

## **Morphological Evaluation of Colorectal Carcinoma with Grading Staging and Histological types**

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### **Abstract**

**Objective:** To evaluate the morphology, grading and staging of colorectal carcinoma (CRC) and to assess the relationship between these parameters.

**Methods:** This cross-sectional study was carried out at the Departments of Pathology, University of Health Sciences and Sheikh Zayed Federal Post Graduate Medical Institute Lahore, Pakistan, over a period of one year. The study consisted of 100 colectomy/ hemicolectomy specimens, received fixed in 10% formalin. The specimens were examined grossly to observe the various macroscopical features of tumours. Haematoxylin and Eosin stained slides were examined to determine the histological type, grade and stage of CRC.

**Results:** Among the 100 cases, 59 were non mucinous adenocarcinomas, of which 4 were in Dukes' stage A, 51 were in Dukes' stage B and 4 were in Dukes' stage C. Cases of nonmucinous CRC of grade I to grade II were 55 in number. In thirty cases of mucinous carcinomas, 18 were in Dukes' stage B and 12 were in Dukes' stage C, of these 2 were of grade I, 20 were of grade II and 8 were of grade III. All the 11 signet ring cell carcinomas were of grade III and in Dukes' stage C.

**Conclusion:** Mucin secreting and signet-ring cell adenocarcinomas of colon and rectum are high grade tumours and presented at an advanced stage (JPMA 60:998; 2010).

### **Introduction**

Colorectal carcinoma (CRC) accounts for about 10 per cent of all cancers (after exclusion of non-melanoma skin cancer) and it is the fourth leading cause of cancer death in the world.<sup>1</sup> CRC is the second leading cause of death from malignancy in the industrialised world.<sup>2</sup> Every year, nearly one million people world wide develop CRC, of which 50 per cent die within 5 years.<sup>3</sup>

Many Asian countries, including China, Japan, South Korea and Singapore, have experienced an increase of two to four times in the incidence of colorectal cancer during the past few decades. The rising trend in incidence and mortality from colorectal cancer is more striking in affluent than in poorer societies and differs substantially among ethnic groups.<sup>4</sup>

The statistics observed by WHO in Pakistan for the year 2005 showed that the CRC was the 8th leading cause of cancer deaths in males and 7th amongst females.<sup>5</sup>

The tumor registry data of Armed Forces Institute of Pathology (AFIP), Rawalpindi (1992-2001) listed in adults, breast carcinoma foremost in females, and prostatic carcinoma in males; followed by carcinoma of skin, lymphomas, colorectal, gastric and urinary carcinomas among the commonest malignant neoplasm in both sexes.<sup>6</sup> According to the Shaikat Khanum Memorial Cancer Hospital (SKMCH) annual cancer registry report (2006) in

adults, breast carcinoma is commonest carcinoma followed by hepatocellular carcinoma, non Hodgkin's lymphoma, cancer of oral cavity and CRC.<sup>7</sup>

Microscopically 98% of all CRC are adenocarcinoma. The major subtypes are non mucinous adenocarcinomas, mucinous or colloid adenocarcinoma and signet ring cell carcinoma. Adenocarcinomas of colon and rectum are graded predominantly on the basis of the extent of glandular appearance and are classified into well, moderately and poorly differentiated adenocarcinomas.<sup>8</sup> Dukes' staging is the most common means of staging the CRC.

The objectives of the study were to evaluate the morphology, grade and stage of CRC and assess the relationship between them.

### **Material and Methods**

This study was conducted at the Department of Pathology, University of Health Sciences, and Sheikh Zayed Federal Post Graduate Medical Institute Lahore and was completed within one year (2007). The study consisted of 100 colectomy/hemicolectomy specimens of CR. Patients of all ages and both sexes were included. After fixation in 10% formalin, each specimen was opened and thoroughly examined grossly to observe the various macroscopic features of the tumour. Multiple 3-5 mm thick representative slices were taken from the tumour including the junction with the adjacent uninvolved tissue. In addition the proximal and

distal resection margins, with at least one random block from the uninvolved bowel, and necessary blocks from the background abnormalities, including polyps or if any other disease process. The mesenteric fat was thoroughly examined for lymph nodes. These tissues were processed for paraffin embedding and subsequent staining by haematoxylin and eosin. For demonstrating the mucin, Alcian blue stain was performed.<sup>9</sup> The tumours were graded as, well, moderately and poorly differentiated according to WHO grading criteria. The pathological stage was determined according to Dukes' staging system.

