Colorectal cancer in young patients under 40 years of age

Comparison with old patients in a well defined Jordanian population

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ABSTRACT

Objectives: To determine the incidence of colorectal cancer (CRC) in young Jordanians and to compare the clinical and pathological characteristics with those in older patients and with those in high risk populations.

Methods: Clinical and pathological data of all the patients with CRC managed at Princess Basma Teaching Hospital, Irbid, Jordan over a 10 year period (January 1990 through December 1999) were recorded. The patients were divided according to age into group one (those <40 years) and group 2 (> 40 years). The 2 groups were compared regarding sex, predisposing conditions, tumor stage at presentation, tumor differentiation, mucin secretion, tumor invasion, presentation with complications and tumor location. The data were compared with those of "high risk" Western populations and with the few reports coming from "low risk" populations, mainly from Kingdom of Saudi Arabia and Egypt.

Results: Out of 202 patients evaluated, 4 were excluded. Group1 constituted 20.2% of the patients, 17.5% of them have predisposing conditions. Comparison between group 1 and 2 revealed the following: female sex (65% versus 50.6%, p=0.104), advanced stages at presentation (65% versus 41%, p=0.005), rectal tumors (50% versus 39.2%) and right side tumors (15% versus 29.1%) (p=0.18). Mucinous and signet ring tumors (30% versus 15.8%, p=0.04), poor tumor differentiation (20% versus 18.3%, p=0.78) and presentation with complications (21% versus 22.2%, p=0.96).

Conclusions: The incidence of CRC in young Jordanians was much higher than high risk populations. Half of the tumors were rectal. Young patients have more advanced stage and more mucin secreting tumors. The relative high frequency and frequency of predisposing conditions calls for family screening and surveillance in the presence of predisposing conditions.

Saudi Med J 2003; Vol. 24 (8): 871-874

Colorectal cancer (tumor) is one of the most common cancers in the Western world. The disease, however, is relatively uncommon under the age of 40 years. The reported incidence of CRC in young patients in such "high risk"populations is usually less than 6% of the total number of patients with CRC.[1-12] By contrast, higher incidences were reported in the scanty reports coming from low risk populations with figures as high as 35%.[13-16] Controversy remains regarding the differences between CRC in the young and old in regard to site, sex, stage, histopathological characteristics and prognosis. The purpose of this study was to determine the incidence of CRC in young Jordanians, to compare the clinical and pathological characteristics with those in

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Received 23rd December 2002. Accepted for publication in final form 17th May 2003.

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the old and to compare our results with those of young patients in Western high risk populations. Emphasis was made on sex difference, tumor site, stage, differentiation, vascular and lymphatic invasion, predisposing conditions and presentation with complications. Three differences between the Jordanian population and those in Western countries make this evaluation worth doing. It is a "low risk population," It is a young population and it has a high rate of consanguineous marriages.

Methods. This is a retrospective evaluation of all the patients diagnosed as having colorectal adenocarcinoma in Northern Jordan over a 10 year period between January 1990 through to December 1999. The data were collected from the files of the patients managed at Princess Basma Teaching Hospital, Irbid, Jordan, which is the main governmental hospital in the region, from the private hospital records and from the single pathology unit at Jordan University of Science and Technology which serves the whole Irbid province. The age of 40 years was used to divide the patients into 2 groups: "young" (under 40 years, group 1) and "old" (above 40 years, group 2). This choice was made to facilitate comparison with other studies, as the age 40 years was the one most frequently used in the literature. The 2 groups were compared regarding sex, predisposing factors (polyposis syndromes, hereditary non polyposis colon cancer (HNPCC) and inflammatory bowel diseases), stage at presentation, the differentiation of the tumor (well, moderate and poor), the mucinous and signet ring subtype, the presence or absence of invasion (lymphatic, vascular or perineural), the presentation with complications (obstruction, perforation and hemorrhage) and tumor location. Hereditary non polyposis colon cancer was diagnosed using the Amsterdam criteria. The tumor location was based on the international classification of diseases (International classification data 9) dividing the large bowel into 3 sites: the right colon (appendix, cecum, ascending colon, hepatic flexure and transverse colon), the left colon (splenic flexure, descending colon and sigmoid colon), and the rectum (rectosigmoid junction and rectal ampulla). Staging of the tumor was based on the modified Dukes'system after operation, pathological evaluation and investigations for distant metastasis: Stage A carcinoma confined to the mucosa; stage B, carcinoma extending into or through the muscularis propia without lymph node or distant metastasis; stage C, carcinoma with lymph node metastasis with no distant metastasis, and stage D, distant metastasis. Investigations to uncover metastasis include computed tomography scan of the chest, abdomen and pelvis and serial carcinoembryonic antigen measurements performed repeatedly according to the follow up program or earlier if symptoms mandate. Other investigations like brain or bone scans were performed as required. The differences between the 2 groups were determined by the Chi-square test. A p value of <0.05 was considered significant.

