

RESEARCH ARTICLE

Histopathological Features of Colorectal Cancer in Al-Madinah Region of Saudi Arabia: 8 Years Experience

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Abstract

Background: To determine the histopathological pattern of colorectal cancer (CRC) among Saudi patients with a view to determine various epidemiological and histopathological features of the disease. **Materials and Methods:** We retrospectively collected and analyzed the demographic and histopathological data of all the patients with CRC diagnosed at King Fahad Hospital, Madinah, Saudi Arabia over a period of 8 years from January 2006 to December 2013. **Results:** Of 324 cases of CRC reviewed, 200 cases (61.7%) were males while 124 cases (38.3%) were females giving a male to female ratio of 1.6: 1. Age of the patients ranged from 20 to 100 years with a mean age 57.9 years. The rectosigmoid region was the most frequent anatomical site (13.6%) involved and adenocarcinoma (88.6%) was the most common histopathological type. The majority of adenocarcinomas (87.3%) were moderately differentiated. A total of 47.8% of patients were in stage B and 43.5% of patients were in stage C of the Aster-Coller classification. Most patients (75.7%) presented with large size tumors. Lymphovascular invasion and lymph node metastasis were recorded in 67.9% and 43.6% of cases, respectively. **Conclusions:** Colorectal cancer is common in our environment and the majority of patients present late with an advanced stage. Screening programs regarding CRC should be enhanced to improve the outcome of the patients.

Keywords: Colorectal carcinoma - histopathology - Madinah - Saudi Arabia

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Introduction

Colorectal cancer (CRC) is the third commonest cancer in the world. There were approximately 1.4 million new cases of CRC diagnosed worldwide in 2012. (Colorectal Cancer Statistics, 2013). More than half of the cases occurred in developed countries; while the lowest incidence was found in Africa and Asia (Ferlays et al., 2013). Every year, the American Cancer Society estimates the numbers of new cancer cases and deaths expected in the United States. They have concluded that the death rates continue to decrease for all 4 major cancer sites including colorectum (Edwards et al., 2010; Siegel et al., 2013). A large study in Europe, observed survival rates of solid tumours including CRC to be highest in Northern Europe, lower in the UK and Denmark, and lowest in the Czech Republic, Poland and Slovenia (Sant et al., 2009). In Africa, incidence of CRC ranked 6th in males and 4th in female population; however recent reviews suggest an increasing trend in overall cancer incidences (Jemal et al 2012). Recent hospital based studies from Africa (Nigeria and Egypt) show a range of 13.4% to 15% CRC diagnosis on colonoscopies (Elbatea et al., 2011; Onyekwere et al., 2013).

Recent reviews of cancer epidemiology of South-West

Asia including Arab countries, found a low incidence of CRC in the Arab countries as compared to Irsael (Salim et al., 2010). The incidences of colon and rectum cancer in the Arab world are relatively low, except Algeria and Yemen (Salim et al., 2009). Studies from other parts of Asia report different demography of CRC than reported in the Western countries such as in Malaysia (Goh et al., 2005; Rashid et al., 2009), Pakistan (Bhurgri et al., 2011) and Iran (Ansari et al., 2006; Omranipour et al., 2012). Recent studies from some parts of Asia such as Vietnam and Iran, have shown high risk of CRC in young population (Quach and Nguyen 2012; Hajmanoochchri et al., 2014).

According to the latest Saudi Cancer Incidence Report (2012), a total of 13,254 new cancer cases were reported in 2009. CRC was second commonest with 1109 (11.3%) new cases, after breast cancer (which accounted for 1331 (13.5%) cases). Within the males, CRC was the commonest i.e. 617 cases (13.4%). Al-Madinah Al-Munawwarah region ranked third out of 13 regions in the diagnosis of CRC (after Riyadh and Eastern regions). But interestingly within the Madinah region, CRC was found to the commonest cancers in both sexes, as compared to national figure of its being second after Breast cancer.

Comparing with the international figures, CRC

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incidences in Kingdom of Saudi Arabia (KSA) are very low, however a recent article predicted a significant increase (fourfold) of CRC burden in KSA, during the coming decades (Ibrahim et al., 2008). A number of excellent reviews (Al-Diab et al., 2012) and epidemiology-based articles (Mosli and Al-Ahwal, 2012) on CRC in KSA have been published in the indexed literature and presented in international conferences as abstracts (Mosli and Al-Ahwal, 2012); but there is a dearth of hospital based retrospective histopathological data on CRC from KSA. Few studies have recently been published from Al Hassa region (Amin et al., 2012), Jeddah (Qayyum and Sawan, 2009; Sibiani et al., 2011) and Riyadh (Guraya and Eltinay, 2006; Aljebreen, 2007); however no such study has been done in Al-Madinah Al-Munawwarah region.

