www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i7.189

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

Histopathological Audit of Gastric Tumours with Special Reference to Expression of MUC2 in Gastric Carcinomas – A Six Month Analysis in a Tertiary Care Centre

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Abstract
Objective: *The study is the histopathological audit of Gastric tumours in the Department of Pathology of RG Kar Medical college in six months, with special reference to MUC2 expression in gastric carcinomas.*
Materials and Methods: *All cases were grossly and microscopically examined and were classified under the WHO classification for Gastric tumours. The cases of Gastric carcinomas were further subjected to immunohistochemical examination by MUC2 and the results were correlated with the histomorphological grading and staging of the tumour.*
Results and Analysis: *There were altogether 20 cases in one year; 15 were of adenocarcinomas, 3 were of lymphoma; 1 of GIST; 1 of gastric carcinoid. Majority of the tumours were located in the gastric antrum/ pyloric region and most of them were moderately differentiated. The well differentiated carcinomas showed high expression of MUC2 and as the grade progressed the expression of MUC2 reduced. Hence MUC2 is inversely related to the grade of gastric carcinoma The expression of MUC2 and its reduction has a therapeutic indication as a high MUC2 expression can lead to fatal pseudomyxoma peritonei which can be limited by Anti- MUC2 therapy.*
Conclusion: *Gastric adenocarcinomas are the most common tumours among gastric neoplasms. They are more common in males. Mean presentation is 40-60 years. The lymphomas are mainly of Non hodgkins type. The expression of MUC2 decreased as the grade of the tumour increased hence the indication of anti MUC2 therapy is ore in lower grades of gastric carcinomas as compared to higher grades*
Keywords: *Gastric neoplasms, MUC2, Gastric cancer.*

INTRODUCTION

The vast majority of both benign and malignant tumours of the stomach are of epithelial origin, with mesenchymal and neuroendocrine tumours being much less common. Gastric adenocarcinoma comprises in excess of 95% of

malignant neoplasms of the stomach. Primary gastric lymphoma is the second commonest malignancy. Gastrointestinal stromal tumours (GISTs) and rare tumours, such as carcinoids, account for the remainder of cases. Gastric carcinoma (GC) is a malignant epithelial tumour of the stomach mucosa with glandular differentiation. It's etiology is multifactorial, most commonly it develops after a long period of atrophic gastritis. It has been seen that the mucinous type of adenocarcinoma is associated with pseudomyxoma peritonei which is a fatal condition. It has been stated that as the gastric tumour starts to show spread or metastasis the expression of MUC2 becomes lower. Mucins are gels which are produced by the mucosal surface to protect them. Stomach normally does not have MUC2 but when a carcinomatous process sets in stomach, a de novo expression of MUC2 is found. It has the characteristics of being expressed more in well differentiated carcinoma . The rate of expression decreases as the carcinoma progresses to moderate or poor differentiation.

OBJECTIVES

- Spectrum of histopathological features of gastric tumours
- To assess any change in expression of MUC2 in relation with different histopathological types and extent of differentiation of gastric carcinoma(GC)

MATERIALS AND METHODS

- **Study settings:** This study was conducted on a group of patients admitted in Department of Surgery, R G Kar Medical College & Hospital, Kolkata.
- All patients were provided with signed informed written consent.
- **Sample size-** 20
- **Time line:** 6 months

All the resection specimens of stomach which came to the department of Pathology were included in the study. Small biopsies were excluded. Clinical records of the patient including age, sex, addictions, co-morbidity and any associated endoscopy and biopsy reports were reviewed and recorded. All the gastric tumours were processed and the slides were stained with Hematoxylin and eosin stain. Immunohisto-chemistry for MUC2 was done on cases of gastric carcinomas to check for its expression.

Measurement of MUC2 expression

MUC2 positivity was defined as positive cell stain in at least 25% of the tumor cells in continuous scales or at least moderate staining in qualitative scales.

