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CHARACTERISTICS OF COLORECTAL CANCER PATIENTS IN KURDISTAN CENTRE FOR GASTROENTEROLOGY & HEPATOLOGY (KCGH)

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ABSTRACT

Background: Colorectal cancer (CRC) is one of the most common types of cancer worldwide. In Asia the incidence of CRC is increasing. It is now the second most common cause of death in western countries.

Objectives: To evaluate the socio-demographic, clinical, endoscopic and histopathological characteristics of patient with colorectal cancer at Kurdistan center for gastroenterology and hepatology (KCGH).

Patients and methods: This is a retrospective cross-sectional study of CRC in Kurdistan center for gastroenterology and hepatology in Sulaimani city/ Iraqi Kurdistan for 14 months from 1st of June 2014 to 31st of July 2015. The records of 2163 colonoscopies were evaluated to find cases of colorectal cancer.

Results: A hundred patients with histologically proved CRC were included in this study (55% male, 45% female); 64 % of patients were above 50 years of age. Mean age was 55.7 ± 16.4 year. The most common presenting symptom was bleeding per rectum (40%), followed by abdominal pain (30%). Site of distribution of tumor was 78% distal colon, 22% proximal colon. The vast majority of cases were adenocarcinoma (97%).

Conclusions: Colorectal cancer was diagnosed in 4.6% of patients who had been referred for colonoscopy at KCGH, male to female ratio was 1.2:1, mostly in the 7th and 8th decades. Bleeding per rectum was the most common presenting symptom and adenocarcinoma was the most common histological type.

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INTRODUCTION

Colorectal cancer (CRC) is the second most common internal malignancy and the second leading cause of cancer deaths in Western countries. The first cause of cancer related death in male is lung cancer and in female is breast cancer (Nicki *et al.*, 2010). The incidence begins to rise at age 40 and peaks at age 60 to 75 years (Mark *et al.*, 2003). Colorectal area is the host to more primary neoplasms than any other organ in the body (Mohd *et al.*, 2010). The incidence of CRC in Iraq is 2.6% compared to 6-13% in the developed countries (Adil H. Al-Humadi, 2008; Summer Saad Abdulhussain *et al.*, 2014). Despite numerous attempts to detect cancer at an early stage, the overall long-term outcome of patients curatively resected has not significantly changed in the last decade, the 5-year survival rate being approximately 60 percent.

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More than half of colorectal adenocarcinomas are still diagnosed only when the disease involves regional or distant organ metastasis (Laohavinij *et al.*, 2010). "CRC" is considered as one of the most preventable cancers, because it might develop from polyps, which can be removed before they become cancerous (Fayez Sandouk *et al.*, 2013). The risk of cancer in adenomatous polyps and villous adenomas under 1 cm in size is only about 1 in 100 (1%), for polyps between 1 and 2 cm in diameter the risk increases to about 1 in 10 and over 2 cm there is a nearly 30% malignancy rate (Muto *et al.*, 2010). Both environmental and genetic factors are important in colorectal carcinogenesis. Environmental factors probably account for over 70% of all 'sporadic' colorectal cancers (Nicki R. Colledge *et al.*, 2010).

Risk factors

Environmental factors

The etiology for most cases of large-bowel cancer appears to be related to environmental factors. The disease is more

common in high socioeconomic group who live in urban areas (Summer Saad Abdulhussain *et al.*, 2014). Diet: The ingestion of animal fats that found in red meats and processed meat leads to an increased proportion of anaerobes in the gut microflora, resulting in the conversion of normal bile acids into carcinogens (Muto *et al.*, 2010). Insulin resistance: The high calories in “western” diets coupled with physical inactivity have been associated with a higher prevalence of obesity; obese teenagers have twofold higher risk for Colorectal Cancer (Elizabeth D. Kantor, 2015). Persons with such excess weight gain develop insulin resistance with increased circulating levels of insulin, leading to higher circulating concentrations of insulin-like growth factor type I (IGF-I). This growth factor appears to stimulate proliferation of the intestinal mucosa (Adil H. Al-Humadi, 2008). Fiber: A high fiber intake was regularly recommended as one way to lower the risk for colon cancer. This recommendation was largely based on observations that countries with a high fiber intake tended to have lower rates of colon cancer than the rates found in countries with a low fiber intake (Zlobec and Lugli, 2008).