Our study is first of its kind in the region of Al-Madinah Al-Munawwarah, KSA, giving detail analysis of the colorectal cancer as diagnosed in the histopathology laboratory of King Fahad Hospital, Al-Madinah Al-Munawwarah.

Materials and Methods

This retrospective study included histopathological reports of all patients with CRC who had undergone colonic endoscopic biopsies and surgical colectomy between January 2006 and December 2013 at the King Fahad Hospital, Madinah, Saudi Arabia. Data of 324 patients were extracted from the hospital computer database and entered into an Excel sheet. Demographic data included the name of the patient, age and sex, diagnosis, tumour site, size, grade, differentiation, presence of lymphovascular invasion and perinural invasion and the status of the lymph nodes. Data were entered and processed using SPSS version 20 (SPSS Inc. Chicago, IL). Tumour classification of histomorphology followed the rules of the World Health Organization. Tumor staging of colorectal cancer was carried out according to Astler Collier modification of Duke's system, dividing it into stage A to D depending upon the extent of local involvement and regional node spread.

Results

A total of 324 patients were included in the study. One hundred and forty cases underwent colonic surgery to remove the tumour. There were 200 cases (61.7%) males and 124 cases (38.3%) females giving a male to female ratio of 1.6: 1. The age of the studied cases ranged from 20 to 100 years with a mean age 57.9 years. The peak age range was 50-59 years. A total of 33 (10.2%; M=18; F=15) were below 40 years of age; while 27 patients (8.3%) were aged above 80 years. The highest number of patients was between the ages of 50 and 59 (29%).

The majority (n=44) of tumors (13.6%; M=30; F=14) arised from recto-sigmoid colon. Tumors originating from sigmoid, ascending and descending colon accounted for 8.9%, 7.4% and 6.2% of cases respectively.

A total of 287 (M=172; F=115) adenocarcinomas representing 88.6% of the encountered lesions was seen making adenocarcinoma (classical) the commonest

histologic type, followed by mucinous adenocarcinoma (10.2%) and signet ring carcinoma (1.2%). Overall histologically, the differentiation characteristics of tumors were: 6.2% well differentiated, 87.3% moderately differentiated, 6.5% poorly differentiated.

Table 1 summarizes the age incidence, tumor site distribution, histological types and tumor differentiation on the basis of gender in our CRC patients.

Tumor stage, size and lymph nodes status were available for 140 cases, who underwent surgical colectomy and lymphadenectomy. Tumor staging was carried out according to Aster-Coller classification. The majority of patients i.e. 47.8% were diagnosed in stage B (n= 67;

Table 1. Histopathological Features of Colorectal Cancer Cases in Relation to Patient's Gender

Variables	Females (n=124) No. (%)	Males (n=200) No. (%)	Total (n=324) No. (%)
Age (years)			
< 40	15 (12.1)	18 (9)	33 (10.2)
40-49	19 (15.4)	35 (17.5)	54 (16.8)
50-59	35 (28.2)	54 (27)	89 (27.5)
60-69	23 (18.5)	49 (24.5)	72 (22.2)
70-79	23 (18.5)	26 (13)	49 (15.1)
> 80	9 (7.3)	18 (9)	27 (8.3)
Site			
Rectum	8 (6.5)	10 (5)	18 (5.5)
Sigmoid colon	13 (10.5)	16 (8)	29 (8.9)
Recto sigmoid	14 (11.3)	30 (15)	44 (13.6)
Descending colon	9 (7.3)	11 (5.5)	20 (6.2)
Transverse colon	2 (1.6)	5 (2.5)	7 (2.2)
Ascending colon	2 (1.6)	22 (11)	24 (7.4)
Unknown	76 (61.3)	106 (53)	182 (56.2)
Histological Type			
Adenocarcinoma (Classical)	115 (92.7)	172 (86)	287 (88.6)
Mucinous adenocarcinoma	9 (7.3)	24 (12)	33 (10.2)
Signet ring carcinoma	0 (0)	4 (2)	4 (1.2)
Differentiation			
Moderate	113 (91.2)	170 (85)	283 (87.3)
Poor	5 (4)	16 (8)	21 (6.5)
Well	6 (4.8)	14 (7)	20 (6.2)

Table 2. Features of Advanced Disease and Aggressive Behaviour of CRC in Our Cases

