

## Colorectal Carcinoma Presentation, Risk Factors and Management

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### ABSTRACT

**Background:** Colorectal carcinoma is the most common gastrointestinal tract cancer worldwide. In men, it is the third cancer after lung and prostate cancer, while in women; it is the third common cancer after lung and breast cancer. Despite the clear relationship with aging, colorectal carcinoma is not strictly a disease of elderly and 6-8 % of cases occur in patients below 40 years of age. Colorectal cancers are of favorable prognosis provided they are diagnosed and treated in early stage. **Objective:** This study aims to assess the patterns of presentation, risk factors, distribution, and management of colorectal carcinoma. **Method:** From October 2008 to October 2010, 70 patients with colorectal carcinoma 41/70, (58%) males and 29/70, (42%) females were admitted to the Gastroenterology and hepatology center. The age, sex, presentation, modes of investigation, stage of the cancer, treatments as well as complications have been described. **Results:** Male: female ratio about 1.4:1 with peak age of incidence is the sixth decade, 19/70, (27%). 17/70, (24%) of cases are below age of 40 most of them were with worse histopathological types and advanced stage. The main presenting symptom was bleeding per rectum 30/70, (56%). The mean of the period between onset of presenting symptoms and final diagnosis was 8 months. The most common sites were rectum 25/70, (36%), 41/70, (58%) were moderately differentiated, 30/70, (43%) were Duke's-C. **Conclusion:** The study highlights the importance of early diagnosis, keeping in mind the increasing incidence of colorectal carcinoma in younger age groups.

**Keywords:** Colorectal CA. Presentation. Risk factors. Investigations. Site of predilection. Surgical management. Complications.

### Introduction:

Colorectal carcinoma is the most common gastrointestinal tract cancer worldwide. (1) In men, it is the third cancer after lung and prostate cancer, while in women; it is the third common cancer after lung and breast cancer. (2,3) It is estimated according to the results of Iraqi cancer registry (in the period between 1995-1997) that it is the 12th most common cancer, with an incidence of about 1.1/100 000 person. (4) Colorectal and anal malignancies are slightly common in men, they represent about 4.4% in males and 3.7 % in females of all malignant tumors registered during the period between 1995-1997. (4) Despite the clear relationship with aging, colorectal carcinoma is not strictly a disease of elderly and 6-8 % of cases occur in patients below 40 years of age. (5) It has been noted recently that there are increase colorectal malignancies in young patients. (6) In a study done in Iraq during the period from 1989 to 1992 found that colorectal and anal malignancies accounts for 40% of all malignant tumors involving stomach, small bowel and large bowel. (7) Colorectal malignancies are of favorable prognosis provided they are diagnosed and treated in early stage. (8)

The etiology of colorectal cancer is unclear, but there is a group of patients regarded as high- risk patients and these include: (1,9)

**A- Age above 50 years.**

**B- Patients with premalignant conditions like:**

*Ulcerative colitis.*

*Crohn's disease.*

*Familial polyposis coli.*

*Hereditary non polyposis colon cancer syndrome.*

*Previous history of colon polyps.*

*Uretrosigmoidostomy.*

**C-Family history of colorectal cancer or polyps.**

The influence of age and sex on the site distribution of large bowel malignancies is widely reported to change with time. There is a relative decrease in frequency in the left side of colon with relative increase on the right. (10,11,12)

Signs and symptoms of colorectal malignancies are non-specific, usually depend on site and type of the tumor.

Following suspicion of these tumors, per rectal examination and fecal occult blood test remain important measures for detecting tumors. (14)

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Endoscopy regarded as the most accurate method for diagnosis as well as to rule out any synchronous carcinoma or polyp that occur in 3-5 % of cases.<sup>(1,16)</sup> The use of modern techniques will increase the diagnostic certainty at early stages, for example, the use of endoscopic ultrasound will give diagnostic accuracy of 90%. Advances in imaging technology have created a number of less invasive but highly accurate tools for screening.

