



## A Clinicopathological Study of Colorectal Carcinoma with Special Reference to Mucin Content

### KEYWORDS

colorectal carcinoma, mucin content, H&E, special stains

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**ABSTRACT** *Colorectal Carcinoma is the most common Gastrointestinal malignancy and is a major cause of morbidity and mortality. Mucin is one pathologic feature considered important for prognosis. Mucins are glycoproteins that are secreted specially by the goblet cells of the gastrointestinal tract. There are two types of mucins - neutral and acidic. In the present study an attempt was made to assess the colorectal carcinomas clinicopathologically with emphasis to age, sex, site, grading and to evaluate the mucin content in the tumor histochemically and to correlate the mucin content with the histological grading. In the study H&E was used as a routine stain for the histological diagnosis and special stain PAS (Periodic Acid Schiff) for presence of mucin and AB/PAS (Alcian Blue/Periodic Acid Schiff) to differentiate neutral and acidic mucins. It was observed that there was a rising trend in young patients and that acid mucins were predominant in comparison to neutral mucin.*

### INTRODUCTION:

Colorectal Carcinoma is a global oncologic problem faced by medical fraternity. It is a major cause of cancer associated with a high rate of morbidity and mortality in the western world[1]. Colorectal Carcinoma ranks among the three most commonly diagnosed malignant diseases worldwide with over one million new cases and approx. 500,000 deaths each year[2]. A higher risk of Colorectal Carcinoma were found in subjects consuming a diet poor in fibres[3] and rich in meat[4]. Non dietary causes include genetic disposition[5].

In India, Colorectal Carcinomas are not as common as in developed countries. According to a study by DN Rao, an estimated number of new colon cancers in 1991 were 5.5 per 1000 in males and 3.6 per 1000 in females whereas rectal carcinomas were 8.1 per 1000 in males and 6.1 per 1000 in females[6]. The same study estimated 0.1 per 1000 new cases for Colorectal Carcinomas in both sexes in Assam[6]. With economic development and changing lifestyle in our country, we have every reason to believe that in the near future Colorectal Carcinomas will be more frequent in our country too. Contrary to the earlier belief, Colorectal Carcinoma is not uncommon and are being diagnosed more frequently in Indian patients. But unfortunately a precise estimate of the magnitude of the problem in India is not possible due to lack of nationwide data storage system.

Colorectal cancer usually presents with altered bowel habits, abdominal pain, lump, weight loss and iron deficiency anemia. Though it is often regarded as a man's disease, the male - female ratio is becoming almost equal nowadays.

Certain pathologic features have been considered important prognostic determinants in adenocarcinoma of colon and rectum. One of the histological features of colorectal cancers with important impact on prognosis and therapeutic management of these patient is the mucin production by the tumour cells usually extruded into the stroma which is described as colloid or mucinous adenocarcinoma.[7]. According to Umpleby et al

Colorectal carcinomas of high mucin content carry a poor prognosis than those with other types of carcinoma[8]. Poor survival rate could be due to imbibition of water by the mucin which swells and cleaves the tissue planes, dispersing the malignant cells[8].

Mucin is a high molecular weight glycoprotein that is synthesized, stored and secreted by the epithelial mucosal cells especially the goblet cells[9]. Mucins' key characteristic is its ability to form gels and serving functions such as lubrication, cell signalling and forming protective chemical barriers[10] and contribute to the innate defensive system in mucosal immunology[11]. It seems that mucins play a role in the process of tumour progression, invasion and metastasis and also in tumour cell survival and protection against the host immune response[12]. Histochemically, the mucins are classified into neutral mucins and acidic mucins.

In the present study an attempt was made to highlight the distribution of the disease with special emphasis to age, sex, site and histopathology of colorectal carcinoma, to evaluate the mucin content in the tumor histochemically and to correlate mucin content with the histological grading.

### MATERIALS AND METHODS:

The study was done in a tertiary care hospital for a period of one year and age, sex, religion, relevant past and family history were noted. These patients had undergone operations like hemi-colectomy, segmental resection, subtotal colectomy, anterior resection, abdomino-perineal resection. Gross features of the specimen were recorded during the period of study.

Sections from normal colon were taken as control(Fig-1). Representative sections were taken and fixed in 10% formalin and processed for paraffin blocks preparation. 2-3 micron sections were cut for H & E ( Hematoxylin & Eosin) staining and histo-chemical stains namely PAS ( Periodic Acid Schiff) for presence of mucin and PAS / AB ( Periodic Acid Schiff / Alcian Blue) for nature of mucin i.e neutral and acidic. Ethical approval was taken from the institutional ethical committee.

**RESULTS AND OBSERVATION:****INCIDENCE:**

**AGE:** Age group of the patients were studied in male and female patients according to different decades of life . Overall the commonest age group was 40 – 49 years which accounted for 30%. The youngest patient was a 25 yrs old male.

**SEX:** There were 33 males and 17 females in the series with male : female ratio of 1.94:1.

**SITE DISTRIBUTION:** It was seen that the commonest site of growth was rectum (59%) followed by ascending colon (16%), transverse colon (12%) , sigmoid colon (8%) and descending colon (6%).

