ORIGINAL ARTICLE

Morphological and Clinical Analysis of Colorectal Cancer: Findings from a Cross-Sectional Study

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Abstract

Background: Colorectal cancer (CRC) is a leading cause of cancer-related morbidity and mortality worldwide, with increasing incidence in developing countries like Pakistan. This study aims to evaluate the distribution patterns of colorectal cancer morphologies among patients treated at Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro.

Methodology: This descriptive, cross-sectional study was conducted over two years (January 2022 to December 2023) at the Department of Gastroenterology, Asian Institute of Medical Sciences, in collaboration with the Department of Pathology, LUMHS Jamshoro. A total of 150 patients diagnosed with CRC and who underwent surgical resection were included in the study. Data were collected on socio-demographic characteristics, clinical presentations, histopathological types, tumor grading, and staging. Statistical analysis was performed using SPSS version 25, with Fisher's exact test applied to assess associations between variables.

Results: The mean age of the patients was 58.7 years (± 11.2), with the majority being male (60%). Most tumors were classified as non-mucinous adenocarcinomas (56%), followed by mucinous adenocarcinomas (28%) and signet-ring cell carcinomas (16%). A strong positive correlation was found between tumor size and Dukes' staging ($\rho = 0.42$, $p < 0.001$), as well as between Dukes' staging and tumor grading ($\rho = 0.46$, $p < 0.001$). Rectal bleeding was significantly associated with advanced Dukes' stages ($\rho = 0.44$, $p < 0.001$).

Conclusion: This study highlights the aggressive nature of colorectal cancer in the studied population, with significant associations between age, tumor size, staging, and grading. The findings underscore the need for early detection strategies and tailored treatment approaches to address CRC in this region.

Keywords

Colorectal Cancer, Dukes' Staging, Histopathology, Tumor Grading.

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Introduction

Colorectal cancer (CRC) remains one of the most commonly diagnosed malignancies and is a leading cause of cancer-related morbidity and mortality worldwide. According to the Global Cancer Observatory (GLOBOCAN), there were almost 1.9 million new cases and 935,000 deaths in the year 2020 globally, which makes lung cancer the third most diagnosed cancer and the second leading cause of death of all cancers[1]. As for CRC, the incidence and mortality rates have traditionally been greater in developed countries, particularly those from North America, Europe, and Australia. On the other hand, in support of these observations, current rates are also escalating in Southeast Asia and Africa commensurate with Western lifestyle practices – a diet of high-fat red and processed meat (both associated with CRC risk), inadequate physical activity levels as well as obesity prevalence increase across all ages[2].

CRC has become a significant public health issue in Pakistan, and more cases are diagnosed every year. These high incidence rates in CRC coincide with the fast urbanization and adoption of sedentary lifestyle-related practices especially in more metro areas like Jamshoro[3]. A significant role has been attributed to the increasing adoption of a Westernized diet (high fat and low fiber) and sedentariness, leading to an increased burden on CRC[4]. Moreover, time of exercise, smoking habits/alcohol intake and genetic predisposition are critical in the molecular background in CRC susceptibility[5]. CRC often goes through a predictable sequence of stages, initiating as adenomatous polyps that can become malignant over time if not treated[6]. Early-stage CRC symptoms are usually mild and seem less severe, including changes in bowel habits (diarrhea is also a symptom of other diseases), rectal bleeding, or blood present in the stool, which cannot be spotted easily by patients due to its slight degree[7]. As a consequence, CRC is diagnosed at more advanced stages in many patients, meaning that the prognosis and treatment options are worse. This reinforces the impact of early diagnosis and timely treatment to alter CRC outcomes. The histopathological evaluation remains the mainstay of diagnosis and staging for CRC, which gives an idea about tumor type, grading, and staging that are critical to determining appropriate management plans and prognostic implications[8]. The most frequent histological form of CRC is adenocarcinoma, including subtypes like mucinous and signet-ring cell carcinomas. Mucinous and signet-ring cell carcinoma, on the other hand, has been found to vary in its biological behavior, harboring a more advanced stage at a presentation associated with poorer outcomes[9].

