A DESCRIPTIVE STUDY OF COLORECTAL CANCER IN HIWA CANCER HOSPITAL, SULAYMANIYAH, IRAQ

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ABSTRACT:
Colorectal cancer is the third most common cancer and the fourth leading cause of death from cancer worldwide. This study provides an overview of changes in sociod-demographic parameters in patients with colorectal cancer (henceforth CRC) disease in a local cancer hospital in Sulaymaniyah province of Kurdistan region of Iraq. The study included 113 patients admitted to Hiwa Cancer Hospital, Sulaymaniyah from January 2014 to December 2015. The data collection lasted for 3 weeks (from 19/12/2015 to 11/01/2016) and was obtained from the management department of Hiwa Cancer Hospital. Several socio-demographic parameters including age, gender, and smoking, as well as biochemical parameters such as liver function, renal function and blood glucose level were studied and statistically analyzed. Results have shown that the majority of CRC patients were neither current smoker nor x-smoker (P-value < 0.05). Males suffered from CRC at an earlier age compared to females (P-value < 0.05). Regarding the biochemical tests, there was no significant correlation between CRC and impaired liver function during the diagnosis process and most of the study patients had a normal liver function test on presentation. In contrast, the correlation between CRC and impaired renal function on presentation was statistically siginificant (P-value < 0.05). No significant difference was noted in the means of hematological and biochemical parameters between males and females, except for white blood cells and serum Aspartate Aminotransferase. White blood cells and total serum bilirubin showed significant differences (P-value < 0.05) between smoker and nonsmoker sub-populations. It was concluded that CRC is one of the common cancers in Sulaymaniyah province. Males develop it at an earlier age compared to females, and the impaired renal function is a significant finding on presentation.

KEYWORDS: Cancer, Colorectal cancer, Hiwa Cancer Hospital, Cancer in Sulaymaniyah

1. INTRODUCTION

Cancer is a disease in which cells divide out of control, in contrast to the normal physiological regulation of cell division. There are many different types of cancer, but they all initiate from uncontrollable growth of abnormal cells (Miller *et al.,* 1990). Recent studies indicate that CRC is the third most common type of cancer and the fourth leading cause of death from cancer worldwide (Lozano *et al.,* 2012; Parkin *et al.,* 2005).

Around 75 to 95% of the diseases are sporadic CRC with no or few genetic defects (Lee *et al*., 2012; Watson & Collins, 2011). Ageing, male gender, high consumption of fat, alcohol or red meat, obesity, smoking, and lack of exercise are some described risk factors for the disease (Watson & Collins, 2011). It usually arises from adenomatous polyp and progresses slowly that takes about 10 to 20 years to develop into malignancy during which a number of genetic changes/mutations take place (Bond, 2000).

The chance of developing CRC increases with age (Society, 2008). The disease mainly occurs in people over the age of 50 (Molanaie *et al.,* 2000), during which more than 90% of CRC cases are diagnosed (Edwards *et al.,* 2010). 5% to 10% of people who develop CRC carry inherited gene defects (mutations) that predispose them to familial CRC syndromes such as familial adenomatous polyposis (FAP) and

hereditary non-polyposis colorectal cancer (HNPCRC) that lead to development of the disease (Edwards *et al.,* 2010).

Furthermore, inflammatory bowel diseases are known to be associated with an increased risk of CRC (Edwards *et al.,* 2010). Crohn's disease increases the risk of CRC by two folds, whereas the risk is 7to 11 fold for Ulcerative colitis and is directly related to the duration of the disease (Roy & Bianchi, 2009).

The present study aims to provide an overview of CRC disease in a local cancer hospital in Sulaymaniyah province of Kurdistan region of Iraq. It studies the correlation between the disease and some socio-demographic characteristics of patients, as well as the biochemical and hematological parameters.

2. MATERIAL AND METHODS

2.1. Data collection

The study included 113 out of 194 CRC patients that were admitted to Hiwa Cancer Hospital from January 2014 to December 2015, as there were no enough data in the applied database on the remainder 81 patients. Data collection on the study subject lasted for three weeks (from 19/12/2015 to 11/01/2016), during which information about the socio-demographic parameters of the patients and some biochemical tests prior to treatment (that were performed as a part of initial work up for the CRC patients) were obtained from the Clinical Portal System of HCH under supervision of the management

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department. This study has been formally permitted and approved by Research and Data Protection Committee in Hiwa hospital.

2.2. Questionnaires

The questionnaire form included information about some socio-demographic parameters of the patients such as gender, age and smoking. The answers to the questions were obtained from the recorded database by the interviewers from the management department.