CT colonography (Virtual Colonoscopy) makes use of helical CT technology and three-dimensional reconstruction to image the intraluminal colon. Pre operative staging allow surgeons to assess the degree of penetration, thus determining which tumor will be amenable to excision and which will benefit from pre operative radiation for down staging.<sup>(17)</sup>

The standard treatment for colorectal cancer is surgery with wide resection and anastomosis. The aim of surgical treatment for cure is to remove the tumor and its lymphatic drainage and provide adequate clear margins ensuring removal of entire tumor burden.<sup>(18)</sup>

Approximately 25% of patients have distant metastasis and are not candidate for surgical resection with curative intent.<sup>(19)</sup> The use of self expandable stents that is introduced endoscopically is a recent advance where it can be used either as a palliative measure or preoperatively to allow single stage operation to be carried out later on in case of intestinal obstruction.<sup>(20)</sup> Adjuvant chemotherapy can be used following resection in patient with high risk of recurrence and they can improve survival in patients with Dukes' C tumor.<sup>(18)</sup>

The risk of recurrence after surgery vary from 20% to 45% this results from incomplete tumor excision, implantation of tumor cells or the development of new growth and the risk can be reduced by total mesorectal excision.<sup>(13)</sup>

So that post operative follow up is important in every case especially those regarded as high risk group and this can be achieved by colonoscopy and barium enema.

The level of carcinoembryonic antigen CEA as a tumor marker can be used also for follow up every three months then annually.<sup>(1,9)</sup>

There is a place for prevention of the development of these cancers in patients with some of polyposis coli and in some cases of ulcerative colitis by performing prophylactic colectomy,<sup>(11)</sup> also there are many reports showing that nonsteroidal anti inflammatory drugs can prevent the development of cancer through its action on inhibiting cyclo oxygenase 2 enzyme, which is over expressed in cancer state.<sup>(21)</sup>

In regard to staging of colorectal cancer, modified Duke's staging system is now the most popularly used method.

Another staging system is the TNM staging system. Colorectal cancer staging is based upon tumor depth and the presence or absence of nodal or distant metastases.

### Patients and Methods

A prospective and retrospective study of a single centre was conducted on seventy patients newly diagnosed to have colorectal carcinoma, of different age groups and gender. All patients were managed at gastroenterology and hepatology teaching hospital-Medical City in Baghdad ,Iraq from October 2008 - October 2010. The data were collected by a special form and the patients were admitted and treated at the surgical department , where investigations carried out to prove the diagnosis and determine the site and the extent of the disease. All patients were evaluated by history , clinical examination, and investigated by the following ;Complete blood picture , ESR , liver function test , renal function test, prothrombin time , partial thromboplastin time , INR , virological assessment. Radiological examination by chest, plain abdominal X-Ray , abdominal ultrasound were done for all the patients and most of them investigated by endoscopy and biopsy and abdominal CT scan and some patients with EUS.

Preoperative bowel preparation (mechanical using saline rectal enemas, oral polyethelenglycol solution, chemical using antibiotics or both) was done for all patients presenting as an elective situation two days before surgery.

Prophylactic antibiotics (Cefuroxime 1g plus Metronidazole 500mg intravenously) were given at induction of anesthesia and continued for two days if no clinical features of sepsis were present. The choice of operation depends on the site of the tumor, the condition of the bowel and the general condition of the patient. Our aim of surgical treatment for cure was to remove the tumor and its lymphatic drainage and provide adequate clear margins ensuring removal of entire tumor burden. Post-operative follow up was performed by measuring the level of carcinoembryonic antigen (CEA) as a tumor marker every three months then annually and by colonoscopy within the first six months and then annually.

Clinical data from physical examination, investigations and operative findings were used for classification of the cases; the staging system used in this study was the modified Duke's staging system. Body mass index calculated by the equation:  $BMI = \frac{Wt (Kg)}{(Ht)^2 M^2}$  (obese patients had a BMI of more than 30) ,alcohol consumption, chronic heavy smoking, hereditary factors (FAP) and non hereditary factors (UC & polyps) were included in this study as risk factors for the development of colorectal carcinoma .

