our study in accordance with findings of Xiong L et al., [5].

In present study, 18 cases were of carcinoma of which one case was poorly differentiated, eight cases were moderately differentiated and nine cases were well differentiated. Histomorphologically, 13 cases were of biliary type and two cases were of intestinal type. Two cases were of papillary adenocarcinoma, both of which were well differentiated. These tumours were named as intracystic (GB) papillary neoplasm with associated invasive ca according to 2010 WHO classification [15]. One case was carcinosarcoma with heterologous differentiation type which accounts for less than 1% of GBC [16]. Other histological variants of GBC were not encountered in present study. Also, reported were three cases of biliary intraepithelial neoplasia or CIS. There were three cases of adenomas of which one presented with multiple adenomatous polyps in the gall bladder as a part of familial adenomatous polyposis syndrome. A total of 2/3 adenomas showed low expression of MUC1 and all adenomas (3/3) showed MUC5AC expression [5]. This is similar to a study done by H. Mohan H et al., who reported 12 cases of GBC and two cases of adenoma out of 1100 cholecystectomies [1]. Sharma SP et al., recorded high incidence of 17.8% which could be related to geographical, ethnic or dietary factors [17]. Kim S-M et al., examined 54 cases of GBC of which 28, 21 and 5 were well, moderately and poorly differentiated carcinomas respectively [18].

In the present study GBC cases (2) with lymph node metastasis and T3 stage ca (7) cases were positive for MUC1. Moderately differentiated ca (8) and all T1 stage ca (6) cases were negative for MUC5AC expression. One case of carcinosarcoma of GB showed MUC1 positivity and lack of MUC5AC expression in epithelial component. There was no significant statistical correlation between age, sex or presence of calculi with expressive rates of MUC1 or MUC5AC. Earlier literature documents varying results of MUC1 expression in GB [5,18]. One study, mentions MUC1 expression of 56.8%, 38.6% and 4.6% in 25 well-differentiated 17 moderately and two poorly differentiated GBC respectively. However, there was no correlation between MUC1 expression and other clinicopathological features such as age, sex, T-stage and nodal status [18]. Another study reports significantly lower positive rates of MUC1 in cases with no metastasis of lymph node as compared to metastasis of lymph node, and invasion of regional tissues ($p<0.01$). The positive rates of MUC5AC were significantly higher in the well-differentiated adenoca cases than those in poorly differentiated adenoca cases ($p<0.05$) [5].

Mucin Expression in Surrounding GB Mucosal Lining

MUC1 was seen in 4.64% cases of secondary hyperplasia and 3.39% cases of adenomatous hyperplasia. 85.71% of dysplasia and 83.33% of GBC cases showed high MUC1 expression especially in invasive areas as seen in literature [18].

Pyloric metaplasia and intestinal metaplasia was seen in 40.22% (253/629) and 12.24% (77/629) cases of GBLs as seen in literature [19]. Pyloric metaplasia was seen in 224 cases of CCC, 15 cases of ACC and 14 cases of GB neoplastic lesions. Intestinal metaplasia was seen in 71 cases of ACC, five cases of ACC and one case of papillary adenocarcinoma of GB. In present study, no case of intestinal metaplasia showed MUC1 expression. However, 33.20% cases of pyloric metaplasia showed MUC1 positivity pointing towards similar characteristics of both lesions for tendency to express MUC1. Similar findings is noted in literature [3]. Duarte I et al., in his study of 162 cholecystectomy specimens found pyloric and intestinal metaplasia in 95.1% and 58.1% of cases [19]. Chronic inflammation owing to gall stones is mentioned in literature as being more responsible for causing both intestinal and pyloric metaplasia which subsequently leads to dysplasia and carcinoma transformation [3].

Mucin Expression and its Correlation with Clinico-Pathological Parameters

One study documented in literature showed lower MUC1 expression in T1 stage tumours than in higher stages. No correlation was observed between MUC1 expression and histopathologic type and grade in their study. However, they found angio-lymphatic

invasion to be associated with depolarized MUC1expression [7]. In the present study, high MUC1 expression was correlated with less differentiated tumours. Xiong L et al., previously examined the correlation of MUC1 and MUC5AC in GB adenoca, finding that the expression of MUC1 is linked with T-stage ($p<0.01$) [5]. Additionally, increased MUC1 expression or decreased MUC5AC expression was associated with decreased overall survival. Furthermore decreased MUC5AC expression was found to be an independent prognostic predictor [5]. MUC1 expression in GB carcinoma may signify histological dedifferentiation, increased proliferative activity and invasiveness [13].

Above findings re enforce the fact that though GB specimens are commonly encountered in surgical pathology, GBC cases are uncommon. It can be stated that the expression of MUC1 and MUC5AC might be closely related to the pathogenesis of neoplastic and non-neoplastic GBLs.

LIMITATION

Smaller sample size of the neoplastic GB lesions owing to its rarity.

CONCLUSION

In this study, 96.18% cases were non neoplastic GBLs of which chronic cholecystitis (87.77%) were predominant. 3.81% of the GBLs constituted for neoplastic lesions of which 75% were gall bladder carcinomas. GBL have significant female preponderance with non-neoplastic lesions having peak incidence during 5th decade of life and neoplastic lesions during 6th decade. MUC1 shows higher rates of expression in neoplastic GBLs. MUC5AC shows higher rates of expression in non neoplastic GBLs. Studying MUC1 and MUC5AC profile in every gall bladder neoplasm and its surrounding mucosa may help to understand the biology of the disease and tumourigenesis pathways enabling us to identify cancer risk patients which could aid in better management.

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