

Evaluation And Management Of Colorectal Carcinoma

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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, distribution, and management of colorectal carcinoma in Gastroenterology and hepatology center. **Patient and Method:** From November 2011 to February 2014, 100 patients with colorectal carcinoma 53 males and 47 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 documented. **Results:** Male: female ratio about 1.1:1 with peak age of incidence is the seventh decade, 21 of patient 21% are equal or below age of 40 most of them were with worse histopathological types and advanced stage. The main presenting symptom was bleeding per rectum 75%. The mean period between onset of presenting symptoms and final diagnosis was 7 months. The most common sites were rectum 52%, 60% were moderately differentiated, 47% 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.

Introduction:

Colorectal carcinoma is the most common gastrointestinal tract cancer worldwide. ^(1,2,3) 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. ^(4,5) 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. ⁽⁶⁾ Colorectal and anal malignancies are slightly more 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. ⁽⁸⁾ 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. ⁽⁷⁾ It has been noted recently that there are increase colorectal malignancies in young patients. ⁽⁸⁾ In a study done in Iraq during the period from 1989 to 1992 it was found that colorectal and anal malignancies accounts for 40% of all malignant tumors involving gastrointestinal tract. ⁽⁹⁾

Colorectal malignancies are of favorable prognosis provided they are diagnosed and treated in early stage. ⁽¹⁰⁾ The etiology of colorectal cancer is unclear, but there is a group of patients regarded as high- risk patients and these include: ^(1,2,3,11)

A- Age above 50 years.

B- Patients with premalignant conditions like:

1- Ulcerative colitis.

2- Crohn's disease.

3- Familial polyposis coli.

4- Hereditary non polyposis colon cancer syndrome. HNPCC

5- Previous history of colon polyps.

6- Uretrosigmoidostomy.

C- Family history of colorectal cancer or polyps.

D- History of malignancy outside the bowel

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. ^(12,13,14)

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Signs and symptoms of colorectal malignancies are non-specific, usually depend on site and type of the tumor. In left colon, cancer might present as bleeding per rectum or change in bowel habit while, in right colon, cancer present usually as anemia with its consequent fatigue, weight loss and fever in 50% of patients. It might cause intestinal obstruction in 10%. The tumor might invade other organs, which lead to other signs and symptoms. Some times colorectal carcinoma can present as metastasis.^(2,3,15) Following suspicion of these tumors, per rectal examination and fecal occult blood test remain important measures for detecting tumors.⁽¹⁶⁾ 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.^(1,18)

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%. 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.⁽¹⁹⁾ 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.⁽²⁰⁾ Approximately 25% of patients have distant metastasis and are not candidate for surgical resection with curative intent.⁽²¹⁾ The use of self expandable stentes that is introduce 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.⁽²²⁾ Adjuvant therapy can be used following resection in patient with high risk of recurrence and they can improve survival in patients with Dukes' C tumor.⁽²⁰⁾

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.⁽¹⁵⁾ 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 fore follow up every three months then annually.^(1,2,3,11) 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,⁽¹³⁾ 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.^(23,37)

Aim Of The Study:

The aim of this study is the assessment of the patterns of presentation ,age and sex distributions ,methods of investigations, pathological distribution ,site ,stage and grade and surgical management and complication of colorectal carcinoma in Gasrotr oentorology and Hepatology teaching hospital and if there is any difference or changes in comparison with other studies done in Iraq as well as world wide.

Setting:

Gastroenterology and Hepatology Teaching Hospital-Medical City,Baghdad,Iraq.

Patient and methods:

In this prospective study , analysis of the data of 100 patients newly diagnosed to have colorectal carcinoma who were treated at Gastroenterology and Hepatology teaching hospital medical city from November 2011 to February 2014.The data were collected by a special form as below 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 include biochemical , endoscopy (upper and lower) and imaging as U/S ,CT, MRI and barium enema .Preoperative bowel preparation (mechanical using rectal enemas ,oral polyethelinglycol solution (coloclean), antibiotics or both) was done for most of the patients presentating as an elective situation two days before surgery but not in case of emergency operations , fluid diet 72 hours prior to surgery ..

Prophylactic antibiotics (ceftriaxone 1 g plus metronidazole 500 mg intravenously)were given at induction of anesthesia and continued for two days if no clinical feature of sepsis were present . The surgical technique depends on the site of tumor , the condition of the bowel and the general condition of the patient include right and left hemicolectomy , segmental resection with anastomosis, anterior resection (high , low and ultralow) , A-P resection , total proctocolectomy with or with out stoma , colostomy or ileostomy only , bypass , stenting and no surgery.

specimens all send for histopathology examination. Most of our patients were referred to oncologist pre and post operatively. Clinical data from physical examination , investigations and operative finding were used for staging system used . in this study the modified Duke 's staging system was used . {table 1}

