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Original Article

Clinico-Epidemiological Study of Colorectal Cancer Patients Diagnosed at Endoscopy Unit of Two University Hospitals in Cairo

Ahmed K. Mahmoud *, Walid M. Gomaa, Diah M. Eltiby

Department of Hepatology, Gastroenterology, and Infectious Diseases, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

ABSTRACT

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*Corresponding author

Email: sawya038@gmail.com

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Background: Colorectal cancer [CRC] is the third most common cancer and the second lethal among both males and females. Despite improved diagnostic methods and preventive healthcare practices, the incidence of CRC is projected to rise by 60% by the year 2035.

The Aim of the work: To study clinical and epidemiological criteria of CRC patients diagnosed at endoscopy unit of hepatology, gastroenterology, and infectious diseases department at Al-Azhar University Hospitals in Cairo by colonoscopy and histopathological examination.

Patients and Methods: The present study is a cross-sectional study which assessed 1175 patients presented to the endoscopy unit of EL Hussein and Sayed Galal University hospital from January 2022 to January 2023. Only 84 patients meet the eligibility criteria and diagnosed with CRC, and were eligible for final analysis. We estimated the relative prevalence of CRC among the enrolled patients at 7.1%.

Results: The mean age of studied patients was 49.56 ± 13.5 years old, males showed higher prevalence of CRC with males to female ratio was = 2.2:1, with 22.6% reporting positive family history. CEA tumor marker was normal among most of the assessed patients accounted for 86% and only 14% showed elevated CEA. As regards demographic data, we found that age was associated with high-risk disease [Grade III disease], as younger patients had higher risk disease compared to elderly. On the other hand, no significant correlation as regards gender, family history, BMI, smoking and dietary pattern.

Conclusion: We reported a higher prevalence of colorectal cancer in males compared to females in this age group the main age of the patients around fifty years. Furthermore, the analysis indicated that the left-sided colon was the most common location for colorectal cancer in both genders. Also, we found that younger age groups demonstrate more aggressive, poorly differentiated and fatal CRC compared to patients older than 40 years old.

Keywords: Colorectal cancer; Colonoscopy; Epidemiology; Risk factors.



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INTRODUCTION

Globally, colorectal cancer [CRC] ranks third in terms of the number of cases diagnosed and second in terms of the number of deaths it causes ^[1]. The incidence and mortality rates of colorectal cancer [CRC] differ worldwide, and this variation can be attributed to various factors, such as existing risk factors, ethnicity, the comprehensiveness of cancer registries, and the availability of screening facilities and management protocols in different geographical areas and countries ^[2].

Thankfully, the incidence of colorectal cancer [CRC] and CRC-related deaths are decreasing in Western countries. However, there has been a noticeable and rapid increase in the incidence and mortality rates of CRC in many developed countries in Asia, Eastern Europe, and South America ^[3]. Although the incidence of colorectal cancer among Arabs is much lower than that of developed countries, the Arab population is not immune to this disease, and the incidence of colorectal cancer in Arab countries has increased in the past decade ^[4].

Risk factors that are widely accepted as causal for colorectal cancer [CRC] include obesity, physical inactivity, certain poor dietary patterns, consumption of red and processed meats, alcohol consumption, and tobacco use. Protective factors include dietary fiber, intake of dairy products or calcium, and the use of aspirin. Additionally, there are other factors that are suggested to have a protective effect, such as probiotics found in yogurt ^[5].

Advancements in the treatment of colorectal cancer [CRC] have resulted in a decline in mortality rates in the second and third categories of countries, despite an increase in incidence ^[6]. Early detection plays a crucial role in improving survival rates, and various methods such as colonoscopies, flexible sigmoidoscopies, computed tomography [CT] colonography, faecal immune-chemistry, and faecal occult blood testing have been effective in detecting and removing polyps at an early stage ^[7].

