Colorectal cancers in Saudi Arabia

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ABSTRACT

Objectives: The aim of this retrospective study is to delineate the histopathological profile of colorectal cancers seen at King AbdulAziz University Hospital, Jeddah, Kingdom of Saudi Arabia and to compare our findings with 12 other studies published in the literature from other areas of the Kingdom of Saudi Arabia.

Methods: Our study group consisted of 39 colorectal cancer patients, who were examined in the department of Histopathology at King AbdulAziz University Hospital, Jeddah, Kingdom of Saudi Arabia, over a period of 4 years from January 1996 to December 2000. The data was retrieved and analyzed. The histopathological characteristics of the tumor such as tumor differentiation, tumor Duke's staging and grade of all the tumors were studied and compared with age of the patients.

Results: We received 2552 gastrointestinal endoscopic specimens during a 4 year period; out of these 276 were colorectal specimens. We found 39 cases (21 males and 17 females) of colorectal cancer during this period, which constituted 1.5% of total endoscopic biopsies and 13.8% of colorectal biopsies. Among these cases there were 31 cases (81%, mean age 56) of colorectal adenocarcinoma, 3 cases (7.6%, mean age 35) of signet cell carcinoma, 2 cases (5%, mean age 55.5) of mucinous adenocarcinoma, one case (2.5%, age 68) of metastatic papillary carcinoma, one case of mixed mucin secreting signet cell carcinoma (2.5%, age 64) and one case (2.5%, age 55) of poorly differentiated squamous cell carcinoma. In our study 21% of patients presented in their 3rd decade of life, 18.4% in the 4th decade, 15.8% in the 5th decade, 26.3% in the 6th decade, 10.5% in the 7th decade and 7.9% in the 8th decade.

Conclusion: Colorectal carcinoma showed frequent presentation in our population. Some malignant lesions showed early presentation as compared to United States of America, with 6.9% cases presenting at a young age and 23.6% of cases presented at middle age. In order to achieve early diagnosis, a comprehensive cancer education program should be planned and executed, and proper screening programs should be launched.

Keywords: Colonic malignancies, rectal malignancies.

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Results from epidemiological studies have provided insights into the etiology of large bowel pathologies especially cancer. Markedly diverse incidences of colorectal cancer exist in various parts of the world and within different regions of a given country. Studies of migrant populations have revealed a role for environmental factors, particularly dietary, in the etiology of colorectal cancers.[1] Genetic factors and inflammatory bowel disease also place certain individuals at increased risk. Sedentary lifestyle, cholecystectomy, and uretero-sigmoidostomy may also increase the risk of developing large bowel cancer.[1] The outlines of colonic malignancies are still not well reported in the Kingdom of Saudi Arabia (KSA). The present situation of this common and serious health problem is less than ideal and indicates that a lot has to be carried out to detect the disease at an earlier stage. The incidence of mortality from these colorectal malignancies in KSA cannot be determined accurately since there is no proper national cancer registry. Preliminary reports from several

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investigators have suggested that carcinoma of the rectum and large bowel is not as common in KSA as it is in Western Europe and North America.[2,3] While it is the most common malignancy arising from organs of the digestive system in the United States of America (USA), it is the 3rd incidence in KSA, followed by esophageal and hepatocelluar carcinomas.[3,4] Oncology textbooks from the West indicate that colorectal carcinoma occurs predominantly in the elderly, with a peak incidence in the 7th decade of life. It is considered to be rare in young adults. Experience at the King Abdul Aziz University Hospital (KAUH) indicates that it is not rare in young Saudi men and women.[4] Until age-adjusted national incidence figures become available to prove the contrary, the presence of large numbers of young patients with colorectal carcinoma could be considered due to a relatively younger median age in Saudi society compared with those in Western countries. Etiology of colorectal cancer is not completely clear. Epidemiologic studies demonstrate the importance of environmental factors, particularly dietary in cancerogenesis. Familial aggregation within a given population shows that genetic factors play an important role. General risk factors are represented by age, sex, and physical activity, while some pathologies increased the risk of developing colorectal cancer or are frankly pre-cancerous (adenomas, ulcerative colitis, Crohn's disease). Due to the influences of these etiological and epidemiological factors it was expected that the epidemiology of colorectal carcinomas in our population would differ from other countries, especially in the Western and Far Eastern countries.[1] In this study we reviewed and analyzed the epidemiology of colorectal carcinoma seen at our hospital and those reported in the literature from different areas of the Kingdom. Special emphasis was given to age of presentation of colorectal carcinomas on our population.