## Data Analysis

The data was entered and analyzed using SPSS version 16.0. Frequencies and percentages are given for qualitative variables. Fisher's Exact test was applied to observe associations between qualitative variables. A p-value of <0.05 was considered as statistically significant.

## Results

A total of 100 formalin fixed colectomy/hemicolectomy specimens of CRC were included in this study. Among these patients, 8 were below the age of 40 years, 5 were above the age of 70 years and 87 were between 41 and 69 years of age. Fifty nine patients were males and 41

**Table-1: Distribution of cases by relationship between Dukes' staging and histological type of colorectal carcinoma (n=100).**

Histological Type	Dukes' A n (%)	Dukes' B n (%)	Dukes' C n (%)
Non-Mucinous	4 (4%)	51 (51%)	4 (4%)
Mucinous	0 (0%)	18 (18%)	12 (12%)
Signet ring type	0 (0%)	0 (0%)	11 (11%)
Total	4 (4%)	69 (69%)	27 (27%)

Fisher' Exact Test =43.44.  
p-value< 0.000.

were females. Among these 100 cases of CRC, 37 were located in the right colon, 30 in the left colon and 33 in the rectum.

Morphologically all 100 cases were of adenocarcinoma. No other microscopical variants were seen in them. Among 100 cases, 59 were reported as non-mucinous adenocarcinoma, 30 as mucinous adenocarcinoma and 11 as signet-ring cell type carcinoma. Regarding histological grades, 15 were reported as grade I, 62 as grade II and 23 as grade III adenocarcinomas. In Dukes' staging, 4 were of Dukes' stage A, 69 were of Dukes' stage B, and 27 were of Dukes' stage C (Table-1).

Among the 59 cases of non mucinous adenocarcinoma, 4 were of Dukes' stage A, 51 were of Dukes' stage B, and only 4 were of Dukes' stage C. In 30

**Table-2: Distribution of cases by relationship of Dukes' staging with grade of colorectal carcinoma (n=100).**

Grade	Dukes' A n (%)	Dukes' B n (%)	Dukes' C n (%)
Grade I	4 (4%)	11 (11%)	0 (0%)
Grade II	0 (0%)	54 (54%)	8 (8%)
Grade III	0 (0%)	4 (4%)	19 (19%)
Total	4 (4%)	69 (69%)	27 (27%)

Fisher' Exact Test= 54.844.  
p-value< 0.000.

**Table-3: Distribution of cases by relationship of grade with histological types of colorectal carcinoma (n=100).**

Histological Type	Grades		
	Grade I n (%)	Grade II n (%)	Grade III n (%)
Non-Mucinous	13 (13%)	42 (42%)	4 (4%)
Mucinous	2 (2%)	20 (20%)	8 (8%)
Signet ring adenocarcinoma	0 (0%)	0 (0%)	11 (11%)
Total	15 (15%)	62 (62%)	23 (23%)

Fisher' Exact Test= 44.417.  
p-value<0.000.

mucinous type of CRC, 18 were included in Dukes' stage B and 12 in Dukes' stage C. All 11 signet-ring cell of CRC were in Dukes' stage C. Significant association was observed between histological type and Dukes' stage of CRC (p-value<0.000) (Table-1).

In 15 cases of grade I adenocarcinoma, 4 were of Dukes' stage A, and 11 were of Dukes' stage B. Among the 62 cases of grade II adenocarcinoma 54 were of Dukes' stage B and 8 were of Dukes' stage C. Four of the 23 cases of grade III CRC were of Dukes' stage B and 19 were of Dukes' stage C. Significant association was observed between histological grade and Dukes' stage of CRC (p-value < 0.000) (Table-2).

Among the 59 cases of non mucinous adenocarcinoma, 13 were reported as grade I, 42 as grade II, and 4 as grade III adenocarcinoma. In the remaining 30 cases of mucinous adenocarcinoma, 2 were of grade I, 20 were of grade II, and 8 were of grade III adenocarcinoma. All 11 signet-ring cell type CRC were reported as grade III carcinoma. Significant association was observed between histological type and grade of CRC (p-value<0.000) (Table-3).