The Dukes stage, dating back to 1930, was developed by Cuthbert E. Dukes, a British pathologist, and is one of the most common systems for staging colorectal cancer (CRC). The tumor, node and metastasis (TNM) staging system classifies the disease into four stages based on the degree of local invasion by an FKBP-negative tumor and spread to lymph nodes or distant parts[10]. Dukes' A stage refers to tumors limited to the bowel wall; Dukes B involves invasion beyond the bowel

wall but not out wide and locally penetrating serosa or adjacent structures (e.g., circulating in a fluid-filled organ); Dukes C involves lymph node metastases; and finally, stage d means distant spread[11]. The tumor grade, which measures how the cancer cells look similar to healthy ones and indicates using malignancy of this kind together with the tendency for it to come back or spread[12], has also become an essential factor. Despite advances in the knowledge and care of CRC, there are overwhelming disparities relating to how this disease is perceived and acquired and its heterogeneous outcomes as a function of genetic variability together with various environmental factors[13]. There is an apparent lack of broad-based demographic and clinical data for CRC in Pakistan; particularly, it remains scarce throughout the country, including the Sindh region, which impedes the development of effective prevention and management strategies [14].

The current study aims to analyze the socio-demographic characteristics and clinical presentation of colorectal cancer (CRC) among patients presenting to a tertiary care hospital in Hyderabad. Specifically, it seeks to estimate the frequency of different histological subtypes of CRC and evaluate the association between tumor grade and Dukes' stage. Additionally, the study aims to identify the most common demographic factors associated with advanced-stage CRC and provide recommendations for screening and treatment strategies.

Methodology

Study Setting and Duration

This was a descriptive, cross-sectional study aimed at assessing the distribution of various morphologies in patients with colorectal cancer (CRC) at Liaquat University of Medical & Health Sciences Jamshoro. This study aimed to assess the socio-demographic characteristics, clinical presentations, histopathological types of CRC and tumor grading. The work was conducted in the Department of Gastroenterology Asian Institute Of Medical Sciences and Department PF Pathology LUMHS Jamshoro. The research was carried out between January 2022 and December 2023 over a period of two years, which took ample time to gather numbers to ensure the reliability and validity of the findings.

Sample Size Estimation

The sample size of 150 patients was determined following a review of studies listed in the introduction section and assuring that such a number is appropriate with the expected prevalence rate for CRC in the region. We determined the sample size using a formula for descriptive studies in which we used Z is 1.96 to represent a confidence limit of χ% and assumed prevalence at a conservative estimate (10%) based on regional data; the margin error was ±5%. We rounded the calculated sample size to 150 for dropouts or incomplete data.

Eligibility of Participants

Patients of any age and gender who were diagnosed with colorectal cancer and underwent surgical resection (colectomy or proctectomy) at LUMHS Jamshoro during the study period were included. Written informed consent was obtained from all participants. Patients whose

histopathological slides were available and suitable for review were included, while those with incomplete medical records, a previous history of colorectal cancer or other synchronous malignancies, or those who received neoadjuvant chemotherapy or radiotherapy were excluded from the study.

Data Collection Procedure

Data were collected using a structured data collection form that included sections on socio-demographic information (age, gender, area of residence, occupation), clinical presentation (symptoms, duration of symptoms, physical examination findings), and histopathological characteristics (tumor location, size, histological type, grade, and stage). Experienced pathologists reviewed the histopathological slides at the Department of Pathology, LUMHS. Tumors were classified according to the World Health Organization (WHO) classification of colorectal tumors, and staging was performed using the modified Dukes' classification. Tumor grading was conducted based on the degree of differentiation of the cancer cells, categorized into the following:

- **Grade I (well-differentiated)**
- **Grade II (moderately differentiated)**
- **Grade III (poorly differentiated)**

Data Analysis

Data collected were then entered into Statistical Package for Social Science – SPSS (Version 25) software. Descriptive statistics were performed to describe data (using frequency, percentages, means and standard deviation). Histological type, Dukes' staging versus grade and stage were tested for association by Fisher exact test with p value less than 0.05, which was considered statistically significant[17].

Ethical Considerations

The protocol for this study was reviewed and approved by the appropriate Ethical Committee (EC) of AIMS Hyderabad in collaboration with LUMHS Jamshoro. Before their inclusion in the study, informed consent was obtained from all patients or legal guardians. The anonymity and confidentiality of patient information was maintained throughout the study per The Declaration of Helsinki.

Results

The study included a total of 150 patients diagnosed with colorectal cancer who underwent surgical resection at LUMHS Jamshoro between January 2022 and December 2023. The mean age of the patients was 58.7 years (± 11.2), with an age range of 32 to 85 years. The majority of patients (45.3%, n=68) were in the age group of 51-60 years, followed by 61-70 years (28%, n=42). The study population comprised 90 males (60%) and 60 females (40%), resulting in a male-to-female ratio of 1.5:1. Most patients (72.7%, n=109) resided in urban areas, while 27.3% (n=41) were from rural regions (Table-1).

