RESEARCH COMMUNICATION

Incidence and Current Trends of Colorectal Malignancies in an Unscreened, Low Risk Population

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Abstract

Introduction: Karachi falls into a low risk region for colorectal (CRC). The incidence rate is known but detailed epidemiology and pathology data regarding the disease are not available. The aim of this study is to describe CRC with reference to incidence, gender; topographic sub-site, tumor morphology, grade and stage at diagnosis and to determine the trends of incidence. Materials and Methods: Four hundred and seventy three cases of colorectal cancer submitted to the Karachi Cancer Registry for Karachi South, years 1995-2002 were reviewed. Cases were analyzed in two time periods (1995-7 and 1998-2002) to facilitate the study of time trends. Results: A total of 151 CRC cases were registered during period one [86 (57%) males; 65 (43%) females] and 322 cases [210 (65%) males; 112 (35%) females] in period two. Age standardized rate (ASR) world per 100,000, crude incidence rate (CIR) and relative frequency in period one were 5.3, 3.2 and 4.1% in males and 5.5, 3.2 and 3.2% in females respectively. Corresponding figures for period two were 7.1, 4.5 and 4.7% for males and 5.2, 2.8 and 2.7% in females. The male, female ratio was equal for colon (1:1). Men had more rectal cancers (2:1) and overall CRC (1.7:1). The mean age of the patients varied with sub-site and gender from 43.7 years to 51.2 years. Cancers of the rectum presented at a relatively earlier age. Less then 5% of the cases were diagnosed in adolescents, 50% above 50 years of age and only 30% above 60 years. The ratio under-40 to above-40 for CRC patients was 0.3, which is much higher than the international average, indicating a younger age group at risk. The first cases were observed in adolescents (15-19 years) and a peak was observed in the seventh decade. Colon to rectum ratio was 1:1 in males and 2:1 in females. Most cases presented with advanced disease, though some down staging was observed in period 2 (1998-2002). Conclusion: The current low but increasing incidence (especially in men), the younger age and advanced stage of CRC at diagnosis reflects a low risk, unscreened population. With existing prevalence of high risk factors in Pakistan, the low CRC incidence may be an artifact. There are concerns that an aging population over the next decade and changing lifestyle patterns may translate into a higher CRC incidence. Screening must be considered as part of the health sector planning for the future and include the high risk younger age groups.

Keywords: Colorectal cancer - Karachi, Pakistan - incidence trends

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Introduction

Colorectal cancer, ICD-10 (International Classification of Diseases 10th Revision) categories C18-C21 (cancer of the colon, recto-sigmoid junction, and rectum) is considered among the top ten malignancies globally with a 25 fold variation worldwide (Parkin, 2005). Higher incidence rates are reported for North America, Australia/ New Zealand, Western Europe, and Japan. A lower incidence is reported for Africa and Asia and intermediate rates for southern parts of South America (Parkin DM, 2005).

In 'Cancer Incidence in Five Continents' (CIV) volume (vol.) eight (VIII) for the five year data (1993-7) the highest age standardized incidence rates per 100,000 (ASR/100,000) were observed in Japan, Hiroshima (59.2) and the lowest in Gambia (0.5), with a 100 fold variation for males (Parkin et al, 2002). In females corresponding ASRS/100,000 were New Zealand (28.6) and Oman (1.6) with an 18 fold variation. In CIV vol. nine (IX), for the 1998-2002 data amongst males the highest and lowest ASRs/100,000 reported were for Canada, Northwest Territories (40.2) and India, Chennai (1.9) with a 21 fold variation (Curado et al, 2007). Likewise amongst females the highest incidence rates were observed in USA, Missouri: Black (31.0) and the lowest in India, Trivandrum

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Table 1. Five Highest and Lowest Age Standardized Incidence Rates (ASR) per 100,000 Reported in Cancer Incidence in Five Continents Volumes VIII (1993-1997) and IX (1998-2002).