Table 1
Modified Dukes' staging system(Astler and Colle

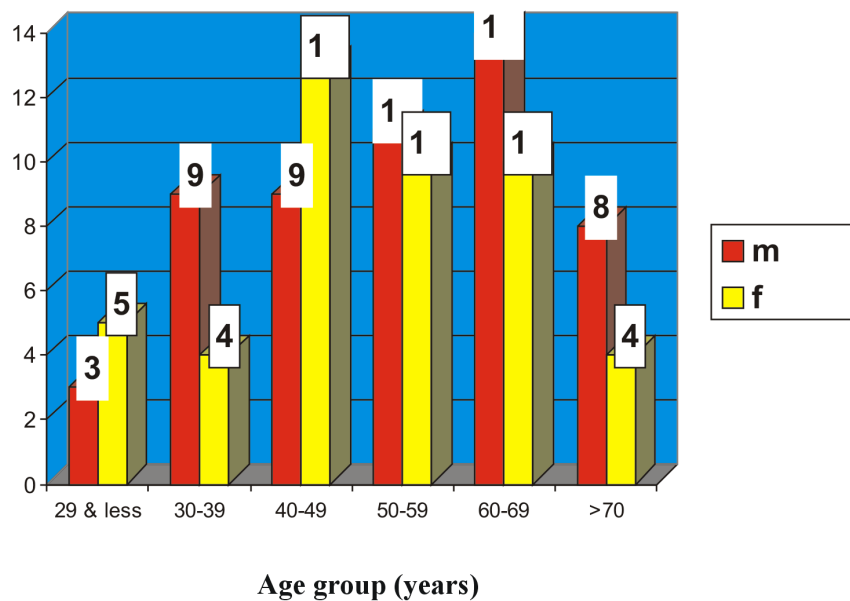
Stage	Extent of tumor	5 years Survival rate
A	Lesion limited to the mucosa.	100%
B1	Lesion limited to the muscularis propria with negative lymph nodes.	66.4%
B2	Lesion penetrating muscularis propria with negative lymph nodes.	53.9%
C1	Lesion limited to the wall with positive lymph nodes.	42.8%
C2	Lesion penetrating through the wall with positive lymph nodes.	22.4%
D	Distant metastasis.	>10%

Results:

There were 53 male patients and 47 female patients. The mean of age was 49.5 years for males and 43.5 years for females, the range of age was 12-80 years. There were 21 patients (21%) below 40 years. The peak age group affected was between 60-69 years age and.

Male to Female ratio is 1.1: 1. There were 4 patient (4%) between 10-20 years, all of them locally advanced CA who require neoadjuvent chemo radiotherapy before surgery. As seen in figure (1).

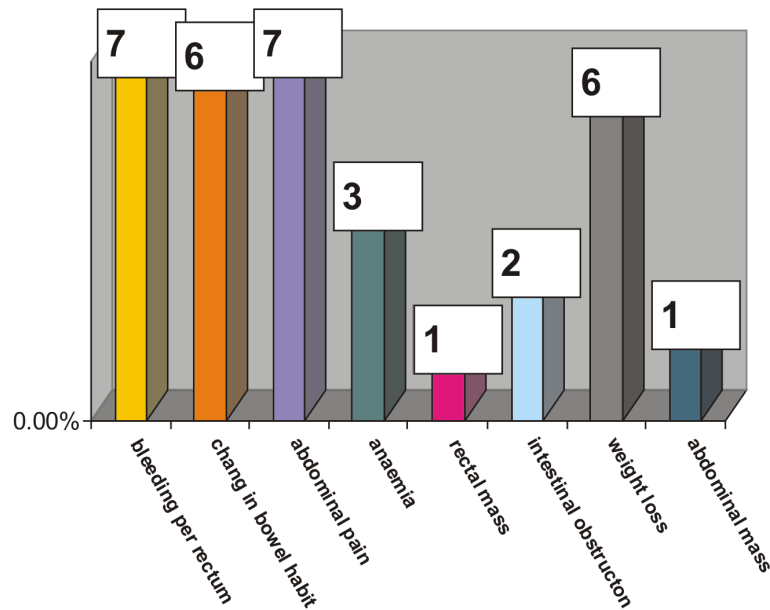
Figure (1): Distribution according to age and sex



Mode of presentation:

The main presenting symptoms was bleeding per rectum and abdominal pain in 75 % of cases followed by change in bowel habit in 65% of cases, patient might have more than one symptom. As seen in figure (2).

**Figure (2):
The main symptoms and signs.**

**Duration of symptoms.**

The mean of the period between onset of presenting symptoms and the final diagnosis was 7 months.as seen in figure (3).

Figure (3)

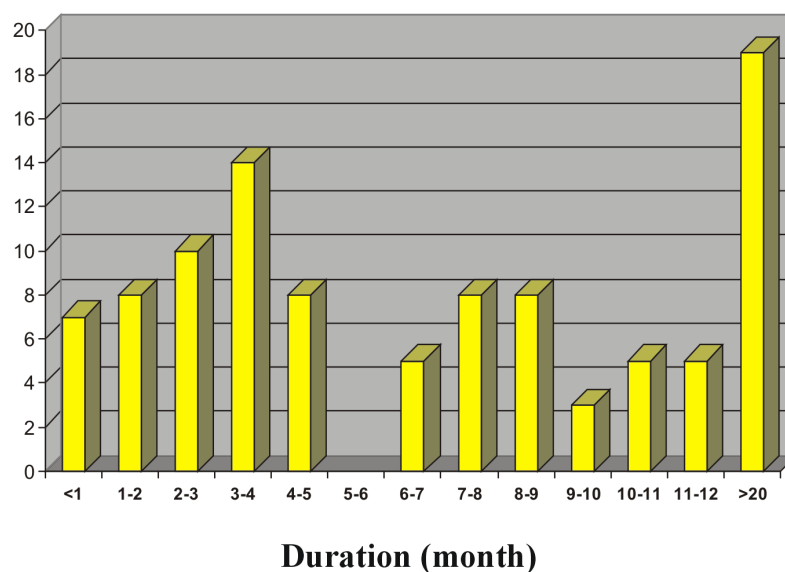


Table 2:
site distribution of colorectal

Site of tumor	Male	Female	Total No.	Percent(%)
Upper rectum	3	6	9	9 %
Middle rectum	4	5	9	9%
Lower rectum	7	6	13	13%
Recto sigmoid	13	10	23	23%
Sigmoid	5	8	13	13%
Ascending colon	4	0	4	4%
Splenic flexure	2	2	4	4%
Transverse colon	0	1	1	1%
Hepatic flexure	4	0	4	4%
Descending colon	0	3	3	3%
Caecum	10	3	13	13%
FAP+CA	3	1	4	4%