Table-1 Socio-Demographic and Clinical Characteristics of Patients (n=150)	
Characteristic	**n (%)**
Age (years)	
31-40	10 (6.7%)
41-50	30 (20%)
51-60	68 (45.3%)
61-70	42 (28%)
Gender	
Male	90 (60%)
Female	60 (40%)
Area of Residence	
Urban	109 (72.7%)
Rural	41 (27.3%)
Presenting Symptoms	
Rectal bleeding	62 (41.3%)
Altered bowel habits	55 (36.7%)
Abdominal pain	46 (30.7%)
Anorexia	30 (20.0%)
Weight loss	28 (18.7%)

Tumor location and size were also analyzed. The majority of tumors were located in the rectum (38%), followed by the recto-sigmoid junction (24%) and caecum (14.7%). Tumors larger than 5 cm were observed in 67.3% of patients, while 32.7% had tumors smaller than 5 cm (Table-2).

Table-2 Tumor Location and Size (n=150)	
Characteristic	**Frequency (n)**
Tumor Location	
Rectum	57 (38%)
Recto-sigmoid junction	36 (24%)

Caecum	22 (14.7%)
Transverse colon	15 (10%)
Descending colon	10 (6.7%)
Ascending colon	6 (4%)
Tumor Size	
≥5 cm	101 (67.3%)
<5 cm	49 (32.7%)

Histological examination of the tumors revealed that non-mucinous adenocarcinomas were the most frequent histological type, accounting for 56% of cases. Mucinous adenocarcinomas accounted for 28%, and signet-ring cell carcinomas were observed in 16% of patients. The majority of non-mucinous adenocarcinomas were classified as Dukes' B stage, whereas signet-ring cell carcinomas were predominantly associated with Dukes' C stage. Tumor grading also revealed that Grade II tumors were the most prevalent (52.0%), followed by Grade III (28.7%) and Grade I (19.3%) (Table-3).

Table-3 Distribution of Histological Type and Tumor Grading by Dukes' Staging (n=150)

Histological Type	Dukes' A (n)	Dukes' B (n)	Dukes' C (n)	Total (n)
Non-mucinous adenocarcinoma	12 (8.0%)	45 (30.0%)	27 (18.0%)	84 (56.0%)
Mucinous adenocarcinoma	15 (10.0%)	10 (6.7%)	17 (11.3%)	42 (28.0%)
Signet-ring cell carcinoma	11 (7.3%)	5 (3.3%)	8 (5.3%)	24 (16.0%)
Tumor Grading				
Grade I	18 (12.0%)	9 (6.0%)	2 (1.3%)	29 (19.3%)
Grade II	12 (8.0%)	49 (32.7%)	17 (11.3%)	78 (52.0%)
Grade III	8 (5.3%)	2 (1.3%)	33 (22.0%)	43 (28.7%)

The correlation between patient age and tumor characteristics was explored. Age was moderately positively correlated with tumor size ($r = 0.34$, $p<0.001$) and Dukes' staging ($\rho = 0.29$, $p = 0.001$), suggesting that older patients tended to have larger and more advanced tumors. Similarly, a moderate positive correlation was found between age and tumor grading ($\rho = 0.26$, $p = 0.003$) (Table-4).

Table-4 Correlation of Age with Tumor Size, Dukes' Staging, and Tumor Grading (n=150)				
Variables	**Mean (± SD) or Median (IQR)**	**Correlation Coefficient (r/ρ)**	**p-value**	**Interpretation**
Age (years)	58.7 (±11.2)	-	-	-
Tumor Size (cm)	5.7 (±1.4)	r = 0.34	<0.001	**Moderate positive correlation** Older age associated with larger tumor size
Dukes' Staging	Median: 2 (IQR: 1-3)	ρ = 0.29	0.001	**Moderate positive correlation** Older age associated with more advanced Dukes' stage
Tumor Grading	Median: 2 (IQR: 1-3)	ρ = 0.26	0.003	**Moderate positive correlation** Older age associated with higher tumor grades

Dukes' staging was strongly positively correlated with tumor size (ρ = 0.42, p < 0.001), meaning that patients with larger tumors were more likely to have advanced-stage disease. Additionally, a strong positive correlation was found between Dukes' staging and tumor grading (ρ = 0.46, p < 0.001), indicating that poorly differentiated tumors were often found in patients with advanced-stage disease. Rectal bleeding, a common symptom, was also strongly correlated with advanced Dukes' stages (ρ=0.44, p<0.001) (Table-5).