Years	Registries	Male ASR	Registries	Female ASR
1993-1997	Japan, Hiroshima	59.2	New Zealand	28.6
Highest	USA, Connecticut: Black	37.6	Canada, Prince Edward Island	28.5
	Japan, Nagasaki	36.9	Japan, Hiroshima	28.0
	Japan, Miyagi Prefecture	34.6	Israel: Jews born in America or Europe	27.8
	Israel: Jews born in America or Europe	34.5	USA, Louisiana, New Orleans: Black	27.7
1993-1997	India, Ahmedabad	1.9	Oman	1.6
Lowest	India, Chennai (Madras)	1.9	India, Ahmedabad	1.3
	India, Trivandrum	1.8	India, Trivandrum	1.2
	India, Karunagappally	0.8	The Gambia	1.1
	The Gambia	0.5	India, Karunagappally	1.0
1998-2002	Canada, Northwest Territories	40.2	USA, Missouri: Black	31.0
Highest	USA, Louisiana, New Orleans: Black	37.2	USA, Illinois: Black	29.7
	USA, Illinois: Black	36.9	USA, Connecticut: Black	29.2
	USA, Missouri: Black	36.6	USA, District of Columbia: Black	28.4
	USA, Michigan, Detroit: Black	36.3	USA, Michigan, Detroit: Black	27.7
1998-2002	Oman	2.5	India, Karunagappally	2.1
Lowest	India, Poona	2.4	India, Delhi	1.9
	India, Trivandrum	2.2	India, Nagpur	1.8
	India, Karunagappally	2.0	India, Chennai (Madras)	1.6
	India, Chennai (Madras)	1.9	India, Trivandrum	1.6

(1.6) with a 19 fold variation. The five highest and lowest rates for each category are given in Table 1.

The current study was conducted to describe CRC with reference to incidence, gender; topographic sub-site, tumor morphology, grade and stage at diagnosis and to determine the trends of incidence in Karachi, for the periods 1995-7 and 1998-2002, corresponding to the CIV volumes VIII and IX (Parkin et al, 2002; Curado et al, 2007).

Materials and Methods

Epidemiological data of malignant tumors of the colon and rectum ICD-10 categories C18-C21 registered at Karachi Cancer Registry (KCR) for Karachi South (KS), during 1st January 1995 to 31st December 2002 were reviewed and analyzed as two time periods 1995-7 and 1998-2002. The time periods coincide with the data published in 'Cancer Incidence in the Five Continents volumes VIII and IX respectively.

The study included clinically diagnosed and microscopically verified cases. Histologically verified cases were initially evaluated on hematoxylin and eosin (H&E) stained sections. Special stains and immunohistochemistry were selectively used. Manual and computerized validity checks for the cancer data were performed as per recommendations of the International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR) (Parkin, 1994), these included checks for multiple primaries and duplication. Cases were categorized by tumor site, age and sex of the patients. Variables recorded were the hospital patient-number, date of incidence, name, age, sex, address, ethnicity, topography, morphology, grade, stage and date of death/last follow-up.

Data were classified using ICD-O3 (International Classification of Diseases-Oncology, 3rd edition) and computerized using a customized version of CANREG-4 software (WHO, 2002). Crude, age standardized incidence rate (ASR) and age specific incidence rates were calculated using the person years of population at risk by sex and 5-year age-groups, based on the 1998 census; population of 893,684 males and 794,920 females, assuming an annual growth rate of 1.94%, as calculated by the Federal Bureau of Statistics.

The definition of incidence used was 'number of new cases occurring, expressed as an absolute number of cases per year or as a rate per 100,000 persons per year'. The latter approximates the average risk of developing a cancer in one year and is used for comparisons between countries or world areas, or within populations over time (Parkin, 2005).

Standardized incidence rate was calculated with an external reference population, the 'world' population with a given 'standard' age distribution (Segi M, 1960). The methodology applied was direct standardization, using 5-year age groups. The rates given are the annual incidence per 100,000 population averaged over the number of years for which data are presented'. Incidence tables were based on ICD-10 (WHO, 1992). The cases were staged using the AJCC/UICC TNM system of staging. Data were analyzed using SPSS 17.0.

