

**Original Article**

## Colorectal Carcinoma: Histopathological Analysis and Changing Trends in Various Parameters

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**Abstract**

*Colorectal cancer (CRC) is one of the major causes of morbidity and mortality world over. The aim of the present study was to analyse CRC according to age, sex, site, grade, stage and other important parameters and to determine the association of anatomical distribution, grade, stage of the tumor with the age of the patient. A cross sectional study was conducted on 100 resected specimens of CRC from January 2011 to July 2015 in our department of Pathology. All the cases were reviewed and the histopathological findings were recorded. The results were analysed using Chi square value ( $\chi^2$ ) and Fischer test. In our study, 100 cases of CRC were taken. The mean age at presentation was 57 years with male preponderance (64%). Colonic tumors were seen in 52% cases as compared to rectal tumors in 29% cases and rectosigmoid in 10% cases. Majority of the tumors were moderately differentiated (46%) and 41% were of TNM stage II. The analysis also revealed a statistically significant correlation between subsite, tumor grade and the age of the patient. Our results indicated an increase in the incidence of colonic tumors as compared to rectal tumors in all the age groups which can have an important clinical implication in selection of screening methods.*

**Keywords:** Age, anatomic distribution, colorectal carcinoma, grade.

**Introduction**

CRC is often seen in the elderly. However, there has been a significant rise in the incidence of CRC in younger individuals. Regarding the site of the tumor, rectal carcinomas were predominant as compared to colonic tumors. Presently, higher incidence of colonic tumors is observed as compared to rectal and rectosigmoid tumors. Thus a shift of tumor location to proximal parts of the colon is observed. With the rising incidence of

CRC world over and its varying trends, continuous monitoring and evaluation with more detailed data can be helpful in early detection and management of the disease.

Colorectal cancer (CRC) is the fourth most common cancer in men and the third most common cancer in women all over the world.<sup>[1]</sup>

The lifetime risk of developing CRC is about 1 in 20 (5.1%) and the mortality rate is also on a rise. The key etiological factors involved in develop-

ment of CRC are environmental, dietary and genetic which may vary with race, age, sex, geographic distribution and anatomic location in the large intestine.<sup>[2,3]</sup> CRC develops through a multistage process resulting from the progressive accumulation of genetic mutations mainly in the Wntsignaling pathway.<sup>[2]</sup>

The majority of carcinomas that arise from the large intestine are epithelial adenocarcinomas that originate from columnar epithelium of the colon and rectum.<sup>[4]</sup>

More than 95% of CRCs are adenocarcinomas. Overall percentage of adenocarcinoma increases with age. The mucinous and signet ring adenocarcinoma are seen more commonly in younger patients. An overall incidence of sigmoid tumors is more followed by rectum and caecum.<sup>[5]</sup>

However, several studies haveshown variations in the site of CRC with an overall proximal shift in its anatomical distribution.<sup>[3]</sup>

This study is undertaken to determine the frequency of occurrence of various clinicopathological parameters in CRC along with the correlation of age with tumor subsite, grade and stage.

**Materials and Methods**

The present cross sectional study was conducted in our department from January 2011 to July 2015. A total of 100 cases of colorectal carcinomas involving the colon & rectum were collected. All the resected specimens of colorectal carcinoma were included in the study and all biopsies, partially fixed and unfixed specimens were excluded. The institutional ethics committee clearance was obtained prior to conducting this study.

The clinical history & endoscopic findings were collected. The gross specimens obtained after surgery were examined in detail. Tissue was fixed in 10% buffered formalin, and processed by paraffin embedding. The blocks were serially cut, each of 3-5µ thickness and the sections counterstained with H & E. All the cases were reviewed thoroughly and the histopathological findings were recorded.

The data was analysed by proportions and tables. Various morphological features were analysed for

their frequency and were correlated with age using Chi square value ( $\chi^2$ ) and Fischer test wherever appropriate. P value of <0.05 was considered to be significant. SPSS version 16.0 (Statistical Product for Services Solutions) was used for analysing the data.

