RESEARCH ARTICLE

Colorectal Cancer in the Kingdom of Saudi Arabia: Need for Screening

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Abstract

Background and Objectives: Colorectal cancer (CRC) is a major health problem in the Kingdom of Saudi Arabia (KSA). Our aim was to characterize the epidemiology of CRC in the Saudi population. Design and Setting: Retrospective analysis of all cases of CRC recorded in the Saudi Cancer Registry (SCR) between January 2001 and December 2006 amongst Saudi citizens in KSA. Patients and Methods: Data were retrieved from the database of the SCR. Descriptive statistics was performed using SPSS. Results: A total of 4,201 cases of CRC were registered in the SCR. The incidence of CRC increased between 2001 and 2006. The mean age of patients at the time of diagnosis was 58 years; most patients were above 45 years of age (n=3322; 79.1%). At the time of diagnosis, 977 patients (23.0%) presented with localized disease and 1,018 (24.0%) had distant metastasis. The most frequent pathological variant was adenocarcinoma (73%), with grade 2 (moderately differentiated) being the most common grade among all variants (61%). For all cancer grades, the frequency of CRC was significantly higher among patients >45 years (P=0.004), who presented with more advanced disease (stages III and IV) (P=0.012). Based on logistic regression, age >45 years was associated with advanced regional presentation (P=0.001). Tumor grade was associated with advanced regional presentation and metastasis. Conclusion: There was an increase in the incidence of CRC between 2001 and 2006. The age at the time of diagnosis was low when compared with reports from developed countries. A nationwide approach is needed to encourage and illustrate the importance of screening programs.

Keywords: Colorectal cancer - incidence - epidemiology - screening - Saudi Arabia

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Introduction

In the year 2005, the population of the Kingdom of Saudi Arabia was estimated at 16,945,484, composed mostly of native Saudis (62%). In that same year, the Saudi Cancer Registry (SCR) reported that colorectal cancer (CRC) was the second most common malignancy among Saudis for all ages (10.3%) and the number one malignancy in males (11.8%) (Al-Eid, 2011). At present, very few reports provide a descriptive epidemiology of CRC in Kingdom of Saudi Arabia, which in general can indicate the magnitude of cancer care in the Kingdom (Mansoor et al., 2002; Ibrahim al., 2008). Thus, the main aim of this study was to characterize the epidemiology of CRC in the Saudi population and to examine the average age of Saudi patients at the time of diagnosis.

Materials and Methods

We conducted a retrospective study in all Saudi patients who were diagnosed with CRC during the period from January 2001 to December 2006. Data was retrieved from the SCR, a population-based registry that started reporting cancer cases from January 1,1994. The SCR strives to compile all cancer data from the Ministry of Health, governmental and private hospitals as well as clinics and laboratories from all regions in the Kingdom of Saudi Arabia (Ministry of Health, 2007).

For all cases of CRC diagnosed during the study period, we recorded demographic data and pathological factors such as cancer location and the TNM stage at the time of diagnosis. The patients were divided into two groups based on their ages; patients less than 45 years and those older than 45. We reported the tumor location, the pathological type and the tumor stage at initial presentation in both age groups. A similar report was made with respect to gender. We calculated the incidence rates for the study population by age and cancer site for 16 age groups (from 0 to 75+ at intervals of 5).

Descriptive statistics was performed using Microsoft Excel 2007 (Microsoft, Seattle, WA). Data were presented as incidences (percent) and frequencies.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 20.0 (SPSS

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Inc., Chicago, IL, USA). CRC grades and stages were compared between patients younger than age 40 and those older than 40 and between patients younger than age 45 and those older than age 45, using Chi-square test where a p value <0.05 was considered statistically significantly. Multinomial logistic regression was performed to identify the predictors of advanced disease. Odds ratios were considered significant if <2 and the confidence interval did not include 1.

Results

A total of 4201 cases of CRC were registered in the SCR between January 2001 and December 2006. The data revealed a general increase in CRC incidence in both genders and in all age groups (Figures 1 and 2). Tables 1 show the incidence of CRC in the different age groups in females and males. The mean age of the patients at the time of diagnosis was 58 years (57 in females and 59 in males), with the majority of patients being older than 45 years (n=3322; 79.1%). There was a slight predominance of newly diagnosed cases in males (n=2274; 54.1%).

