

*Full Length Research Paper*

# Colorectal Cancer in Saudi Arabia King Abdul Aziz University Hospital: A Five Year Experience

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**Colorectal cancer (CRC) ranks first in males and third in females among all cancers in Saudi Arabia. Its frequency of diagnosis has increased significantly over the past ten years. Genetic and environmental factors may have played important roles in the increase in CRC incidence in Saudi Arabia. Using a retrospective study, we studied all patients diagnosed with CRC by endoscopy at King Abdul Aziz University Hospital in Jeddah, Saudi Arabia. For each patient, we collected demographic data, endoscopic findings, hemoglobin results, CEA levels at diagnosis, radiological findings and methods of treatment offered. We included 177 patients in the final analysis. The sample comprised mostly males 103 (58.2%), and 72 (40.0%) were Saudis. The mean age was 56.6±SD 13.3 years old. Male patients were older than female patients (P=.046). Approximately one-third of all patients were younger than 50 years old (50 patients). Most of the patients 164 (92.7%) had a single lesion on the left side rectum (52, 29.4), sigmoid (41,23.2%) and rectosigmoid (46, 26%). We reported lymph node involvement in 90 (50.8%) patients and distant metastasis (DM) in 50 (28.2%) patients. The carcinoembryonic antigen was higher in patients with DM P <.001. A total of 168 patients received chemotherapy or had a hemicolectomy for the tumor. We reported tumor recurrence in 27 (15.3%) patients. The mean survival was 4.832±.44 years. In conclusion, the diagnosis and prevalence of CRC is increasing in Saudi Arabia. As such, CRC screening programs are recommended for both the prevention and early detection of CRC.**

**Keywords:** Colorectal cancer, incidence, metastasis, chemotherapy, radiotherapy, Saudi Arabia.

## INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed cancer among males and the fourth most common among females worldwide ( Parkin et al, 2002). In terms of occurrence, it is more common in males than in females (Colon cancer Incidence and mortality rates,

2010; Rim et al., 2009). The Kingdom of Saudi Arabia (KSA) is considered to be a country with a low CRC incidence; however, CRC incidence and related mortalities have been steadily increasing in the country over the past twenty years (Ibrahim et al., 2008; Al Eid and Manalo, 2006). It now ranks first among all cancers in males and third among females in Saudi Arabia. In countries such as the United States, which has a high CRC incidence and established surveillance programs that result in the early detection and removal of pre-

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**Table 1.** Demographic data of patients diagnosed with colon cancer at KAUH via colonoscopy between 2005 and 2009.

|         |     | Nationality |        |       | Age      |               |
|---------|-----|-------------|--------|-------|----------|---------------|
|         |     | Saudi       | Yamani | Other | Mean age | Std Deviation |
| Male    | 103 | 38          | 25     | 40    | 58.4     | 13.99665      |
| Females | 74  | 34          | 21     | 19    | 54.4     | 11.92606      |
| Total   | 177 | 72          | 46     | 59    | P=.046   |               |

cancerous colonic polyps, the incidence of CRC and its related mortalities have decreased over the past 15 years (Rim et al., 2009; Jackson et al., 2006). In contrast, past data on CRC from KSA suggest a potentially alarming increase in CRC in the coming decades, surveillance programs are not yet established in KSA (Ibrahim et al., 2008). Genetic predispositions, such as the K-RAS mutation, have been linked to CRC for many years, (Parsons and Meng, 2009) though those variables have been insufficiently investigated in KSA (Abubaker et al., 2008). Other environmental factors and the westernization of the Saudi diet may play roles in the increased CRC incidence in KSA, but such hypotheses must be further assessed. To address these questions, we carried out a six-year descriptive study involving patients diagnosed with CRC at King Abdul Aziz University Hospital in Jeddah, Saudi Arabia

## METHODS

### Design of the retrospective descriptive study

**Study population:** Patients diagnosed with CRC via colonoscopy at King Abdul Aziz University Hospital in Jeddah, Saudi Arabia, between January 2005 and December 2009.

**Inclusion criteria:** All patients diagnosed with CRC via colonoscopy and confirmed by tissue biopsy.

Patients were excluded if their demographic data were incomplete or if they could not be contacted for follow-up shortly after the colonoscopic examination. Patients who were diagnosed before 2005 but had only a follow-up colonoscopy after treatment during the study period were not included. Patients who had their first diagnostic colonoscopy in another center during the study period and completed treatment and follow-up at King Abdul Aziz University Hospital were also excluded.