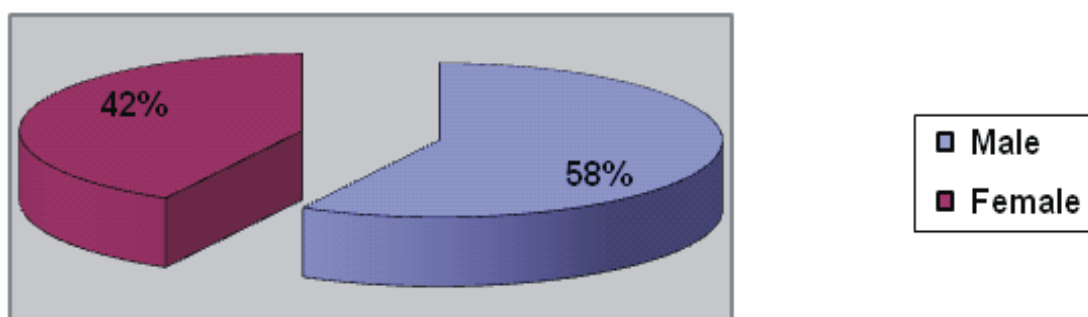
**Results and Tables:**

Age distribution, **table (1)** showed that 19/70, ( 27%) of patients were found in the (50-59 years) age group recording the highest occurrence. Also we found that 17/70, (24.3%) of patients were below 40 years old.

**Table (1): Age distribution.**

<i>Age (years)</i>	<i>No.</i>	<i>%</i>
< 20	1	1.4%
20-29	6	8.6 %
30-39	10	14.3 %
40-49	16	23%
<b>50-59</b>	<b>19</b>	<b>27%</b>
60-69	10	14.3 %
= 70	8	11.4%
<b>Total</b>	<b>70</b>	<b>100%</b>

**Figure (1): Sex distribution. / M:F ratio = 1.4 : 1**



**Table (2): Risk factors for colorectal carcinoma**

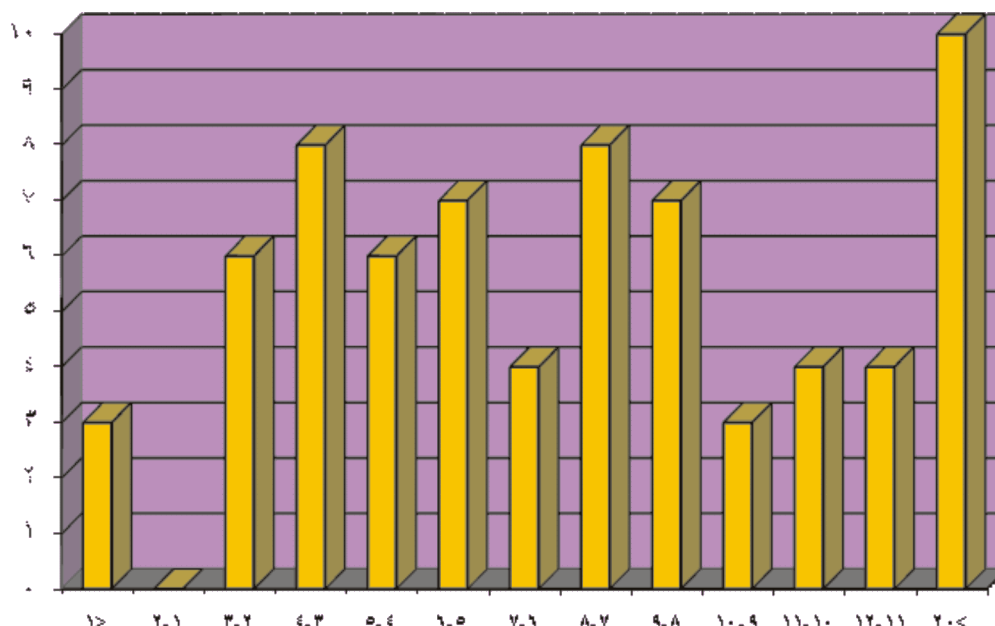
<i>Risk factors</i>			<i>No.</i>	<i>%</i>
<i>Dietary</i>	High fat and/or low fiber diet		<b>51</b>	<b>73%</b>
	Large BMI		30	43%
	Alcohol consumption		13	18.5%
	Cigarette smoking		45	64%
<i>Non dietary</i>	<i>Hereditary</i>	FAP	2	3%
	<i>Non hereditary</i>	UC	2	3%
		Family history	4	5.7%
		Polyps	9	13%