Methods. King Abdul Aziz University Hospital is a tertiary care hospital located in Jeddah, KSA. In an attempt to delineate the spectrum of colorectal pathologies, data on colonic endoscopic biopsies and surgical colectomy specimens received in the time frame of 4 years between January 1996 to December 2000 were retrieved from the records of the laboratory keeping track of age, gender, histopathological diagnosis, cytological diagnosis and frozen section diagnosis. Mean age for each individual leison were derived. Histological charecterstics such as tumor differentiation, grading and Duke's staging are tabulated and cross tabulated with age in **Table 1** to get the particular histological characteristics of colorectal malignancies for each age group. Similarly, we separately compared these histological characteristics among the young and middle age groups with a similar large study by Bedikian et al[5] from Riyadh, KSA in **Table 2**. Twelve other studies discussing epidemiology of cancers or specifically colorectal cancer in KSA were found in the literature. The data was comparatively analyzed in **Table 3**. Our results were compared with other studies from different regions of KSA to

Table 1 - Summary of age and sex distribution of malignant colorectal carcinoma cases with their histological differentiation, grading and staging according to age range.

Age Range	Sex		Differentiation			Grade of tumor			Duke's stage					Total
	Male	Female	Well	Moderately	Poorly	I	II	III	NA*	A	B	C	D	
30-39	3	4	3	4	0	5	0	2	1	3	1	2	0	**7**
40-49	5	1	1	5	0	1	5	0	0	1	1	4	0	**6**
50-59	3	5	1	6	1	1	7	0	1	2	5	0	0	**8**
60-69	5	5	4	3	3	4	6	0	1	3	3	3	0	**10**
70-79	3	1	0	3	1	1	2	1	1	1	1	0	1	**4**
80-89	1	1	1	0	1	1	0	1	0	1	0	0	1	**2**
90-100	1	0	1	0	0	1	0	0	0	1	0	0	0	**1**
Total	**21**	**17**	**11**	**21**	**6**	**14**	**20**	**4**	**4**	**12**	**11**	**11**	**2**	**38**

NA* - not applicable, Grade 1 - highly differentiated and limited to mucosa, Grade II - well to moderately differentiated with infiltration of bowel wall, Grade III -moderately to poorly differentiated with metastasis, Duke's stage A - mucosal/submucosal, Duke's stage B - extension to muscularis and serosa, Duke's stage C - extension to serosa with positive lymph nodes, Duke's stage D - metastasis.

Table 2 - Comparison of tumor pathological findings in 2 studies among young (<29) and middle (30-49) age groups.

Pathological findings	**Ibrahim***		**Bedikian et al[4]**	
	Age Group		**Age Group**	
Duke's staging	**Young**	**Middle**	**Young**	**Middle**
A Mucosal/submucosal	0	4 (30%)	0 0	0 0
B Extension to muscularis and serosa	0	2 (15%)	4 (16.5%)	11 (24.0%)
C Extension to seros and positive nodes	0	6 (46%)	8 (33.5%)	7 (15.0%)
D Metastasis	0	0 0	11 (46.0%)	23 (50.0%)
Unknown	0	0 0	1 (4.0%)	5 (11.0%)
Tumor differentiation	**0**	**13 (100%)**	**24 (100%)**	**46 (100%)**
Well differentiated	0	4 (30%)	2 (8.0%)	3 (6.5%)
Moderately differentiated	0	9 (69%)	9 (38.0%)	25 (54.0%)
Poorly differentiated	0	0 0	12 (50.0%)	11 (24.0%)
Undifferentiated	0	0 0	0 0	1 (2.0%)
Unknown	0	0 0	1 (4.0%)	6 (13.0%)
Total	**0**	**13 (100%)**	**24 (100%)**	**46 (100%)**
*present study				

Table 3 - Summary of comparison between 12 studies describing percentage of colorectal cancer among all malignancies with male to female ratio and ranking.

Authors	**Total**	**%**	**Mean Age**	**Male: Female**	**Rank**
Mahboubi[7]	**341**	(3.04)	53.5	1.70:1	11
Bedikin[4]	**100**	0	55.0	4.00:1	0
Sami[8]	**25**	(5.8)	0	3.40:1	5
El-Akkad[2]	**33**	(3.0)	0	1.06:1	4
Sahd Salim[10]	**35**	(3.8)	53.0	15.00:1	7
Ajarim[11]	**0**	(3.9)	0	0	8
Tandon P[12]	**0**	(3.9)	0	1.00:1.19	5
Al Saigh[13]	**0**	(6.3)	0	1.13:1	4
Khan AR[14]	**0**	(4.7)	0	1.00:1	6
Agop YB[5]	**331**	0	0	1.10:1	0
Abdel Rahman[6]	**18**	0	0	1.10:1	0
Willen R[9]	**0**	(5.0)	0	1.00:1.1	6
Ibrahim*	**38**	0	56.0	1.20:1	0
Total	**921**	**(4.2)**	**54.4**	**1.70:1**	**7**
*present study					

Table 4 - Age distribution in 4 different studies reported from the Kingdom of Saudi Arabia with their mean ages of presentation.

