RESEARCH ARTICLE

Descriptive Epidemiology of Colorectal Cancer in University Malaya Medical Centre, 2001 to 2010

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Abstract

Background: Colorectal cancer is the second most frequent cancer in Malaysia. Nevertheless, there is little information on treatment and outcomes nationally. We aimed to determine the demographic, clinical and treatment characteristics of colorectal cancer patients treated at the University Malaya Medical Centre (UMMC) as part of a larger project on survival and quality of life outcomes. Materials and Methods: Medical records of 1,212 patients undergoing treatment in UMMC between January 2001 and December 2010 were reviewed. A retrospective-prospective cohort study design was used. Research tools included the National Cancer Patient Registration form. Statistical analysis included means, standard deviations (SD), proportions, chi square, t-test/ ANOVA. P-value significance was set at 0.05. Results: The male: female ratio was 1.2:1. The mean age was 62.1 (SD12.4) years. Patients were predominantly Chinese (67%), then Malays (18%), Indians (13%) and others (2%). Malays were younger than Chinese and Indians (mean age 57 versus 62 versus 62 years, p<0.001). More females (56%) had colon cancers compared to males (44%) (p=0.022). Malays (57%) had more rectal cancer compared to Chinese (45%) and Indians (49%) (p=0.004). Dukes' stage data weres available in 67%, with Dukes' C and D accounting for 64%. Stage was not affected by age, gender, ethnicity or tumor site. Treatment modalities included surgery alone (40%), surgery and chemo/radiotherapy 32%, chemo and radiotherapy (8%) and others (20%). Conclusions: Significant ethnic differences in age and site distribution, if verified in population-based settings, would support implementation of preventive measures targeting those with the greatest need, at the right age.

Keywords: Colorectal cancer - epidemiology - ethnic variation - Kuala Lumpur - Malaysia

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Introduction

Colorectal cancer is a major public health problem globally. Overall, it ranks as the third most frequent cancer worldwide, and the third and second most frequent cancer in men and women respectively (Jemal et al., 2011). The incidence of colorectal cancer in Asia, and particularly South East Asia, has assumed the global trend. Presently, colorectal cancer is the third most frequent cancer in Asian men and women (Pourhoseingholi, 2012).

Colorectal cancer is the second leading cancer among the general population in Malaysia, according to the Ministry of Health annual report 2011 Yahaya et al (2010). Colorectal cancer accounts for 12.7% of all cancers diagnosed, comprising 15.7% and 10.4% of male and female cancers respectively. Nearly equal numbers of colon and rectal cancers were diagnosed (4,547; 15.7 per 100,000 versus 4,689; 16.2 per 100,000) with similar mortality rates (241; 0.83 per 100,000 versus 229; 0.79 per 100,000).

The upward trend in incidence of colorectal cancers in Asia is influenced by lifestyle and environmental factors such as smoking, obesity, physical inactivity and, to some extent, the ethnic background of the patients (Chong et al., 2009; Tsukuma et al., 2011). This suggests an urgent need to understand the differential burden of colorectal cancer in countries in Asia (Hyodo et al., 2010). Therefore, study of the epidemiologic characteristics of colorectal cancer in Malaysia is both necessary and timely, in order to guide the establishment of screening services, plan colorectal cancer prevention public health education and awareness campaigns and improve treatment outcomes.

Consequently, we aimed to study the epidemiologic characteristics, survival and health-related quality of life (HRQOL) of the colorectal cancer patients treated at the University Malaya Medical Centre (UMMC) over a ten-year period. This paper reports the first components of the research whose aim was to determine the demographic, clinical and treatment characteristics of colorectal cancer patients treated at the UMMC between January 2001 and

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Materials and Methods

Colorectal cancer patients treated at UMMC between 2001 and 2010 were studied. Data was retrieved from patients' medical records retrospectively from January 2001 to December 2008, and prospectively from January 2009 to December 2010. The Malaysian National Cancer Patient Registry-Colorectal cancer (NCPR) form (version 1.0) was used to record the data. The form was primarily designed to obtain data for the newly established National Colorectal Cancer Registry by the Clinical Research Centre (CRC), Malaysia (Wendy and Radzi, 2008). Each patient's unique national identity card as well as hospital registration number was used to identify and link their medical records. In this study, only Malaysian citizens or permanent residents with a diagnosis of colorectal cancer were included.