**Table (3): Clinical presentation**

<i>Clinical feature</i>	<i>No.</i>	<i>%</i>
Bleeding per rectum	39	56%
Changeable bowel habit	34	48.5%
Abdominal pain	28	40%
Anemia	27	38%
Mass	18	26%
Tenesmus	13	18.5%
Anorexia	6	8.5%
Abdominal distension	6	8.5%

**Figure (2)**

The mean of the period between onset of presenting symptoms and the final diagnosis was 8 months

**Table (4): Investigation methods**

Investigation	Findings	No.	%
Abdominal U/S	Colonic mass	15	21%
	Colonic wall thickening	7	10%
	Liver metastasis	5	7%
	Ascites	3	4%
	Negative/Inconclusive	40	57%
Double contrast Barium enema	Irregular filling defect	6	8.5%
	Stricture	3	4%
Endoscopy	Ulcerative lesion	31	44%
	Stricture	17	24%
	Cauliflower lesion	13	18%
	Uncompleted	9	13%
CT scan with oral and IV contrast	Pelvic mass	17	26%
	Colonic wall thickening	15	21%
	Ascites	3	4%
	Liver metastasis	5	7%
Plain abdominal x-ray	Distended large bowel	15	23%
	Normal	55	78%
EUS	T3N1	4	5.7%
	T3N0	4	5.7%

**Table (5): Site distribution of colorectal cancer**

<i>Site</i>	<i>No.</i>	<i>%</i>
Rectum	25	36%
Sigmoid	16	23%
Caecum	6	8.5%
Rectosigmoid	6	8.5%
Transverse colon	5	7%
Ascending colon	4	5.7%
Descending colon	2	2.8%
Hepatic flexure	1	1.4%
Splenic flexure	1	1.4%
Total colon (FAP+UC )	4	5.7%
Total	70	100%

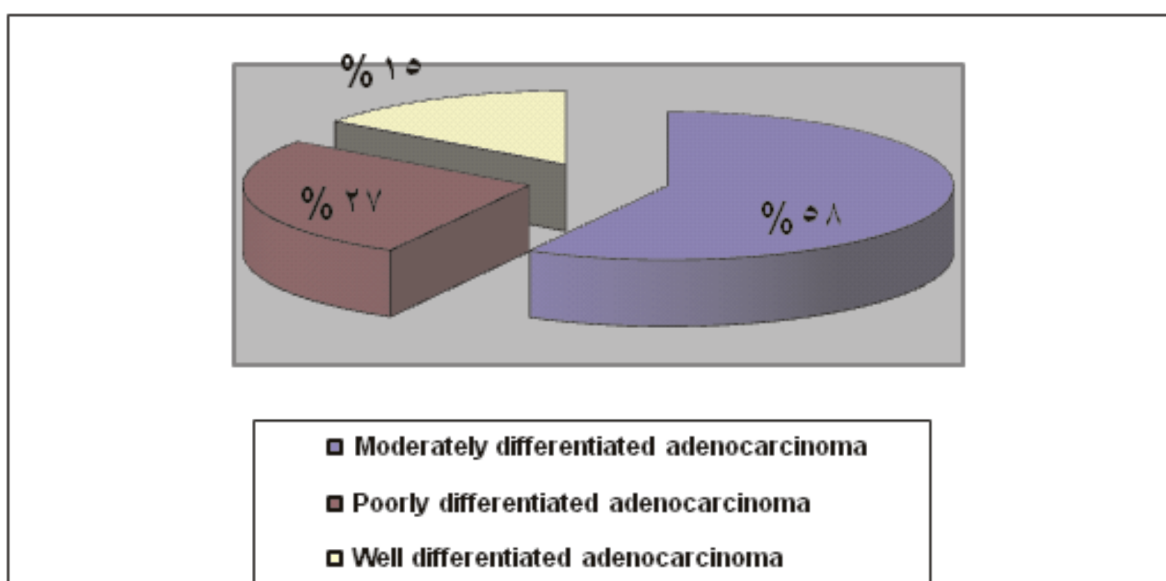
**Table (6): Modality of surgical treatment**

