

## RESEARCH ARTICLE

# Characteristics of Young Colorectal Cancer in Brunei Darussalam: an Epidemiologic Study of 29 Years (1986-2014)

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### Abstract

**Background:** Colorectal cancer (CRC) is the most common gastrointestinal cancer and the incidence is increasing. CRC is more common with increasing age, but a proportion occurs in young adults, termed young CRC. This study assessed the incidence and the demographic of young CRC in Brunei Darussalam. **Materials and Methods:** All histologically proven CRC between 1986 and 2014 registered with the Department of Pathology cancer registry were reviewed and data extracted for analyses. Young CRC was defined as cancer in patients aged less than 45 years. The various population groups were categorized into locals (Malays, Chinese and Indigenous) and expatriates. **Results:** Over the study period, there were 1,126 histologically proven CRC (mean age  $59.1 \pm 14.7$  years, Male 58.0%, Locals 91.8% and 8.2% expatriates). Young CRC accounted for 15.1% with the proportion declining over the years, from 29% (1986-1990) to 13.2% (2011-2014). The proportion of young CRC was highest among the indigenous (30.8%), followed by the expatriates (29.3%), Malays (14.3%) and lowest among the Chinese (10.8%). The mean age of young CRC was  $35.9 \pm 6.2$ ; lowest among the indigenous ( $33.5 \pm 6.7$ ), expatriate ( $34.9 \pm 6.0$ ) group and the Malays ( $35.6 \pm 6.5$ ) compared to the Chinese ( $38.6 \pm 4.6$ ), a similar trend being observed in the non-young CRC groups. There were no difference between the genders and tumor locations (rectum or colon) between the young and the non-young CRC cases. Female young CRC was significantly younger than male ( $p < 0.05$ ) without any significant variation between the various population groups ( $p > 0.05$ ). **Conclusions:** Our study showed that the young CRC accounted for 15.1% of all CRC with declining trend observed over recent years. Young CRC was more common among indigenous, expatriates and Malays and least common among the Chinese. There were no differences in the gender and tumor locations.

**Keywords:** Brunei - colorectal cancer - young cancers - incidence

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### Introduction

Colorectal cancer (CRC) is the commonest gastrointestinal cancers and the incidence is increasing, particularly in the developing nations (IARC, 2012; Somi et al., 2014). However, in some of the developed nations of Northern America and Northern Europe, the incidence rates are actually declining, due in part to the effect of CRC screening carried out (IARC 2012; Austin et al., 2014). Through screening, CRC are being detected early resulting in curative treatment and prevention of the development of CRC through the removal of premalignant lesions. Currently, screening for the average risk population (general population) starts at 50 years, sooner for those with risk factors such as personal or family history of CRC or advanced colorectal neoplasms (Levin et al., 2008; Qaseem et al., 2012; Sung et al., 2015).

In the absence of a formal CRC screening program, any screening carried out in our setting has been done opportunistically and followed the recommendations

of accepted international guidelines (Levin et al., 2008; Qaseem et al., 2012; Sung et al., 2015). A recent national health screening program for government servants that included CRC screening through fecal occult blood testing has shown CRC screening in our setting to be feasible (Chong et al., 2013).

CRC is mainly a disease of the mature adult or the elderly demographic and generally considered uncommon among the younger population. However, in certain parts of the world, especially the less developed nations, Young CRC variably defined as CRC diagnosed in those ages younger than 45 to 50 years old, is not uncommon (Hav et al., 2011; Mosli et al., 2012; Quach et al., 2012). Even in the developed nations, there are reports of increasing incidence of Young CRC (Siegel et al., 2009; Meyer et al., 2010; Ahnen et al., 2014). Therefore, it is important to be aware of the characteristics of Young CRC so that effective healthcare planning, including CRC screening can be planned to take into account the Young CRC. In Brunei Darussalam, the incidence of CRC is also increasing

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(Chong et al., 2009) and Young CRC (defined as 45 years of younger) was 18.5% based on our previous study. This study looked at latest rate and also the demographic of Young CRC in Brunei Darussalam.

## Materials and Methods

### Setting

Brunei Darussalam is a developing nation located on the northeast corner of the Borneo Island in South-East Asia. It has an estimated population of 420,000 (2012 Census) with Malays being the predominant group (68%), followed by the Expatriates (~20%), Chinese (11%) and the Indigenous group (<5%). The health coverage is provided free to the Citizen and permanent residents (Locals) and payment is required for the Expatriate groups. Each district has a government hospital served by multiple strategically located health centres or clinics. The only tertiary referral centre (RIPAS Hospital), a 550 bedded hospital covering all subspecialties is located in the Capital (Bandar Seri Begawan) and house the State Pathology (Department of Pathology), which receives and processes all tissue specimens from all the health institutions and centres with the country. A cancer registry which captures all tissue proven malignancies is maintained by the Department of Pathology, RIPAS Hospital from 1984 to the present day.