Variables	Females (N=52) No. (%)	Males (N=88) No. (%)	Total (N=140) No. (%)
Stage of disease			
A	5 (9.7)	3 (3.4)	8 (5.7)
B1	14 (26.9)	17 (19.3)	31 (22.1)
B2	11 (21.1)	23 (26.2)	34 (24.3)
B3	2 (3.8)	0 (0)	2 (1.4)
C1	11 (21.2)	20 (22.8)	31 (22.1)
C2	5 (9.7)	21 (23.8)	26 (18.6)
C3	1 (1.9)	3 (3.4)	4 (2.9)
D	3 (5.7)	1 (1.1)	4 (2.9)
Tumor size			
<4cm	18 (34.6)	16 (18.2)	34 (24.3)
≥4cm	34 (65.4)	72 (81.8)	106 (75.7)
Lymph Node			
Negative	33 (63.5)	46 (52.3)	79 (56.4)
Positive	0 to 3	18 (20.5)	28 (20)
> 3	9 (17.3)	24 (27.2)	33 (23.6)
Lymphovascular invasion			
Negative	18 (34.6)	27 (30.7)	45 (32.1)
Positive	34 (65.4)	61 (69.3)	95 (67.9)
Perinural invasion			
Negative	41 (78.8)	67 (76.1)	108 (77.1)
Positive	11 (21.2)	21 (23.9)	32 (22.9)

M=40; F=27) and 43.5% in stage C (n=61; M=44; F=17), whereas 5.7% (n=8) and 2.8% (n=4) of patients were in stage A and stage D respectively. The size of the tumor was less than 4 cm in 34 cases (24.3%; M=16; F=18), while equal to or more than 4 cm in 106 cases (75.7%; M=72; F=34). Seventy-nine cases (56.4%) had negative lymph node metastasis and 61 cases (43.6%; M=42; F=19) had positive lymph nodes. Of the latter group, 28 cases (20%; M=18; F=10) had metastases in one to three lymph nodes and 33 cases (23.6%; M=24; F=9) in more than three lymph nodes. Ninety-five patients (67.9%; M=34; F=61) had lymphovascular invasion, while 45 (32.1) showed no lymphovascular involvement. Perineural invasion was noticed in 32 cases (22.9%; M=21; F=11). Table 2 summarizes all the features of advanced disease and aggressive behavior of CRC in our patients.

Discussion

Colorectal cancer (CRC) is the third commonest cancer in the world, but has been reported to be on a decrease in the developed world (Edwards et al., 2010; Siegel et al., 2013). Although presently Africa and Asia, including KSA are considered to be low incidence regions, but alarmingly a recent report predict that the CRC incidence in KSA will raise four folds in coming decades (Ibrahim et al., 2008). A number of recent epidemiology based work from KSA has been published and few hospital based research from different regions are also available (Aljebreen, 2007; Qayyum and Sawan, 2009; Sibiani et al., 2011; Amin et al., 2012). No such work has been done in the region of Al-Madinah Al-Munawwarah; although CRC has been reported to be most common cancer in this region according to the Saudi Cancer incidence report (2012).

A total of 324 patients of CRC were reported during the study period, out of which 184 had only biopsy reports, while 140 were colonic surgery specimens. There were 200 cases (61.7%) males and 124 cases (38.3%) females giving a male to female ratio of 1.6: 1. These figures show a higher CRC diagnosis in male sex as compared to the ratios provided by Globocan 2012 for the whole world (Ferlays et al., 2013); and UK (Bowel Cancer Statistics Report UK, 2014). Regionally, our report of CRC male to female ratio is close to that reported by Azadeh et al. (2008) from Iran. Another investigation also from Iran by Fazeli et al. (2007), has reported almost same male to female ratio. Citing two studies from KSA, regarding the male to female ratio for CRC; Aljebreen (2007) has reported a ratio of 1.38:1; while Al-Ahwal and Abdo Al-Ghamdi (2005) has reported a male to female ratio of 1.13: 1 from their hospital based study of Western region. But while reviewing the Saudi Cancer Registry data from 1994 to 2004, Al-Ahwal et al. (2013), have recently calculated the male to female ratio of 1.95:1. Thus there is a wide variation in the male to female ratio figures internationally and regionally.

In our study group, CRC diagnosis was made in patients aged from 20 to 100 years with a mean age 57.9 years; most of the patients being above 40 years. These figures are consistent with the Western (Fuszek et al., 2006; Bowel Cancer Statistics Report UK, 2014) and Eastern

(Kotepui et al., 2013) figures. Only thirty three (10.2%) patients were below 40 years of age, although some of the studies have reported unusually high proportions of CRC in younger population e.g. Cambodia (Hav et al., 2011), Vietnam (Quach and Nguyen, 2012), Nepal (Kansakar and Singh, 2012) and Iran (Azadeh et al., 2008; Safaee et al., 2012). Within the KSA, our age related observations are consistent with that of other reviews and researches. Mosli and Al-Ahwal (2012), reviewed the Saudi Cancer Registry data from 2001 to 2006 and calculated the mean age of CRC diagnosis to be 58 years, with the majority of patients being older than 45 years of age (77%); while Amin et al. (2012) from Al-Hassa region reported diagnosis of CRC in more than two third cases after the age of 50 years. And almost similar observations were made by Sibiani et al. (2011) from Jeddah in their five years study at King Abdul Aziz University Hospital. But within KSA also, there is only one study from Riyadh reporting unusually high number of CRC diagnosis in young patients, although the number of cases were only 57 patients, out of which Thirty-six patients (63%) were found to be younger than 40 years (Guraya and Eltinay, 2006).