Results

Four hundred and seventy three cases of colorectal cancer submitted to the Karachi Cancer Registry (KCR) for the years 1995-2002 were reviewed. A total of 151 [86 (57%) in males; 65 (43%) in females] cases were registered during period one (1st January 1995 to 31st December 1997); 322 cases [210 (65%) in males; 112 (35%) in females] were registered in period two i.e. from 1st January 1998 to 31st December 2002 (table 2). The age standardized rate (ASR) world per 100,000 and crude incidence rate (CIR) in period one were 5.3 and

Table 2. Crude (CIR), and Age Standardized Incidence Rates (ASR) per 100,000, Relative Frequency (RF) and Mean Age at Presentation of Colorectal Cancers in Karachi South

Site	Colon (C18)	Rectum/anus (C19-21)	Large bowel (C18-21)	Colon (C18)	Rectum/anus (C19-21)	Large bowel (C18-21)
Male		1995-7			1998-2002	
Number	40	46	86	101	109	210
CIR*	1.5	1.7	3.2	2.2	2.3	4.5
ASR**	2.4	3.0	5.4	3.6	3.5	7.1
Mean age***	46.3	50.5	48.5	51.2	47.0	49.0
95%CI	40.9; 51.6	45.6; 55.3	45.0, 52.1	48.2; 54.2	43.6; 50.5	46.7; 51.3
SD	16.6	16.3	16.5	15.3	18.1	16.9
Range***	76 (8-84)	79 (16-95)	87 (8-95)	69 (17-86)	70 (15-85)	71 (15-86)
Female		1995-7			1998-2002	
Number	41	24	65	73	39	112
CIR	1.8	1.0	2.8	1.8	1.0	2.8
ASR	3.6	1.9	5.5	3.5	1.7	5.2
Mean age***	50.6	45.3	48.6	50.1	43.7	50.1
95%CI	45.8; 55.4	38.5; 52.1	44.8; 52.5	44.8; 55.3	38.9; 48.4	44.8; 55.3
SD	15.2	16.0	15.6	16.2	14.7	16.2
Range***	62 (19-81)	55 (16-71)	65 (16-81)	64 (11-75)	58 (17-75)	64 (11-75)

*Crude incidence rate (CIR); **age standardized rate (ASR); ***years

3.2 in males and 5.5 and 3.2 in females respectively. The corresponding figures for period two were 7.1 and 4.5 for males and 5.2 and 2.8 in females (Table 2). In KS colorectal cancers accounted for 4.4% (4.0% period one; 4.6% period two) cases in males and 2.8% (3.1% period one; 2.7% period two) cases in females (Bhurgri et al, 2000; 2002). Male, female ratio for CRC was 1.7:1, for colon 1:1 and for rectum 2:1.

The mean ages of the patients varied with the sub-site and gender (Table 2) from 43.7 years in female patients suffering from rectal cancer in 1998-2002 to 51.2 years in males suffering from cancer colon for the same time period. Less then 5% of the cases were diagnosed in adolescents i.e. those above 14 years and below 20 years of age [period one 2 (2.3%) cases in males; 2 (3.1%) in females and in period two, 6 (2.4%) and 5 (4.5%) cases in males and females respectively]. A case of childhood colorectal cancer was also observed. Approximately half the cases were observed above 50 years of age and 30% above 60 years. The ratio under-40 to above-40 CRC patients was 3:1.

Age-specific incidence rates varied with the site of the malignancy and the gender, however the first cases were observed in adolescents (15-19 year age group) and a peak was observed in the 65-69 year age group (Figures 1-2). Younger patients presented with poor histological differentiation, mucin secreting cancers and a more advanced stage at diagnosis. Overall presentation was of a moderate grade malignancy with a regional spread of disease at diagnosis (Table 3).

Colon to rectum ratio was 1:1 in males and 2:1 for females in both time periods. The most common sub-