Demographic variables studied were: age at the time of diagnosis, gender and ethnicity. The clinical characteristics included are; tumor site, Dukes stage, and tumor cellular differentiations. The treatment variables were surgery, type of surgery, urgency of surgery, chemotherapy and radiotherapy.

Exploratory data analysis was done to identify the missing data and guide the choice of statistical test. Age and other quantitative variables were summarized using mean and standard deviations, while gender, ethnicity and other categorical variables were summarized using proportions and percentages. The Chi squared (Chi2) test was used to compare differences in proportions between categorical variables. Differences in means for two or more numeric variables were examined using t-test and ANOVA respectively. Where differences were observed, post hoc (Bonferroni) analysis was performed to understand the nature of the differences. A two-tailed significance level of 0.05 was used. Analysis was done using SPSS version 21.0 for windows, (SPSS Inc., Chicago, Illinois, USA). This project was approved by the ethics committee of the University Malaya Medical Centre (PPUM/UPP/300/02/02, MEC 770.2).

Results

Demographic characteristics of the patients

The final sample consisted of 1212 colorectal cancer patients. The male to female ratio was 1.2:1. Sixty-seven per cent were Chinese, 18%, were Malays, 13% Indians, and 2%other ethnic groups.

The mean age was 61 years (SD13); the majority were more than 60 years of age (59%), and 7% were aged 40 years and below. There was no significant difference in mean age between male [61 years (SD 12)] and female [61 years (SD 14)] patients (t (N=1212) =0.672; p=0.502). There was no difference in mean age between patients diagnosed in 2001-2005 [60 years (SD 13)] and those diagnosed in 2006-2010 [61 years (SD 13)] (t (N=1212) =1.173; p=0.241). Interestingly, the mean age differs significantly between ethnic groups (F (N=1212) =11.83; p<0.001). Further post hoc (Bonferroni) analysis reveals that Malays (57 years) were diagnosed at a younger age compared to the Chinese (62 years) (p<.001), and Indians (62years) (p=0.022) respectively. So also 'others' minority group (54 years) present at far younger age than the Chinese (p=0.024) and Indians (p=0.014). Demographic characteristics are presented in Table 1.

Clinical characteristics and co-morbid conditions

Details of the co-morbid medical conditions, clinical characteristics can be found in Table 2. The majority of patients had their cancer located at the rectum (32%), followed by the sigmoid colon (20%), recto sigmoid junction (13%) and caecum and ascending colon (12%). Females had more colon cancer (56%) compared to males (44%); the difference was statistically significant (χ^2= 7.668, p =0.022). Malays tended to have more rectal cancers (57%); whereas Chinese (55%) and Indians (52%) had more colon cancers. This difference was also statistically significant (χ^2=17.28, p=0.008).

At the time of diagnosis, 26% had hypertension and 16% had diabetes mellitus. Pre-operative carcino-embryonic antigen was elevated in 21% of patients. High-grade tumors (i.e. poorly and undifferentiated tumors) were present in 5% of patients.

In relation to staging, only 5% had Dukes' stage A. The majority were Dukes' C (45%) followed by B (31%) and D (19%). There was no significant difference in stage distribution, between males and females (χ^2= 0.815, p=0.846), nor between ethnic groups (χ^2=6.710, p=0.876). Similarly, stage did not differ among the age groups (χ^2=20.13, p=0.065). Table 3 shows Dukes' stage distribution according to patients, disease and treatment characteristics.

Information on histological grade was available in

Table 1. Demographic Characteristics of Patients (n=1212)

Characteristics		n	%
Age groups (years)	≤ 39	83	6.8
	40-49	121	10
	50-59	291	24
	60-69	410	34
	≥ 70	307	25.3
	Mean age (SD)*	61(13)	-
Gender	Male	668	55.1
	Female	544	44.9
	Ratio male: female	1.2:1	-
Ethnic groups	Chinese	808	66.7
	Malays	225	18.6
	Indians	157	13.0
	Others	22	1.7
Diagnosis Year	2001	79	6.5
	2002	100	8.3
	2003	100	8.3
	2004	137	11.3
	2005	134	11.1
	2006	136	11.2
	2007	144	11.9
	2008	153	12.5
	2009	115	9.5
	2010	114	9.4

*SD standard deviations

Table 2. Comorbid Medical Conditions and Clinical Characteristics of Colorectal Cancer Patients (n=1212)