Inflammatory bowel disease (IBD)

Patients with long-standing inflammatory bowel disease (IBD) having higher risk to develop CRC. Cancers develop more commonly in patients with ulcerative colitis (UC) than in those with Crohn's disease (CD). The risk of CRC in a patient with IBD is relatively small during the initial 10 years of the disease, but then it appears to increase at a rate of 0.5 to 1% per year. Cancer may develop in 8-30% of patients after 25 years. The risk is higher in younger patients with pancolitis (Muto *et al.*, 2010).

Genetic factors

Patients with the highest risk for CRC are those who have a hereditary CRC syndrome. The dominantly inherited syndromes include familial adenomatous polyposis (FAP) and Lynch syndrome (Summer Saad Abdulhussain and Osama Hasan Othman, 2014; Laohavinij *et al.*, 2010; Fayez Sandouk *et al.*, 2013; Muto *et al.*, 2010; Elizabeth D. Kantor, 2015; Zlobec and Lugli, 2008; William *et al.*, 2012).

Ureterosigmoidostomy

Colon cancer develops in 5-10% of people 15 to 30 years after ureterosigmoidostomy to correct congenital extrophy of the bladder. Neoplasms characteristically are found at a site distal to the ureteral implant where colonic mucosa is chronically exposed to both urine and feces (Muto *et al.*, 2010).

Tobacco use

Cigarette smoking is linked to the development of colorectal adenomas, particularly after 35 years of tobacco use (Muto *et al.*, 2010).

Clinical features

More often the symptoms of CRC are anemia and changes in

bowel habit. For right sided tumors also melena can occur. For rectal cancer it is not uncommon that fresh blood and / or mucus in faeces as well as changes in bowel habit are the cause for seeking consultation. In later stages symptoms of CRC can be significant weight loss, loss of appetite, fatigue and obstruction, or a palpable lump in abdomen or rectum (Annette *et al.*, 2011; Friedenreich *et al.*, 2010)

Screening

It is thought that most CRC arise from preexisting adenomas (Aitken *et al.*, 1996). Adenocarcinoma of the colon and rectum grows slowly, and a long interval elapses before it becomes large enough to produce symptoms. Early diagnosis depends on proper regular screening (Nicki *et al.*, 2010; William *et al.*, 2012). All patients with symptoms suggestive of colorectal neoplasia should undergo an evaluation of the colon by colonoscopy or by flexible sigmoidoscopy plus barium enema or CT colonography (virtual colonoscopy) (Winawer *et al.*, 2003).

The rationale for CRC screening programs is that the earlier detection of localized, superficial cancers in asymptomatic individuals will increase the surgical cure rate. Such screening programs are particularly important for individuals having a family history of the disease in first-degree relatives. Most programs directed at the early detection of CRC have focused on digital rectal examinations (DRE) and fecal occult blood testing. The digital rectal examination should be part of any routine physical evaluation in adults at any age (Muto *et al.*, 2010). Higher adenoma detection rates in screening colonoscopy were associated with lower lifetime risks of colorectal cancer (Reinier *et al.*, 2015). Effective screening tests include immunochemical methods for fecal occult blood (i-FOBT) using antibodies to human globin with potential increase in patients' compliance; because no dietary restrictions are needed (Mark *et al.*, 2003).

Fecal (stool) DNA (deoxyribonucleic acid) tests have been under continuous development over the past several years. These tests are designed to detect in stool samples any number of DNA markers shown to be associated with CRC (Renée *et al.*, 2011). Colonoscopy is also recommended for screening by the American Cancer Society at age of 50 years. Colonoscopy is often considered the gold standard for detection of colorectal polyp, and deaths from CRC can undoubtedly be reduced through removal of adenomatous polyps (Mark and Robert Berkow, 2003; William *et al.*, 2012). Computed tomographic colonography (CTC), or virtual colonoscopy, was more sensitive than barium enema in detecting colorectal cancer and large polyps (Winawer *et al.*, 2003).