Tables 2 show the frequency of CRC by site among the different age groups in females and males. The most common location of CRC was the rectum (n=1176; 28.0%) followed by the sigmoid colon (n=798; 19.0%) and the recto-sigmoid junction (n=630; 15.0%) (Figure 3). Most cases of CRC (n=2856, 68.0%) were found on the left side of the colon. Isolated right-sided lesions were documented in 14.0% of the cases.

Overall, a total of 977 patients (23.0%) presented with localized disease and 1018 patients (24.0%) had distant metastasis at the time of diagnosis. The remaining patients (n=2206) had various degrees of regional extension or an unknown stage. The most frequent pathological variant

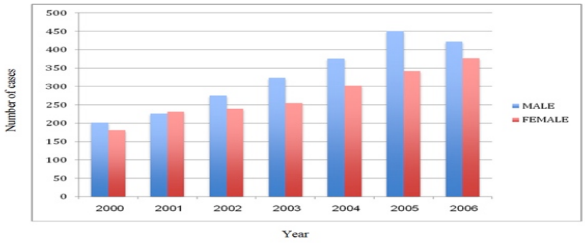

Figure 1. Cases of Colorectal Cancer per Year in Both Genders. The data represents the number of cases in males and females, irrespective of the age.

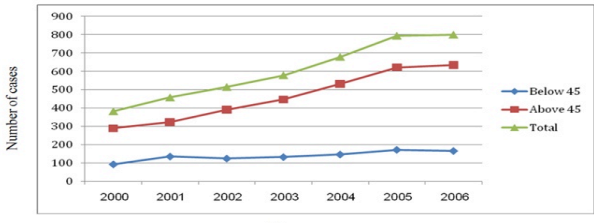

Figure 2. Cases of Colorectal Cancer per Year in Both Age Groups. The number of colorectal cancer cases among patients below and above age 45 years from 2000 to 2006 is shown.

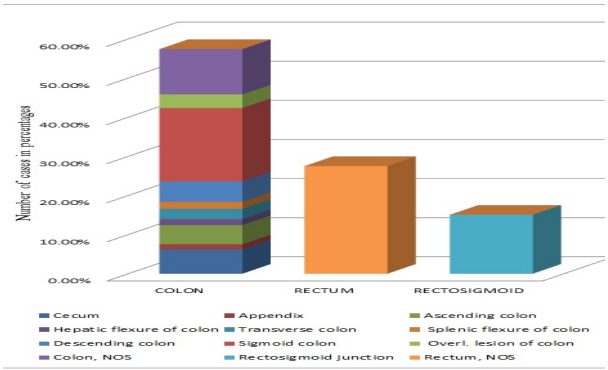

Figure 3. Frequency of Colorectal Cancer by Site. Each bar represents the percentage of cases by cancer location. The most common location was the rectum (n=1176; 28.0%). In general, most cases were found on the left side of the colon (n=2856, 68.0%), while 14.0% were isolated right-sided lesions.

Table 1. Incidence of Colorectal Cancer in Different Age Groups in Females[a] and Males[a]

Site	All Ages (n)	Age Unkn (n)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
Females																		
Colon	1144	1	0	0	0	0.1	0.4	0.7	1.2	2.2	4	6.1	9.4	12.2	17.2	16.5	15	20.6
Rectum	783	0	0	0	0	0.1	0.1	0.4	0.6	1.9	2.5	5	7	7.3	9.6	11	11	17.1
Colorectal	1927	1	0	0	0	0.2	0.5	1.1	1.8	4.1	6.5	11.1	16.4	19.5	26.8	27.5	26	37.7
Males																		
Colon	1268	0	0	0	0	0.1	0.2	0.5	0.7	2	3.3	6	7	13.6	19.3	24	26	24.2
Rectum	1006	1	0	0	0	0.1	0.1	0.2	1	1.6	2.4	4.9	6.2	12.5	14	18.9	21.1	17
Colorectal	2274	1	0	0	0	0.2	0.3	0.7	1.7	3.6	5.7	10.9	13.2	26.1	33.3	42.9	47.1	41.2

[a]Data are presented as incidence (percent) unless otherwise stated, Unkn=unknown.

Table 2. Frequency of Colorectal Cancer by Site in Different Age Groups in Females[a] and Males[a]

Site	All Ages (n)	Age Unkn (n)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
Females																		
Colon	1144	1	0	0	1	4	19	33	48	74	102	116	128	128	158	114	87	131
Rectum	783	0	0	0	0	4	7	18	25	63	64	94	95	76	88	76	64	109
Colorectal	1927	1	0	0 1	8	26	51	73	137	166	210	223	204	246	190	151	240	
Males																		
Colon	1268	0	0	0	3	4	10	26	29	68	94	128	106	136	167	169	137	191
Rectum	1006	1	0	0	1	4	4	11	40	55	68	104	94	125	121	133	111	134
Colorectal	2274	1	0	0	4	8	14	37	69	123	162	232	200	261	288	302	248	325

[a]Data are presented as frequencies., Unkn=unknown.