Characteristics		No.	%
Co morbidity	Hypertension	318	26.2
	Diabetes	196	16.2
Colon cancer	Appendix	6	0.5
	Caecum	69	6.0
	Ascending colon	72	6.3
	Hepatic flexure	35	3.0
	Transverse colon	48	4.2
	Splenic flexure	33	2.9
	Descending colon	44	3.8
	Sigmoid colon	245	21.4
	Colon NOS	44	3.8
Rectal cancer	Recto-sigmoid	156	13.6
	Rectum	383	33.4
	Ano rectal	13	1.1
	Unknown	64	-
Dukes stage	A	41	5.0
	B	256	31.5
	C	366	44.9
	D	151	18.6
	No HPE/Unknown	398	-
Grade	Low	802	66.2
	High	60	5.0
	Unknown	350	28.8
Preoperative CEA	Not elevated (≤ 5.0ng/ml)	543	44.8
	Elevated (≥ 5.1 ng/ml)	256	21.1
	Not taken/unknown	413	34.1

Table 3. Dukes Stage Distribution according to Selected Patients Characteristics (n=814)

Characteristics	A (n=41)	B (n=256)	C (n=366)	D (n=151)	P value
Period of diagnosis					0.077
2001-2005	16(4.8)	105(31.3)	139(41.1)	76(22.6)	
2006-2010	25(5.2)	151(31.6)	227(47.5)	75(15.7)	
Age					0.065
≤ 39	-	16(32.0)	24(48.0)	10(20.0)	
40-49	1(1.2)	19(23.2)	42(51.2)	20(24.4)	
50-59	10(5.0)	57(28.6)	91(45.7)	41(20.6)	
60-69	18(6.4)	83(29.4)	131(46.5)	50(17.7)	
≥ 70	12(6.0)	81(40.3)	78(38.8)	30(14.9)	
Gender					0.846
Male	24(5.3)	141(31.1)	208(45.9)	80(17.7)	
Female	17(4.7)	115(31.1)	158(43.8)	71(19.7)	
Ethnicity					0.678
Chinese	27(4.9)	172(31.5)	243(44.5)	104(19.0)	
Malays	9(6.0)	39(26.2)	71(47.7)	30(20.1)	
Indians	5(4.8)	38(36.2)	47(44.8)	15(14.3)	
Others	-	7(50.0)	5(35.7)	2(14.3)	
Site					0.398
Colon	18(4.1)	141(31.9)	208(47.1)	75(17.0)	
Rectal	22(6.2)	112(31.7)	152(43.1)	67(19.0)	
Treatment modalities					<.001*
Surgery alone	30(73.2)	116(45.3)	91(25.0)	62(41.1)	
Surg+chemo/radio	6(14.6)	77(30.1)	168(46.0)	67(44.4)	
Surg+chemo+radio	4(9.8)	28(11.0)	51(14.0)	8(5.3)	
Chemo±radio only	1(2.4)	18(7.0)	36(10.0)	7(4.6)	
Palliative	-	17(6.6)	20(5.0)	7(4.6)	

*chi square (x^2) significant at p-value ≤0.05, **CEA; carcino embryonic antigen

862 patients. As shown in Figure 1, the ratio of high grade tumors between the younger age group (≤39 years) and the older (≥ 40 years) was 2.5:1 (15.8% *vs* 6.3%); this difference was statistically significant (χ^2=7.35, P< 0.007). Males (57%) had low grade tumors compared to female (44%). Conversely, more females (58%) had high grade tumors than male (42%). The difference was statistically significant (χ^2=4.496, p=0.026). Ethnicity was not associated with tumor grade (χ^2=1.54, p=0.674).

Table 4. Treatment Modalities, Operation Types and Patients Presentation

Characteristics	n	%
Treatment modality (n= 1212)		
Surgery alone	488	40.3
Surgery plus Chemo/Radio	393	32.4
Surgery plus Chemo and Radio	116	9.6
Chemo and Radio alone	101	8.3
Palliative	114	9.4
Type of operation (n=997)		
AR(AR, HAR, ULAR,LAR)[a]	261	26.2
APRb	101	10.1
Rt hemi colectomy plus (Ext)[c]	215	21.6
Lf hemi colectomy plus (Ext)[d]	78	9.9
Sigmoid colectomy	96	9.6
Subtotal/total colectomy	56	5.6
Transverse colectomy	13	1.3
Hartman's procedure	68	6.8
Laparotomy	11	1.1
Otherse	98	9.8
Urgency of operation (n=997)		
Elective	481	48.2
Emergency	134	13.4
Unknown	382	38.2