### Cases and data collection

All histologically proven CRC diagnosed over a 29 years period between 1986 and 2014 were identified from the cancer registry maintained by the Department of Pathology. Cases from 1984 and 1985 were excluded as data on age were not available. In this study, Young CRC was taken as any CRC diagnosed in those age younger than 45 years (<45 years old).

Demographic data (age, gender and population groups) and tumour locations were extracted for analyses. The population groups were categorised into Locals (citizen or permanent residence of Brunei Darussalam) and Expatriates (foreign nationals). The Local group consisted of the Malays, Chinese and Indigenous groups. The Expatriates or foreign nationals consisted mainly

of the nationals from the South-East Asia nations (most from Malaysia, Thailand, Indonesia and the Philippines), Indian Subcontinent (India and Bangladesh) and smaller group of Caucasians.

### Statistical analyses

Analyses were carried using the SPSS version 16.0. Comparisons were made for the scores between genders, race (Malay and non-Malay), levels of education and marital status. The Student t test and Analysis of Variance (ANOVA) were used to compare the continuous variables and the Chi-square was used for categorical variables. A p value of less than 0.05 was taken as significant.

## Results

In total, there were 1,126 histologically proven CRC over the study period. The Locals population accounted for 91.8% of all CRC cases, and the Expatriate groups accounted for the remaining 8.2%. Among the Locals, the Malays accounted for the most followed by the Chinese, consistent with the national population breakdown. The mean age at diagnosis of CRC was  $59.1 \pm 14.7$  years old.

The most common tumor type was adenocarcinoma, followed by neuroendocrine tumor and lymphoma.

Among all CRC; Chinese had the highest mean age at diagnosis compared to the other groups (Table 2).

Young CRC accounted for 15.1% of all CRC (Figure 1). The proportion of Young CRC was highest among the Indigenous (30.8%), followed by the Expatriates (29.3%), Malays (14.3%) and lowest among the Chinese (10.8%).

Over the years, the proportion of Young CRC declined from 29% in 1986-1990 to the lowest recorded of 9% in 2001-2005, before increasing to 13.2% in 2011-2014 (Figure 2a). The decline were seen in both the major population group; the Malays and Chinese (Figure 2b).

Among the tumor locations (Rectum vs. colon) and genders, there were no differences between the Young and the Non-Young CRC with colon tumor accounting or two-third and male gender slightly predominating (Table 1).

The overall mean age of diagnosis of Young CRC was  $35.9 \pm 6.2$  years old. Chinese Young CRC had the highest mean age at diagnosis compared to the other groups, a

**Table 1. Socio-demographic Characteristics of Subjects with CRC and the Tumor Characteristics**

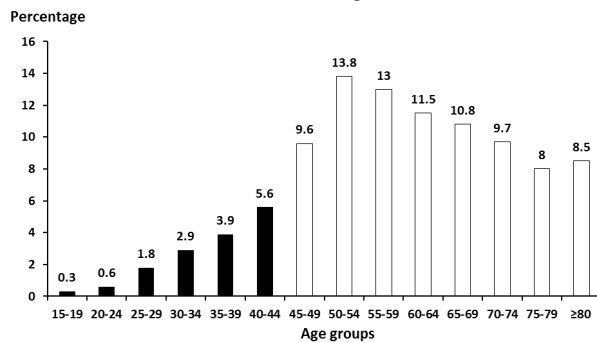
Variable		Overall (N=1,126) n (%)	Young CRC (n=170) n (%)	Non Young CRC (n=956) n (%)	p value
Gender	Male	653 (58.0)	93 (54.7)	560 (58.6)	0.346
	Female	473 (42.0)	77 (45.3)	396 (41.4)	
Population groups	Local	1,033 (91.8)	143 (84.1)	890 (93.4)	<0.001 For trend
	Malay	739 (65.7)	106 (62.4)	633 (66.3)	
	Chinese	268 (23.8)	29 (17.1)	239 (25)	
	Indigenous	26 (2.3)	8 (4.7)	18 (1.9)	
	Expatriates	92 (8.2)	27 (15.9)	65 (6.6)	
Tumor types	Adenocarcinoma	1,094 (97.2)	158 (93.5)	935 (97.8)	0.019 For trend
	Neuroendocrine tumor	16 (1.4)	5 (2.9)	11 (1.2)	
	Lymphoma	10 (0.9)	4 (2.4)	6 (0.6)	
	Others	6 (0.5)	2 (1.2)	4 (0.4)	
Locations *	Rectum	372 (35.2)	49 (32.7)	323 (35.2)	0.484
	Colon	685 (64.8)	101 (67.3)	584 (64.4)	