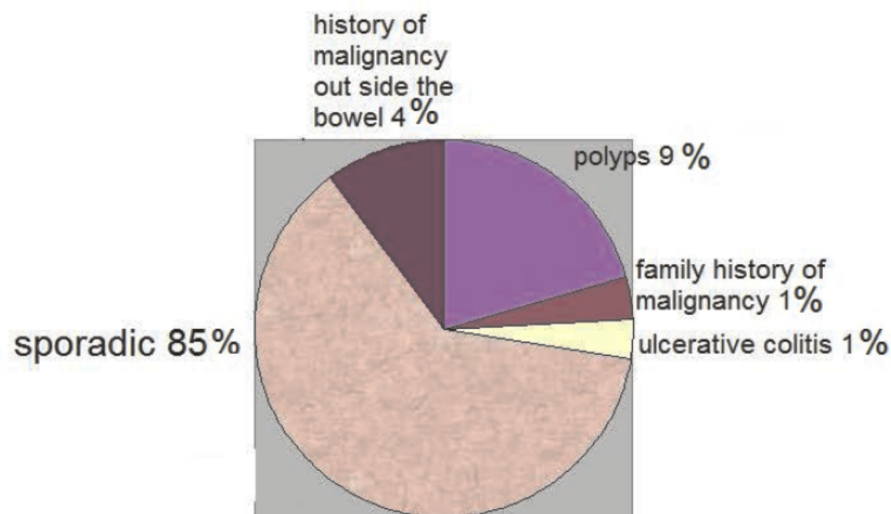
The commonest site of the tumor was ate the rectum in 31% followed by rectosigmoid in 23%,sigmoid colon and caecum in 13 % , transverse colon tumor was the least 1.1%.

The right colon 22% , the left colon 74% and whole the colon 4%. as seen in table2.

Predisposing factors.

15patients were found to have predisposing factors.9% of them had adenomatous polyps, 4% had history of malignancy outside the bowel,1 % had family history of colorectal carcinoma , 1% were with ulcerative colitis and 85% of patients were found to be sporadic .as seen in figure(4).

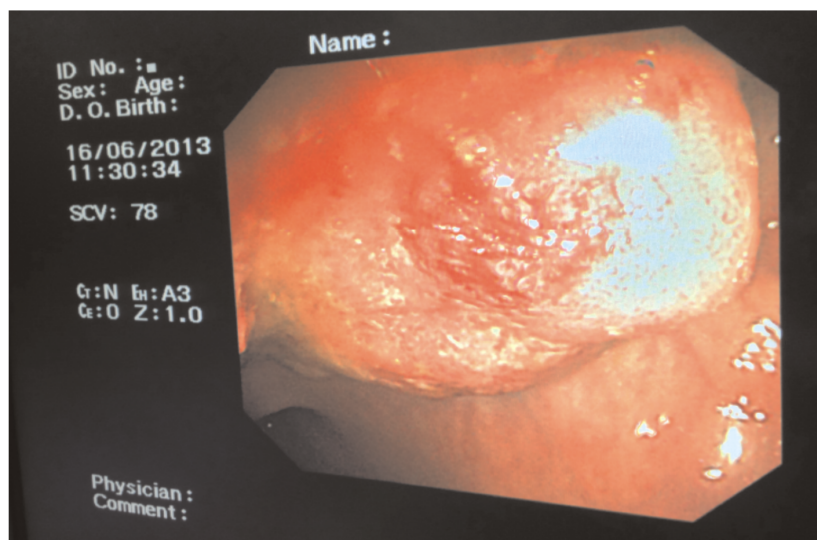
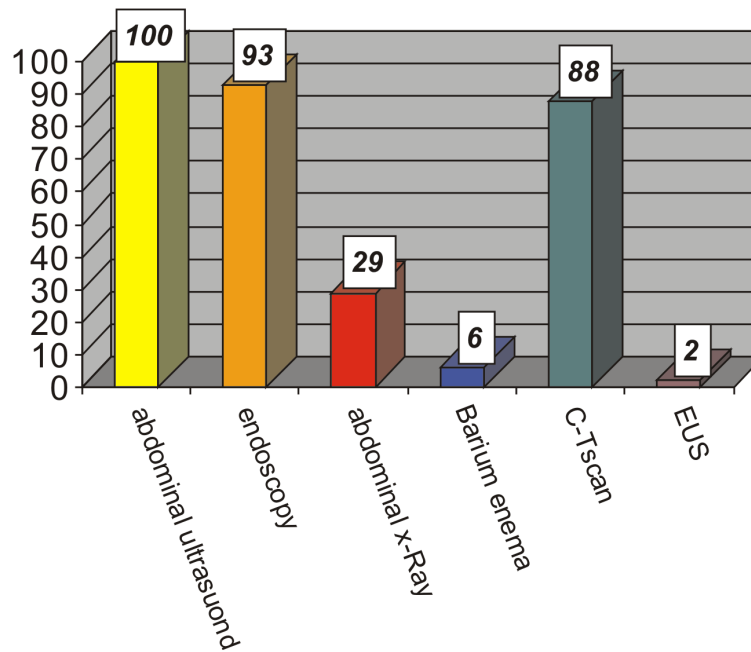
Figure (4):



Investigations:

The most common performed investigation was abdominal ultrasonography, for all patients followed by endoscopy (colonoscopy) 93%. CT scan done for about 88% of patient . as seen in figure(5).