Table 1 - Comparison between young (≤40 years) and old (>40 years) Jordanian patients with colorectal cancer.

Variables	**Group 1 (≤40 years) n=40 patients (20.2)**	**Group 2 (>40 years) n=158 patients (79.8)**	**p-value**
Male:Female ratio	1:1.86	1:1.03	p=0.104
Stage Dukes			p=0.005
A	1 (2.5)	2 (1.3)	
B	13 (32.5)	83 (52.5)	
C	13 (32.5)	46 (29.1)	
D	13 (32.5)	19 (12)	
Unknown	0	5	
Biopsy only	0	3	
Site			p=0.180
Right	6 (15)	46 (29.1)	
Left	14 (35)	50 (31.7)	
Rectum	20 (50)	62 (39.2)	
Differentiation			p=0.778
Moderate	24 (68.5)	93 (65.5)	
Well	4 (11.4)	23 (16.2)	
Poor	7 (20)	26 (18.3)	
Mucinous and signet ring	12 (30)	25 (15.8)	p=0.040
Invasion	(35.7)	(36)	p=0.980
Complications	9 (21)	35 (22.2)	p=0.962

Results. A total of 202 patients were diagnosed as having CRC over the 10 year period. Four patients were excluded because of uncertainty about the exact age. One hundred and ninety-eight patients form the basis of this study. Forty patients were under the age of 40 years (group 1), an incidence of 20.2%. There were 29 patients between 31 and 40 years, 9 patients between 21 and 30 years, 1 patient between 11 and 20 years and one patient between 0 and 10 years. Predisposing conditions (polyposis syndromes, HNPCC and inflammatory bowel diseases) were present in 17.5% of the patients in group 1 (4 with HNPCC and 3 with polyposis syndromes). No predisposing conditions were confirmed in any patient in group 2. The clinical and pathological characteristics of the 2 groups and the differences among them are summarized in **Table 1**. Females constitutes 65% of the patients in group 1 versus 50.6% in group 2 (p=0.104). Advanced stages (Dukes C and D) were encountered more frequently in group 1 (65% versus 41%, p=0.005). Group 1 patients had more rectal tumors (50% versus 39.2%) and less right side tumors (15% versus 29.1%), however, the site difference did not reach a statistical difference (p=0.180). Mucinous and signet ring pathology was encountered in 30% of the patients in group one versus 15.8% in group 2 (p=0.040). The degree of tumor differentiation was not different between the 2 groups (p=0.778) and the same incidence of invasion (vascular, lymphatic and perineural) was

encountered (35.7% versus 36%, p=0.980). A similar percentage of patients presented with complications (21% versus 22.2%, p=0.962).