Table 3. Gender-wise Distribution of Grade and Stage of CRC at Presentation

	1995-1997		1998-2002	
Male	Colon	Rectum	Colon	Rectum
Grade*	(n=40)	(n=46)	(n=101)	(n=109)
I	14 (35.0)	12 (26.1)	16 (15.8)	29 (26.6)
II	18 (45.0)	25 (54.3)	53 (52.5)	44 (40.4)
III	8 (20.0)	7 (15.2)	30 (29.7)	30 (27.5)
Unknown	-	2 (4.3)	2 (2.0)	6 (5.5)
Stage				
Localized	16 (40.0)	19 (41.3)	34 (33.7)	29 (26.6)
Regional spread	18 (45.0)	21 (45.7)	58 (57.4)	73 (67.0)
Distant spread	6 (15.5)	2 (4.33)	6 (5.9)	2 (1.8)
Unknown	-	4 (8.7)	3 (3.0)	5 (4.6)
Female	Colon	Rectum	Colon	Rectum
Grade*	(n=41)	(n=24)	(n=101)	(n=109)
I	7 (17.1)	2 (8.3)	13 (17.8)	8 (20.5)
II	22 (53.7)	15 (62.5)	43 (58.9)	22 (56.4)
III	10 (24.4)	6 (25.0)	15 (20.5)	8 (20.5)
Unknown	2 (4.9)	2 (8.3)	2 (2.7)	1 (2.6)
Stage				
Localized	10 (24.4)	8 (33.3)	24 (32.9)	8 (20.5)
Regional spread	22 (53.7)	16 (66.6)	40 (54.8)	29 (74.4)
Distant spread	8 (19.5)	-	7 (9.6)	1 (2.6)
Unknown	1 (2.4)	-	2 (2.7)	1 (2.6)

*Grade I-well differentiated, II-moderately differentiated, III-poorly differentiated

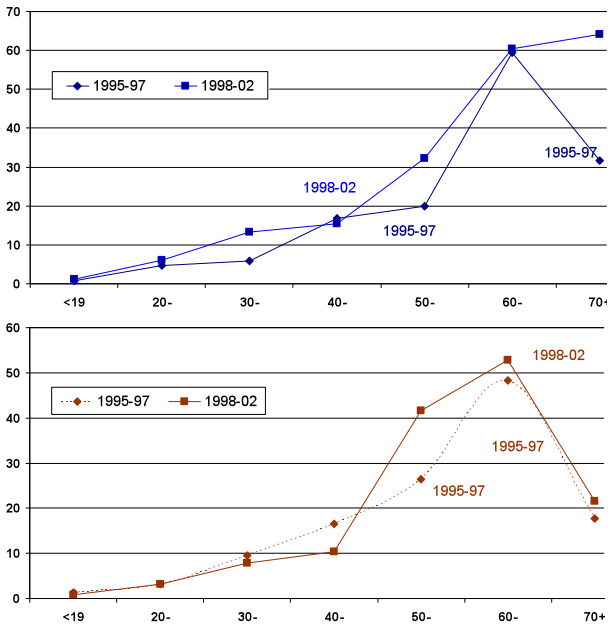

Figure 1. Age-dependent Rates. a) Male; b) Female

Table 4. Gender-wise Distribution of CRC by Site of Presentation (ICD-O3 coding)

Topography		1995-1997		1998-2002	
		Male	Female	Male	Female
Colon		n=40	n=41	n=101	n=73
Cecum	C18.0	6 (15.0)	5 (12.2)	13 (12.9)	13 (17.8)
Appendix	C18.1	-	1 (2.4)	1 (1.0)	3 (4.1)
Ascending	C18.2	6 (15.0)	6 (14.6)	11 (10.9)	11 (15.1)
Hepatic flex	C18.3	1 (2.5)	-	2 (2.0)	1 (1.4)
Transverse	C18.4.	1 (2.5)	-	8 (7.9)	2 (2.7)
Splenic flex	C18.5	-	-	-	2 (2.7)
Descending	C18.6	-	-	10 (9.9)	1 (1.4)
Sigmoid	C18.7	9 (22.5)	8 (19.5)	24 (23.8)	21 (28.8)
Overl. lesion	C18.8	17 (42.5)	21 (51.2)	32 (31.7)	19 (26.0)
Laterality					
Right		14 (35.0)	12 (29.2)	35 (34.7)	30 (41.1)
Left		9 (22.5)	8 (19.5)	34 (33.6)	24 (45.5)
Synchronous		17 (42.5)	21 (51.2)	32 (31.7)	19 (26.0)
Rectum		n=46	n=24	n=109	n=39
Rect	C19.9	7 (15.2)	2 (8.3)	11(10.1)	4 (10.3)
Rect, NOS	C20.9	25 (54.3)	20 (48.8)	77 (70.6)	27 (69.2)
Anus, NOS	C21.0	3 (6.5)	1 (4.2)	3 (2.8)	1 (2.6)
Anal canal	C21.1	11 (23.9)	1 (4.2)	18 (16.5)	7 (18.0)
Distant		8 (19.5)	-	7 (9.6)	1 (2.6)
Unknown		1 (2.4)	-	2 (2.7)	1 (2.6)