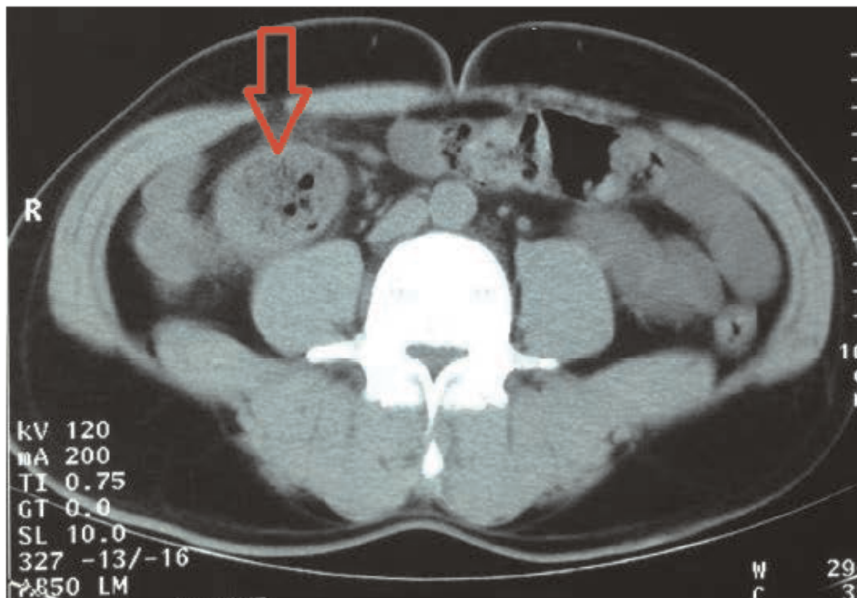
Figure (5):pre operative investigation.



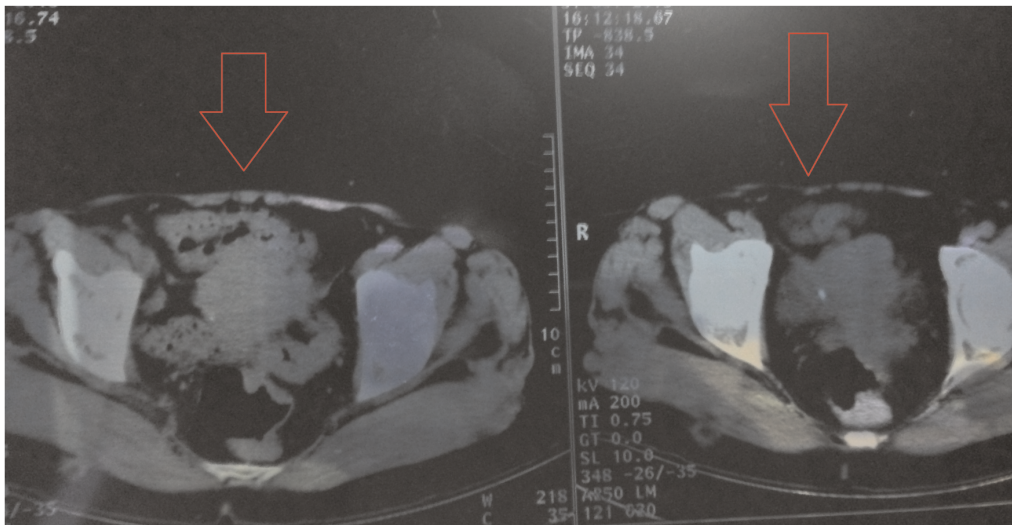
Picture (1): patient with rectal tumor colonoscopy show fungated, ulcerated mass at the rectum 7 cm from anal verge.



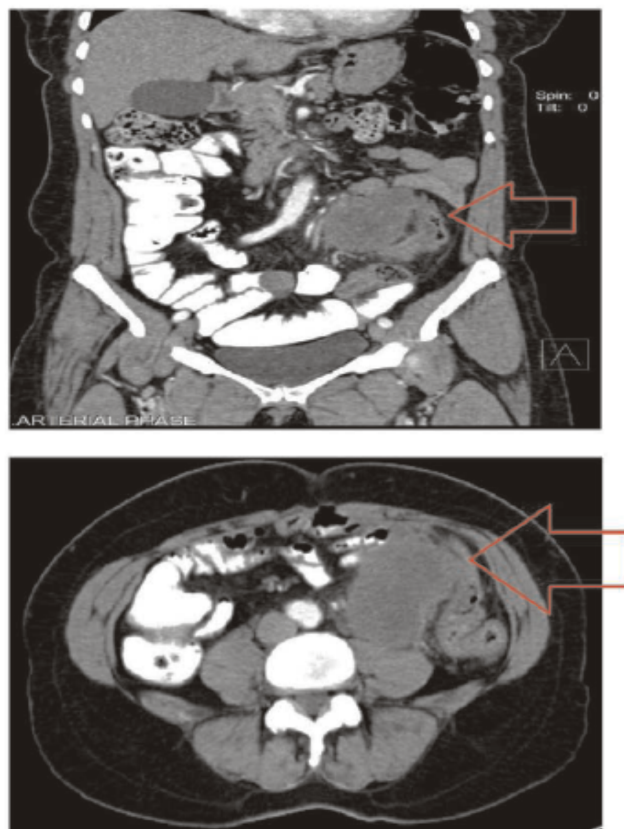
Picture (2):
colonoscopy showed the pathology at 50 cm from anal verge has ugly looking mass obstructed lumen (splenic colonicCA).