For each patient, we obtained the following demographic data: age, sex and nationality. We then reviewed the patient files and hospital information systems to obtain colonoscopy results and the hemoglobin and carcinoembryonic antigen (CEA) findings at normal diagnosis normal (0-3.4). We also reviewed the results of the computed tomography (CT) performed both at diagnosis and during the entire follow-up process. The

CT enabled us to identify regional infiltrates, mesenteric and para-aortic lymph node involvements, distal metastasis and metastasis with recurrence during follow-up. From the treated patients, we also obtained data regarding the types of treatment (e.g., chemotherapy, radiotherapy, surgical management or other combinations). The duration of follow-up and the outcomes at the end of follow-up were determined for each patient.

**Statistical method:** We used the Statistical Package for Social Science software (SPSS 16) to determine the frequencies, means and standard deviations (SD). We also used the independent T- test to assess differences in ages and mortalities between males and females and to assess the mortalities between patients with and without advanced disease. A P value of .05 or less was considered significant. We used Kaplan-Meier survival analysis to assess survival.

## RESULTS

From January 2005 to December 2009, 192 patients were diagnosed with CRC by colonoscopy; of these patients, 8 were excluded because of incomplete data or lack of follow-up shortly after diagnosis. Two patients were excluded because the biopsy results showed colonic lymphoma, whereas another two patients had features characteristic of carcinoid tumor upon biopsy and were thus excluded. Two females were excluded because they had advanced cervical cancer invading into the colon, while another patient had CRC on top of chronic ulcerative colitis and was thus excluded. The final analysis included 177 patients; most were males (103,58.2%). Of, 72 (40.7%) were Saudis, and 105 (59.3%) were non-Saudi and mostly Yemenis (Table 1). The mean age was 56.6±SD 13.2822 years. Male patients were more likely to be older than the females, with mean ages of 58.4 and 54.4 years, respectively (P=.046). A total of 12 patients (6.8%) were younger than 40 years old, while 50 (28.2%) were younger than 50 years old. The largest number of occurrences was in 2009, with 59 patients. Only two patients had received a screening colonoscopy at the time of diagnosis due to a family history of CRC, while the rest were either asymptomatic or symptomatic, had rectal bleeding from distal lesions,