Studies in general population samples have found certain demographic variables, such as higher education, higher income, having health insurance, and being married to be associated with high CRC screening rate. Factors such as lack of symptoms, lack of time, inconvenience, lack of interest, cost, discomfort associated with the procedure, and embarrassment have been found to be common barriers to CRC screening (William *et al.*, 2012; Annette *et al.*, 2011; Friedenreich *et al.*, 2010; Aitken *et al.*, 1996; Winawer *et al.*, 2003; Reinier *et al.*, 2015; Renée *et al.*, 2015).

Aims of the study

- 1- To study the sociodemographic characteristics of patients with CRC at KCGH.
- 2- To study the colonoscopic and histological characteristics of CRC among patients referred to KCGH for colonoscopy.

Patients and Methods

This is a retrospective cross sectional study conducted in KCGH in Sulaimani city /Kurdistan-Iraq; from 1st of June 2014 through 31 July 2015. A total of 2163 patients were included; all were referred for colonoscopy.

The study started after obtaining approval from Scientific and Ethical committee of Directory of Health of Sulaimani. *Brief history, physical examination and viral screening for Hepatitis B, C and HIV(human immune deficiency virus) were performed before colonoscopy*, demographic data recorded, weight in kilograms and height in centimeters were measured, BMI(body mass index) (kg/m^2) was calculated from the reported values.

Inclusion criteria

All patients referred to KCGH for colonoscopy.

Exclusion criteria

- 1- Unprepared patients.
- 2- Noncompliance/incomplete study.

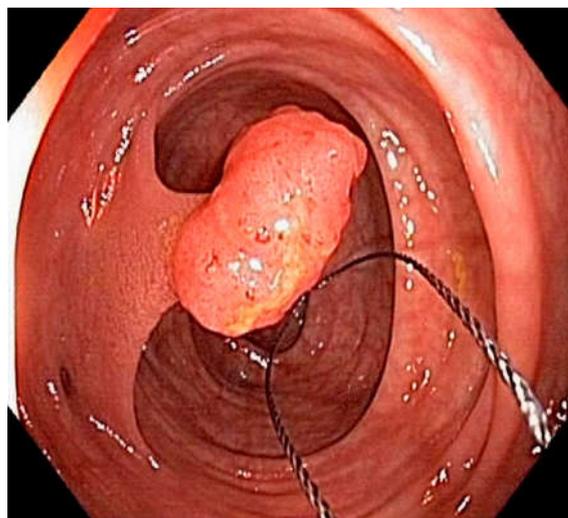
Written Informed consent was obtained from every patient before colonoscopy, the patients were prepared 2 days before colonoscopy with (Poly ethylene glycole) and (Bisacodil) and details of preparation were given to every patients.

The procedures were performed under conscious analgesia using intravenous midazolam (2.5-5 mg) and pethidine (50-100 mg) with doses escalated according to response, monitoring pulse rate, O₂ saturation and BP(blood pressure) were used during the procedure. All the procedures were performed by certified gastroenterologists. The colonoscopy done by using Olympus EVIS EXERA (CF-Q180AL).

When any lesion was found during procedures, 4-8 biopsies were taken for histopathological examination, after completing colonoscopy, the patient transferred to the recovery room for 30-60 minutes for monitoring the vital signs and general condition and when they become stable they were discharged. All the data of patients were registered in special retrieval system in KCGH.

RESULTS

Out of 2163 colonoscopies which had been performed during the study period, 100 patients were diagnosed as CRC which constitute 4.6%. The mean age of patients with CRC was 55.7 ± 16.4 year (55% were males and 45% were females). Male to female ratio was 1.2:1 as shown in Fig.1.



Picture 2. Large bowel polyp



Picture 3. Large bowel cancer

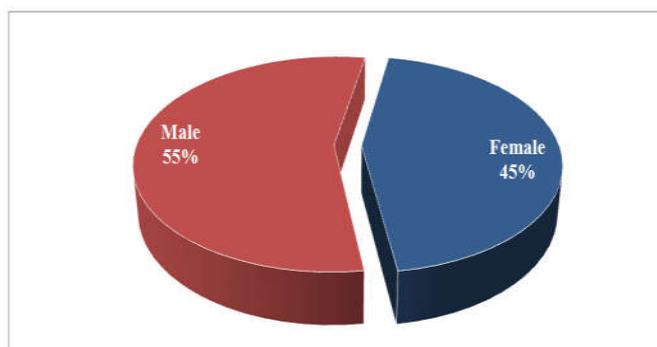


Fig. 1. Colorectal cancer and gender

The incidence of CRC was increasing with age and the peak age was in 7th and 8th decades. As shown in Figure 2.