Rect, Rectosigmoid junction

Table 5. Gender-wise Distribution of CRC by Site of Morphology (ICD-O3 Coding)

		1995-1997		1998-2002	
		Colon	Rectum	Colon	Rectum
Males		(n=41)	(n=24)	(n=101)	(n=109)
Carc, NOS	M8000-20	4 (10.0)	3 (6.5)	4 (4.0)	6 (5.5)
SCC, NOS	M8070-2	-	6 (13.0)	1 (1.0)	11 (10.1)
AC, NOS	M8140	29 (72.5)	32 (69.6)	79 (78.1)	63 (57.8)
Mucin AC	M8480-1; M8490	5 (12.5)	3 (6.5)	14 (13.9)	24 (22.1)
B-cell	M9680, 87	2 (5.0)	1 (2.2)	2 (2.0)	1 (0.9)
Other	M8240-60; M8720, M8800	-	1 (2.2)	1 (1.0)	4 (3.6)
Females		(n=41)	(n=24)	(n=73)	(n=39)
Carc, NOS	M8010-20	-	-	3 (4.1)	1 (2.6)
SCC, NOS	M8070-2	-	1 (4.2)	2 (2.8)	6 (15.4)
AC, NOS	M8140	35 (85.4)	16 (66.7)	47 (64.4)	27 (69.2)
Mucin AC	M8480-1; M8490	6 (14.6)	4 (16.7)	19 (27.1)	5 (12.8)
Diffuse B	M9680	-	2 (8.3)	-	-
Other spec	M8240, - M8936,	1 (4.2)	2 (2.7)	-	-

Data are No and %; SCC, Squamous cell carcinoma; AC, adenocarcinoma

site of colon involved was sigmoid colon; however approximately half the cases presented as advanced synchronous disease where identification of the site of origin was difficult (Table 4). Right cancers were more than left sided cancers of colon. Histological stratification indicates that the most common morphology was adenocarcinoma, and mucinous adenocarcinoma (Table 5. Microscopic confirmation was 99.0%.

Discussion

Colorectal cancer (also called cancer of the large bowel) is a common malignancy in developed countries but occurs much less frequently in the developing world. Worldwide in terms of incidence, colorectal cancers rank fourth in frequency in men and third in women (Parkin et al., 2005).

On a global perspective, Karachi falls into a low risk region for colorectal cancers, similar to regions in the Indian Subcontinent and other developing countries (Peedikayil et al., 2009; Curado et al, 2007; Parkin et al., 2002; s2005). CRC accounted for 4.4% cases in males and 2.8% in females. This is approximately half the global estimate of 9.4% for colon and rectum cancers (Parkin et al, 2005). In Karachi CRC ranked lower in both genders. In males it ranked ninth in 1995-7, but rose in hierarchy to the seventh ranking in 1998-2002. In females the cancers remained at rank eight and nine respectively.

The wide geographical variations for colorectal cancers, especially the differences in the more developed and the less developed countries are co-related with environmental exposures to risk factors which are labile and change over time. High risk factors include per capita consumption of meat (Armstrong and Doll, 1975) and fat (Prentice and Sheppard, 1990). A correlation has been found with physical inactivity, excess body weight, and a central deposition of adiposity (Giovannucci, 2002). There is a strong prevalence of these risk factors in Pakistan. The low incidence in KS may thus be a reflection of lower life expectancy, and there are concerns that an ageing population may be translate into a higher CRC incidence. Aspects which cannot be ignored are protective dietary factors viz. traditional spices, which may have positive associations. This has been reported from India (Nayak et al., 2009).

The occurrence of large bowel cancer is strongly related to age, with 84% of cases arising in people who are 60 years or older (Cancer Statistics, 2007); more than 90% of CRC occur after age 50 (Giovannucci and Wu, 2006). Approximately 50% of our cases were observed above 50 years and only 30% of the cases were diagnosed above 60 years, indicating a younger age of patients at risk (figures 1-2). In KS, the incidence of colorectal cancer started to rise after age 35 and increased rapidly after age 50, peaking in the seventh decade. This pattern is also observed in other countries (Giovannucci E and Wu K, 2006). As the population in Pakistan ages over the next decade or two, we should expect an increase in the number of cases in the older age groups.