Table 3. Differences Between the Age Groups With Regards to Tumor Grade and Localization

Variable	Age <45 years	Age >45 years	Total (n)
Cancer Grade			(P-value=0.004)
Grade I (well differentiated)	68 (12.6%)	473 (87.4%)	541
Grade II (moderately differentiated)	364 (14.2%)	2198 (85.8%)	2562
Grade III (poorly differentiated)	72 (21.0%)	271 (79.0%)	343
Grade IV (undifferentiated anaplastic)	4 (10.0%)	36 (90.0%)	40
Unknown	116 (16.2%)	599 (83.8%)	715
Total	624 (14.9%)	3577 (85.1%)	4201
Tumor Localization			(P-value=0.012)
Localized	210 (21.5%)	767 (78.5%)	977
Regional: Direct ext	145 (20.4%)	566 (79.6%)	711
Regional: Lymph node inv	82 (25.4%)	241 (74.6%)	323
Regional: Direct ext. and lymph node inv	165 (27.8%)	428 (72.2%)	593
Regional: NOS	2 (25.0%)	6 (75.0%)	8
Distant metastases	247 (24.3%)	771 (75.7%)	1018
Unknown	115 (20.1%)	456 (79.9%)	571
Total	966 (23.0%)	3235 (77.0%)	4201

*Data are presented as frequency (percent) unless otherwise specified, ext=extension; inv= involvement, NOS=not otherwise specified.

Table 4. Association Between Advanced Disease and Tumor Grade on Logistic Regression

Tumor Grade	P-value	Odds ratio	95% Confidence Interval
Regional: Direct Extension			
Grade 1	<0.01	5.464	3.620-8.248
Grade 2	<0.01	10.068	7.247-13.987
Grade 3	<0.01	5.727	3.337-9.831
Grade 4	0.009	4.236	1.429-12.560
Regional: Lymph Node Involvement			
Grade 1	<0.01	4.154	2.256-7.648
Grade 2	<0.01	12.671	7.885-20.361
Grade 3	<0.01	10.546	5.436-20.462
Grade 4	0.03	4.825	1.164-20.000
Regional: Direct Extension and Lymph Node Involvement			
Grade 1	<0.01	2.962	1.847-4.750
Grade 2	<0.01	9.698	6.867-13.697
Grade 3	<0.01	10.934	6.538-18.284
Grade 4	0.279	2.151	0.537-8.613
Distant Metastases			
Grade 1	0.018	1.523	1.076-2.156
Grade 2	<0.01	3.063	2.403-3.906
Grade 3	<0.01	4.338	2.819-6.676
Grade 4	0.023	2.841	1.155-6.990

was adenocarcinoma (73%), with grade 2 (moderately differentiated) being the most common grade among all variants (61%). For all cancer grades, the frequency of CRC was significantly higher among patients > 45 years (P=0.004) (Table 3). Patients older than 45 years presented with more advanced disease (stages III and IV) compared to younger patients (P=0.012) (Table 3). On logistic regression, age >45 years was associated with advanced regional presentation (direct extension and lymph node involvement) (P=0.001, odds ratio=1.796, 95% confidence interval=1.289-2.503). Tumor grade was associated with advanced regional presentation and metastasis (Table 4).

Discussion

The analysis of this data from the SCR reflects the trend of CRC between January 2000 and December 2006 in the Kingdom of Saudi Arabia. Unfortunately, it is difficult to make relevant comparisons with most studies conducted in the Kingdom because the majority of the few studies that were conducted are hospital-based (Al-Radi et al., 2000; Isbister et al., 2000; Ayyub et al., 2002; Al-Ahwal and Al-Ghamdi, 2005; Sibiani et al., 2011) and therefore do not reflect the trend of the disease among Saudis in the Kingdom. However, this striking trend does mirror similar recent reports from other countries (Eser et al., 2010; Matsuda al., 2010; Matsuda et al., 2011).