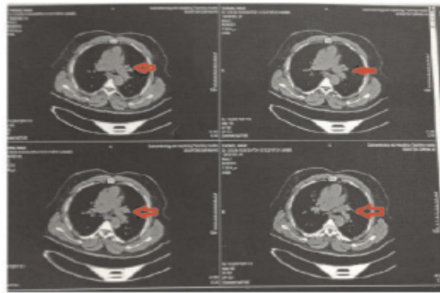
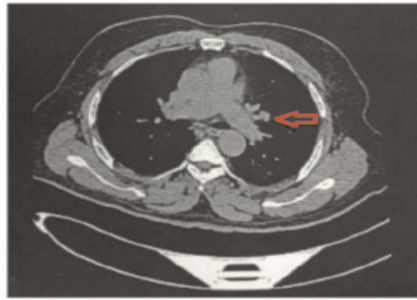
Picture (3): CT scan show well defined lesion projected from terminal ileum extended to the cecum causing sever narrowing to the lumen with multiple ulceration, enhance after Contrast injection in keeping with neoplastic lesion.



Picture (4):
CT scan show well defined mass projected from the rectum (32x24 mm) irregular outline enhanced after contrast injection.



Picture (5):
show hypodense mass 7.5 cm involving sigmoid colon in keeping with recurrence sigmoid CA after resection.

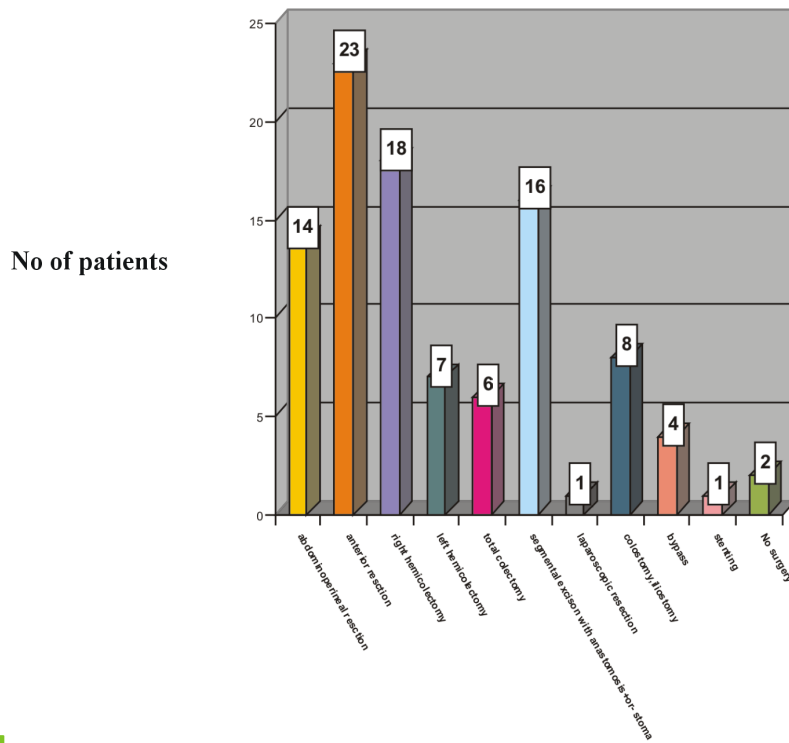


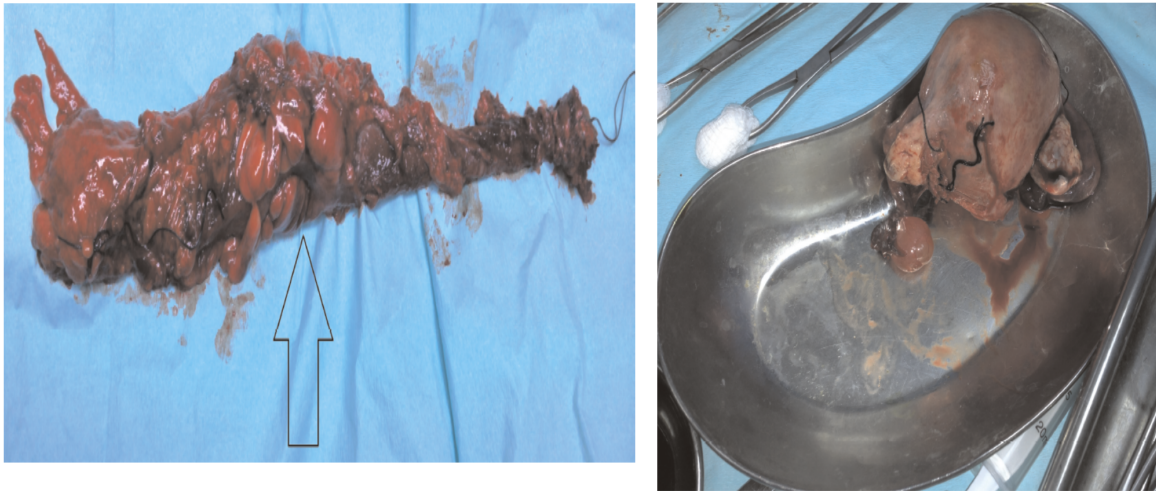
Picture (6): CT scan show mass lesion 4.5 cm in sigmoid colon (arrowhead) enhancement after contrast injection colonoscopic biopsy reveal villous adenoma with moderate nuclear atypia.

Modalities of treatment.