The mean ages of the patients varied with the sub-site and gender from 43.7 years to 51.2 years (table 2). This mean age is lower then reported elsewhere. Even in India, where reportedly, the age for CRC is low, the mean age at diagnosis is 58.4 years (Peedikayil et al, 2009). Five percent of our cases are observed in adolescents. Studies from India also report a higher incidence of CRC in adolescents, an observation which correlates with our findings (Gupta S et al, 2010). The ratio (0.3) of under-40 to above-40 CRC patients is comparable to figures reported by the Indian National Cancer Registry (approximately 0.2), less than reported by Gupta et al

(0.64) but much higher than international average (0.07). This pattern of involvement may suggest a genetic origin. Generations of consanguineous marriages would favor clustering of mutations in families. This aspect needs further study.

A rising incidence of the disease is observed in males, which may be a genuine increase or an artifact. There is likelihood that partially this increase may be a result of improved diagnostic facilities or better registration over time. The first results of a registry can show some under-registration especially in developing countries. It is also argued that though the risk of CRC is labile to environmental change, this would manifest over generations and probably not within a period of 5 years. Nonetheless we cannot overlook this observation entirely as an artifact as colorectal incidence rates are increasing rapidly in all countries (with the exception of North America) since 1985. This is observed even in countries where the overall risk was formerly low, especially in Japan, but also elsewhere in Asia (Parkin et al, 2001). We need to study the KS trends with care as this is an unscreened population.

There is a male predominance for CRC (1.7:1) and rectal cancers (2:1) in KS with an equal ratio for colon (1:1). A male predominance has also been reported for rectal cancers from other countries (Keating et al, 2003). For overall CRC, the American Cancer Society, 2009, reported a slightly higher incidence in males than in females (1.4:1) between 1995-9, whereas New Zealand reported an equal gender ratio (Keating et al, 2003). The colon to rectum ratio was 1:1 in males in both time periods and 2:1 for females. The ratio of colon to rectal cancer incidence in high-risk populations is 2:1 or more (rather more in females). In low-risk countries, colon and rectal cancer rates are generally of the same magnitude (Parkin, 2005). This finding is also supported by Keating et al who reported a roughly equal distribution of CRC in the rectum, left colon and right colon (proximal to the splenic flexure) in New Zealand and other developed countries.

In KS right sided colon cancers were more common than the left side, as observed elsewhere (Peedikayil et al, 2009) however half the cases in 1995-7 and a third in period two, in both genders were synchronous, affecting both sides, indicating the advanced stage at diagnosis. In developed countries only 3% of the patients have synchronous tumors. The American Cancer Society has reported a preponderance of left colon carcinomas in males and right colon carcinomas in females. This was observed in our data, if rectal cancers are included in the classification of right sided cancers. In colon per se, the sharp demarcation of laterality was masked by the synchronous advanced cases.

In Karachi, we observed an advanced stage at presentation unlike the international stage distribution reported (14% Dukes stage A, 43% stage B, 43% stage C) (Keating J et al, 2003). We had used the TNM system of staging for our data, as majority of the clinicians and pathologists used that system of staging. Nonetheless no case was diagnosed equivalent to as Dukes stage A. Approximately a third of the cases were localized (equivalent to Dukes Stage B) and two thirds presented as regionally spread disease (equivalent to Dukes stage C). A number of cases were even diagnosed with distant metastasis. Some down staging was observed in period 2 (1998-2002), but was negligible. Rectal cancers presented relatively earlier then cancers of the colon, an observation also reported by other authors (Keating et al, 2003)

Younger patients presented with poor histological differentiation, mucin secreting cancers and a more advanced stage at diagnosis. An observation also reported by Gupta et al.

In conclusion, the current low but increasing incidence(especially in men), the younger age and advanced stage of CRC at diagnosis reflects a low risk, unscreened population. With existing prevalence of high risk factors in Pakistan, the low CRC incidence may be an artifact. There are concerns that an ageing population over the next decade and changing lifestyle patterns may translate into a higher CRC incidence. Screening must be considered as part of the health sector planning for the future and include the high risk younger age groups.