So,

- POSITIVE MUC2- >25% STAINING
- NEGATIVE MUC2- < 25% STAINING

RESULTS

- A total of 20 cases of stomach tumours were analysed .Out of the 20, 15 turned out to be carcinoma (Table I), 3 were cases of lymphoma, 1 was of GIST (Gastrointestinal stromal tumour), 1 was of Gastric Carcinoid.
- Out of 3 cases of lymphoma, 2 were of Diffuse Large B cell type.(Table II)
- It is found in our study that incidence of stomach cancer in fundo- cardiac is almost equal to that in pyloric- antral region.(Table III)
- The mucinous adenocarcinoma of stomach comprises of 41% of all the gastric carcinomas(Table III)
- The intestinal phenotype of gastric carcinoma does not seem to have any predilection for any site in stomach whereas the diffuse type is found more in the Fundo-cardiac region and the Mucinous type is found more in the pyloric- antral region.(Table III).
- Table IV shows that more well differentiated the gastric carcinoma, more is the MUC2 expression and the expression decreases as the histological grade of the carcinoma increases.

- We find that the mucinous adenocarcinomas in general shows positive MUC2 expression and the diffuse type is negative for MUC2 expression, but we cannot not find any specific relation between the intestinal phenotype and MUC2 expression.(Table V and figure V)
- Histiological grade of Gastric Carcinoma and MUC2 expression is inversely proportional to each other and statistically significant.
- MUC2 expression decreases the rate of lymphovascular invasion increases and it is found to be statistically significant.

TABLE I- Distribution of Gastric tumours according to histological subtype

TYPE OF GASTRIC TUMOURS	NO. OF CASES	%
GASTRIC CARCINOMA	15	75%
LYMPHOMA	3	15%
GIST	1	5%
CARCINOID	1	5%

FIGURE I- Pie chart showing cases in each category

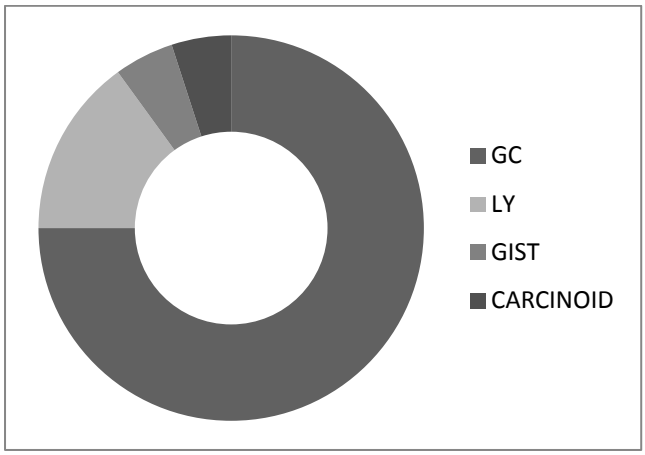


TABLE II- Distribution of cases according to the different types of lymphoma

Lymphoma	No. of cases	%
DLBCL	2	66.7%
MALTOMA	1	33.3%

GRAPH II- Pie chart showing distribution of lymphoma

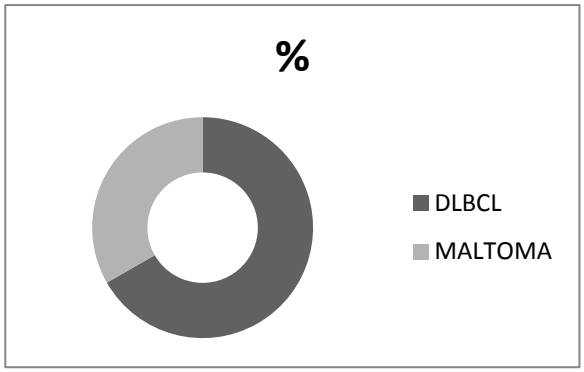


TABLE III- Distribution of the histological subtypes of gastric carcinoma according to sites of occurence

TYPE OF GC	NO. OF CASES	SITE IN STOMACH	
		F-C	P-A
INT	5(33.3%)	2(40%)	3(60%)
DYS	4(26.7%)	4(100%)	0
MU	6(40.0%)	2(33.3%	4(66.7%