The most common operation performed was anterior resection

Figure (6):treatment

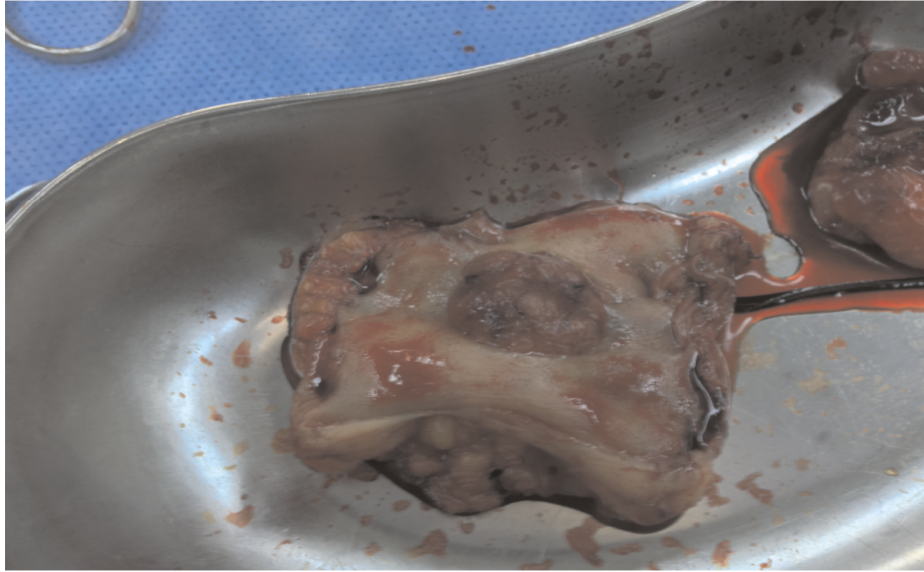




Picture (7):
show gross pathology of lower rectal tumor- arrowhead- with abdomino perineal resection+
hysterectomy + bilateral salpingo oophorectomy.



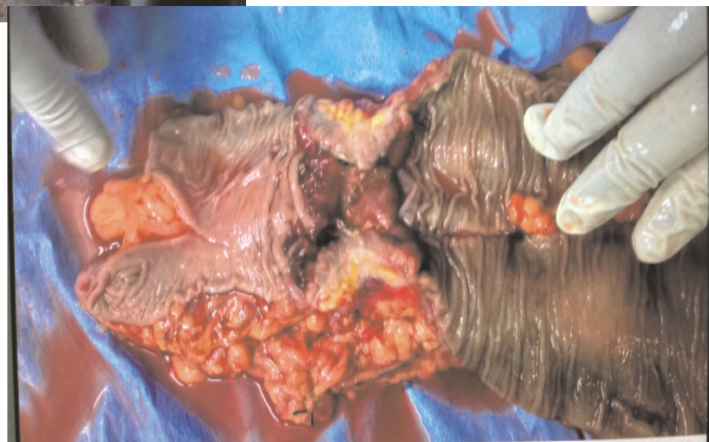
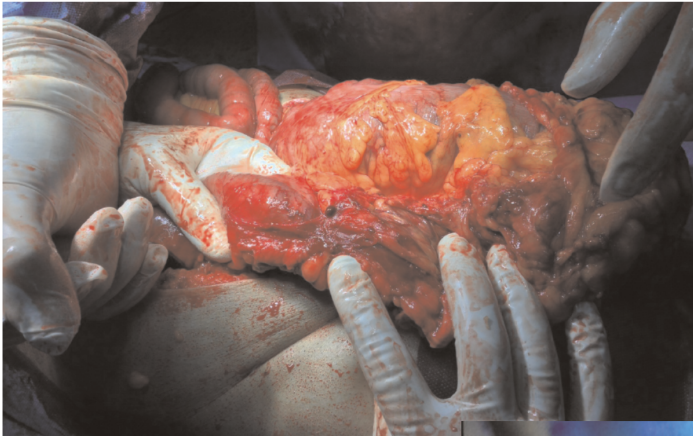
Picture (8):
show gross pathology of right hemi colectomy of cecal tumor .



Picture (9):
show gross pathology of segmental anterior resection of ugly upper rectal polyp with dysplastic change.



Picture (10):
show gross pathology of sigmoid tumor with segmental resection and anastomosis



Picture (11): splenic colon tumor with left hemi colectomy and Double Barrel colostomy.

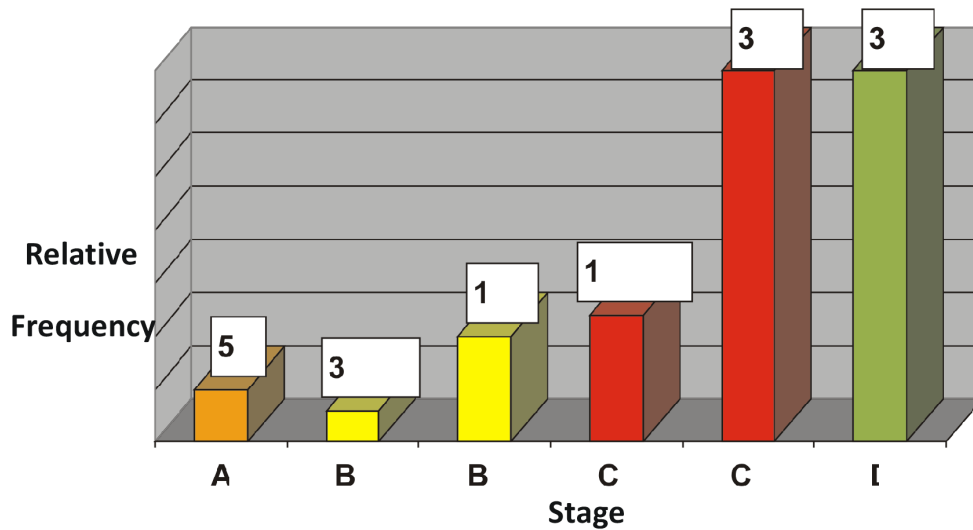


Picture (12): show panproctocolectomy with end ileostomy of FAP patient with high grade dysplasia.