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Conflict of Interest/Competing interests: None

References

American Cancer Society. Cancer Facts & Figures (2009). American Cancer Society. http://www.cancer.org/Research/CancerFactsFigures/index. Accessed June 25, 2009.

Armstrong B, Doll R (1975). Environmental factors and cancer incidence and mortality in different countries with special reference to dietary practices. *Int J Cancer,* **15**, 617-31.

Bhurgri Y, Bhurgri A, Hassan SH, et al (2000). Cancer incidence in Karachi, Pakistan: First results from Karachi Cancer Registry. *Int J Cancer*, **85**, 325-9.

Boyle P ,Leon ME (2002), Epidemiology of colorectal cancer. *Br Med Bull*, **64**, 1-25.

Boyle P, Langman JS (2000). ABC of colorectal cancer epidemiology. *BMJ,* **321**, 805-8

Census Bulletin-1 (1998). Population and Housing Census of Pakistan, Population Census Organization Statistics division, Federal Bureau of Statistics, Government of Pakistan.

Curado MP, Edwards B, Shin HR, et al eds. (2007). Cancer Incidence in Five Continents, Vol. IX, IARC Scientific Publications No.160, Lyon, IARC.

Giovannucci E, Wu K. Cancers of the colon and rectum. In: Schottenfeld D, Fraumeni J, eds. Cancer. Epidemiology and Prevention. 3rd ed. Oxford University Press; 2006

Giovannucci E (2002). Modifiable risk factors for colon cancer. *Gastroenterol Clin North Am*, **31**, 925-43.

Gupta S, Bhattacharya D, Acharya AN, Majumdar S, Ranjan P, Das S (2010). Colorectal carcinoma in young adults: a retrospective study on Indian patients: 2000-2008. Colorectal Dis. Colorectal Dis. 2010 Jan 27 [Epub ahead of print].

Keating J, Pater P, Lolohea S, Wickremesekera K (2003). The epidemiology of colorectal cancer: what can we learn from the New Zealand Cancer Registry? *N Z Med J*, **116** , 1174

McKeown-Eyssen G (1994). Epidemiology of colorectal cancer revisited: are serum triglycerides and/or plasma glucose associated with risk? *Cancer Epidemiol Biomarkers Prev*, **3**, 687–95.

Office for National Statistics, Cancer Statistics registrations: registrations of cancer diagnosed in 2007, England. Accessed 22nd January 2011.

Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108

Parkin DM, Bray F, Devesa S (2001). Cancer burden in the year 2000: the global picture. *Eur J Cancer*, **37**, S4–S66.

Parkin DM, Pisani P, Ferlay J (1999). Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer*, **80**, 827-41.

Parkin DM, Chen VW, Ferlay J (eds.) (1994). Comparability and Quality Control in Cancer Registration, IARC Technical Report No.19 International Agency for Research on Cancer.

Parkin DM, Whelan SL, Ferlay J, Teppo L, and Thomas DB, eds. (2002), Cancer Incidence in Five Continents, Vol. VIII. IARC Scientific Publications No.155, Lyon, IARC.

Peedikayil MC, Nair P, Seena SM, Radhakrishnan L, Sadasivan S et al (2009) Colorectal cancer distribution in 220 Indian patients undergoing colonoscopy. *Indian J Gastroenterol*, **28**, 212-5.

Prentice RL, Sheppard L (1990). Dietary fat and cancer: consistency of the epidemiologic data, and disease prevention that may follow from a practical reduction in fat consumption. *Cancer Causes Control*, **1**, 81–7.

Nayak SP, Sasi MP, Sreejayan MP, Mandal S (2009). A case-control study of roles of diet in colorectal carcinoma in a South Indian Population. *Asian Pac J Cancer Prev*, **5**, 65-8.

Segi M (1960). Cancer Mortality in Selected Sites -in 24 Countries (1950-57), Sendai, Tohoku University School of Public Health.

WHO (1992). International Statistical Classification of Diseases and Health Related Problems 10th Revision, Geneva, World Health Organization.