**HISTOLOGICAL TYPE OF CARCINOMA:**

Among the 50 cases, 45 (90%) cases were histologically diagnosed as Adenocarcinoma and 5 (10%) cases as Mucinous adenocarcinoma(Fig-2).

**TUMOUR DIFFERENTIATION (GRADING):** There were 23 (46%) cases of moderately differentiated carcinomas followed by 18 (36%) cases of well differentiated carcinoma and 9 ( 18 %) cases of poorly differentiated carcinoma.

**MUCIN CONTENT:** Following PAS stains, the results were tabulated (Table 1) according to the mucin content into different grades ranging from (+) to (+++) (mild, moderate, marked). Mild mucin were detected in 27 cases, moderate mucins in 3 cases and marked mucins in 5 (10%) cases. In most cases mucin content was considerably less. In 15 (30%) cases no mucin was detected.

Tumours with mucin content <50% were labeled as non – mucinous adenocarcinoma and while tumours with mucin content >50% were included in mucinous adenocarcinomas. On the basis of mucin content, 50 cases of colorectal carcinoma were divided into non–mucinous adenocarcinoma (n=45 ; 90%) and mucinous adenocarcinomas (n=5 ; 10%) .

PAS was done for the presence of mucin (Fig-3). Then Alcian blue – PAS staining was applied for the nature of the mucin : acid and neutral mucin( Fig-4 ).

**Table 1 below shows staining results of AB – PAS :**

MUCIN	MILD	MODERATE	MARKED
ACIDIC MUCIN	26	3	5
NEUTRAL MUCIN	1	0	0
NO MUCIN	15		

Of the 50 cases, 34 (68%) cases showed predominantly presence of acidic mucins ( mild in 26 (52%) cases , moderate in 3 (6%) cases and marked in 5 (10%) cases ). Mild neutral mucin was present in 1 (2%) case .There was absence of mucin in 15% cases.

**GRADING OF TUMOURS WITH MUCIN CONTENT:**

Out of the 50 cases there were 41 (82%) low grade tumours and 9(18%) high grade tumours(Table 2). Mucinous carcinoma showed a higher proportion of high grade tumours i.e 5 cases(55%) as compared to non-mucinous carcinomas which was 4 cases(44.4%).

**Table 2 depicting grades of tumours with mucin content:**

GRADE	MUCIN CONTENT		TOTAL
	PRESENT	ABSENT	

LOW GRADE	30	11	41
HIGH GRADE	5	4	9
TOTAL	35	15	50

**DISCUSSION:**

Amongst the gastrointestinal malignancy , colorectal carcinomas are the commonest variety. Although common in the developed countries, recent trends have shown that its incidence is increasing in the developing countries as well. In this section the finding of the present study will be discussed in context to other relevant studies

**Age Distribution:** In the present study, the commonest age group for colorectal carcinoma was 40-49 yrs which accounted for 30% of the cases. The age incidence of our study is consistent with the findings of Shah and Wani[13], who suggested that the commonest age group is 40-60 yrs. It is also slightly consistent with the findings of Qing et al [14] who found to be between 50-59 yrs. He also suggested that younger oriental patients were more common in comparison to white population .Though in the present study the commonest age group is 40-49 yrs, an important finding of the study was that 50% of the patients were below the age of 50 yrs.

**Sex Distribution:** In this study the male : female ratio was 1.94:1. In studies done by Smiddy & Goligher[15] ,Prabhakar[16], Tahilyani[17] ,D N Rao[6],Qing et al[14]and Leishram et al[18] it was found that incidence was more in males than in females which was slightly consistent with the present study.

**Site distribution:** The anatomic distribution shows that rectum accounted for 56%.Our findings regarding the site of tumour is not exactly consistent with other authors but it matches with them like the rectum as the commonest site[14,18,19].

**Histological patterns:** In a study by O'Connel et al[19],87.4% of the patients had adenocarcinoma and 11.6% had mucinous adenocarcinoma which was consistent with the present study i.e adenocarcinoma was 90% and mucinous carcinoma was10% .

**Table 3: Percentage of mucinous carcinomas in various series:**

SERIES	MUCINOUS ADENOCARCINOMA (%)
UMPLEBY ET AL (1985) <sup>[8]</sup>	11(U.K.),15(USA), 13.5(ARGENTINA)
SASAKI ET AL (1987) <sup>[21]</sup>	10-15
AJCC (2002) <sup>[22]</sup>	5-15
DU W. ET AL (2004) <sup>[23]</sup>	10-20
PRESENT STUDY	10

**Mode of differentiation:** In a study by Yamamoto et al[24] there were 19.7% well differentiated colorectal carcinomas, 65.9% moderately differentiated and 14.2% were poorly differentiated carcinomas. Leishram et al [18] suggested that 31.48% of the cancers are well differentiated, 37.4% were moderately differentiated and 31.4% are poorly differentiated. In our study we found 22% well differentiated,60% moderately differentiated and 18% poorly differentiated carcinomas which are slightly consistent with the other authors findings.