<i>Site</i>	<i>Operation</i>	<i>No.</i>	<i>%</i>
Rectum	Abdomino-perineal resection	21	30%
	Low anterior resection	2	2.8%
	Colostomy	2	2.8%
Sigmoid	Anterior resection	15	21.6%
	Colostomy	1	1.4%
Rectosigmoid junction	Resection + EEA	5	7.2%
	Colostomy	1	1.4%
Caecum	Right hemicolectomy	6	8.6 %
Transverse colon	Extended right hemicolectomy	3	4.3 %
	Resection + EEA	2	2.8%
Ascending colon	Right hemicolectomy	4	5.7%
Descending colon	Left hemicolectomy	2	2.8%
Hepatic flexure	Extended right hemicolectomy	1	1.4%
Splenic flexure	Left hemicolectomy	1	1.4%
FAP & ulcerative colitis	Procto-colectomy + ileostomy	4	5.7%
<b>Total</b>		<b>70</b>	<b>100%</b>

**Table (7): Stages of colorectal cancer**

<i>Duke's stage</i>	<i>No.</i>	<i>%</i>
A	3	4.2%
B1	10	14.3 %
B2	12	17.1%
<b>C1</b>	<b>16</b>	<b>23%</b>
<b>C2</b>	<b>14</b>	<b>20%</b>
D	15	21.4%
<b>Total</b>	<b>70</b>	<b>100%</b>

Histological grading, **figure (3)** clarified that 41/70,(58%) had moderately differentiated adenocarcinoma, 19/70,(27%) had poorly differentiated adenocarcinoma while the remaining 10/70, (15%) of cases had well differentiated adenocarcinoma

**Figure (3): Grades of colorectal cancer**

**Table (8): pathological findings in young and old patients.**

	<i>No of patients</i>	
<i>Grad of the tumor</i>	<i>&lt; 40 year</i>	<i>&gt;40 year</i>
Well differentiated	2	9
Moderately differentiated	9	31
Poorly differentiated	6	13
<i>Duke's classification</i>		
A	0	3
B	4	18
C	7	22
D	6	10

**Table (9): Postoperative morbidity and mortality.**

<i>Complications</i>	<i>No.</i>	<i>%</i>
Wound infection	3	4.2%
Wound dehiscence	2	2.8%
Chest infection	2	2.8%
DVT	2	2.8%
Fistula	1	1.4 %
Intra-abdominal sepsis	1	1.4 %
Renal failure	1	1.4 %
Mortality	2	2.8%



## Discussion:

Colorectal cancer continues to be the most common cancer in the gastrointestinal tract world wide.<sup>(1)</sup> The male to female ratio(M:F) is about equal.<sup>(11)</sup>