Authors	Age Range								Total	Mean Age
	<19	20-29	30-39	40-49	50-59	60-69	70-79	80-89		
Mahboubi[7]	5	20	44	55	81	79	46	11	341	53.5
Bedikin[4]	0	6	13	17	25	30	12	6	100	55.0
Sahd Salim[10]	0	3	8	8	7	4	3	2	35	53.0
Agop YB[5]	24		46		291				331	0
Ibrahim*	0	0	8	7	6	10	4	3	38	56.0
Total	**6.9%**		**23.6%**		**73.4%**				845	54.4
*present study, <29 - young age group, 30-49 - middle age group.										

develop a brief but more complete picture of colorectal malignancies in KSA.

Results. We received 2552 gastrointestinal endoscopic specimens during a 4 year period; out of these 276 were colorectal specimens. We found 39 cases (21 males and 17 females) of colorectal cancer during this period, which constituted 1.5% of total endoscopic biopsies and 13.8% of colorectal biopsies. Among these cases there were 31 cases (81%, mean age 56) of colorectal adenocarcinoma, 3 cases (7.6%, mean age 35) of signet cell carcinoma (SCC), 2 cases (5%, mean age 55.5) of mucinous adenocarcinoma, one case (2.5%, age 68) of metastatic papillary carcinoma, one case of mixed mucin secreting SCC (2.5%, age 64) and one case (2.5%, age 55) of poorly differentiated squamous cell carcinoma. On analyzing the distribution of these malignancies in the large bowel, 2 cases (5%) were located in the cecum, 5 cases (12.8%) were located in the ascending colon, 11 cases (28.2%) in the sigmoid colon and 14 cases (35.9%) were located in the rectum. Overall histologically, the differentiation characteristics of tumors were: 28.9% well differentiated, 55.3% moderately differentiated, 15.8% poorly differentiated; grading of these malignancies were: 36.8% grade I, 52.6% grade II, 10.5% grade III; staging of these malignancies: 31.6% were in stage Duke's A (mucosal/ submucosal), 28.9% were in stage Duke's B (extension to muscularis and serosa), 28.9% were in stage Duke's C (extension to serosa with positive lymph nodes) and 5.2% were in stage Duke's D (metastasis). Differentiations, grades and stages of our cases are cross tabulated with age in **Table 1** to get the particular histological characteristics of colorectal malignancies for each age group. Similarly, we separately compared these histological characteristics among the young and middle age groups with a similar large study by Bedikian et al from Riyadh[5] in **Table 2**. Thirteen other studies discussing epidemiology of cancers or specifically colorectal cancer in KSA were found in the literature. There data was comparatively analyzed in **Table 3**. The mean percentage and ranking of colorectal carcinoma out of all malignancies that came from these 12 studies[2-14] was 4.2% and 7th respectively. The mean male to female ratio was 1.7:1. Mean age of presentation from 4 studies was 54.4 years. In our study 21% patients presented in their 3rd decade of life, 18.4% in the 4th decade, 15.8% in the 5th decade, 26.3% in the 6th decade, 10.5% in the 7th decade and 7.9% in the 8th decade. The detailed age distributions of 845 colorectal malignancies from 5 different studies is tabulated in **Table 4**. It was found that 6.9% cases presented at a young age (<20 years), 23.62% cases presented at middle age (30-49 years) and 73.4% cases presented after 50 years.