Modified Dukes staging of the patients.

The most pathological stage according to modified Dukes staging system was C2 and D in 35 % for each stage.as seen in figure (7).

Figure (7)



Degree of differentiation of colorectal cancer.

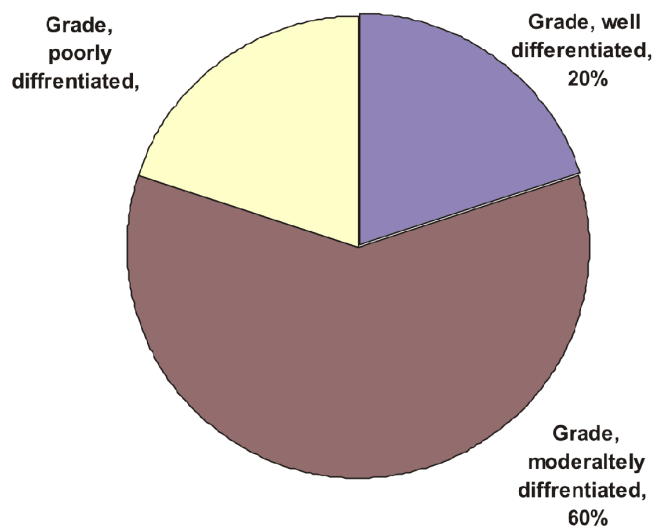


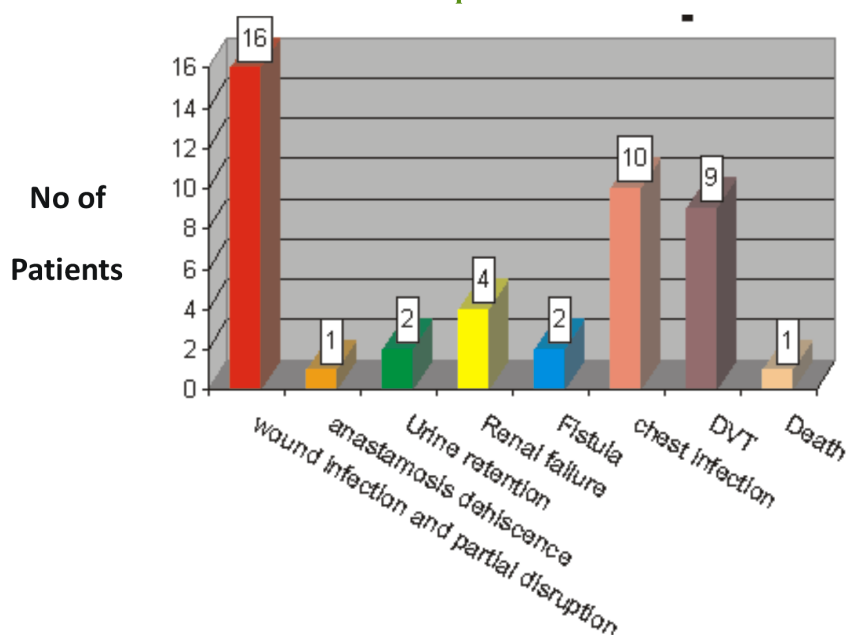
Figure (8)

Grading of 100 patients depending on histopathological findings revealed that, moderately differentiated adeno carcinoma represent the commonest pathological grade 60%.

morbidity and mortality.

During period of hospitalization, the commonest complication was wound infection in 16 . 1 patients died during the period of hospitalization due to pulmonary embolism and 1 patient had anastomosis dehiscence that needed re exploration.

**Figure (9):
Complications**



In patients less than 40 years, 87.5 % had moderately & poorly differentiated carcinoma and 87.5% had Duke's stage C & D.

**Table (3):
pathological finding in young and old patients.**

	No of patients		total
	< 40 year	>40 year	
Grad of the tumor			
Well differentiated	4%	16%	20%
Moderately differentiated	24%	36%	60%
Poorly differentiated	4%	16%	20%
Duke's classification			100%
A	0	5%	5%
B	4%	9%	13%
C	16%	31%	47%
D	12%	23%	35%
Total			100%

Discussion :

Colorectal cancer continues to be the most common cancer in the gastrointestinal tract world wide.^(1,2,3) The male to female ratio(M:F) is about equal.⁽¹³⁾ In this study the (M:F)ratio was 1.1:1.1. In study by I. Palibrk et al the (M:F)ratio was 1.2:1⁽³²⁾

. Although colorectal carcinoma is a disease of older patients it was found that 21% of our patients were under the age of 40 years, this is higher than many studies done world wide like McCoy and Parks(U.K 1984) who reports 0.9%⁽⁹⁾ and Smith et al(USA1989) who reported 4.8%⁽²⁴⁾, while in Iraq 2008 Waseem had reported 17.5%⁽³¹⁾

The peak incidence of colorectal cancer was between 60-69 years age group, it is similar to the result of other study done in Iraq between January 1996 and jun 1997⁽²⁵⁾

The commonest presenting symptom was bleeding per rectum in 75 % followed by change in bowel habit in 65% of our patients, while the results of 2008 Waseem et al, bleeding per rectum in 63% followed by change in bowel habit in 55%⁽³¹⁾, other study done in Iraq had showed 43.9% bleeding per rectum and 57.5% change in bowel habit^(13,26)