GRAPH III A-

GRAPH III B -

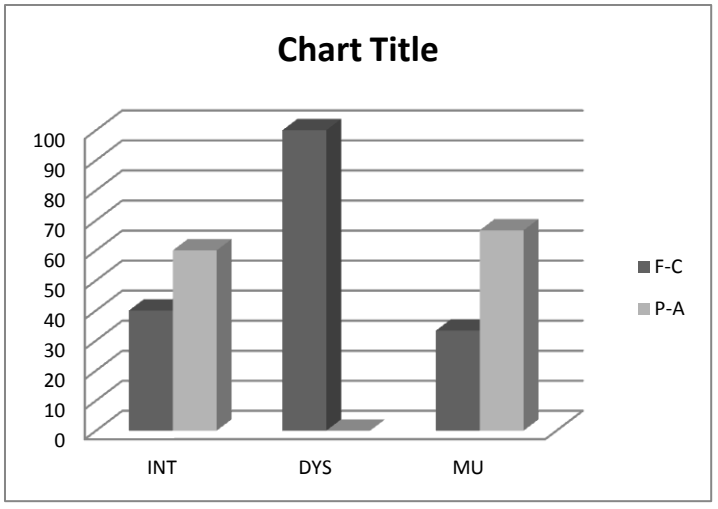


TABLE IV-Distribution of cases according Grade and MUC2 expression

GRADE OF STOMACH CANCER	MUC 2 EXPRESSION	
	Positive	Negative
WD(5)	4(80%)	1(20%)
MD(7)	3(42.8%)	4(57.1)
PD(3)	0	3(100%)

GRAPH IV

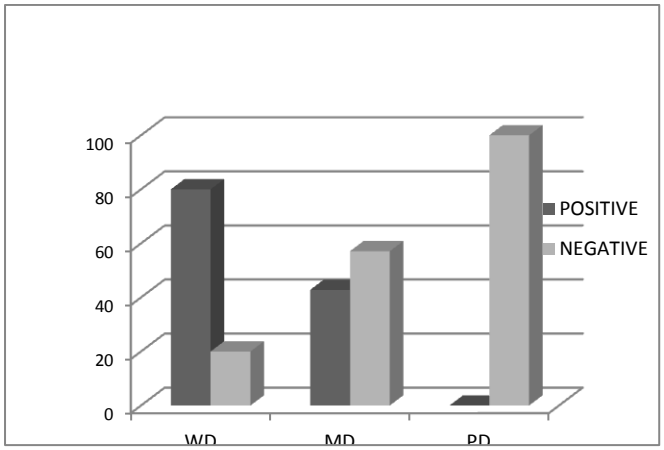
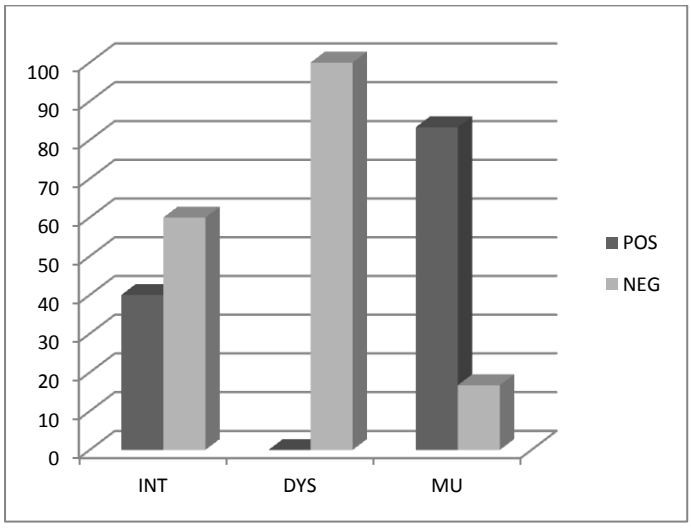


TABLE V Distribution of the histological subtypes of gastric carcinoma according to MUC2 expression

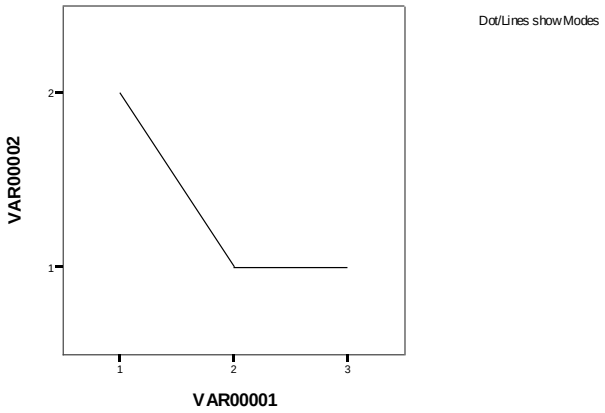
TYPE OF GC	NO. OF CASES	MUC2 EXPRESSION	
		POSITIVE	NEGATIVE
INT	5(33.3%)	2(40%)	3(60%)
DYS	4(26.7%)	0	4(100%)
MU	6(40.0%)	5(83.3%)	1(16.7%)

