

Retrospective Review of Epidemiological, Pathological and Clinical Features of Colorectal Cancer Diagnosed by Colonoscopy at King Hussein Medical Center

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ABSTRACT

Objective: To find out different characteristics and variables of patients diagnosed as Colorectal cancer at King Hussein Medical Center.

Methods: A total of 204 cases of colonic cancer patients aged 16 years or more were identified over 4 year-period between January 2006 and December 2009 were reviewed at King Hussein Medical Center. The patients were divided into 2 groups according to their age; those < 55 years, and those > 55 to compare the study variables between the two age groups.

Results: Seventy five (37%) patients with colonic cancer aged under 55 years and 129 (63%) were 55 years or older. Colonic cancer was more common in men at both age groups than that in women. Localized disease was more common in the young age group. Left side colonic cancer was the most common in both age groups. Nodal involvement was almost similar in frequency in both age groups. Distant metastases were more common in the old age group > 55 years. At diagnosis, 48 (23.5%) of patients had advanced cancers (stage D) with either nodal or distant metastases. Moderately differentiated adenocarcinoma was the most common histological finding. Surgery was undertaken on 134 (65.7%) patients, with a postoperative mortality of 2 (1.5%) patients. Anti-cancer chemotherapy was given to 91 (44.5%) patients and radiotherapy was used in 7 (3.4%) patients. Eleven (5.3%) patients received chemo-radiotherapy and 20 (9.1%) patients received the three modalities of treatment.

Conclusion: This study showed that; the frequency of colonic cancer increases with age, at the same time there is a considerable number of patients diagnosed at young age. It is common in our patients with colorectal cancers to present with advanced disease. Colorectal cancer in our group of patients had more aggressive pathological features at presentation in the young age group. Earlier diagnosis of these cancers could well serve as an achievable solution and may improve survival.

Key word: Colonoscopy, Colonic cancer, Epidemiology, Rectal cancer, Malignancy, Rectal bleeding.

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Introduction

Colorectal cancer includes cancerous growths in the colon, rectum and appendix.⁽¹⁾ With 655,000 deaths worldwide per year, colorectal cancer is a major health problem worldwide, where it is the second leading cause of cancer and cancer-related death.⁽²⁾ The lifetime risk of developing colon cancer in the United States is about 7%.⁽³⁾ Furthermore, the incidence of the disease is rising.⁽⁴⁾ Colorectal cancer is one of the most prevalent malignancies in men as well as women. Sex differences in incidence and mortality rates have been reported and attributed to biological and environmental factors, including diet and hormones.⁽⁵⁾

Certain factors increase a person's risk of developing the disease.⁽⁶⁻¹²⁾

The symptoms of colorectal cancer depend on the location of tumor in bowel and whether it has spread to elsewhere in the body.⁽¹³⁾ In the United States, colonoscopy or Faecal occult blood test (FOBT) plus sigmoidoscopy are the preferred screening options.^(14,15) The most common colon cancer cell type is adenocarcinoma which accounts for 95% of cases.^(16,17) The systems for staging colorectal cancers depend on the extent of local invasion, the degree of lymph node involvement and whether there is distant metastasis.⁽¹⁸⁾

The treatment depends on the staging of the cancer. When colorectal cancer is caught at early stages it can be curable.⁽¹⁹⁻²¹⁾ Surgery remains the primary treatment while chemotherapy and/or radiotherapy may be recommended depending on the individual patient's staging and other medical factors. Survival is directly related to detection and the type of cancer involved.⁽²²⁾ Survival rates for early stage detection is about 5 times that of late stage cancers.⁽²³⁾ CEA level is also directly related to the prognosis of disease, since its level correlates with the bulk of tumor tissue.⁽²⁴⁾

The present study aimed to look at epidemiological data including; Age, Site, histology, stage, and tumor differentiation for patients diagnosed as colorectal cancer at King Hussein Medical Center and to compare the data of patients less than and greater than 55 years of age.

Methods

A retrospective descriptive epidemiological review of a cohort of patients diagnosed as colonic cancer at King Hussein Medical Center. King Hussein

Medical Center is a teaching hospital, attached to it 7 tertiary care hospitals. It receives referrals from all medical sectors in different parts in Jordan. It serves most of the Jordanian population including the armed forces personnel.