Twenty percentages of CRC patients were below age of 40 years, 30% were between 40-59 years and 48% was above 60 years, family history of CRC was positive in 2% of cases both of them with first degree relatives, only those two patients came for screening colonoscopy. The Mean BMI was 21.5 ± 3.03 . Most patients 73% had normal BMI as shown in Tab.1.

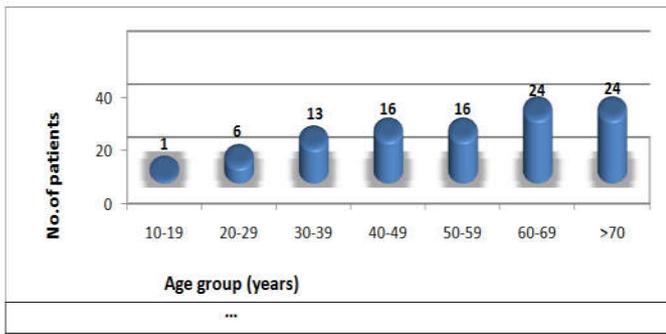


Table 1. Demographic characteristic of patients with CRC

Variable	Total no.&%
Age/ year	
< 40	20
40 - 59	32
≥ 60	48
Family history of CRC	2
BMI	
< 18.5 Kg/m ²	14
18.5 – 24.5 Kg/m ²	73
> 25 Kg/m ²	13

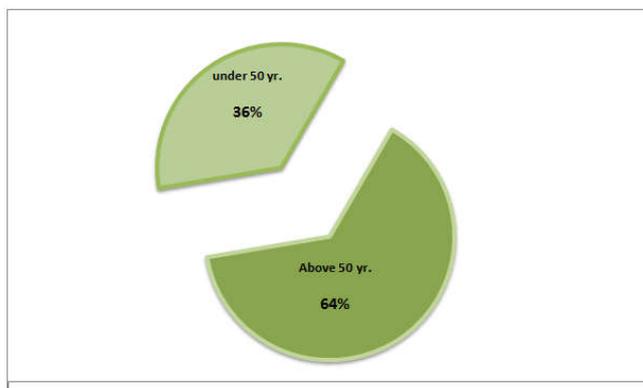


Fig. 3. Colorectal carcinoma and age 50 years

Thirty six patients 36% were below age of 50 years and 64% were above age of 50 years as shown in Figure 3. The most common presenting symptom was bleeding per rectum 40% followed by abdominal pain 30% as shown in Figure 4.

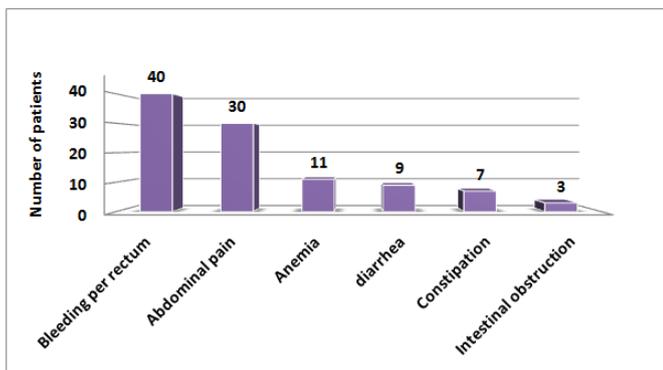


Fig. 4. Presentation of patients with colorectal cancer

Anal inspection showed abnormality in 10% Figure 5.

Digital rectal examination of patients with CRC was Negative in 65% of cases but abnormal in 35%; as shown in Figure 6. (during DRE 65% of patients with CRC were negative, in 22% there were a mass, 8% had stenosis).