GRAPH V



GRADE OF GC vs MUC2

Variable	*Spearman's Rho*	*p*
• Grade of GC	1.000	*0.010(sig)*
• MUC2 Exp	-0.685	



MUC2 vs LVSI

Variable	*Spearman's rho*	*P*
• MUC2	1.000	*0.004(sig)*
• LVSI	- 0.745	

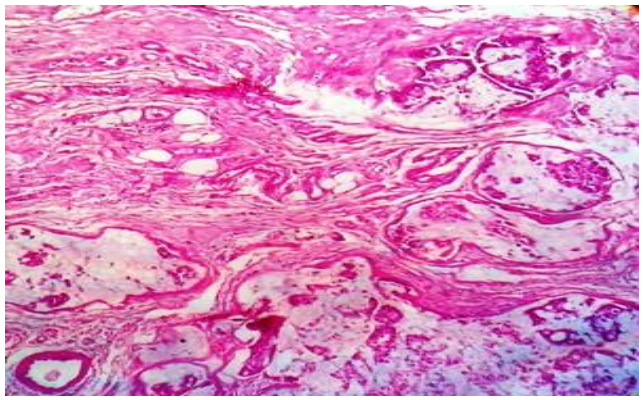


FIG 1- Photomicrograph showing histopathological features of Gastric carcinoma- Mucinous type (low power view)

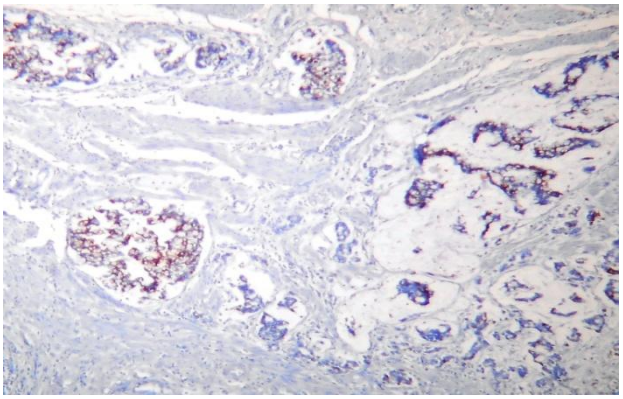


FIG 2- Photomicrograph showing positive expression of MUC2 in mucinous subtype of gastric carcinoma

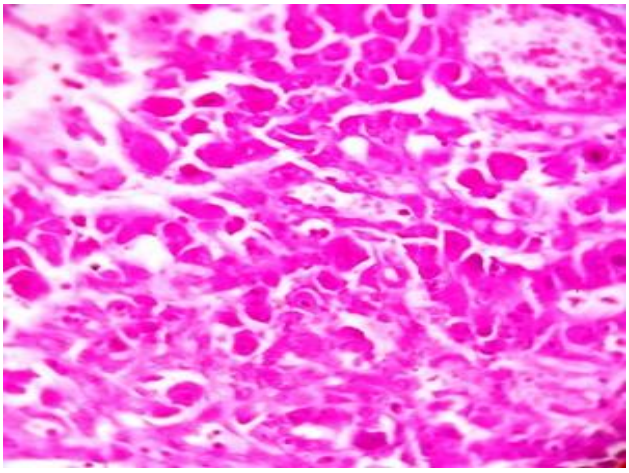


FIG3 Photomicrograph showing histopathological features of Gastric carcinoma- Mucinous type (low power view)

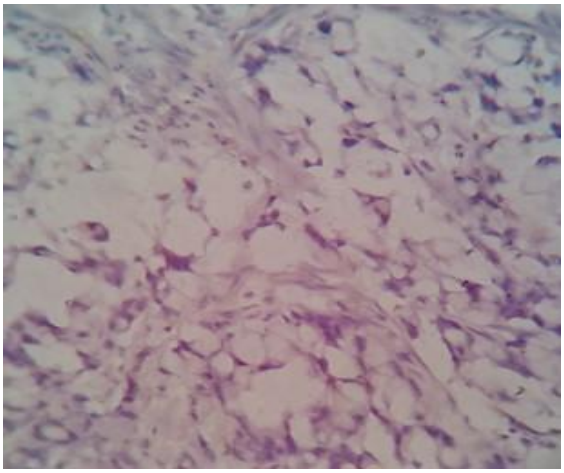


FIG 6- Photomicrograph showing negative expression of MUC2 in dyscohesive gastric carcinoma.