*Note. [a] Anterior resection including high, low and ultralow anterior resection; [b]Abdomino Perineal Resection; [c] Right hemi colectomy including (extended right); [d] Left hemi colectomy including (extended left) and; [e] Other procedures e.g. appendectomy

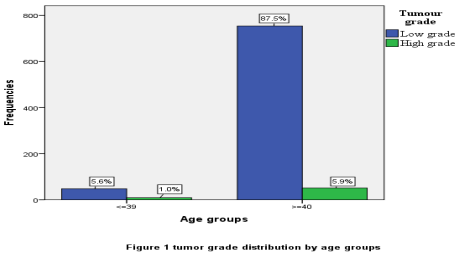

Figure 1 tumor grade distribution by age groups

Figure 1. Tumor Grade Distribution by Age Groups

Treatment characteristics

Treatment characteristics are shown in Table 4. Surgery (82%) was the most common treatment strategy used during the study period. Of the surgeries performed, 11% were emergency operation. The commonest procedures were anterior resection (all types; 26%); followed by right hemi-colectomy (all types; 22%); and abdomino-perineal resection (10%). Further analyses showed that 40.3% had surgery alone, 32.4% had surgery and chemotherapy or radiotherapy, 8.3% had chemotherapy and radiotherapy, 9.6% had surgery, chemotherapy and radiotherapy and 9.4% had palliative care only.

Discussion

Colorectal cancer is no longer predominantly a disease of the Western world. Colon and rectal cancers are now a major public health problem in Malaysia, yet there is little data on its management, as national data is currently focused on epidemiology, and is limited by under-reporting. Hospital-based clinical and epidemiologic

research remains a valuable means of understanding the current burden of colorectal cancers in countries with limited data at the national level. In addition to being the primary sources for national level epidemiological data, hospital-based data provides more clinically-rich information on patients, including treatment and outcomes of treatment. It therefore contributes significantly in the resource management for patients, hospitals and the country (Nadathur, 2010). In this research, we studied a ten-year cohort of colorectal cancer patients treated at the UMMC. Findings were compared with previous literature from Malaysia and other countries.

Regarding the demographic, clinical and treatment characteristics, our patients are generally similar to other patients in Malaysia and other South East Asian countries. We found mean age to be around 60 years, more male patients and over two-thirds are of Chinese ethnicity. These findings are similar to the earlier studies in Malaysia (Zarihah et al., 2003; Goh et al., 2005; Ooi et al., 2005; Chong et al., 2009; Hassan et al., 2010).

The mean age was slightly lower than reported in Singapore, Japan and the Western world (Vines et al., 2003). Similar to earlier reports, this study reiterates that a significant proportion of Malays present at younger age compared to the Chinese and Indians (King and Kutty, 1971). A recent study from Jeddah Saudi Arabia reports mean age of 58 for male and 53 for female (Mosli and Al-Ahwal, 2012) and Iran mean age of 57.7 for male and 56.6 for female (Hajmanoochehri et al., 2014). Possible explanations are yet to be unveiled. However, genetic factors might be responsible. These findings are important when screening services are considered in the Malaysian multi-ethnic society. Future research is needed to understand the risk factors and pathogenesis of colorectal cancer among the different ethnic groups in Malaysia.

No significant difference between males and females was observed in our study. This is similar to a recent study from Iran (Hajmanoochehri et al., 2014). Previous studies, however, suggested that males have a higher risk for colorectal cancer (Mosli and Al-Ahwal, 2012; Shah et al., 2014). This is said to be due to exposure to dietary, lifestyle risk sex-specific exposure to/or metabolism of environmental risk factors, differences in screening experiences and access to medical care (de Kok et al., 2008; Koo and Leong, 2010). It is possible that males in our population are less likely to demonstrate health-related help-seeking behavior, and thus are under-diagnosed compared with females.

The higher incidence in Chinese patients is in line with the earlier observation that ethnicity may play a role in the etiology of colorectal cancers in Asia (Yee et al., 2009; Pourhoseingholi, 2012). Although previous Malaysian national cancer registry reports have shown the Chinese having the highest incidence of colorectal cancer (Zarihah et al., 2003; Lim et al., 2004; Zainal Ariffin et al., 2011; Shah et al., 2014), local registries have sometimes contradicted this; this was attributed to dissimilarities in the local ethnic distribution. However, given the proportion of Chinese colorectal cancers far exceeds their proportion in our catchment area, it is likely to reflect a true increased risk. Similar findings were reported from Brunei (Chong et al., 2009). As expected, Indians have the lowest figures. Pathy et al. (2012) concluded that colorectal cancer incidence among Indians remains the lowest compared to other races in Asia.