In this study the (M:F) ratio was 1.4 : 1. Although colorectal carcinoma is a disease of older patients we found that 17/70, (24%) of our patients were under the age of 40 years, this is higher than many studies done worldwide like McCoy and Parks(U.K 1984) who reports 0.9%<sup>(7)</sup> and Smith et al(USA1989) who reported 4.8%<sup>(22)</sup>, while in Iraq 2000 Rhman had reported 35.5%<sup>(11)</sup>. Kakil I et al<sup>(41)</sup>

conducted 20% of colorectal cancer patients to be less than 40 years. The peak incidence of colorectal cancer was between 50-59 years age group, this is in difference to the result of other study done in Iraq between January 1996 and jun1997<sup>(23)</sup> and 2008<sup>(43)</sup> who recorded that the peak incidence was between 60-69 years age. In respect to the risk factors of colorectal cancer, included in this study; *High fat and/or low fiber diet* ;51/70, (73%) ,this was in agreement with that of: Schottenfeld D<sup>(29)</sup>, Steinmetz KA et al<sup>(30)</sup>, Favero A et al<sup>(31)</sup> and Levi F et al<sup>(32)</sup>: who also found high fat and/or low fiber diet as a risk factor for colorectal cancer.

*Lack of physical activity and large body mass index* ;30/70, (43%) and this is in accordance with that of: Thune I<sup>(33)</sup>, Martinez ME et al<sup>(34)</sup>, Slaterry ML et al<sup>(35)</sup>, Giovannucci E et al<sup>(36)</sup> and Willet WC et al<sup>(37)</sup>: who also reported a correlation between lack of physical activity, large body mass index and colorectal cancer. *Alcoholism*; 13/70,(18.5%) and this concedes with that of: Longnecker MP et al<sup>(38)</sup>, Baron JA et al<sup>(39)</sup> and Boutron MC et al<sup>(40)</sup>: who also found higher incidence of colorectal cancer among alcoholic patients. *Cigarette smoking* ;45/70, (64%) and this goes with that of: Yamada K et al<sup>(42)</sup> who also conducted a relationship between cigarette smoking and colorectal cancer.

*Non dietary factors* included hereditary risk which was found in two cases with FAP 2/70, (3%) ,*non hereditary* risk was in the form of ulcerative colitis 2/70,(3%), family history of colorectal cancer 4/70, (5.7%) and polyps 9/70, (13). Jarvinen et al found that ulcerative colitis represents 1.7% and FAP 0.6 %<sup>(25)</sup>, also it is the same finding of other study done in Iraq 2001<sup>(26)</sup>.

The commonest presenting symptom was bleeding per rectum in 39/70, (56%) of our patients followed by change in bowel habit in 34/70, (48%), while the results of Rhman and Al-Janabi were 55% for bleeding per rectum and 24% for change in bowel habit<sup>(11)</sup>, other study done in Iraq had showed 43.9% bleeding per rectum and 57.5% change in bowel habit<sup>(24)</sup>. Talib A. Majid and Waseem M.Sh.<sup>(43)</sup>, Al-Bahrani ZR and Al-Hadithi R<sup>(44)</sup>,

also reported bleeding per rectum and change in bowel habit as the most common presentation symptom of colorectal cancer. Other symptoms were including pain, anemia, weight loss, abdominal mass and others.

There was delay for more than 8 months from the onset of presenting symptoms to the time of definitive diagnosis, this is about the same of other studies done in Iraq<sup>(43)</sup>

which had recorded a delay for more than 7 months . Therefore any of presenting symptoms should be take in consideration and patient should be investigated properly and at early time.

All patients enrolled in our study were underwent abdominal U/S examination and 61/70,(87%) of them underwent endoscopic examination.

When colorectal cancer is suspected, colonoscopy is the diagnostic study of choice, it provide access to examine the entire colon ,allows biopsy of colonic lesion. The colonoscopy was uncompleted in 9/70, (13%) of cases, so completion barium enema was necessary<sup>(26)</sup>.

EUS is very sensitive and specific (>90%) for bowel wall involvement. Lymph node involvement is detected by EUS with a specificity of approximately 85%. Eight of our patients underwent an EUS examination , 4/70, ( 5.7%) were with T3N0 and the others were T3N1 .