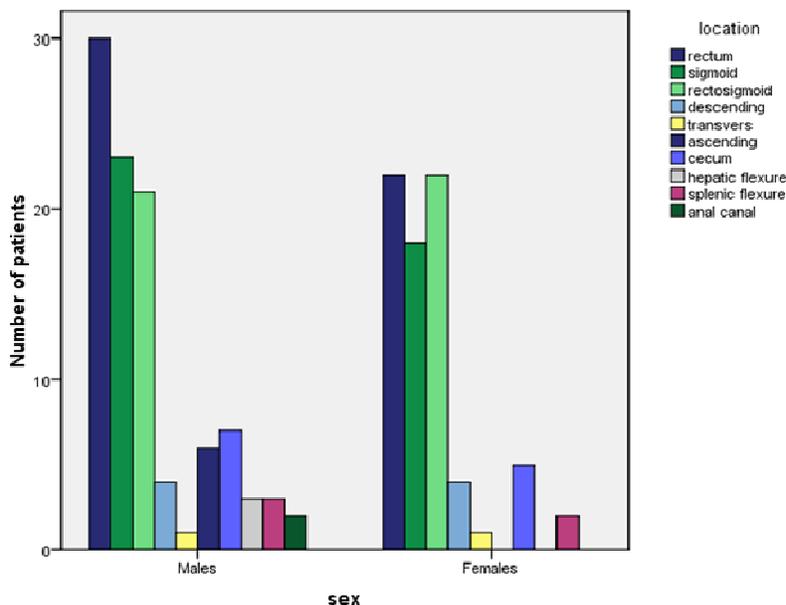


Figure 1. Tumor location in relation to gender

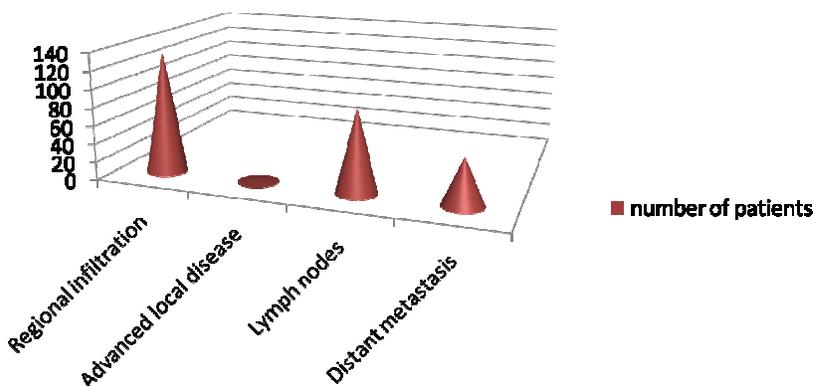


Figure 2. Number of patients according to tumor infiltration and metastasis

experienced unexplained abdominal pain from lesions in the sigmoid colon and above, or had a colonoscopy for unexplained anemia. Two patients had acute abdominal pain due to colonic perforation from the tumor. Ten patients (5.6%) had a history of previously resected CA colon, and seven (4%) had a history of colonic polyp removal. The most common location was the rectum, with 52 (29.4%), followed by the rectosigmoid, with 46 (26%) (Figure 1). Male patients had higher rates as compared to females in the rectum, rectosigmoid and sigmoid regions. Most patients (164; 92.7%) had a single lesion; 10 (5.65%) patients had 2 lesions, 2 patients (1.13%) had 3

or 4 lesions, and a single patient (.56%) had multiple lesions. A total of 136 (76.3%) patients had regional infiltration, while 2 with the disease had severe local infiltration with a frozen pelvis. Distant metastases at diagnoses mainly involved the liver, though three patients had lung metastasis (two at diagnosis and one with recurrence), two patients had brain metastasis (one at diagnosis and one with recurrence), and one patient had multiple bony metastasis (refer to Figure 2 for tumor infiltration and metastasis). Of those patients who were younger than 50 years of age, 38 (76%) had locally advanced disease, 14 (28%) had lymph node metastasis,

**Table 2.** Number of patients who received chemotherapy and surgery.

|                  | Operated hemicolectomy 108 |    | Permanent colostomy |
|------------------|----------------------------|----|---------------------|
| Chemotherapy 100 | Yes                        | No |                     |
| Yes              | 72                         | 26 | 2                   |
| No               | 36                         | 31 | 1                   |

and 6 (12%) had distant metastasis. The mean hemoglobin level at diagnosis was  $10.844 \pm 0.384$ . There was no difference in the Hb between patients with and without advanced local disease, and similarly, the mean Hb levels were not different between the patients with and without distant metastasis ( $P = .74$  and  $.67$ , respectively). The serum CEA values were normal in a majority of the patients (0-3.4), though patients with distant metastasis were more likely to have high CEA levels as compared to those without distant metastasis, with mean values of 517.6 and 13.8, respectively ( $P$  value  $< .001$ ). The histological features of the patients were variable from moderately to poorly differentiated adenocarcinomas. The majority of the patients (168, 95%) had either received chemotherapy or right or left hemicolectomies according to tumor location (Table 2). Thirty-six patients with a localized disease received only a resection without chemotherapy, three (1.7%) had permanent colostomies for advanced obstructing rectal or rectosigmoid lesions, and another three (1.7%) had preoperative colon stenting for obstructing tumors. In 2009, 26 patients received chemotherapy; they had post-chemo hemicolectomies in 2010 after finishing the planned chemotherapy cycles. A total of 35 (19.8%) received radiotherapy, while two of those who received radiotherapy had tumors involving the anal canal. Recurrence during follow-up was reported in 27 patients (15.3%), and 18 of them (66.7%) had liver or lung metastases with the recurrent tumors. The location of the primary tumor did not affect the recurrence, though patients with advanced primary disease and metastasis were more likely to have recurrences ( $P = .04$ ). The mean duration of recurrence was  $2.2 \pm 0.514$  years. The duration of follow-up was less than one year (2-6 months) in 71 patients (40.1%); all of them had locally advanced disease with lymph node and/or distant metastasis. For the remaining 106 patients (59.9%), the mean duration of follow-up was  $2.16 \pm 0.26$  years. At the time of the final analysis, 67 patients (37.9%) were still alive, and 37 (20.9%) had been documented as dead. The remaining 73 (40%) could not be contacted for follow-up. The death rate was not affected by age, sex or nationality, though it was higher in patients with metastasis and advanced disease as compared to those without metastasis ( $P = .003$ ). The mean survival time was  $4.832 \pm 0.44$  years. All of the reported deaths were directly related to the CA colon complications, though one patient died from a chest infection complicated by respiratory failure.