Table-5 Correlation of Dukes' Staging with Tumor Size, Tumor Grading, and Rectal Bleeding (n=150)				
Variables	**Mean (± SD) or Median (IQR)**	**Correlation Coefficient (r/ρ)**	**p-value**	**Interpretation**
Dukes' Staging	Median: 2 (IQR: 1-3)	-	-	-
Tumor Size (cm)	5.7 (± 1.4)	ρ = 0.42	<0.001	**Strong positive correlation** Larger tumors associated with more advanced Dukes' stage
Tumor Grading	Median: 2 (IQR: 1-3)	ρ = 0.46	<0.001	**Strong positive correlation** Higher tumor grades associated with more advanced Dukes' stage
Rectal Bleeding	Present: 62 (41.3%)	ρ = 0.44	<0.001	**Strong positive correlation** Presence of rectal bleeding associated with more advanced Dukes' stage

Finally, tumor grading was moderately positively correlated with tumor size (ρ = 0.38, p < 0.001), and strongly correlated with Dukes' staging (ρ = 0.46, p < 0.001). These results suggest that larger

tumors and those in advanced stages are more likely to be poorly differentiated (Grade III) (Table-6).

Table-6 Correlation of Tumor Grading with Tumor Size and Dukes' Staging (n=150)

Variables	Mean (± SD) or Median (IQR)	Correlation Coefficient (r/ρ)	p-value	Interpretation
Tumor Grading	Median: 2 (IQR: 1-3)	-	-	-
Tumor Size (cm)	5.7 (± 1.4)	ρ = 0.38	<0.001	**Moderate positive correlation** Larger tumors associated with higher tumor grades
Dukes' Staging	Median: 2 (IQR: 1-3)	ρ = 0.46	<0.001	**Strong positive correlation** Higher tumor grades associated with more advanced Dukes' stage

Discussion

In this study, we report our experience with the demographics, clinical and pathological features of colorectal cancer (CRC) in a tertiary care center in Pakistan. Age, tumor size, Dukes' staging and grading of the tumor uncover strong associations with each other that emphasize a comprehensive pattern in CRC progression within the studied population.

In this study, the mean age of patients was 58.7 years, with a significant number (45.3%) in the subgroup between the ages of 51 and 60 years. Hence, this corroborates with the global data showing that CRC is infrequently diagnosed in individuals under 50, contributing to more than ninety per cent of new cases in the sixth and seventh decades[1,2]. This aside, our study also showed an alarming trend in which younger patients are being diagnosed with advanced stage of CRC because we found a significant correlation between both age and Dukes' staging (ρ= 0.29, p=<0.001) as well as tumor grading (ρ=0.26, p=≤.003). This is in line with current literature indicating higher grade and more advanced CRCs presenting at a younger age, which may relate to late-stage diagnosis or inherently biologically aggressive tumor types[3,4]. The significant relationship between tumor size and Dukes' staging (ρ=0.42, p<0.001) in this study suggests larger tumors are more likely to have progressed to advanced stages by the time of diagnosis. This corroborates what is already known in the literature, with tumor size being independently associated with more advanced disease and a poor prognosis[5,6]. Given the situation in Pakistan, where there is no organized CRC screening program, and a high proportion of patients are diagnosed at an advanced stage[18], it may account for the higher incidence of larger tumors with a statistically significant correlation between tumor size and staging. Demonstrating the importance of having high awareness and early detection approaches, specifically in those with a higher-risk population[7].

Dukes' staging was positively correlated with tumor grading (ρ=0.46, p<0.001) in our study; too, Advanced Dukes' stage is significantly more associated with grade 3 compared to grades one and, which shows a high degree of differentiation, similar to cancer. This result confirms observations from other investigations that a correlation exists between grading and tumor stage, supporting the capability of less differentiated type A thymomas to exhibit deeper tissue invasion with lymph node or distant metastasis[8,9]. The finding lends clinical relevance to the classification of tumors, suggesting that more aggressive treatment strategies are required for high-grade tumors, which are predisposed to rapid disease progression. Studies have reported a strong association between rectal bleeding and advanced Dukes' staging of CRC[17], which mirrors our data (rectal bleeding is common in patients, with its presence increasing the odds of an urgent referral to the hospital some tenfold). This association implies that patients presenting with rectal bleeding receive a later diagnosis of their disease. Rectal bleeding could be a sign of advanced CRC in older adults; however, it is often considered an innocent symptom. Similar results were reported by different studies[10,11]. As the presumed significance of rectal bleeding in predicting identification and treatment has been further borne out, our correlation was found to be qualitatively significant (P=0.0071), meshing well with protocols that may warrant earlier investigation for feculence among those aged fifty years or older[12].