Thus, we conducted a cross section study aiming to study clinical and epidemiological criteria of CRC patients diagnosed at Endoscopy unit of Hepatology, Gastroenterology and Infectious diseases Department at Al-Azhar university hospitals in Cairo by colonoscopy and histopathological examination.

PATIENTS AND METHODS

This is a cross-sectional study which assessed 1175 patients presented to the endoscopy unit of EL Hussein and Sayed Galal University hospital from January 2022 to January 2023. Only 84 patients were diagnosed with CRC and were eligible for final analysis. We included all patients diagnosed with CRC at Endoscopy unit during the study period. The current study excluded patients who were under 18 years old, had previously received chemotherapy or any treatment for colorectal cancer [CRC], or had any other type of cancer. All patients underwent a thorough medical history assessment, clinical examination, and laboratory tests, including complete blood count, liver and kidney function tests, C-reactive protein [CRP], and carcinoembryonic antigen [CEA] as tumor markers. Patients also underwent an initial pelvi-abdominal CT scan, followed by a metastatic workup, and were then referred to an endoscopist for colonoscopy examination.

RESULTS

The mean age of studied patients was 49.56 ± 13.5 years old, males showed higher prevalence of CRC with males to female ratio was = 2.2:1, with 22.6% reporting positive family history. Regarding the presenting symptoms, we found that, history of bleeding, constipation, and abdominal pain were the most reported presenting symptoms accounting for more than 40% of the included patients, while 60.7% were diagnosed with iron deficiency anemia, and 52.3% showed weight loss [Table 1].

Laboratory findings of the included patients are summarized in table 2, CEA tumor marker was normal among the majority of the assessed patients accounted for 86% and only 14% showed elevated CEA.

Abdominal CT images detected colonic masses among 86% of the included patients, while Metastatic workup showed that 37% has LN metastasis, while 18% had distant metastasis at the time of presentation. Regarding colonoscopy, full visualization of colonic lumen was achieved in 95.2% of the included patients. While only 4 patients had obstructed lumen and failure of visualization beyond detected lesions. Obstructed lumen was reported in 10.8% of the included patients, 6% were partially obstructed and 4.8% were totally obstructed [Table 3].

Histopathology examination showed that 91.7% of the examined specimens were adenocarcinoma, and only 7 patients had mucinous adenocarcinoma with signet ring appearance, grade II disease was the most reported accounting for 81% versus 19% as grade III [Table 4].

As regards demographic data, we found that age was associated with high risk disease [Grade III disease], as younger patients had higher risk disease compared to elderly. On the other hand, no significant correlation as regards gender, family history, BMI, smoking and dietary pattern [Table 5].

Table [1]: Demographic characteristics of the included patients

| Demographics and co-morbidities | | percentage |
|---------------------------------|-------------------------|----------------|
| Age | Mean [SD] | 49.56 [13.589] |
| | Median [range] | 57 [24,78] |
| Sex | Female | 26 [31%] |
| | Male | 58 [69%] |
| Family History | Negative Family history | 65 [77.4%] |
| | Positive Family history | 19 [22.6%] |
| BMI | Mean [SD] | 28.39 [4.688] |
| | Range | [27-44] |
| Smoking | No | 60 [71.4%] |
| | Yes | 24 [28.6%] |
| Diet | Inappropriate diet | 54 [64.3%] |
| | Appropriate diet | 30 [35.7%] |
| Chronic diseases | No | 49 [58.3%] |
| | Diabetes | 29 [34.5%] |
| | Hypertension | 25 [29.76%] |
| | Chronic kidney disease | 2 [2.4%] |
| | Ischemic heart disease | 4 [4.8%] |
| Presentation | Bleeding | 37 [44%] |
| | Constipation | 38 [46%] |
| | Abdominal Pain | 45 [53.6%] |
| | Iron deficiency anemia | 51 [60.7%] |
| | Weight loss | 44 [52.3%] |