This analysis shows that there was a steady increase of CRC incidence from the year 2000 to the year 2006, and the incidence was greater in males than in females. Similar observations have been made in other studies, including those that were conducted in the Kingdom of Saudi Arabia (el-Akkad et al., 1986; Al-Madouj and Al-Zahrani, 2005; Ibrahim al., 2008). However, the reasons why colorectal cancer is more common in men than women are not clear. In one study it was suggested that factors such as diet, body size, physical activity, hormones and family history of CRC could be responsible for the greater frequency amongst males than females (Fancher et al., 2011; Statistics, 2011).

According to the present study, the average age at diagnosis of CRC in the Kingdom of Saudi Arabia was 58 years. One report by Al-Ahwal et al. in 2002 showed a similar mean age (59 years) for CRC diagnosis in the western region of the Kingdom of Saudi Arabia (Al-Ahwal and Al-Ghamdi, 2005). When compared with reports from developed countries (Moore et al., 2010) (Sankaranarayanan et al., 2010), the mean age at diagnosis of CRC is lower in the Kingdom. In England, some researchers reported that between 1996 and 2004 the mean age at diagnosis of CRC was 68.4 years in men and 69.0 years in women (Jones et al., 2009); In Australia, the median age at diagnosis of CRC in 2008 was reported to be 70 years (Ageing, 2008), similar to that is reported in the United States (Liang, 2010) and Sweden (Derwinger et al., 2010). Contrary to our findings, reports from neighboring countries that share our country's topographic and climatic characteristics show that patients younger than 45 years of age have more advanced disease at the time of diagnosis when compared with those older than 45 (Al-Jaberi et al., 2003). There are also reports that at initial presentation, more aggressive and advanced disease has been detected in patients younger than 50 years (Isbister, 1992). This population of young patients presenting with early-onset advanced CRC are thought to have a higher risk of long-term mortality compared to age-matched controls (Forbes et al., 2010). This makes them a population that should be targeted for further studies to elucidate the biology of CRC and to identify more effective prognostic factors than the

traditional staging system and hence a more aggressive approach (Forbes et al., 2010; Liang, 2010)

Regarding the etiology, genetic factors may play a role but dietary factors would likely be a true cause of this phenomenon (Genkinger and Koushik, 2007; Arafa et al., 2011; Zandonai et al., 2012). More attention should be paid to positive family history, obesity management and smoking cessation in reducing the incidence of cancer (Aune et al., 2011), which can be achieved by widespread nationwide patient education rather than personal efforts which is overall cost effective when conducted effectively (Lansdorp-Vogelaar et al., 2010; Lansdorp-Vogelaar et al., 2011). Adhering to CRC screening programs is also an issue. Various factors and considerations might contribute, but cultural limitations and screening literacy may be the leading ones (Ravichandran et al., 2010; Ravichandran et al., 2011). Further research and surveys may be helpful to further prove that this is indeed true. However, this also should be one of the main targets of nationwide patient education campaigns.

In the midst of declining CRC incidence worldwide (Fancher et al., 2011), a more strict adaptation of screening programs is likely necessary. As cost effectiveness is a cornerstone behind the concept of screening, especially if it is correlated to national mortality data, different screening methods have been proposed and adapted worldwide depending on both resource availability and population preference. Both invasive and non-invasive methods are available with different notions as to the comparable overall cost-effectiveness. Fecal occult blood testing and stool DNA detection are examples of non-invasive methods compared to potentially invasive modalities like colonoscopy (Misra et al., 2011; Sobhani et al., 2011; Wilschut et al.; 2011; Goede et al., 2012).

In 2008, some authors predicted that there will be an increase CRC incidence in the Kingdom of Saudi Arabia during the next decade due to possible westernization of our dietary habits and lack of proper screening, which is also another reason to implement such a strict approach (Ibrahim et al., 2008). Whether or not we should start screening at a lower age is another question, which has been repeatedly brought up in other countries with similar epidemiological observation (Davis, 2011; Ganapathi et al. 2011). Proper identification of cases of Lynch syndrome and other familial causes of CRC is necessary, as this group should be managed differently. This has become a focus of attention in other countries like the United Kingdom (Anning et al. 2011).

In conclusion, the incidence of CRC in the Kingdom of Saudi Arabia has been on a constant rise over the past few years. The age at the time of diagnosis is lower when compared with results from developed countries. Further research is needed to identify the cause of this observation, and this may be a reason to implement more strict guidelines for colon cancer screening and to consider starting this at a younger age. This calls for a more organized nationwide approach focused on patient education that encourages and illustrates the importance of CRC screening programs.

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