**Results**

A total of 100 cases of CRC were studied for the various clinicopathological parameters as shown in Table1.

**TABLE1:** Clinicopathological variables in CRC

Clinicopathological parameters		Frequency	Percentage (%)
Age (years)	20-40	13	13
	41-60	43	43
	>60	44	44
Sex	Male	64	64
	Female	36	36
Tumor size (cm)	<5	33	33
	≥5	67	67
Tumor location	Colon	52	52
	Recto-sigmoid	10	10
	Rectum	29	29
	Not specified	9	9
Tumor type	Well differentiated	42	42
	Mod. differentiated	46	46
	Poorly differentiated	3	3
	Undifferentiated	2	2
	MUC*	4	4
	MANEC**	3	3
Histological Grade	1	32	32
	2	56	56
	3	10	10
	4	2	2
Lymph node metastasis	Positive	38	38
	Negative	62	62
Lymphovascular invasion	Present	11	11
	Absent	89	89
Perineural invasion	Present	4	4
	Absent	96	96
Mitosis	1-4	37	37
	≥5	63	63
Necrosis	<50%	72	72
	>50%	28	28
Modified Duke's Stage	A	0	0
	B	62	62
	C	38	38
TNM stage	I	20	20
	II	41	41
	III	39	39

\*MUC: Mucinous adenocarcinoma, \*\*MANEC: Mixed adenoneuroendocrine carcinoma

Correlation of anatomic distribution, grade and stage of the tumor was done with respect to age of the patient as shown in Table 2

**TABLE 2:** Anatomic distribution, grade and stage of CRC with respect to age

Variables		Age groups (yrs)		
		20-40	41-60	>60
Site (p value 0.033)	Colon	38.5	44.2	63.6
	Rectum	30.8	39.2	18.2
	Rectosigmoid	0	9.3	13.6
	Not specified	30.8	7	4.5
Grade (p value 0.049)	1	38.5	18.6	43.2
	2	38.5	69.8	47.7
	3	23.1	9.3	6.8
	4	0	2.3	2.3
TNM Stage (p value 0.085)	I	30.8	9.3	27.3
	II	23.1	53.5	34.1
	III	46.2	37.2	38.6
Modified Duke's stage (p value 0.715)	A	0	0	0
	B	53.8	65.1	61.4
	C	46.2	34.9	38.6

The mean age at presentation in CRC was 57 yrs. Males were 64% and females were 36%. Maximum number of cases were of >5 cm diameter (67%). The commonest location was colon 52%, followed by rectum 29% and rectosigmoid 10%. Percentage of cases in right hemicolon, left hemicolon, transverse colon and sigmoid being 19%, 5%, 3%, 25% while rectal carcinomas accounted for 29% of cases. Moderately differentiated tumors were the most frequent (46%) followed by well differentiated (42%). MANEC cases were few (3%). Grade 2 cases were 56 %, grade 1 were 32 %, grade 3 were 10% and grade 4 carcinomas were 2%. Metastatic nodal deposits were seen in 38% cases. Carcinomas with modified Duke's stage B were most common(62%) and 41% were TNM stage II. Lympho vascular invasion and perineural invasion were associated with 11% and 4% cases respectively (as depicted in Table).