Table [2]: Laboratory findings of the included patients

| | Mean ± SD | Range |
|--------------------|---------------|-----------|
| CRP [mg/dL] | 11.6±12.7 | 0-48 |
| Creatinine [mg/dL] | 1.2±0.6 | 0.5-4.3 |
| AST [IU] | 22.8±3.7 | 10.6-31.8 |
| ALT [IU] | 24.7±4.8 | 14-40.1 |
| HB [gm/dL] | 10.2±2.6 | 3.9-15.2 |
| TLC [10/cc] | 5103.0±2178.8 | 2.4-10668 |
| Platelets [10/cc] | 332.0±70.8 | 98-560 |

Table [3]: CT imaging and endoscopic findings among the included patients

| | Variable | present |
|----------------------|-------------------------|------------|
| CT imaging | Lymph nodes Mets | 37% |
| | Distant Mets | 18% |
| | Detectable colonic mass | 86% |
| Colonoscopy | Not full visualized | 4.8% |
| | Full visualized | 95.2% |
| Obstruction | Not obstructed | 89.3% |
| | Partially obstructed | 6.0% |
| | Total obstruction | 4.8% |
| Site of colonic mass | RT colon | 20 [23.8%] |
| | LT colon | 57 [67.9%] |
| | upper rectum | 5 [6.0%] |
| | Lower rectum | 2 [2.4%] |

Table [4]: Histopathology findings of the included patients

| | | N [%] |
|---------------------------|----------------|------------|
| Histopathology | Adenocarcinoma | 77 [91.7%] |
| | Signet ring | 7 [8.3%] |
| Histological grade | Grade II | 68 [81%] |
| | Grade III | 16 [19%] |

Table [5]: Logistic Cox regression for demographic factors associated with high-risk disease [Grade III]

| | | Univariate Analysis | | Multivariate Analysis | |
|------------------------|----------------------------------|----------------------|--------------|-----------------------|--------------|
| | | OR [95 % CI] | P-value | OR [95 % CI] | P-value |
| Age | Less than 40 y | 1 | | 1 | |
| | More than 40 y | 0.9[0.07,0.8] | 0.007 | 0.9[0.8,0.9] | 0.030 |
| Gender | Male | 1 | | 1 | |
| | Female | 0.6[0.2,2.4] | 0.56 | 0.2[0.03,2.09] | 0.2 |
| Family history | Negative | 1 | | 1 | |
| | Positive | 0.8[0.2,2.6] | 0.781 | 0.4 [0.1,2.2] | 0.361 |
| BMI | Obese [class I, II, III] | 1 | | 1 | |
| | Average [<30 kg/m ²] | 1.1[0.9,1.2] | 0.065 | 1.1[0.9,1.3] | 0.065 |
| Smoking | Absent | 1 | | 1 | |
| | Present | 0.6[0.1,1.8] | 0.383 | 0.9[.163,4.984] | 0.905 |
| Dietary pattern | Inappropriate diet | 1 | | 1 | |
| | Appropriate diet | 1.2[0.3,4.1] | 0.679 | 4.3[0.5,35] | 0.163 |

DISCUSSION

Colorectal cancer [CRC] is the third most common cancer and the second deadliest among both males and females. The development of colon cancer is influenced by significant environmental and genetic risk factors [8].

Around 5% of all colorectal cancer cases are caused by two inherited syndromes, namely Familial Adenomatous Polyposis and Lynch syndrome [9]. The process of normal colonic epithelium transforming into a precancerous lesion and eventually an invasive carcinoma requires the accumulation of somatic [acquired] and/or germline [inherited] genetic mutations over a period of 10-15 years [10].

Many European and North American people tend to consume red meat and alcohol, live a sedentary lifestyle, have low-fiber diets, smoke, and become obese. These lifestyle choices have led to consistently high rates of colorectal cancer in these regions. As Asian societies, such as India, Japan, and Saudi Arabia, have adopted similar Western lifestyle patterns, they have also experienced an increase in the incidence of colorectal cancer in recent years [11].