The clinical features observed in our cohort of patients reflect the current trend in colorectal cancer in most developing nations. As expected, patients in UMMC had more rectal cancers (involving recto-sigmoid, rectum and ano-rectal sites). These cancers are as well more among the male population compared to female. Also, rectal cancers were more in the Malay ethnic groups. These findings are similar to the findings of a recent study from a review of surgeries relating to colorectal cancers in the northern state of Kedah (Hassan et al., 2011).

One of the most striking observations is that two-thirds of patients had advanced stage (Dukes' C and D), irrespective of their gender, age or ethnicity. Law et al (2009) reported that the ethnic background of rectal cancer patients in UMMC was not associated with pre-hospital delays, and others have suggested that access to health care, rather than ethnicity or racial background, determines stage at presentation (Hassan et al., 2009; Laiyemo et al., 2010). Similarly, African-Americans are at increased risk of presenting with late stage cancers, and poorer overall outcomes, compared to Caucasians, mainly due to difficulties with health care access (Sabounchi et al., 2012). Other factors affecting delay in diagnosis of colorectal cancer in our settings are poor knowledge of the symptoms, attitudes to screening as well as health care personnel failure to suspect colorectal cancer in patients presenting with a rectal bleeding (Hashim et al., 2010; Kong et al., 2010; Hashim et al., 2011). Advanced colorectal cancer disease in 2/3rd of the patients was also reported among patients in other Asian counties (Amin et al., 2012; Hajmanoochehri et al., 2014)

Our younger (≤ 40 years) patients had significantly higher tumor grade compared to older age groups. This is in line with previous studies where colorectal cancers were found to be more aggressive, spread faster and are associated with a poor prognosis in younger age groups (Chou et al., 2011; Amin et al., 2012). The higher proportion of young Malays affected suggests that this section of the population may need to be screened at a younger age than the Asian Pacific guidelines suggest.

Treatment delivered in our center is in accordance with evidence-based recommendations. The use of surgery as the primary treatment modality, and indications for adjuvant chemo- and radiotherapy, are well established in the literature. As summarized by the National Institute of health and Care Excellence full guidelines 2011, the choice of treatment modality depends on presentation as emergency or otherwise, pre-treatment staging, presence of co-morbidities, metastasis, tumor site, level of risk for local recurrences (rectal cancer). The decision on the final treatment modality will depends on proper assessment of these parameters and decision of both the management team and a well-informed patient.

Not surprisingly, the majority of our patients received surgery, even those with metastatic disease, where the aim was either curative resection or surgical palliation of a symptomatic primary. A significant proportion also

received chemotherapy in the form of adjuvant therapy, and a few had radiotherapy depending on the tumor location, stage and general wellbeing of the patient; this reflects the late stage of presentation of our patients.

Our study has several strengths, including the use of a large sample of patients, from a tertiary hospital, with a functional multi-disciplinary team dedicated to the care of colorectal cancers. The exclusion of non-Malaysian patients is useful as we want to identify any environmental associations. The other point is that our data encompasses a longer time frame than any of the registry data, and has more clinical treatment data.

Apart from the strengths listed above, some limitations need to be highlighted. One limitation is in the retrospective component of the study. Patients were identified using ICD codes from the hospital medical records. This coupled with the lack of synoptic histopathology reporting and other patient details in the early years (before 2008) limit the completeness of data. Our finding therefore, needs verification in larger population-based dataset.

In conclusion, systematic data collection monitoring of patients follow up to ensure quality data are obtained for both hospital based studies should be undertaken. In addition, synoptic reporting of histopathology examinations is urgently needed. At the same time, for any measure control and preventive measures to work, the characteristics and differences identified among colorectal cancer patients must be considered. For example, health education and screening campaigns should target both men and women equally, and screening should be carried out at younger age for the Malays compared to the Chinese and Indians.

This study adds to the scant body of knowledge regarding characteristics of patients with colorectal cancer, and thus provides a foundation for further studies on the subject matter. Further research is needed to clarify the risk factors of colorectal cancer among the different ethnic groups in Malaysia, the role of tumor biology, genetics, and lifestyle risk factors in explaining differences in how colorectal cancers present and behave.

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