\*Based on 1,057 cases with tumor locations recorded

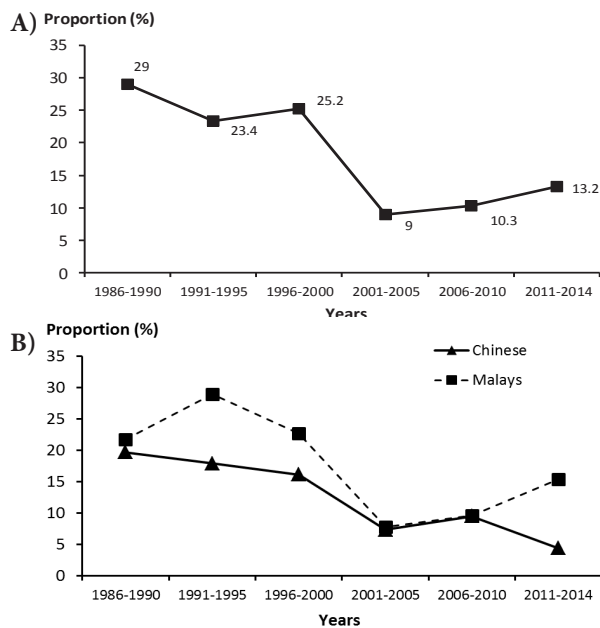
**Table 2. Mean Age of Diagnosis of Young CRC between the Genders and the Various Population Groups Compared to the Non-Young CRC**

Variables		Young CRC	p value	Non-Young CRC	p value
Gender	Male	36.8 ± 5.7	0.029	63.5 ± 11.2	0.368
	Female	34.7 ± 6.7		62.9 ± 12.0	
Population groups	Malays	35.6 ± 6.5	0.056 for trend	62.8 ± 11.4	<0.001 for trend
	Chinese	38.6 ± 4.6		65.9 ± 11.4	
	Indigenous	33.5 ± 6.7		62.4 ± 12.2	
	Expatriates	34.9 ± 6.0		58.1 ± 10.5	
	Rectum	35.7 ± 6.1		0.729	
Colon	35.3 ± 7.0	63.4 ± 11.6			

\*Student t test and ANOVA used for comparisons



**Figure 1. The Age Group Breakdown of Patient with CRC.** Black Shading Bars Indicate Young CRC and white Shading Indicating Non-Young CRC Cases



**Figure 2. The Proportion of Young CRC over the Study Periods.** A) All; B) Malays and Chinese, Separately

trend following those categorized as non-Young CRC (Table 2).

Among the tumor locations (Rectum vs. colon) and genders, there were no differences between the Young and the Non-Young CRC with colon tumor accounting for two-third and male gender slightly predominating (Table 2).

## Discussion

Overall, there is a rising trend in the total number of CRC diagnosed in Brunei Darussalam over the study period. This is not unexpected considering that the

population is increasing and growing older. In our previous study, we showed that the age standardised rate (ASR) was increasing, but still lower than the rates reported from the developed or more developed nations (Chong et al., 2009; IARC, 2012). In any population of patients with CRC, a proportion is categorized as young CRC, defined as CRC diagnosed age 45 or younger. Following current screening recommendations (Levin et al., 2008; Qaseem et al., 2012; Sung et al., 2015), these patients would not have been considered for screening. Therefore it is important to be aware of the characteristics of cancers among younger population, including young CRC so that a comprehensive healthcare plan can be formulated.