The medical records for all patients aged 16 years or more who underwent colonoscopy and diagnosed as colonic cancer by histopathology between January 2006 and December 2009 were reviewed. Data collected in form of the number of the patients, age, sex, reason for doing colonoscopy, endoscopic findings, site, size, histology reports including stage, and tumor differentiation.

Colonic preparation before all lower gastrointestinal examinations done using Dulcolax (Biscodyl 5mg tab) and Foretrans (Macrogel 4000-64gm) or castor oil and normal saline. Patients gave written, informed consent that included endoscopic intervention prior to the colonoscopy being performed. The endoscopy room set up, the instruments, and medical staff was the same for all the patients. Uni-stiffness endoscopes were used (CF-240AI/AL or CF-260AI; Olympus Optical, Tokyo, Japan, or Pentax EC 3840L). The patients were evaluated well before, and during the procedure that the endoscopist will be ready for dealing with any complication. Conscious sedation with i.v. midazolam (Dormicum; Switzerland) and Pethidine 25 mg IV was provided at the patients' request. Otherwise, they did not receive analgesia. Intravenous hyoscine butylbromide (Buscopan; Germany) was used as an antispasmodic agent if the patient had no contraindications (e.g. prostatic hyperplasia requiring therapy, narrow-angle glaucoma, and tachyarrhythmia) when needed.

To ensure that all information was actually recorded, the pathology reports as well as the hospital records were screened. We arbitrarily subdivided the patients into 4 periods, each one of one year's period, to compare the number of patients with colonic cancer per year. At the same time we divided all the patient for two age groups, those less than 55 years old and 55 years or older, to compare different characteristics and variables of patients by each age group.

Patients with familial cancer were excluded from the analysis to find out whether there is any change in the age group that presented with colonic cancer. Colorectal cancer considered familial depending on the medical history, if two or more of the first degree relative of the patient had colorectal cancer.

Chi-Square was used for statistical analysis.

Table I. Number of colorectal cancer during the period of study

Year	Number of patients	%
2006	41	20
2007	46	23
2008	55	27
2009	62	30

Table II. Male: female ratios by age group

	< 55 (years)		> 55 (years)		P- Value
	N (75)	%	N (129)	%	
Male	39	52	78	61	
Female	36	48	51	39	
	0.127	0.127	0.042	0.042	

Table III. Main cause of presentation

cause of presentation	Number	%
Family history of colonic cancer	8	4
Rectal bleeding	80	40
Change in bowel habit	60	29
Weight loss	6	3
Abdominal pain	17	8
Abdominal or rectal masses	6	3
Post intestinal obstruction	13	6
Melena with normal upper endoscopy	5	2.5
Metastasis cancer; searching for the primary	3	1.4
Iron deficiency anemia	6	3

Table VI. Number and percentage of patients by anatomical site and age group

Site	< 55 (years)		> 55 (years)		P- Value
	N (75)	%	N (129)	%	
Right colon	19	25	37	29	0.096
Left colon	53	71	72	56	0.047
Rectum	3	4	20	16	0.064

Table V. Tumor pathology

Histopathology	< 55 (years)		> 55 (years)		P- Value
	N (75)	%	N (129)	%	
Adenocarcinoma	62	83	115	89	0.139
Mucinous adenocarcinoma	8	11	8	6	0.126
Signet-ring carcinoma	2	3	2	2	0.024
Lymphoma	3	4	4	3	0.973

Table VI. Tumor stage (Dukes's stage)

Dukes's stage modified (equivalent TNM stage): Description	< 55 (years)		> 55 (years)		P- Value
	N(75)	%	N(129)	%	
A (stage I): Localized to mucosa and sub-mucosa	14	19	10	8	0.009
B (stage IIA and IIB): Extending into or through muscle layer without lymph node involvement	22	29	26	20	0.025
C (stage IIIA-C): Lymph node involvement	24	32	60	47	0.062
D (stage IV): Distant metastases	15	20	33	26	0.096

Table VII. Tumor differentiation

Differentiation	< 55 (years)		> 55 (years)		P- Value
	N (75)	%	N (129)	%	
Well	6	8	4	3	0.066
Moderately	61	82	113	88	0.092
Poorly	4	5	8	6	0.085
Undifferentiated	4	5	4	3	0.138

P-value was considered significant if less than 0.05. The percentages were calculated by dividing the number of patient diagnosed to have colorectal cancer in each age group over the total number of patients of the same age. The retrospective review complied with the ethical guidelines of the royal medical services ethical committee.