The anatomical site of tumor within the colorectum was not available on the record in 182 cases. Out of the available 142 records; 64% (n=91) were from sigmoid colon and rectum, while the remaining 36% were proximal. Our findings are consistent with the observations by Fuszek et al. (2006), from Hungary, who found almost two thirds of all CRC on left side and also commented that their findings are in contrast to Western European and North American trends of increasing proximal CRCs. Within the region, Fazeli et al. (2007) from Iran, found 83.6% CRCs in the distal parts. Similar were the observations by the Saudi Arabian investigators Amin et al. (2012) who found 62.7% CRCs on left side, while Sibiani et al. (2011) reported as high as 92.7% left sided CRC in their study. Aljebreen (2007) from Riyadh found left-sided lesions and rectal cancers in his 76% and 48% of all CRC tumors respectively. Another national study by Guraya and Eltinay (2006) have reported a higher frequency of right sided colonic tumors than left sided tumors. (57.8% vs 42.2%) in their five years experience at King Khalid University Hospital, Riyadh.

Adenocarcinoma (classical) was the most common histopathological type seen in 88.6% of cases, followed by mucinous adenocarcinoma (10.2%) and signet ring carcinoma (1.2%). Overall histologically, the differentiation characteristics of tumors were: 6.2% well differentiated, 87.3% moderately differentiated, 6.5% poorly differentiated. In the recent literature, there are only three regional studies to compare the grades of adenocarcinoma. Azadeh et al. (2008) from Iran found predominantly well differentiated adenocarcinomas (39.1%) in their 1138 CRC patients. However our results are consistent with two other studies, first a different study from Iran and second from Western region of KSA. Fazeli et al. (2007) from Iran found 96.2% adenocarcinoma, out of which around 53% were moderately differentiated. Similarly Al-Ahwal and Abdo Al-Ghamdi (2005) sharing their experience from two hospitals in the Western region of KSA, found moderately differentiated adenocarcinoma

in majority (38.7%) of their cases. They also correlated between the age groups to find that the young patients had more poorly differentiated tumors than the older age group (>40 years) patients.

Tumor stage, size and lymph nodes status were available for 140 cases that underwent surgical colectomy and lymphadenectomy. In our study, the size of the tumor was greater than and equal to 4 cm in 75.7% (106 cases) and less than 4 cm in only 24.3% (34 cases). Tumor staging was carried out according to Astler-Coller classification. The majority of patients presented either in stage B (47.8%) or stage C (43.5%), whereas 5.7% and 2.8% of patients were in stage A and stage D respectively. Similar were the observations of other investigators from KSA, in their recent work. Amin et al. (2012) reported Duke's C and D stages in 22.5% and 40.1% of lesions respectively. While Aljebreen (2007) found 68% of lesions in Duke's stage C. Guraya and Eltinay, (2006) reported Dukes B and C in 92.9% patients. Although Fazeli et al. (2007) from Iran, did not report their findings of tumor staging in Astler-Coller Classification; they however found most of their younger age group patients in advanced stages. Al-Ahwal and Abdo Al-Ghamdi (2005) in their 111 patients from Western region of KSA, similarly report most of tumors in advanced stages; and concluded that young patients had more advanced stage and poorly differentiated tumors.

Seventy-nine cases (56.4%) had negative lymph node metastasis and 61 cases (43.6%; M=42; F=19) had positive lymph nodes. Of the latter group, 28 cases (20%; M=18; F=10) had metastases in one to three lymph nodes and 33 cases (23.6%; M=24; F=9) in more than three lymph nodes. Reviewing the recent literature; Fuszek et al. (2006), from Hungary report lymph node metastases in 47.7%. Sibiani et al. (2011) from King Abdul Aziz University Hospital Jeddah, included 177 patients in the final analysis and reported lymph node involvement in 90 (50.8%) patients and distant metastasis in 50 (28.2%) patients. Amin et al. (2012) from Al Hassa region, KSA report that metastatic CRC was diagnosed in 62.7% cases and concluded that Saudi patients present late with distant metastasis and advanced disease stage.

Thus our findings are consistent with the finding of other investigators from West, the region and KSA that the patients with CRC presented with a more advanced disease and that CRC is biologically more aggressive as evidenced by large size tumor and the high frequency of nodal metastases and lymphovascular invasion. Screening programs regarding CRC should be enhanced to improve the diagnosis of CRC and outcome of the patients.

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