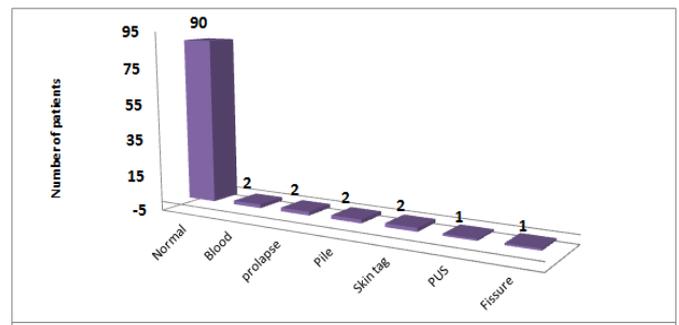


Fig. 5. Anal inspection in colorectal cancer

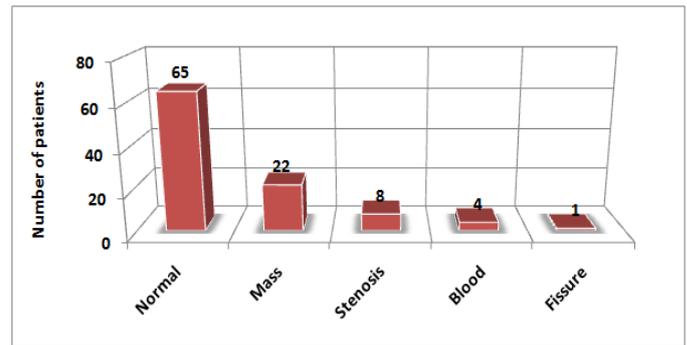


Fig. 6. Digital rectal examination in patients with colorectal cancer

Colonoscopic findings of CRC lesion showed that in 77% of cases had mass (53% non-obstructing, 24% obstructing) and 23% showed ulceration as shown in Figure 7.

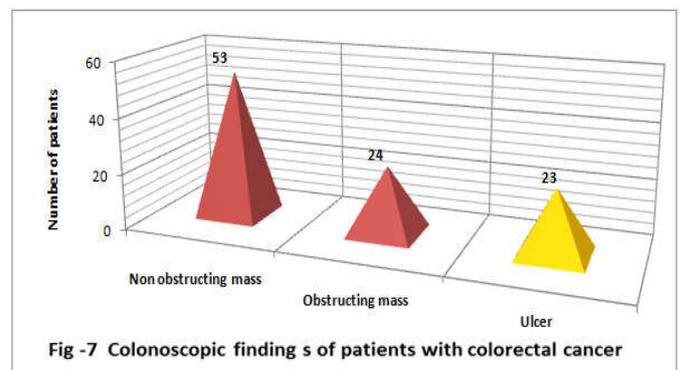


Fig -7 Colonoscopic findings of patients with colorectal cancer

Seventy eight (78%) of CRC were in Distal colon and 22% in Proximal colon; however; the commonest site of tumor was in Rectum 38% Figure. 8.

Proximal colon = [cecum, ascending colon, and transverse colon] (Gonzalez *et al.*, 2001).

Distal colon = [descending colon, sigmoid colon, rectosigmoid, rectum and anorectal] (Gonzalez *et al.*, 2001).

Blood group of the patients with CRC: 51% of the patients had blood group (A) and 31% had blood group (O) as shown in Figure 9.