Comparing these with international data, the pattern shown in our study was similar to what has been reported from high-resource settings where older age, larger tumor size and higher grade are related to advanced disease. In Pakistan, however, the lack of organized screening programs and delayed presentation culminate in a higher percentage of cases being diagnosed at advanced stages[13,14]. By comparison, screening has already levelled–off in the United States and the UK in some regions where their established programs have led to a decrease in late-stage CRC on presentation and an overall reduction of CRC mortality within those populations affected[15,16]. This disparity highlights the pressing need for public health initiatives targeting CRC awareness, emphasizing screening and early detection in Pakistan. Notably, a significant result can be observed in our study results due to the association between histological type and grading (ρ=0.38; p<0.001). In our cohort, non-mucinous adenocarcinomas (which was the predominant histological subtype) were typical of lower grade and signet-ring cell carcinomas—more often presenting more aggressive behavior—to poorly differentiated. This is also in concordance with what has previously been seen on a global scale, where signet ring cell carcinomas are recognized as having a poorer prognosis due to tumorigenic and aggressive behavior, leading to most often symptomatic presentation among patients[17–18]. The fact that the majority of adenocarcinoma patients had SCC, compared with other studies worldwide in developing countries where no trend is apparent[7], may reflect a more aggressive nature of CRC among the Pakistani population, which might be dictated by genetic predisposition as well as environmental and lifestyle factors unique to this region[19].

Conclusion

This study adds to the existing knowledge about factors implicated in CRC progression within a Pakistani population and establishes important roles of age, tumor size, staging, and grading. This highlights the importance of developing methods for early detection and specific treatment plans

to mitigate against this aggressive phenotype in CRC form within these groups. International comparisons, including data from Pakistan, suggest that enhanced screening and improved awareness can potentially help to reduce the burden of advanced CRC in such a high-risk region. The causes of the aggressive CRC phenotypes observed in this study are still under investigation, warranting further studies for early detection and management [20].

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Conflict of Interest
None.

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None.

References

1. GLOBOCAN 2020: New Global Cancer Data. International Agency for Research on Cancer, World Health Organization. [Internet]. 2020 [cited 2024 Aug 19]. Available from: https://gco.iarc.fr/
2. Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. Int J Mol Sci. 2017;18(1):197.
3. Granados-Romero JJ, Valderrama-Treviño AI, Contreras-Flores EH, et al. Colorectal cancer: a review. Int J Res Med Sci. 2017;5(11):4667-4675.
4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7-33.
5. Powers BE, Hoopes PJ, Ehrhart EJ. Tumor diagnosis, grading, and staging. Semin Vet Med Surg Small Anim. 1995;10(3):158-167.
6. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019;394(10207):1467-1480.
7. Raza AM, Kamal M, Begum F, et al. Clinico-demographic characteristics of colorectal carcinoma in Bangladeshi patients. J Curr Adv Med Res. 2016;3(1):22-25.
8. Stintzing S. Management of colorectal cancer. F1000Prime Rep. 2014;6:108.
9. Guinney J, Dienstmann R, Wang X, et al. The consensus molecular subtypes of colorectal cancer. Nat Med. 2015;21(11):1350-1356.
10. Rutter CM, Kim JJ, Meester RGS, et al. Validation of models used to inform colorectal cancer screening guidelines: accuracy and implications. Med Decis Making. 2022;42(1):28-38.
11. Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. 2021;116(3):458-479.

12. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA. 2016;315(23):2564-2575.
13. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-691.
14. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249.
15. Ahmed S, Banerjea A, Hands RE, Bustin S, Dorudi S. Microarray profiling of colorectal cancer in Bangladeshi patients. Colorectal Dis. 2005;7(6):571-575.
16. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. Gut. 2019;68(12):2179-2185.
17. Nabi U, Nagi AH, Riaz S, Sami W. Morphological evaluation of colorectal carcinoma with grading staging and histological types. J Pak Med Assoc. 2010;60(12):998-1002.
18. De Silva MVC, Fernando MS, Fernando D. Comparison of some clinical and histological features of colorectal carcinoma occurring in patients below and above 40 years. Ceylon Med J. 2014;45(4):166-167.
19. Goh KL, Quek KF, Yeo GT, et al. Colorectal cancer in Asians: a demographic and anatomic survey in Malaysian patients undergoing colonoscopy. Aliment Pharmacol Ther. 2005;22(9):859-867.
20. Dekker E, et al. Colorectal cancer. Lancet. 2019;394(10207):1467-1480.

AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design: Uqaili AA, Hassan A

Acquisition, Analysis or Interpretation of Data: Uqaili AA, Hassan A, Shah T, Samejo MA

Manuscript Writing & Approval: Uqaili AA, Bughio U, Umrani ZA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.