The rates of young CRC reported in the literature vary between parts of the world. Our study showed that young CRC accounted for 15.1%, with a declining trend observed over recent years. The proportion was as high as 29% in 1986-1990, dropping to as low as 9% in 2001-2005. In the more developed nations such as North America and northern Europe (Canada; overall 3.36% defined as ≤45 years) (McKay et al., 2014), the rates are typically less than 5%. The rates of young CRC in the more developed nations in the Asia-Pacific regions are also low; Hong Kong: overall 4.1%; Men 3.3% and Women 5.3% (Hong Kong Cancer Registry, 2012) and South Korea: overall 7.2%; Men 6.8% and Women 7.8% (National Cancer Centre, Korea 2011). In contrast, rates from developing or less developed nations are higher. A study from Saudi Arabia using the same definition as our study reported a rate of 20.9% (Mosli & Al-Ahwal, 2012). In South-East Asia, the rates ranged from 11.5% in Malaysia (National Cancer Registry Report 2007) to as high as 28% in Vietnam (<50 years of age) (Quach & Nguyen, 2012). However, the Vietnam study had used <50 as young CRC. The rate reported in Cambodia was 29.8% based on age less than 40 years (Hav et al., 2011). Our rates are comparable to rates reported in Malaysia, a South-East Asia nation that share almost similar population demographic to Brunei apart from Indians. The rate for young CRC in Malaysia among the Chinese was 7.0% (men 5.9% and women 8.3%) but much higher rate among the Malays with rate of 15.9% (men 14.8% and women 17.3%). Among the Indians, the rate was 9.0%; men 9.5% and women 8.3% (National Cancer Registry Report, 2007). Generally, young CRC is more common in the less developed nations.

In our study, the proportion of young CRC was highest among the Indigenous group followed by the Expatriates, and least common among the Chinese. This suggests that the ethnic or national background is important predictive

factor. The Indigenous group only accounted for a small proportion of the population but had the highest proportion of young CRC. In Brunei, the Indigenous group is from the interior and has genetic, social and cultural differences to the other groups (Malays and Chinese). There are also differences in the environmental factors due to their culture and lifestyle. However, with modernization and adoption of a modern lifestyle, such differences are becoming less important. Similarly, the Expatriate group also accounted for a small proportion of the CRC cases but had a high proportion of young CRC. The main reason for this is the age demographic of the Expatriate group in the country. Generally, expatriates are those in the productive age; hence younger than the Local population. This is reflected in the mean age of diagnosis of CRC compared to the other groups. The same reason apply to the other groups; differences in the population pyramids; Malays still having a broader based pyramid as compared to the Chinese with a more smaller based similar to the population pyramid of more developed nations.

Contrary to the increasing trend reported in other countries (Siegel et al., 2009; Ahnen et al., 2014; Austin et al., 2014), our study showed decline in the proportion of Young CRC over the recent years. The decline was seen in both the Malays and Chinese, the two major ethnic groups in the country. It is uncertain if such trends will also be seen among the Expatriates and Indigenous groups. We did not assess these groups as the overall number of cases was small. Again, the likely explanation for this observation is the change in the population pyramids. Fewer young populations, especially among the Chinese can be accounted for by smaller family units (fewer children per family) and also the continued population movement (i.e. emigrations) which is not seen in the Malays.

In our study, we found that female young CRC were significantly younger compared to their male counterpart. Among the various populations, the Chinese were the oldest, youngest among the Indigenous and Expatriate groups, with a trend towards significance. Similar differences were also observed in the non-Young CRC groups. Such findings need to be taken into account when planning future healthcare.

We did not find any difference in the distribution of tumor (rectum vs. colon) between young and non-Young CRC groups, similar to findings from other studies looking at early onset CRC (Hav et al., 2011; Quach & Nguyen, 2012) or overall CRC cases (Cai et al., 2014). However a study from the United States reported a higher incidence of rectal cancer in persons younger than 50 years compared to older adults (Fairley et al., 2006), and several other studies have reported increasing incidence of rectal cancer among the younger population (Siegel et al., 2009; Meyer et al., 2010; Ahnen et al., 2014). This is a concern but the reason for this is unknown and requires further studies. It will be interesting to see if such trend will be seen in the future in developing nations such the South-East Asia nations. These findings have important implications as the screening age for CRC may need to be reduced.

Currently, there is no formal screening program for CRC in Brunei Darussalam and any screening carried out are on an opportunistic basis. Currently, a formal

CRC screening program is being evaluated and being considered. Based on our findings, screening age may need to be lowered from the recommended screening age of  $\geq 50$  years (Levin et al., 2008; Qaseem et al., 2012; Sung et al., 2015). Reducing the screening age will increase the number of people being screened, and this may stretched the available resources. However, we previously showed that screening for CRC starting at 40 years old was feasible (Chong et al., 2013). This program was the Integrated Health Screening for government servants which included CRC screening using a single fecal occult test as the initial test with those positive for fecal occult blood or with family history of CRC referred for screening colonoscopy.

In conclusion, our study showed that Young CRC accounted for a sizable proportion of CRC cases with one in eight cases. The proportion of Young CRC is particularly high among the Indigenous and Expatriate groups. The least common was among the Chinese. Overall, there is a declining trend in the proportion of Young CRC. Despite of Young CRC, the actual total number of Young CRC cases is actually increasing due to population growth. Therefore it important to take into consideration those categorized as Young CRC when planning a CRC screening program.

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