**Mucin Content:** PAS is a versatile and widely used technique for the demonstration of glycoproteins , carbohydrates and mucins. The Alcian blue- PAS technique is a simple procedure and appears to differentiate between neutral mucins and acid mucins. On the basis of mucin content we found adenocarcinoma (mucin> 50%) to be 10%, non-mucinous carcinoma (mucin<50%) comprising of 60% and no mucin in 30% of cases .The predominant mucin that was observed was acidic

mucin, 2% cases had mild neutral mucin. According to Suma KS, Nirmala[25], the incidence of mucinous adenocarcinoma (mucin >50%) were 19%. 14.4% cases had mucinous component <50% whereas there was no mucin in 66.96% cases. In a study done by Hadi NI et al[26], mucinous adenocarcinoma was 20% and non-mucinous adenocarcinoma was 80% and the predominant mucin detected was acidic mucin. Ionila M et al[27] observed that acidic mucins were predominant. Nikumbh RD et al[28] also observed that acidic mucins were predominant with traces of neutral mucin. In another study Ali U et al[29] found prevalence of acidic mucin.

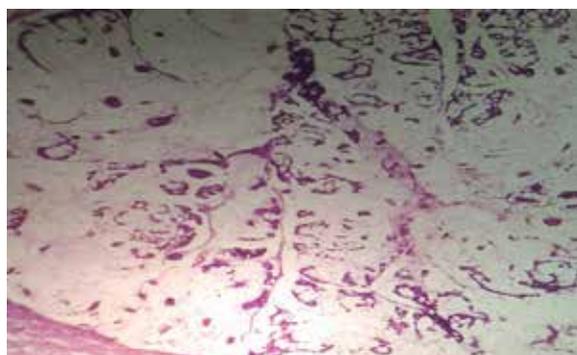
**Grading of tumours with mucin content:** High grade tumours accounted for 18% and low grade tumours comprised of 82%. Out of the high grade tumours 55.5% were mucinous carcinomas and 44.4% were non-mucinous carcinomas. In a study by Hadi NI et al[26] there were 85.71% low grade tumours and 14.28% high grade tumours. They also found that mucinous adenocarcinomas showed a higher proportion of high grade tumours as compared to non-mucinous adenocarcinomas which were consistent with the above author.

#### CONCLUSION:

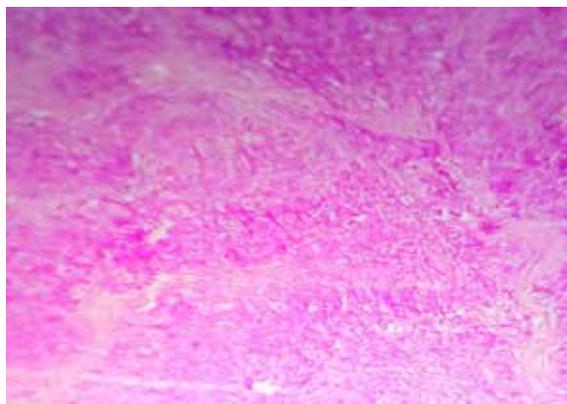
It was observed that colorectal carcinoma occurred in an early age group and moderately differentiated types formed the major group. So possibly there is hidden risk factor and hence a mass screening programme should be initiated. Regarding the mucin study, the acidic mucins were predominant. No definite conclusion could be made between tumour grading and mucin content. But mucin detection may be a valuable clue in early diagnosis and may help in reducing mortality. Although IHC is an advanced diagnostic modality, mucin study may provide a valuable and cost-effective tool for diagnostic histopathology.



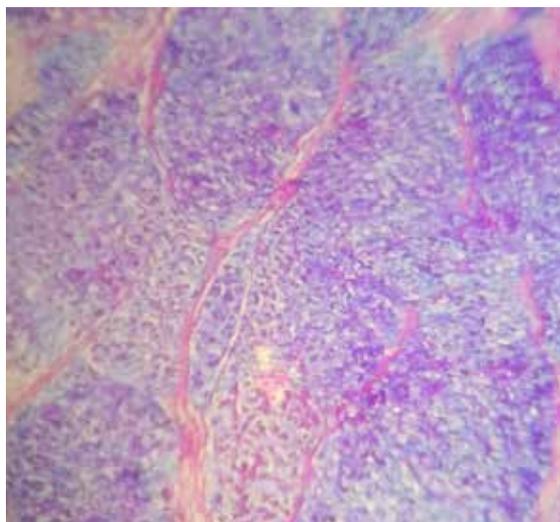
**Fig -1: Photo micrograph showing normal colon after AB/ PAS stain**



**Fig – 2 : Photomicrograph showing Mucinous Adenocarcinoma with H&E stain**



**Fig – 3 : Photomicrograph showing Mucin with PAS stain**



**Fig – 4 : Photomicrograph showing Acidic Mucin (blue) and Neutral Mucin (magenta) with Alcian blue / PAS stain.**

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