Discussion. World-wide cancer of the colon and rectum emerges as the 3rd most frequent form of cancer in males and the 4th in females.[1] Patients with colorectal cancer suffer from a considerable excess mortality during the first 6 to 8 years after diagnosis, and the cure rate, which is in the order of 35-40%, has remained largely unchanged over several decades.[1] The incidence rates show a steep rise with age, marked international differences, increasing incidence in developing countries, adjustments in cancer risk within a few decades in populations who move from low to high risk areas, and no consistent differences in relation to race. In addition, the incidence rates display a complex network of relationship to age, sex, segment of the large bowel and secular trends.[1] The exact etiology of colorectal cancer is not well established. Well defined genetic syndromes and environmental factors have been hypothesized to have a significant role in the

pathogenesis of carcinoma of the colon and rectum.[15] The risk of developing colon carcinoma has been found to be higher than the general public in the patients with history of ulcerative colitis, familial polyposis, Gardner's Syndrome, Turcot Syndrome, partial resection of colon cancer, and family history for colon cancer and other adenocarcinomas.[15,20] Support for the theory that environmental factors are important comes from the observation of marked variation in incidence of colorectal carcinoma in the various parts of the globe.[16,17] It is high in North America and Western Europe, and low in South America, Africa and Asia. Studies of immigrants to the USA have indicated that those coming from countries with low incidence of colon carcinoma will assume the colon cancer risk of the region in which they settle. Most researchers have found a direct correlation between increased fat intake in the diet and the increase incidence of colon cancer.[15,19] The low incidence of colorectal carcinoma in most developing countries had been attributed to the fiber-rich diet consumed in these countries. It has been shown that fiber-rich diet gives protection against colonic carcinogenesis.[20,21] The effect of dietary changes being introduced through urbanization and acceptance of Western diet by the Saudi society is likely to have its impact on the incidence of colorectal carcinoma in this country during the coming decades. Carcinoma of the colon and rectum in the young is expected to occur primarily in the cancer-prone group such as patients with ulcerative colitis and familial polyposis.[15,18] In our study only 3 patients had ulcerative colitis, indicating that, as in the elderly, colorectal cancer in the young may arise in the absence of these precancerous conditions. Another important fact noticed in our study was that SCC had much earlier presentation as compared to others. All the 3 cases of SCC in our series presented in their 3rd decade of life. Although colorectal carcinoma is primarily a disease of adults in Western countries,[16,17] in our study, 21% patients presented in their 3rd decade of life, 18.4% in the 4th decade, 15.8% in the 5th decade, 26.3% in the 6th decade, 10.5% in the 7th decade and 7.9% in the 8th decade. The detailed age distribution of 845 colorectal malignancies from 5 different studies shows that 6.9% cases presented at a young age (< 20 years), 23.62% cases presented at middle age (30-49 years) and 73.4% cases presented after 50 years. This fact should be borne in mind when the physician sees a young Saudi patient with large bowel symptoms. Very frequently the establishment of the diagnosis of colorectal cancer is significantly delayed as such a possibility is not properly entertained. In a large similar study by Bedikian[5] who analyzed colorectal cancer patients presenting in the first 4 decades of life, found that symptom duration was much longer than that described in the USA (median 4-4.5 months versus 2-3 months, and symptom duration > one year in 21% of patients versus 10%).[5,13,14] He stressed that another finding indicative of delayed diagnosis of cancer is the high incidence of frank rectal bleeding as the presenting complaint. Sixty-two percent of the patients in the young group and 47% of the older group had frank rectal bleeding as the presenting complaint. The delay in diagnosis of the malignancy in Saudi patients translated into poor prognosis due to a lower resectability rate. In our study staging of these malignancies were: 31.6% were in stage Duke's A (mucosal / submucosal), 28.9% were in Duke's B (extension to muscularis and serosa), 28.9% were in Duke's C (extension to serosa with positive lymph nodes) and 5.2% were in Duke's D (metastasis). The value of early diagnosis of colorectal carcinoma cannot be over emphasized if progress in the therapy of this malignancy is to be made. Public education campaigns in the Western countries have resulted in an increase in awareness of the "warning signals of cancer" and of the need for early diagnosis of cancer, important elements aimed at cure of cancer. However, the Saudi public has not yet been made aware of these warning signals. In one study only 15% of 250 Saudi nationals indicated they had heard of the "warning signals of cancer" and that unusual bleeding and change in bowel habits could be associated with the possibility of cancer (4.8% and 1.6% of the subjects).[5,24]

In conclusion, in order to achieve early diagnosis, a comprehensive cancer education program should be planned and executed. It should aim at educating the young and the old. It should reach them in the classrooms as well as in the homes. To achieve this, efficient use of the press and audiovisual media is necessary. The public must be informed of the cancer warning signals and the benefits of regular checkups and availability of screening programs for high-risk groups. Routine preventive examinations and medical consultations for symptoms, which persist despite proper therapy, must be encouraged. The unfavorable outlook for young adults with carcinoma of the colon and rectum emphasizes the importance of systematic study of these patients.

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