Although better methods of diagnosis and preventative medical measures can decrease the likelihood, it is projected that the number of cases of colorectal cancer [CRC] will rise by 60% by the year 2035. This estimate suggests

that there will be around 2.2 million new cases and 1.1 million deaths caused by CRC every year [3,12].

The reason for this increase in CRC cases is because of the expected economic growth in countries with a low-to-moderate Human Development Index [HDI]. Not only are residents of developed nations at risk, but immigrants from low-to-moderate HDI countries are also more likely to develop CRC. Additionally, with the possibility of higher levels of carcinogen emissions and exposure due to climate change, the risk of CRC may rise even more [13].

In Egypt, colorectal cancer is the seventh most prevalent type of cancer, accounting for 3.47% of male cancer cases and 3% of female cancer cases. In 2015, the estimated number of patients diagnosed with colon cancer [excluding rectal cancer] was just over 3,000 [14].

Numerous studies have compared colon cancer on the right side of the colon to that on the left side. The findings indicate that tumors on the right side have a poorer prognosis than those on the left side. Some authors have even suggested that these two types of tumors should be treated as separate entities requiring different treatment approaches [15].

We conducted a cross-sectional study aiming to study clinical and epidemiological criteria of CRC patients diagnosed at Endoscopy unit of Hepatology, Gastroenterology, and Infectious

diseases Department at Al-Azhar university hospitals in Cairo by colonoscopy and histopathological examination.

We enrolled 84 patients diagnosed with Colorectal Carcinoma who were presented to EL Hussein and Sayed Galal University hospital during the period between January 2022 to January 2023.

In the current study, the mean age of studied patients was 49.56 [SD 13.5], ranging from [24 to 78 years] which are similar to the study done by **Wahib *et al.*** [16] [50.38 ±11.26 years]. Twenty-six patients [31%] were females, while 58 of 84 patients [69%] were males with males to female ratio was 2.2:1.

Globally males showed higher incidence and mortality compared to females [17]. Our findings are similar to ones reported in Egyptian study, they found that males were predominantly diagnosed with CRC [16], however they were more significantly detected during screening, and females were more commonly presented to emergency department with perforated colon or acute obstruction [18].

These findings disagree with **Metwally *et al.*** conducted a retrospective over 12 years and found that female was predominantly affected with CRC among 340 medical records diagnosed in a tertiary care hospital with female: male ratio 1.2:1 [19].

The current research found that 22.6% of the participants had a family history of colon cancer. A meta-analysis that included a large number of studies revealed that having a positive family history of colorectal cancer in first-degree relatives was linked to a substantially higher risk of developing colorectal cancer, with a relative risk of 1.87 [95% CI: 1.68-2.09; P < 0.00001] [20].

In the current study diabetes was the most common reported comorbidity 34.5%, followed by Hypertension in 29.76%, and ischemic heart disease in 4.8% of the enrolled patients.

These findings were slightly higher than reported by **Gheybi *et al.***, who screened 11,656 CRC patients and indicated that the most common comorbidities associated with colon and rectal cancers were hypertension, affecting 25.9% and 22.0% of patients respectively, and diabetes, affecting 17.3% and 15.6% of patients respectively [21].

Pule *et al.* assessed 7115 Australian patients diagnosed with CRC and found that diabetes mellitus and hypertension were the commonest comorbidities affecting patients with CRC accounting for 9% and 10% respectively for all cases [22].

Abu-Freha *et al.*, assessed comorbidities among patients diagnosed with CRC as risk factors for mortality, they found that hypertension affected >40% of the included patients while diabetes only was reported among 10% [23].

We believe this huge variability of prevalence of different comorbidities between different studies are explained by the difference in the assessed population and baseline prevalence of comorbidities among those cohorts, as well as age and gender of the assessed cohorts of patients.