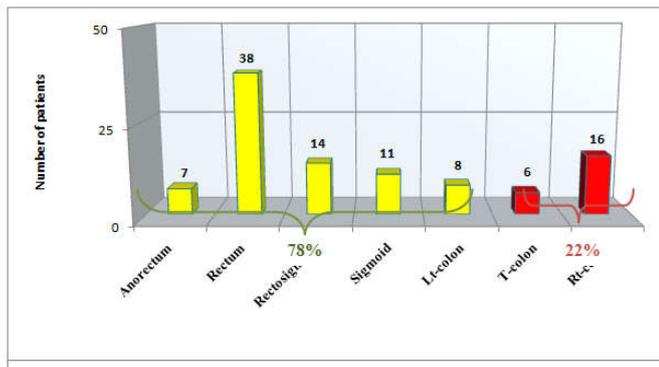


Fig. 8. Site of colorectal cancer by colonoscopy

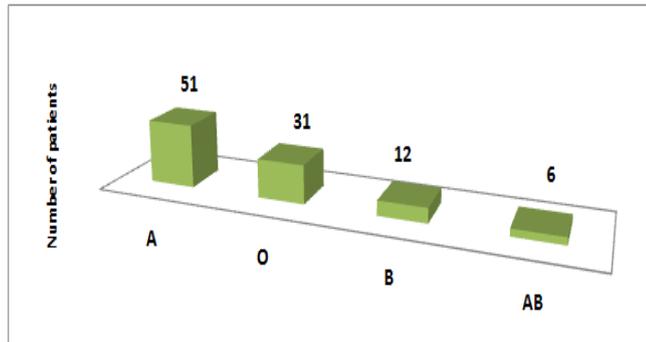


Fig.9. Distribution of colorectal cancer according to blood group

Regarding histopathological types of CRC: 97% were Adenocarcinoma, 1% neuroendocrine tumor (NET), 1% small cell cancer and 1% squamous cell carcinoma, Figure-10.

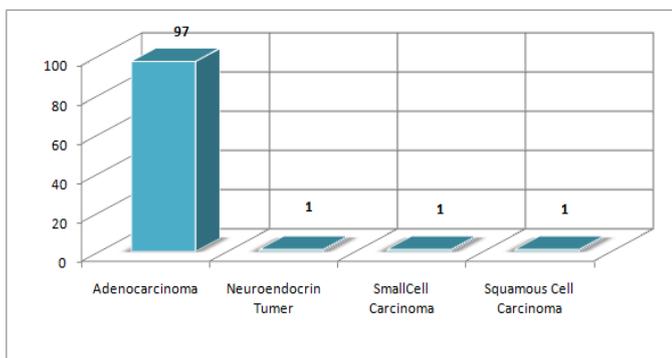


Fig.10. Histopathology of colorectal cancer

DISCUSSION

It is well established that colorectal cancer can largely be prevented by early detection and removal of adenomatous polyps (Lindmark and Kolon och rectum, 2008) and it's curable if diagnosed early (Fang *et al.*, 2010). No age group is exempt from disease; adenocarcinoma of colon has been reported in a nine-month-old girl (David *et al.*, 2002; Ahmed Gado *et al.*, 2014). Attempting to define accurate epidemiological characteristics of CRC patient is essential for any preventive and curative intention; this study is one attempt in this direction. From 2163 colonoscopies done during period of study at KCGH; 100 patients diagnosed to have CRC. The Mean age was 55.79 ± 16.4 in this study which is comparable to the result of previous study done in Sulaimani city where

the mean age was 53.7 years (Taha Alkarboly *et al.*, 2014). Also it is comparable to a study done in Sri Lanka in which the mean age was 55 ± 15 years (Chan *et al.*, 2010).

In current study 55% were males and 45% were females, male to female ratio was 1.2:1. This finding is comparable to the previous studies done in Iraq regarding the male: female ratio and peak age group affected by the disease (Sabeha M. Al-Bayati and Farkad Jasim, 2009) the corresponding distribution worldwide is 1.4:1 (Jacques Ferlay *et al.*, 2011), and China 1.25:1 (An-Gao Xu *et al.*, 2010). In this study the 7th and 8th decades were the most frequent age group affected by CRC which is in concordance with regional and international studies, CRC also occurred more frequently in the 7th & 8th decades in Saudi Arabia (Al-Ahwal *et al.*, 2005). Our results show that 20% of CRC patients were below 40 years and it was comparable to studies done in Saudi Arabia, Sudan and Iran in which CRC below age of 40 years old ranged between 17–36% (Al-Ahwal *et al.*, 2005; Abdalla *et al.*, 2007; Roya Dolatkah *et al.*, 2015).

Most patients 73% had normal BMI, and it was comparable to study done in Sulaimani in which More than half of patients had normal body mass index (Taha Alkarboly *et al.*, 2014), probably this might due to devastating consequences of CRC on health of affected patients. There were 2% with positive family history of CRC, while in Iran 35.1% had a family history of cancer (Roya Dolatkah *et al.*, 2015). This probably due to underreporting in our study due to retrospective design. In the current study, 36% of CRC patients were below 50 years, approximately 43 percent of colorectal cancer in Iran occurs before 50 years of age (Safae *et al.*, 2010). While in United States more recent reviews have shown that only 12% of CRC patients were under 50 years of age (Koo *et al.*, 2012).