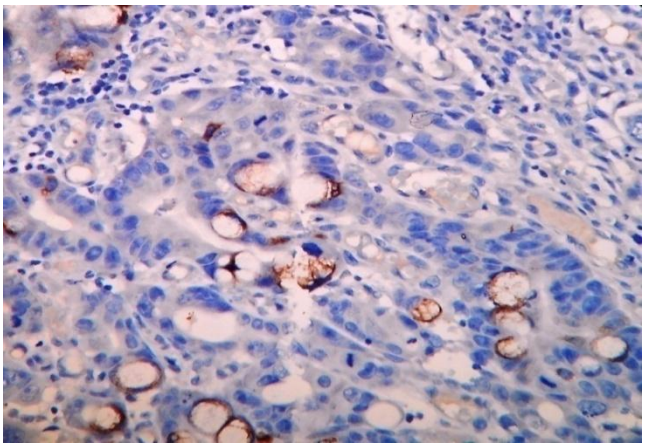


FIG 4- Photomicrograph showing positive expression of MUC2 in mucinous subtype of gastric carcinoma (high power view)

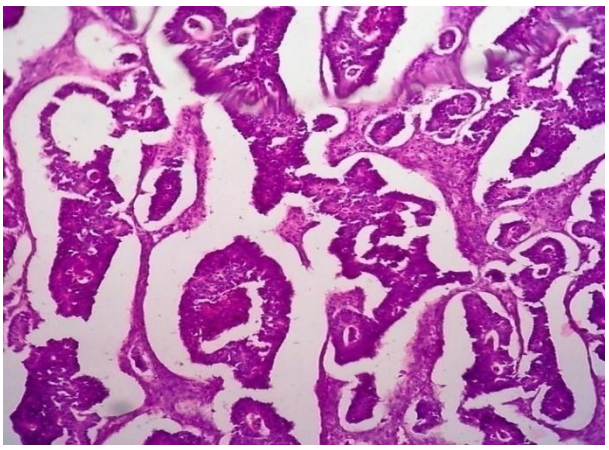


FIG7 Photomicrograph showing histopathological features of Gastric carcinoid.

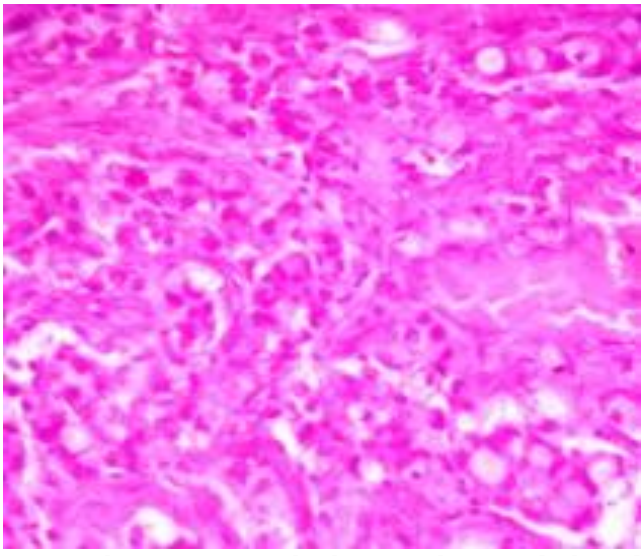


FIG 5 Photomicrograph showing histopatholgical features of dyscohesive gastric carcinoma

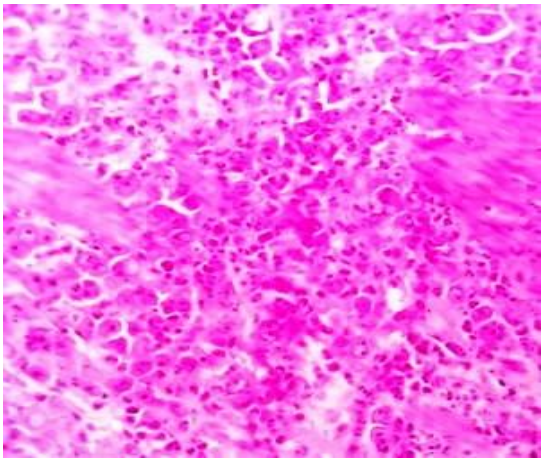


FIG8 Photomicrograph showing histopathological features of Non Hodgkin lymphoma(Diffuse Large B cell Lymphoma)