Discussion. Patients with CRC 40 years of age and below constituted 20.2% of all the patients diagnosed. This figure lies far above that reported in "high risk "Western communities of 2-6%[1-6] but similar to that in nearby "low risk"countries such as Kingdom of Saudi Arabia (KSA) and Qatar (23% & 20%).[13,14] A higher figure (35.6%) was reported in Egypt, which is another low risk community.[15] Having excluding referral bias and ensuring comparison with similar Western populations, these high figures can be partly explained on demographic basis being coming from countries with a young population. However, this calls for further epidemiologic and genetic studies to identify other explanations for this high incidence. We encountered more females in the young group compared to the old, but the difference was not statistically significant (65% versus 50.6%, p=0.104). However, this figure is higher than that reported in Western countries (45-55%).[2,5] Predisposing conditions were present in 17.5% of our young patients (HNPCC 10% and polyposis syndromes 7.5%). These figures are similar to the average Western figures (HNPCC 1.4-8.1% and polyposis (5-8.9%)[2-5,17] although higher figures were expected as of the high consanguineous marriages in our society. We encountered more rectal tumors (50% versus 39.2%) and less right side tumors in the young compared to the old (15% versus 29.1%). However, the site difference was not statistically significant when it was taken as a whole. The Western figures were contradictory in this regard. Some reported higher rectal frequency in the young,[10,18,19] some reported lower rectal frequency,[6] some reported less right side tumors in the young[2] and some reported no difference.[7] Contrary to our results, more patients with proximal lesions were encountered in young Saudi patients,[13] while the results from Egypt were similar to ours where more than half the patients were having rectal tumors.[15] Our young patients had more advanced tumors (Dukes C and D) compared to the old (65% versus 41%, p=0.005). The Western figures are divided in this regard: the majority showed more advanced tumors in the young[2,3,6,17,18,20-22] some showed more advanced tumors in the old[23] and some showed no difference.[4,7,10] Never the less, our results parallel the general trend noticed in high-risk Western communities. In the literature review by Heys et al[1] the median number of patients presenting with Dukes C and D was 64% (31-79%) compared to 47% in the old (18-61%).[1] Figures from KSA showed more young patients with localized disease and nodal involvement while older patients had more distant metastasis.[13] Our young patients proved to have significantly higher incidence of mucin secreting and signet ring tumors compared to the old (30% versus 15.8%, p=0.04). Although this incidence varies widely in Western communities (11-88%, median 23%),[1] there are more studies showing a higher proportion of mucin secreting tumors in the young than not.[1,2,7,10] Similar figures to ours were reported in Saudi and Egyptian patients.[13,15] Poorly differentiated tumors were encountered in 20% of our patients with no significant difference between the young and old (20% versus 18.3%, p=0.778). Our figure parallels the median figure of 27% encountered in young Western patients.[1] Contrary to our results, there were Younger Saudi patients with poorly differentiated tumors (33.8%).[13]

A pathological evaluation of tumor invasion (vascular, lymphatic and perineural) revealed no difference between the young and the old although the data in this regard was lacking in a significant number of our patients. This issue was not dealt within most of Western reports. Similar results to ours were published from Singapore.[4] The proportion of patients presenting with complications (obstruction and perforation) was similar in the young and old (22.5% versus 22.2%). We found only one western report dealing with that and showed a similar incidence (obstruction 17%, perforation 9%).[5] Controversy exists regarding the prognosis of CRC in the young compared to the old. The previous hypothesis that the prognosis is worse in the young[24,25] was argued against by many. Some found similar prognosis when stage for stage comparison was made.[3-6,23] Others even reported better survival in the young.[7,17] It was difficult for us to carry out a comparison regarding prognosis because of the following reasons: 1. Most of the young patients received adjuvant therapy while most of the old patients were denied that 2.The non-cancer mortality was limited to the old patients. 3.The surgical technique was not standardized which affects the out come especially in rectal cancer, which accounts for half of the cases.

In conclusion, young patients with CRC account for 20.2% of the cases diagnosed, 17.5% of them have predisposing conditions. Half of the tumors were rectal with less right side lesions compared to the old. They have more advanced stage and mucin secreting lesions but similar differentiation, invasion and complications compared to the old. This relative high frequency and frequency of predisposing conditions calls for family screening and surveillance in the presence of predisposing conditions.

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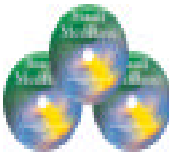

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Abstract

Of 1600 saudi patients who underwent lower gastrointestinal tract endoscopy at the Armed Forces Hospital, 40 (2.50%) had adenomatous polyps, 12 (0.75%) had colorectal cancer, 149 (9.31%) had *Schistosoma Mansoni*, and 5 (0.31%) had schistosomal polyps but with no associated malignancy. Despite the high incidence of *S.Mansoni*, there was no increase in the incidence of colorectal cancer in these patients. Of 1846 Saudi patients seen at the Oncology Department, 346 (18.74%) had gastrointestinal malignancy (307 in the upper gastrointestinal and 39 in the lower gastrointestinal tract). This distribution of neoplasms in the alimentary tract is almost the reverse of that seen in the West. There is a low incidence of adenomatous polyps and colorectal cancer in Saudi patients compared to the Western population. This might be due to genetic, dietary, and environmental factors. The present study also confirms previous studies from Egypt that *S.Mansoni* infestation does not play a role in or predispose to large bowel malignancy.