## DISCUSSION

Our data showed that over a six-year period, 185 patients had a diagnosis of CRC by colonoscopy. This number is much less than the number reported by Al-Ahwal et al. in 2006 from the same center (KAUH); they reported 90 cases of CRC over a 10-year period between 1993 and 2002 (Al Ahwal and Al Ghamdi, 2006). Similarly, Al Jebreen from King Khalid University Hospital in Riyadh reported 113 cases of CRC over 10 years between 1995 and 2005 (Aljebreen, 2007). The larger numbers of patients and shorter periods in our study as compared to these two aforementioned studies suggests a true increase in CRC incidence in KAS (Ibrahim et al., 2008). We found that the number of patients diagnosed during the final year of the study (2009) was higher than the previous year, with an increase of 33.3%. In their report on CRC between 2003-2007 from King Abdul Aziz Medical City in Riyadh, Al Huzaim and co-workers found that CRC diagnosis had increased over the past seven years (Al-Huzaim, 2010). In our data, we did not find any difference in disease severity and mortality between Saudis and non-Saudis or between Saudis and Yemenis. This finding is different from the figures from the United States, where the data have shown variable disease severities and mortalities among different ethnic groups (Rim et al., 2009; Thompson et al., 2006). In our cohort, the number of males was greater than that of females, which is a finding that is consistent with both local and international figures (Colon cancer Incidence and mortality rates, 2010; Rim et al., 2009; Ibrahim et al., 2008; Aljebreen, 2007; Al-Huzaim et al., 2010; Murphy et al., 2010). Similar to our data, Murphy and colleagues showed that the higher incidence of CRC in males was reported across all tumor locations. This finding was less prominent in our cohort, as fewer patients had right-sided colonic tumors than left-sided tumors. In our cohort, female patients had a younger mean age than males. The mean age in our CRC population was also younger than the figures from the United States and other countries (Colon cancer Incidence and mortality rates, 2010; Rim et al., 2009; Thompson et al., 2006). Nevertheless, the mean ages were consistent with that of patients who had CRC based on local data from KSA (Aljebreen, 2007; Al-Huzaim et al., 2010; Al-Ahwal and Al-Ghamdi, 2005). Approximately, one-third of our patients were younger than 50 years old, 38 (76%) of them had advanced local disease, and 9 (18%) had

died of CRC. Many previous local, regional and international data have suggested that CRC at a young age is associated with severe diseases and higher mortality rates as compared to CRC at an older age (Isbister, 1992; Al-Jaberi et al., 2003; Endreseth et al., 2006). However, in our cohort, there was no difference in mortality in relation to age because disease severity was the most predictive factor for mortality. O'Connell et al. reported a similar finding in a 10-year report of California patients with CRC (Connell et al., 2004). A 2007 study by Guraya et al. in Riyadh showed an increase in CRC incidence among King Khalid University Hospital patients; in that report, however, there was a tendency toward a rightward shift of the tumor in terms of location (Guraya and Eltinay, 2006). In our data, most of the patients had left-sided lesions. Only 20% of our patients had localized resectable disease because the CRC screening program was not yet established and because CRC awareness is limited in KSA. In a 26-year review of patients with CRC, Dozois et al. found that young patients less than 50 years old were more likely to be symptomatic and more likely to have advanced disease (Dozois et al., 2008). Most of the lesions in our patients were localized in the distal colon and the rectum, a finding similar to previously reported local data (Aljebreen, 2007; Al-Huzaim et al., 2010; Al-Ahwal and Al-Ghamdi, 2005). Our patients had well-differentiated to poorly-differentiated adenocarcinomas, which is the most common type of colonic malignant tumor in KSA. Only a few patients had lymphomas or other malignancies; this finding is also consistent with previous local data on colorectal malignancies (Al-Huzaim et al., 2010; Al-Ahwal and Al-Ghamdi, 2005; Qayyum and Sawan 2009). In conclusion, we have demonstrated that CRC in our KSA population presents in younger ages and in more advanced disease states as compared to other countries. In addition, the incidence of CRC has increased as compared to data reported in previous local studies. Our findings have added to previous local data on CRC over the last 10 years, and our study highlights the importance of establishing awareness about CRC and screening programs in KSA. In addition, educational programs for families with first-degree relatives with CRC should be offered. Future studies investigating the genetic markers of CRC in KSA may enable individualized treatment options for those patients with markers that can predict high risk of disease recurrence or progression (Qayyum and Sawan, 2009; Abubaker, 2009).

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