Results

A total of 232 patients with colonic cancer were identified over 4 year-period between 2006 and 2009. Twenty eight patients with familial cancer were excluded from the analysis. Two hundred four patients actually included in the study as in Table I, which showed that the number of patients diagnosed to have colorectal cancer per year is increasing. The average mean patient ages were 55.3 years, median 47 years.

One hundred seventeen (57%) of the total patients studied were male, and 87 (43%) were female. 75 (37%) of the patients were less than age 55, and 129 (63%) were 55 or older. As shown in Table II, colorectal cancer affects significantly (P- value; 0.042) more males in the older age group (> 55 years). There were less females, overall, with colonic tumors seen in all age groups.

The main indications for colonoscopies were rectal bleeding (40%), change in bowel habit constipation (29%), and post intestinal obstruction searching for underline cause (6%), as shown in Table III. There were 7 (3.4%) of the patients had a major complication related to the procedure in form of perforation (4 patients), significant bleeding not necessitating blood transfusion (3 patients). Minor complications were abdominal distension 25 (12%) patients, mild abdominal pain in 14 (7%) patients, sedation overdose in 8 (4%) patients, and severe abdominal pain without evidence of perforation 7 (3.4%) patients.

Left colon colorectal cancer was the most common site of presentation for our patients in both age groups. 19 patients (25%) with right side colonic cancer were under 55 years old, which is not statistically significant comparing with the older age group, whereas more patients with left situated lesions tended to be significantly more in the older age group (> 55) (Table IV).

Adenocarcinoma was the most common type of colorectal cancer diagnosed at both age groups. Signet-ring carcinoma was more common in younger age group (<55 years). The less well differentiated and perhaps more aggressive tumors-

mucinous carcinoma and lymphoma were more common among younger patients. There were 177 (87%) patients registered with adenocarcinoma, 35 % of these patients were less than 55 years. (Table V).

Although localized diseases (Dukes's A (stage I) and B (stage IIA and IIB)) were significantly more common among the younger age group (< 55 years), whereas regional node involvement and distant metastases were more frequent in older age group (>55 years). Distant metastases were also more common in the old age group (> 55 years). At diagnosis, 48 (23.5%) of all patients had advanced cancers with either nodal or distant metastases regardless of their age group (Table VI).

Only 32 (15.7%) of the younger patients had tumors which were less than 4cm in diameter, whereas 59 (29%) of the over 55 age group had tumors of this size. Moderately differentiated carcinoma was the most common histological type of colorectal cancer diagnosed at both age groups. Whereas well differentiated carcinoma was more common in younger age group (Table VII).

Surgery was undertaken on 134 (65.7%) patients, with a postoperative mortality of 1.5%. Anti-cancer chemotherapy was given to 91 (44.5%) patients and radiotherapy was used in 7 (3.4%) patients. Eleven (5.3%) patients received chemo-radiotherapy and 20 (9.1%) patients received the three modalities of treatment.

Discussion

King Hussein Medical Center serves medical care for any body in Jordan including the armed forces personnel, which makes our sample represents the whole Jordanian population. The male to female ratio was 1.4: 1. Seventy five (37%) of our patients were less than 55 years old, which is a considerable number to have colorectal cancer at this age, and 39 (52%) of them were men which may indicate increase of colorectal cancer among young age.⁽²⁵⁾

The most common presentations for patients seen at King Hussein Medical Center with colorectal cancer were; Rectal bleeding, change in bowel habit and abdominal pain. Colonoscopy is a widely used diagnostic and therapeutic intervention. The procedure is usually well tolerated, with less than 0.5% of patients developing complications.⁽²⁶⁾ In our study colonoscopy was safe and well tolerated. There were 7 major complications related to the procedure. Four patients had colonic perforation; two occurred while trying to bypass through a tumor

in the descending colon. Minor complications were noticed in about 20% of the patients in form of mild abdominal pain, distension, sedation overdose and severe abdominal pain experienced during the procedure, but for all nothing was done apart from reassurance and they left the endoscopy unite in a very good conditions and mostly asymptomatic.