Other symptoms were including pain, anemia, weight loss, abdominal mass and others. Multiple symptoms presented in 80% of our patients and it was single only in 20%. Most tumor were seen on the left side of the colon mainly the rectum, sigmoid and rectosigmoid junction (54%), nearly the same findings of other studies done in Iraq^(13,26,29), while McCoy and Parks findings were 32% at rectum and sigmoid with 45% at splenic flexure and descending colon⁽⁹⁾, so the tumors are more predominantly at the left side with rectosigmoid predilection. In our study The right colon in 22%, *Shyamal Kumar Halder et al* found that the right colon is more commonly affected (33.3%) than left colon if we consider colonic cancer in isolation. If growths involving rectum, then rectum becomes the commonest site of affection in either age group.⁽³⁵⁾

Pre-existing factors were found only in 15 patients that have been analyzed, from these cases; polyps and villous adenoma presented with carcinoma account for 9% followed by history of malignancy outside the bowel 4%, then family history of colorectal carcinoma 1%, then ulcerative colitis 1%. Jarvinen et al found that ulcerative colitis represents 1.7% and FAP 0.6 %⁽²⁷⁾, also it is the same finding of other study done in Iraq 2001⁽²⁸⁾

The measures required to foster early detection of cases through proper methods for diagnosis are very vital.

All patients enrolled in our study underwent abdominal ultrasonic examination and 93% of them underwent endoscopic examination.

CT scan underwent to 88% of our patient, while other study done in Iraq 15% had CT due to the availability of CT in our center^(13,26,29,31)

. 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 pitfalls of colonoscopy are an occasional incomplete examination of right colon 5-10% of cases, so completion barium enema some time is necessary.⁽²⁸⁾

EUS is very sensitive and specific (>90%) for bowel wall involvement. Lymph node involvement is detected by EUS with a specificity of approximately 85%.

CT scan of abdomen and pelvis is useful in identifying metastatic disease, however, is not useful in gauging the depth of disease.

In our study the abdominoperineal resection done in 14% of cases followed by palliative colostomy, ileostomy in 8%, in comparison to McCoy and Parks abdominoperineal resections of the rectum were in 16.6% and stoma in 6.45%⁽⁹⁾

The relatively high percent of palliative stoma may be contributed to the delayed presentation and advanced disease. 2 patients in this study did not undergo any surgical procedure either because of their advanced disease or because of their refusal to take the risk of surgery.

Neoadjuvant and adjuvant therapy with 5-FU based chemotherapy and radiotherapy to the pelvis is given with the goal of decrease the chance of distant metastatic and improving local control . Regarding the grading of the tumor, the percent of well differentiated carcinoma was 20% ,while moderately differentiated was 60 % and poorly differentiated was 20 %, it is nearly the same finding of other study done in Iraq⁽²⁹⁾, while McCoy and Parks found that well differentiated carcinoma was (41.39%), moderately differentiated was (22.9%) and poorly differentiated was (35.48%).⁽¹⁰⁾ other world wide study, showed that moderately differentiated adenocarcinoma (45%).⁽³⁵⁾

This difference probably attributed to late presentation of cases in our study that subsequently affects health changes the aggressiveness of pathological grade. 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 47% ,Duke D account for 35% ,Duke B represent 13% and Duke A was only 5%. McCoy and Parks, where Duke C 41.9%, D 38.7%, B 12.9% and Duke A was 6.4 %.⁽¹⁰⁾ In the present study the post operative complication was 51.1% , It is the same results of other study in Iraq.⁽²⁶⁾ Ashok Kumar et al had post operative complications in (51.8%).⁽³³⁾ as shown in table 4

Table 4:
Show comparison between our study & Ashok Kumar et al complication rate

Complication	Our study	Ashok Kumar et al
wound infection	16%	n = 27, 25%
chest infection in	10%	Did not happen
DVT	9%	Did not happen
Anastomosis leak	1%	n = 16, 14.6%
fistula	2%	Did not happen
urine retention	2%	Did not happen
renal failure	4%	Did not happen
died	(1%)1 patients	1.85 %
anastomotic stricture	Did not happen	n =19, 17.6%
intra-abdominal bleed	Did not happen	n = 4, 3.7%
intestinal obstruction	Did not happen	n = 16, 14.6%

Risk factors for anastomosis leaks include : male sex, distance of the tumor from the anal verge, Advanced age (greater than 60 years), emergency surgery, malnutrition, severe critical illness, and use of high-dose steroids, smoking, and alcohol abuse have been documented.^(33,36) Most of our young patients had tumor staged with histopathological 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.^(9,25) *Shyamal Kumar Halder et al*, show the patients of younger age group presented in advanced stage all patients received neo-adjuvant therapy.⁽³⁵⁾ Our study 4% of patient between 10-20 years with advanced loco regional adenocarcinoma that received neoadjuvant chemo radiotherapy, while the results of Gangmi Kim et al showed 5 % between 10-20 years, all patients presented with an advanced disease stage and had aggressive histologic types.⁽³⁴⁾ The advanced stage of disease may be attributed to the late presentation of patients and may be the change in the natural history of the disease from pathological point of view.

Conclusion :

- 1-Colorectal cancer shows an increasing incidence especially In young age patients most of them with worse histopathological types and advanced stage.
- 2- There was a delay in the presentation and diagnosis of this disease among our patients.
- 3- The commonest presenting symptom of colorectal malignancy is bleeding per rectum, changes in bowel habit (especially of recent onset) with or without abdominal pain regardless the age.
- 4- Most tumor were seen on the left side of the colon mainly the rectum, sigmoid and rectosigmoid junction.

Recommendation:

1. Considering the result of this study that 21% of colorectal CA presented below 40 years age which make us aware of cancer in young age group presented with bleeding per rectum or change in bowel habit and therefore full investigation should be

considered.

2. High risk patient should undergo regular checking by physical examination, imaging and colonoscopy.
3. Neoadjuvant therapy should be considered for advanced locoregional disease before surgery.

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