**Gross photographs of Colorectal carcinoma resected specimens**



**B. Ulcerative growth pattern in the rectum**



**C. MANEC of ascending colon**

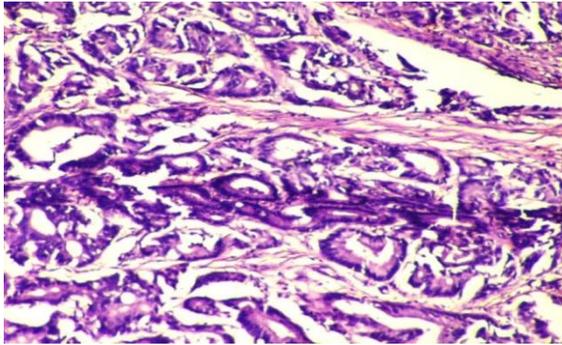


**D. Infiltrative growth pattern in the colon**

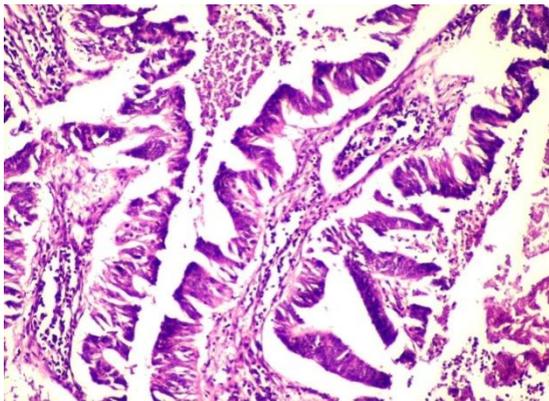


**A. Ulceroproliferative growth in the rectum**

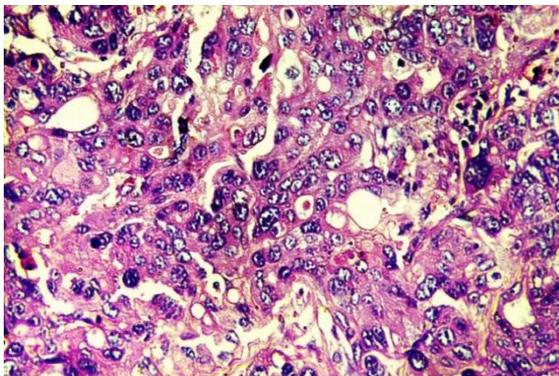
## Microscopy in CRC



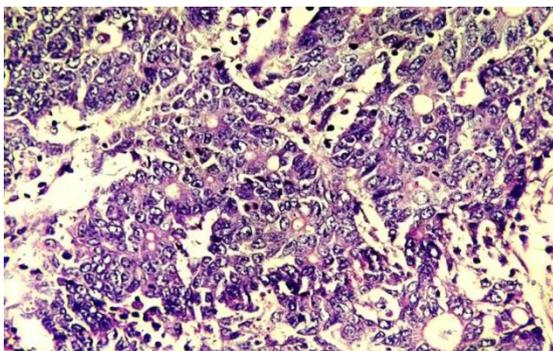
**A. Well differentiated adenocarcinoma**  
[H&E, 200x]



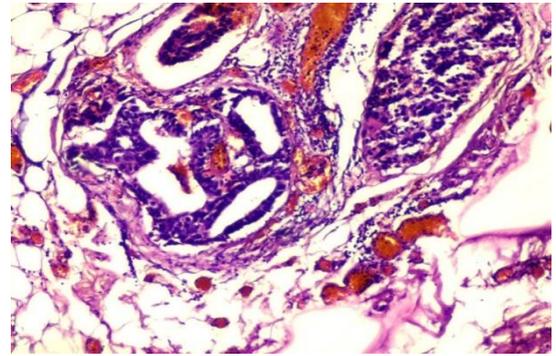
**B. Moderately differentiated adenocarcinoma** [H&E, 200x]



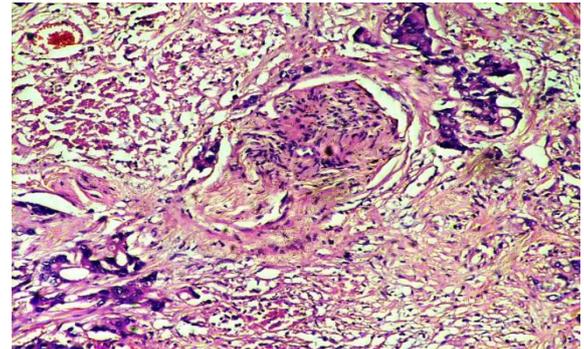
**C. Poorly differentiated adenocarcinoma**  
[H&E, 200x]