DISCUSSION

Gastric carcinomas comprise of a major chunk of gastric tumours. The next common tumour is gastric lymphoma. In our study, DLBCL was found to be the most common lymphoma in the stomach which was not concurrent with Raderer et al[1] who claimed that in gastric lymphoma spectrum Marginal zone lymphoma formed the major chunk followed by DLBCL (Table II). This was followed by 1 case of GIST and gastric carcinoid each comprising 5% each of the study spectrum which was found concurrent with the existing research.

Incidence of cancer in fundic-cardiac area and pyloric-antrum area has almost become equal. Table no.III has depicted the distribution of gastric cancer according to the site. It was observed that out of 15 cases of Gastric Carcinomas, 8 were in fundo- cardiac region. and 7 were in pyloric-antral region i.e 47% of the Gastric Carcinomas occurred in the Pylorus and antrum and rest in fundus and cardia. Robbins and Cotran[2] have agreed that the incidence of cancer in pylorus and antrum was reducing and that in fundo-cardiac region was on the rise.

In our small study spectrum, 40% of the Gastric Carcinomas were of Mucinous type. The Intestinal and the diffuse (poorly cohesive including signet ring WHO 2010) type made up 33% and 27% respectively.(Table no. III). Our finding did not match with WHO[3] data which found that mucinous adenocarcinoma of stomach comprised of only 10% of the gastric carcinomas.

Table IV shows the relation between MUC2 expression and histological grade of the Gastric carcinoma. Normal gastric mucosa did not show MUC2 expression. Intestinal metaplasia, specially incomplete type, led to de novo expression of MUC2[4] It was seen that MUC2 expression was positive in 80% of well differentiated carcinomas and the expression decreased as the histological grade of the carcinoma progressed and the expression was negative in all poorly differentiated carcinomas. Our finding was found concordant with Boltin D and Niv Y[5] and İlhan Ö et al[6] who also agreed that MUC2 expression was inversely proportional to the histological grade of Gastric carcinoma.

In the course of analysis we saw that out of 6 cases, 5 cases of Mucinous type of Gastric Carcinomas were positive for MUC2 expression and all the cases of diffuse (poorly differentiated Gastric carcinoma) were negative for MUC 2.(Table V)

Moving on to comparison of data statistically, a correlation between MUC2 expression and histological grade of Gastric carcinoma by Spearman's rho nonparametric correlation test has been shown. The correlation was inversely proportional at -0.744 and statistically significant at 0.01 ($p<0.05$). The associated graph also shows an inverse relation. Our study was found concordant with Utsunomiya T et al[7] who said that patients with MUC2+ mucin antigen staining in the gastric carcinoma showed significantly better survival than those with MUC2- mucin antigen staining. MUC2 antigen expression was a prognostic factor associated with a favorable outcome in patients

Lymphovascular invasion and perineural invasion has been noted to be higher in cases having reduced MUC2 expression.

CONCLUSION

Gastric carcinoma comprises of major chunk of the gastric tumours followed by lymphoma, GIST and carcinoid. Mucinous adenocarcinomas are more common histological type in our population. As carcinomatous processes set in stomach, it leads to de novo expression of MUC2. So MUC2 can be used as a potential marker for precursor lesion.

As the grade of the carcinomas increases MUC2 expression decreases. So, anobjectivity in reporting the grade of tumour on the basis of MUC2 expression can also help to determine adjuvant chemotherapy.

MUC2 expression is positive in almost 80% mucinous adenocarcinomas and almost absent in

the diffuse type.The intestinal type shows variable expression of MUC2.

As pseudomyxoma peritonei is a fatal condition associated with mucinous type, high MUC2 expression can help in assisting the treatment protocol by addition of anti-MUC2 therapy. Hence it also indicates that anti MUC2 is required more in low grade mucin secreting tumours than in high grade tumo urs as MUC2 is expressed more in the well differentiated tumours.

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