The effects of dietary changes being introduced through organization and acceptance of western diet by Jordanians is likely to have its impact on the incidence of colorectal cancer in the future but the data reported previously and in the present study are still likely to represent the disease as it was before the effects of western influences because these influences need time to have an effect.⁽²⁷⁾ The present study has confirmed higher incidence of colorectal cancer among young patients. There tended to be high numbers of early stage tumors in younger patients.

Colorectal cancer disease seems to be more common in the young in Jordan than in the West.⁽²⁸⁾ The disease was widely and rapidly disseminated before presentation. This may be the pattern of the epidemiology of the disease in the so called low risk countries in which it could be argued that there are a higher proportion of younger people with more aggressive turn over. Diagnosis was delayed in these patients and there was a higher percentage of more malignant tumors and, as a consequence, a very low overall survival rate was reported for the group. Regardless of their mode of treatment survival seemed to be particularly poor. It was concluded that this reflected the more aggressive behaviour of carcinoma in young patients.

It is not possible to comment on survival and so it is difficult to determine whether, young patients survive as long if not longer than older patients with the same disease. However; when up to- date census information becomes available and a National Cancer Registry is established then it may be possible to answer these questions. In the meantime it may be assumed that survival was poor in young Jordanians because of the generally low survival rates observed in relation to high tumor grade and poor differentiation.⁽²⁹⁾

Left colon colorectal cancer was the most common site of presentation for our patients in both age groups. Although localized diseases (Dukes's A (stage I) and B (stage IIA and IIB)) were significantly more common among the younger age group (<55 years), whereas regional node

involvement and distant metastases were more in frequency in older age group (>55 years). Moderately differentiated carcinoma was the most common type of colorectal cancer diagnosed at both age groups. Well differentiated carcinoma was more common in younger age group (< 55 years).

Mucus producing tumors were more frequent in the younger age (11% vs. 6%) and signet ring carcinoma was found in four patients, two of whom were in the younger age group. The overall incidence of signet ring and mucinous tumors in Jordan was not obviously different from what would be expected in a high risk country.⁽³⁰⁾ In Jordan, however, these tumors occurred more frequently in the young. This difference in age distribution of these more aggressive tumors may account for the diverse reports relating to survival of patients with colorectal cancer in high and low risk countries.

With regard to anti-cancer chemotherapy at our institution for patients with stage III colon (node-positive without clinically detectable metastasis), adjuvant chemotherapy for a total of 6 months is standard. This therapy can be delivered according to several different regimens using different drugs. Patients with stage II colon cancer considered to be at a high-risk for relapse (less than 13 analyzed lymph nodes, T4 lesion, bowel obstruction or perforation, lymphovascular or perineural invasion, poorly differentiated histology, microsatellite instability) and confers a worse prognosis and generally warrants adjuvant chemotherapy for stage II colon cancer.

The present report however is able to record a fair sized population of young Jordanians who is known to come from a low risk country and who has all been registered at one institution, albeit with the biases of an institutional series. It is felt that there may be real differences in the disease and its presentation at least in high and low risk countries. This may explain why the literature abounds with diverse reports about age and survival in colorectal cancer.

Whether a change to a more Western way of living with all of the dietary implications of such a change or whether a public awareness campaign about the early signs and symptoms of cancer will alter the characteristics of the disease in Jordan remains to be seen. It seems to be more likely that factors which are responsible for the development of the disease itself and changes in them would be more likely to change the pattern of a disease than any early

detection measures that could be taken. This study of 75 (37%) young Jordanians under the age of 55 provides a base-line for epidemiological studies of colorectal cancer in this age group in the future.

Deficiencies in our study are; First: we do not know the actual prevalence of colonic cancer in the general population of Jordan to compare. Second: genetic testing is not available, which is important in identifying subjects who need revision of their diagnosis. Third: The number of colonic cancer patients, even it is rising in Jordan, but still statistically not significant to give a firm idea about the prevalence of colonic cancer in Jordan.

Conclusion

In our study, the frequency of colonic cancer increases with age, at the same time there is a considerable number of patients diagnosed at young age. With a frequent diagnosis of colonic cancer, the indications for colonoscopy should not be too strict. A rapid and definitive diagnosis can be made. We believe that negative endoscopic result is as of value as the positive one, this gives relief to the patient and his treating physician. We are in need for a multi disciplinary team to deal with major problem of colonic cancer and more research is needed to establish the possible etiology of its increasing frequency.

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