The trend of CRC to affect patients younger than 50 years of age should promote responsible medical authority to review the local guideline regarding screening colonoscopy in our locality, which mandate decreasing age of screening for CRC below the age of 40 years; the limitation probably would be total cost, facilities, discomfort etc....

The percentage of screening for CRC is still very low (2%) even in tertiary center like KCGH. This probably due to low public medical awareness due to lack of national medical education on mass media. A study done in Kingdom of Saudi Arabia revealed that lack of screening and consequent advanced stage at diagnosis might lead to the increase in colorectal cancer mortality in Saudia Arabia (Al-Ahwal and Al-Ghamdi, 2005). In this study, Bleeding per rectum was the most common presentation 40% among CRC patients which is comparable to study done in Sweden which was a classical symptom of CRC and frequent first symptom⁽³⁴⁾ while in study done in Kirkuk-Iraq the main presenting symptom was abdominal pain 42.4% (Summer Saad Abdulhussain and Osama Hasan Othman, 2014). Abdominal pain was the 2nd common presentation 30% which makes colonoscopy preliminary investigation of paramount importance in excluding CRC in any patient with irritable bowel syndrome particularly if he/she more than 40 years and not responding to short empiric treatment or subtle alarming features (Talib *et al.*, 2009). In this study, chronic non bloody diarrhea was the

presentation in 5% of patients and bloody diarrhea 4%; the sum will be 9% (bloody and non-bloody diarrhea) which means diarrhea was more frequent presentation than constipation 7% this mandate colonoscopy work up for chronic diarrheal patients to exclude CRC as a cause of (spurious diarrhea) phenomena (Aras *et al.*, 2015).

In this study, anal inspection of CRC patients revealed abnormality among 10%; this revealed that superficial evaluation can miss serious diagnosis. While comprehensive Digital rectal examination increase yield to 35% of abnormal finding; so lack of enthusiasm by some physicians to do the proper digital rectal examination especially in female patients would miss or delay diagnosis, This simple, safe and cheap procedure can be of great help in the early diagnosis of rectal pathologies (Elisabeth Del Giudice *et al.*, 2014). In this study, 38% of CRC cases were in rectal area which means trend toward increase in rectal tumor in our locality particularly in younger age group, as compared with the incidence of rectal cancer which is 47% in Western countries (Robert E. Sedlack *et al.*, 2008), while it is 30% in the United Kingdom (More than 40,000 people are diagnosed with colorectal cancer - or bowel cancer - in the UK each year, with around one third of these being rectal cancer) (Monahan and Clark, 2013). In Egypt 37.2% of the patients presented with primary lesions in the rectum (Darlene Veruttipong *et al.*, 2012). In Korea and Japan as reported by Sun-II Lee, *et al.*, an increased incidence of rectal cancer by 2.5 times during 1992-2002 (Sun-II Lee *et al.*, 2008).

In the current study 78% of patients had CRC in distal colon (up to splenic flexure). Multiple studies have shown an increase in the incidence of right-sided colon cancers in the United States (Jennifer *et al.*, 2011). Which make flexible sigmoidoscopy more informative & even easier in our patients, because it means doing proper flexible sigmoidoscopy up to splenic flexure will detect the majority (78%) of cases. Although blood group (A) associates with gastric cancer (Edgren *et al.*, 2010), in the current study 51 % of patients had blood group (A) and 31% of group (O). In two large prospective cohorts, they did not observe a statistically significant association between ABO blood group and risk of colorectal cancer⁽⁴⁴⁾. Histopathological examination revealed that 97% had adenocarcinoma, 1% had squamous cell carcinoma, 1% had small cell carcinoma and 1% had neuroendocrine tumor (NET) which is in concordance with other study that found adenocarcinoma constituted 97.8% of the colon cancer (Summer Saad Abdhussain *et al.*, Osama Hasan Othman, 2014; Rosenberg *et al.*, 2008). In conclusion we need to implement earlier screening protocol for our patients to prevent the dire consequence of CRC.

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