Worldwide, 5% to 10% of colorectal cancers are caused by inherited gene mutations that have been passed down from one generation to the next within a family. An additional 10% to 15% of cases are diagnosed in individuals who have a family history of colon or rectal cancer [24].

We found that patients were mainly presenting with constipation, bleeding, and abdominal pain. On the other hand, signs were mainly iron deficiency anemia [25] and weight loss.

These findings are consistent with global reports that indicated change of bowel habits and chronic constipation are main presenting symptoms of cancer colon, followed by occult blood in stool that leads to IDA and consequently leading to easy fatigability, dyspnea and other anemic manifestations [6, 26, 27].

In the present study, there was an association between high grade disease and younger population. Our findings agree with **Mueller *et al.***, who found that young patients [<40 years old] are more commonly diagnosed with T4-tumors, lymph node metastases, and poorly differentiated [G3] tumors [28].

Other authors reported poor differentiation [G3] ranging between 20%-27% of the included patients [29-31].

In the current study, 86% of the included patients had normal tumor marker, while 12 patients [14%] had elevated CEA. In patients who have had surgical resection and adjuvant chemotherapy for colorectal cancer, CEA is a robust prognostic biomarker [32].

Our findings were inconsistent with several studies that indicated CEA can be found elevated among 80-90% of patients newly diagnosed with CRC [33,34].

During endoscopic examination we found 4.8% of the assessed patients were incompletely visualized by colonoscope and they had totally occluded lumen. We found that positive CT imaging, obstructed lumen and grade III disease were associated with the sign of unexplained IDA.

This rate was lesser than reported in other studies, **Coronel et al.** reported the rate of complete occlusion was 16.7% [35], and it was reported in a systematic review to range between 4.4% to 24%, with more prevalence among patients diagnosed with rectal, rectosigmoid, and sigmoid cancer colon [7].

Histopathology examination of the included patients in our study showed that 91.7% had adenocarcinoma pathology, while 7 patients had signet ring, grade II disease was found 81%, and grade III disease was apparent in 16 patients.

These findings are consistent with most of literature which emphasized that 90% of CRC are carcinomas, 80% of it is adenocarcinoma [36], a subcategory of adenocarcinoma is mucinous differentiation which affect patients with aggressive disease and young age <40 years, and 10% are other types as neuroendocrine, hamartomas, mesenchymal, and lymphomas [10, 17].

In the present study, right sided cancer colon was reported in 23.8%, left sided cancer colon was found in 67.9%, 5 patients had upper rectal disease, while only 2 patients had middle rectal disease.

Patients with right-sided colorectal cancer [RCRC] tend to have a poor response to conventional chemotherapies, but they have shown more encouraging outcomes with immunotherapies due to their high antigenic load. To develop effective treatment strategies and improve treatment options, it is crucial to consider right-sided and left-sided tumors as distinct entities and develop treatment plans that take into account the differences between these tumors [37].

It has been shown that most of the CRC [about 70%] tend to occur in the left side, whereas a small percentage [about 10%] occurs in the right side [38, 39].

Our data showed that multivariate analysis showed that younger age <40 years was an independent predictor for mortality after adjustment for other tumor and clinical characteristics.

These findings are consistent with global trends of mortality and incidence of Although mortality rates for CRC have decreased in older adults, there has been a gradual increase in mortality rates for individuals under the age of 50, reaching an estimated 1.9 deaths per 100,000 individuals in 2018. This trend has been observed in various countries across the world, including the United States, Canada, the United Kingdom, Sweden, Switzerland, Italy, Australia, Egypt, and several Asian countries [40-43].

We had few limitations in the form of small sample size, single institute study which hinder the generalizability of the results of the current study. We finally concluded that epidemiological and clinical characteristics are similar to those reported globally, we found that younger age groups demonstrate more aggressive, poorly differentiated and fatal CRC compared to patients older than 40 years old.

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