2.3. Biochemical Tests

As a major part of routine work up for the newly diagnosed CRC patients, physicians from the HCH perform a number of biochemical tests including complete blood count (CBC), liver function test (alanine transaminase [ALT], aspartate transaminase [AST] and total serum bilirubin [TSB]), renal function test (blood urea and serum creatinine), and the blood glucose level test.

2.4. Statistical analysis

After giving each data an identification address (ID), the obtained data were arranged on a Microsoft Excel Datasheet, and statistical analyses were performed using the SPSS software program version 18.0. Standard methods were used including means, percentages, standard deviation and standard error to describe the demographic and biochemical variables. T-test Chie square test and ANOVA one way were applied to compare the means of different variables. In this study, a P-value of ≤ 0.05 is considered as statistically significant.

3. RESULTS

3.1. The relation between gender and smoking in CRC.

Out of 113 patients that were included in the current study, 54 (47.8%) of them were males and 59 (52.2%) patients were females, which indicates a slightly female predominance (male to female ratio was 1:1.1). Among the males, 11(20.4%) and 43 (79.6%) patients were smokers and non-smokers, respectively. In contrast, only 4 (6.8%) female patients were smokers and 55 (93.2%) of them have never smoked in their life. The median age was 49.5, 60 and 57 years for males, females and both genders together (Table 1).

Table 1. Socio-demographic characteristics of the patients and some biochemical parameters in males and females (P <0.05).

		Gender		
		Male (%)	Female (%)	Both (%)
Number		54 (47.8%)	59 (52.2%)	113 (%)
Median age		49.5	60	57
Smoking	Yes	11/54 (20.4%)	4/59 (6.8%)	15/113 (13.3%)
	No	43/54 (79.6%)	55/59 (93.2%)	98/113 (86.7%)
Liver Function Test	Normal	38/54 (70.3%)	50/59 (84.7%)	88/113 (77.9%)
	Abnormal	16/54 (29.6%)	9/59 (15.2%)	25/113 (22.1%)
Renal Function Test	Normal	9/54 (16.7%)	21/59 (35.6%)	30/113 (26.5%)
	Abnormal	45/54 (83.3%)	38/59 (64.4%)	83/113 (73.5%)

- Normal: standard level of the parameters.
- Abnormal: at least one of the parameters higher/lower than the normal range.
- P< 0.05: statistically significant.

3.2. The relations between both liver and renal functions with smoking in CRC

98 (86.7%) of the participants of the study were non-smokers and the rest 15 (13.3%) were smokers. On the one hand, among the non-smokers, 73 (74%) patients had abnormality (ies) in the renal function while only 20 (20.4%) of them had a problem in the liver function parameters. On the other hand, 5 (33%) and 10 (67%) smoker patients showed abnormal liver and renal function tests, respectively (Table 2).

Table 2. The relation between both liver and liver function parameters and smoking habit in colorectal cancer patients (P > 0.05).

		Smoking		
		Yes (%)	No (%)	All (%)
Number		15/113 (13.3%)	98/113 (86.7%)	113 (100%)
Liver Function Test	Normal	10/15 (66.7%)	78/98 (79.6%)	88/113 (77.9%)
	Abnormal	5/15 (33.3%)	20/98 (20.4%)	25/113 (22.1%)
Renal Function Test	Normal	5/15 (33.3%)	25/98 (25.5%)	30/113 (26.5%)
	Abnormal	10/15 (66.7%)	73/98 (74.5%)	83/113 (73.5%)

- Normal: standard level of the parameters.
- Abnormal: at least one of the parameters higher/lower than the normal range.
- P> 0.05: not significant.

3.3. The relation between male and female CRC with different age categories

In the present study, the age of the patients was randomly categorized into three age categories. Out of 54 male patients; 21 (38.9%), 25 (46.3%), and 8 (14.8%) of them were between the ages of 18 - 49, 50 - 69, and ≥70 years old, respectively (Table 3). In the remaining 59 female patients, 16 (27.1%), 31 (52.5%), and 12 (10.6%) of them belonged to the respective age groups as the males.

Table (3): Prevalence of colorectal cancer in males and females in different age categories (P< 0.05).

		Age Categories			Total
		18 - 49	50 - 69	≥ 70	
Gender	Male	21	25	8	54
		38.9%	46.3%	14.8%	100.0%
		18.6%	22.1%	7.1%	47.8%
	Female	16	31	12	59
		27.1%	52.5%	20.4%	100.0%
		14.2%	27.4%	10.6%	52.2%
Total		37 (32.7%)	56 (49.6%)	20 (17.7%)	113 (100.0%)

3.4. The relation between CRC and blood glucose level in male and female

Figure 1 illustrates the relation between blood glucose level and CRC. Only 36 patients demonstrated abnormal blood glucose level and the remainders (77 patients) had normal blood glucose level.
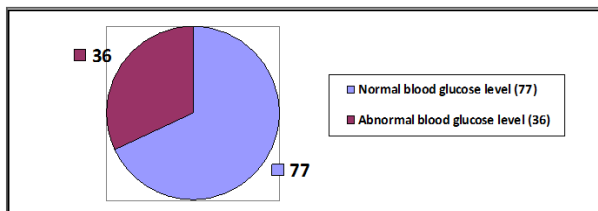
Figure 1. The relation between CRC and blood glucose level at presentation.