CT scan of abdomen and pelvis is useful in identifying metastatic disease, however, is not useful in gauging the depth of disease, but is useful in staging. Abdominal and pelvic MRI have not been shown to be superior to CT scan at this time in staging of rectal cancer ,but are started to gain popularity when EUS is not readily available.<sup>(27)</sup>

Most tumor were seen on the left side of the colon mainly the rectum, sigmoid and rectosigmoid junction 47/70, (67%), nearly the same findings of other studies done in Iraq<sup>(11,24,43)</sup>. Neil J<sup>(13)</sup>

who also found that the most commonly involved site was the rectum, next to it was the sigmoid colon, followed by the caecum. While Mc coy and Parks findings were 32% at rectum and sigmoid with 45% at splenic flexure and descending colon<sup>(7)</sup> , so the tumors are more predominantly at the left side with rectosigmoid predilection.

In respect to the surgical procedures used to treat our patients, abdomino-perineal resection was the most commonly used modality 21/70, (30%) next to it was anterior resection which was employed in 17/70, (23%) of cases, and right hemicolectomy in 14/70, (20%). Palliative colostomy was performed in 4/70, (5.7%) .McCoy G.F., Parks<sup>(8)</sup> reported abdomino-perineal resection and right hemicolectomy to be the most commonly employed procedures (25% and

In respect to staging of the colorectal adenocarcinoma using modified Dukes staging system, most cases presented with Dukes C at time of diagnosis which account for 30/70, (43%), Dukes B account for 22/70, (31%), Dukes D represent 15/70, (21%) and Dukes A was only 3/70, (4.2%). Kakil I et al<sup>(41)</sup> who also conducted that most of the patients with colorectal cancer were found in the category of Duke stage B and C (about 70%). According to McCoy and Parks, Dukes C 41.9%, D 38.7%, B 12.9% and Duke A was 6.4%<sup>(8)</sup>. This was about the same for other studies done in Iraq<sup>(43)</sup>.

Most of our young patients had tumor staged C and D with histo-pathological reports of moderately to poorly differentiated adenocarcinoma which may suggest that carcinoma of large bowel is more malignant and aggressive in young patients and this is also reported in other studies.<sup>(7,23)</sup>

Regarding the grading of the tumor, well differentiated carcinoma was 10/70, (15%), while moderately differentiated was 41/70, (58%) and poorly differentiated was 19/70, (27%). It is nearly the same finding of other study done in Iraq<sup>(27,43)</sup>. Rahman M and Al-Janabi KH<sup>(11)</sup>, who reported moderately differentiated adenocarcinoma in (79%) of their colorectal cancer cases, while McCoy and Parks found that well differentiated carcinoma was (41.39%), moderately differentiated was (22.9%) and poorly differentiated was (35.48%)<sup>(8)</sup>.

The most common postoperative complication in this study was wound infection in 3/70, (4.2) patients followed by wound dehiscence, chest infection and DVT in 2/70, (2.8) for each. Fistula was found in 1/70, (1.4%), this was the same for intra-abdominal sepsis and renal failure. It is about the same results of Hassan A.H., Ameen N.<sup>(24)</sup> and Talib A. Majid & Waseem<sup>(43)</sup>. There were 2 deaths among this study one of them was due to sepsis and renal failure and the other one was because of pulmonary embolism.

### Conclusions:

1. There is an increase in the incidence of colorectal carcinoma in young age, most of them were with worse histopathological types and advanced stage.
2. Bleeding per rectum and change in the bowel habit are the common presenting features with the rectum being the most common site.
3. Dietary and non dietary risk factors for colorectal carcinoma including high fat / low fiber diet, family history and colonic polyps.

### Recommendations:

- 1) Raising the index of suspicion of colorectal carcinoma especially in patients with bleeding per rectum and recent change in bowel habit whatever their age is.
- 2) Bearing in mind the risk factors for colorectal cancer so as to avoid them / use them for earlier

detection of colorectal carcinoma at a better stage and grade and eventually improving the prognosis of the disease.

- 3) Screening for colorectal carcinoma so as to detect the disease at early stages.

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