Associated background abnormalities, synchronous carcinoma, ulcerative colitis (UC), Crohn disease (CD) and Familial Adenomatous Polyposis (FAP) were not found in any of the 100 cases. Of the 100 CRC in this study that revealed adenomatous polyp at the edge of the tumours were 15 in number. Circumferential margin (CRM) involvement by the tumour was not seen in any of the 33 rectal carcinomas. In a total of 100 cases, 27 cases revealed metastatic tumour deposits in regional lymph nodes.

## Discussion

A total of 100 specimens of CRC were included in this study. Grading, histological typing and staging of CRC were carried out.

Determination of tumour type is critical because different tumour types vary regarding the radiosensitivity, local behaviour, and propensity for regional and systemic metastasis. The histological grade of tumours is an important indicator of the potential for local invasion or systemic metastases. Tumour staging as determined by clinical evaluation, imaging studies and histological evaluation are necessary to establish the extent of the tumour, both locally and systemically.<sup>10</sup>

In this study, among 59 non-mucin producing adenocarcinomas, 55 were well or moderately differentiated and are diagnosed at an early stage either in Duke's stage A or B. Poorly differentiated non-mucin producing adenocarcinoma in Duke's stage C were four in number. Thirty mucin producing and 11 signet-ring cell carcinomas were high grade tumours and were diagnosed in Duke's stage B or C which in comparison with the non mucinous tumours, is an advanced stage. This result is consistent with the studies reported by others in which the mucin secreting tumours are high grade tumours and presented at an advanced stage.<sup>11,12</sup> In this study all 11 cases of signet-ring cell type adenocarcinoma presented in Duke's stage C, indicate low rates of curative resection and poor prognosis. This result is also in accordance with another study reported by Bittorf et al in which signet-ring cell type CRC were diagnosed at an advanced tumour stage with a significantly higher frequency of distant metastases.<sup>13</sup>

In reviewing these 100 cases it was revealed that patients with poorly differentiated tumours (Grade-III) showed deep invasion of bowel wall and lymph node metastases as compared to well (Grade I) or moderately differentiated (Grade-II) tumours. This result is similar to the study performed by Chung et al.<sup>14</sup> The findings suggest that histological grading is important adjuncts to the clinical evaluation and treatment planning of patients with CRC.<sup>14</sup>

CRC in patients under 40 years of age usually have a poor prognosis. Most such patients presented with an advanced tumour stage.<sup>15</sup> In our study, 8 patients were below 40 years of age, 2 of them had a moderately differentiated mucin secreting adenocarcinoma, 1 in Dukes' stage B and 1 in Dukes' stage C. Six patients had poorly differentiated signet ring cell adenocarcinoma in Dukes' stage C. The result shows that patients younger than 40 years presented with advanced lesions (Dukes' stage C) and were either a mucinous or signet-ring cell carcinoma. These findings match the study conducted by Taylor who concluded that poor prognosis in patients less than 40 years of age is not due to late symptoms reporting or delay in diagnosis, but due to

morphologically more aggressive disease.<sup>16</sup> Mucoïd and signet ring cell carcinomas are common in young age.<sup>17</sup> Young patients with CRC tended to have poorly differentiated, mucin producing and more advanced tumours, a lower operative mortality rate, higher incidence of synchronous and metachronous CRC, normal p53 expression and a higher incidence of microsatellite instability (MSI).<sup>18</sup>

The number of lymph nodes infiltrated by the carcinoma is an important prognostic indicator.<sup>19</sup> In this study a successful attempt was made to isolate at least 14 lymph nodes from each of the 100 CRC cases including the Dukes' stage A and B which was in accordance with the criteria laid by Wong et al<sup>20</sup> for accurate staging.

CRC is affecting younger age group in our set up. In the present study 8 cases (8%) were below the age of 40 years while in the other studies 43.8% and 45.6% cases were below 40 years of age.<sup>21,22</sup> CRC is not a rare pathology in our country, its early detection is very important as it saves the life of the patients.

Among 100 CRC cases in the present study, 15 revealed foci of adenomatous polypi at the edge of the tumours. Adenomatous foci were not found in the remaining 85 CRC cases probably because all those tumours were fairly advanced, well developed and invasive.

## Conclusion

It is concluded that non mucinous tumours are usually well differentiated and present at an early stage (Dukes' stage A or B) whereas mucin secreting tumours or signet-ring cell adenocarcinomas of colon and rectum are poorly differentiated and are diagnosed at a more advanced stage.

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