➢ Normal: standard level of the parameters. Abnormal: at least one of the parameters higher than normal.

3.5. The relation between CRC and some Hematological and Biochemical parameters in both genders

Figure 2 explains the relation between the biochemical and hematological parameters in different genders of CRC patients. Among the liver function parameters (ALT, AST, and serum total bilirubin) only serum AST showed a significant (*P<0.05*) difference between the male and female patients (Figure 2). The blood glucose level and renal function tests (blood urea and serum creatinine) showed no significant alteration in either genders. On the contrary, among the hematological parameters (hemoglobin [HGB], haematocrit [HCT], mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], platelet [PLT] and white blood cells [WBC]) only WBC was significantly (*P<0.05*) altered in both male and female patients.
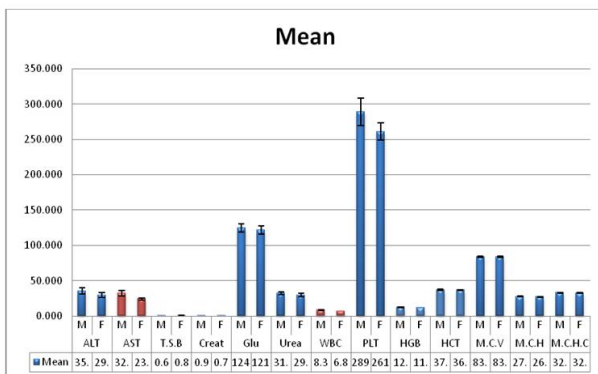

Figure 2. The relation between CRC and some Hematological and Biochemical parameters in different genders (Mean ± SE). The red color of the columns means there is a significant *(P<0.05)* difference between the means of the same parameters. Error bar indicats the standard error of the mean. Alanine transaminase [ALT], aspartate transaminase [AST] and total serum bilirubin [TSB], serum creatinine[Creat], glucose [Glu], hemoglobin [HGB], haematocrit [HCT], mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], platelet [PLT] and white blood cells [WBC].

3.6. The relation between CRC and some Hematological and Biochemical parameters among smoker and non smoker patients

This graph illustrates the relation between CRC and some hematological and biochemical parameters in smoker and non smoker patients. Only AST and TSB showed a significant (*P<0.05*) alteration in smoker and non-smoker patients. All the remaining parameters have not significantly changed *(P>0.05)*.
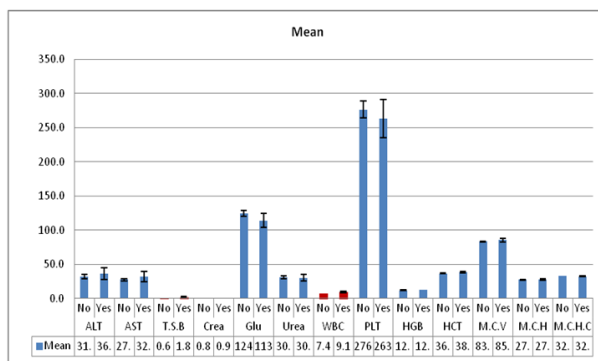

Figure 3. The relation between all paramiters and smoking (Mean ± SE). The red color of the columns indicates a significant difference between the means of the same parameters. Error bar indicats the standard error of the mean. Alanine transaminase [ALT], aspartate transaminase [AST] and total serum bilirubin [TSB], serum creatinine[Crea], glucose [Glu], hemoglobin [HGB], haematocrit [HCT], mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], platelet [PLT] and white blood cells [WBC].

4. DISCUSSION

In the present study, the majority of CRC patients were between the 5th and 7th decades of life which is consistent with the results of other studies (Al-Humadi, 2009; Cook *et al.,* 2013 and Rasouli *et al.,* 2017). A previous study demonstrated that CRC occurs in older age groups (above 70 years) (Clark *et al.,* 1985), furthermore, however, Ono *et al.,*(2002) have showed that the disease may occur more frequently in the middle aged group in both genders with a possible explanation that the molecular and pathophysiological changes occurring throughout the life progressively modify the molecular homeostasis of colonic epithelial cells leading to neoplasia (Ono *et al.,* 2002).