**D. Undifferentiated adenocarcinoma**  
[H&E, 200x]



**E. Vascular invasion** [H&E, 200x]



**F. Perineural invasion** [H&E, 200x]

**Discussion**

With the steady rise in the incidence of CRC, it is essential to apply appropriate diagnostic techniques to reduce the morbidity and mortality associated with it.<sup>[6]</sup>

The mean age at presentation in our study was 57 years. In concordance with our study, Efremidou et al<sup>[7]</sup> observed a higher frequency of CRC in older age ( $p = 0.002$ ), similarly Musthafa et al<sup>[8]</sup> and Chattar-Cora et al<sup>[9]</sup> found mean age at diagnosis to be 58.4 and 60.4 years respectively. In the West, the incidence of colon and rectal cancers have shown an increase between the age group of 50-80 years.<sup>[10]</sup>

Although CRC is often seen in the elderly, some studies have reported a significant rise in the incidence of CRC in younger individuals.<sup>[11,12]</sup> Deoet al<sup>[13]</sup> reported a mean age at presentation of 45.3 years and Suryadevara et al<sup>[10]</sup> reported the mean age to be 47 years in males and 51 years in females. Regarding the site of the tumor, we found a higher incidence of colonic tumors as compared to rectal and rectosigmoid tumors. In contrast, Suryadevara<sup>[10]</sup> found 80% of their cases as rectal cancers, Chattar-Cora et al<sup>[9]</sup> found tumors of

distal colon and rectum to be more than 70%. Peedikayil et al also found most of the tumors distal to the splenic flexure.<sup>[8]</sup>

In agreement with our study, Musthafa et al saw an overall proximal migration of CRC.<sup>[8]</sup> Also in the West a shift of tumor location to proximal parts of the colon is observed.<sup>[14]</sup> This trend has been noticed also in Asian countries like Korea and Japan. In Japan this shift was seen due to a decrease in the incidence of rectal cancer.<sup>[15,16]</sup>

The influence of age of the patients on the subsite of the tumor was studied and it was found that incidence of colonic tumors was more followed by rectal and rectosigmoid tumors under each category of age groups considered and this association was statistically significant (p value <0.05). Also, as the age advanced, percentage of colonic and rectosigmoid carcinomas increased, while no such trend was seen in rectal cancers.

Musthafa et al<sup>[8]</sup> observed that proximal lesions presented at a later age as compared to distal lesions (63.2 years for the right colon and 58.5 years for the rectum) and this difference in ages was significant. Seydaolu et al<sup>[17]</sup> observed an increase in the incidence of right-sided colon cancers in advanced age groups (>70yrs) of males and increase in younger age groups (>50yrs) of females. There was a corresponding continuous decline in the percentage of rectal cancer in both genders.

On the contrary, Friedenberget al and Gomez et al concluded that the variations in subsite was unrelated to age or gender distribution.<sup>[18,6]</sup>

This proximal shift mainly occurs in industrialized countries, where the incidence of neoplasm is greater. All the current epidemiological studies report a large geographic variation in the anatomic distribution of lesions<sup>[19]</sup>, due to different causes including the impact of environmental risk factors such as diet<sup>[20]</sup> and the difference in the frequency of hereditary CRCs.<sup>[21]</sup>

With regard to grade of the tumor, statistically significant (p value <0.05) association was seen between the age of the patient and tumor grade. In the age group of 20-40 yrs, there was an equally high prevalence of well and moderately different-

iated carcinomas (38.5% each). In increasing age groups, predominance of moderately differentiated carcinoma was seen.

TNM stage and Modified Duke's stage however did not show a significant relationship with the age factor. However, no significant studies pertaining to correlation of grade and stage have been documented in the literature.

### Conclusion

We found a proximal shift in the anatomic distribution of CRC from rectum to colon and a significant correlation of subsite and grade of the tumor with the age of the patient. The apparent shift in location and its variation with the age may have an importance in changing the screening strategies of CRC. With the rising incidence of CRC world over and its varying trends, continuous monitoring and evaluation with more detailed data can be helpful in early detection and management of the disease.

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No conflicts of interest

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