The DNA damages certainly increases in with ageing, suggesting frequent stochastic cellular insults (Taylor *et al.,* 2003). Aging also increases (rather than decreasing) epithelial proliferation in human colon (Roncucci *et al.,* 1988). The incidence of CRC is uncommon under the age of 50 years especially sporadic CRC and continues to increase up to the age of 85 years (Holt *et al.,* 2009). The exact mechanism is unclear but recent studies have focused on the importance of SIRT1 deacetylase in suppressing tumorogenesis and colon neoplastic growth (Sinclair, 2005). The present results showed that the male gets it in younger age than female which is consistent with other studies, however, the overall incidence and mortality are similar in both genders.

The age-specific incidence is earlier in men for both colorectal adenomas and carcinoma and the disease seems to appear many years earlier in men compared to woman, probably due to protection effect of estrogen and progesterone. A study have shown that postmenopausal estrogen/progesterone hormone treatment in women can lower colorectal neoplasia risk by as much as 30% (Rex *et al.,* 2009). The renal function test is another important point in the current study patients that has a significant relationship with CRC in both Genders. Among eleven case-reports within the medical literature of colonic adenocarcinoma metastatic to the kidney, none occurred via direct invasion (Ono *et al.,* 2002). In the majority studies, result demonstrated that renal metastasis from primary colon cancer is very rare, except for a unique case-report of a 51-year-old female with extra luminal colonic adenocarcinoma that directly invaded the kidney (Nelson *et al.,* 2011).

The relationship between CRC and the impaired renal function showed an important diminution in 31(17%) patients (GFR < 60 ml/min/1.73m2). Mild impairment (GFR between 60–90 ml/min/1.73m2) of the renal function was observed in 87 (48%) patients and only 65 (35%) patients had a normal function (GFR > 90 ml/min/1.73m2) (Velciov *et al.,* 2013).

In this study, the elevated WBC count had a statistically significant increase (P<0.05) in the incidence risk and mortality of CRC in men and women. Studies have indicated a relationship between chronic inflammation and malignancy with long-standing inflammatory bowel diseases (Crohn's disease and ulcerative colitis) and subsequent elevation of WBC count being a relevant example of inflammation induced CRC (Lee *et al.,* 2006; Prizment *et al.,* 2011).

The association between cigarette smoking and CRC has been inconsistent among studies. However, the results of this study showed no significant relationship between CRC and smoking. A previous study has reported a 20% to 60% increase in the risk of CRC among active smokers. However, neither the U.S. Surgeon General nor the International Agency for Research on Cancer (IARC) have classified this relationship as causal probably due to the effect of other confounding factors (Hannan *et al.,* 2009).

The liver is the most frequent and often unique site of metastasis in CRC, both at the time of diagnosis and after an apparently radical surgery for the primary tumor. Results from the current study showed no significant abnormality in liver functions parameters of CRC patients, however, approximately half of the patients with CRC present at some stage with hepatic metastasis (Scheele, 1993). According to previous studies, liver metastases are diagnosed in 10–25% of patients at the time of resection of their primary colorectal tumor and, eventually, up to 70% of patients with CRC can develop liver metastases (Wanebo *et al.,* 1978; Welch & Donaldson, 1979). Unfortunately, in the present study, a precise recording of the cancer stages of the study subjects was not available, and hence they could not be taken into consideration.

4.1. Strengths and Limitations

To our knowledge, this is the first study investigating the relationship of these important parameters with CRC at Hiwa Cancer Hospital in Sulaimani province. The significant relationship of elevated WBC count with CRC may raise the possibility of an inflammatory background of these tumours in the study population and its future consideration. Additionally, Kurds, Arabs, Christians, and other backgrounds that currently live in Sulaimani province are included in the study and this makes the results more representative of the study population. Furthermore, significantly impaired renal function on presentation can help oncologists to appreciate the importance of pre-treatment work up and guide them choose the best possible management strategy. On the contrary, lack of enough data on 81 out of 194 study subjects and their exclusion from the study might have negatively influenced proper assessment of the targeted parameters and subsequently the results were obtained. In addition to that, the stage of the disease, which is an important confounder, was not considered during statistical analysis and hence the effect of confounding bias on the results is expected.

5. CONCLUSIONS AND RECOMMENDATIONS

It was concluded from the study that CRC is one of the common cancers in Sulaymaniyah Province. Males develop both colorectal adenomas and carcinoma at an earlier age compared to females. Among all the investigated study parameters, the impaired renal function is a significant finding on presentation. In a sub-group analysis, WBC count and total serum bilirubin were significantly different between smoker and nonsmoker. Future colaborative studies are recommended for a better understanding of the relationship between study parameters and CRC disease.

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