RESEARCH COMMUNICATION

Trends in Rectal Cancer Incidence - Indian Scenario

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Abstract

The objective was to analyse time trends of rectal cancer for the Indian population by gender, year of diagnosis, and age. Published data for Indian registries were obtained from "Cancer Incidence in Five Continents" and /or individual Indian registries for different time periods. Mean annual percentage change (MAPC) in incidence rates for seven Indian registries was computed using relative difference between two time periods (earliest and latest) and estimation of annual percentage change (EAPC) was computed for three registries by log-linear regression model using SAS version 8.1. The age standardized incidence rate (ASR) of rectal cancer during 2004-2006 ranged from 0.0 to 5.0 per 100,000 population with a male preponderance in most Indian registries. Among males, excepting for the Southern cities, all other registries revealed a decreasing trend/no change in the MAPC both in crude incidence rate (CR) and ASR. However, in females, an increase in MAPC in CR was noted in several registries. Statistically significant increase in EAPC in CR was observed in all the three registries ranging from 1.45% to 3.99% in males while in females the increase was 1.13% in Mumbai and 1.76% in Bangalore. Further studies are required to understand these changing trends and factors that operate in the aetiology of rectal cancer in the Indian scenario. Higher incidence in males indicates the need for greater attention to understand the causes of gender disparities.

Keywords: Rectal cancer - Indian scenario - trend - estimated annual percentage change

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Introduction

Significant variations in the distribution of rectal cancer have been reported globally (Parkin, 2004; Center et al., 2009). It is now the fourth most common cancer in men and the third most common cancer in women worldwide, (Parkin et al., 2005; Garcia et al., 2007). It was once a disease primarily observed in developed countries in whose populations risk factors for rectal cancers are commonly present (Popkin, 2004) which are, physical inactivity, obesity, a diet low in fruits and vegetables and smoking (Giovannucci and Wu, 2006; Botteri et al., 2008; Giovannucci, 2002). However, in recent years, high rectal cancer rates have been reported in newly developed countries around the world in which the risk was once low (Parkin et al., 2002). Worldwide, the incident number of rectal cancer cases in both sexes during 2008 was estimated to be 12,35,108 cases with an age standardised incidence rate (ASR) of 17.3 per 100,000 person years (Ferlay et al., 2010).

India is a country with diverse societies with a variety of cultural and dietary practices that have evolved over thousands of years. Epidemiological transitions in developing countries like India have shown an increasing burden of non communicable diseases like cardiovascular disease, diabetes as well as cancer. Although cancer rates in India are lower than those seen in Western countries, increasing life expectancy and adoption of newer lifestyles are bringing about an increase in the rates (Sinha et al., 2003). In India, rates for oral and oesophageal cancers are some of the highest in the world. In contrast rates for rectal, prostate and lung cancers are one of the lowest. The estimated ASR of rectal cancer in India was 4.3 and 3.5 per 100,000 in males and females respectively (Ferlay et al., 2010).

A systematic trend analysis may help to understand the alterations in incidence with regard to time, place and person distribution and changing cancer risk. These trends will indicate the increasing burden of cancer if any, and help in making future projections on the load of cancer and requirements for management. The present communication makes an attempt to analyze the time trends of rectal cancer for Indian population by year of diagnosis and age. This study may prompt the conduct of further studies to search for risk factors for rectal cancer.

Materials and Methods

Incidence rates [age-standardized to the world-standard population, crude rate, as well as age-specific] for

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rectal cancers between 1968 and 2002 were obtained from volumes III-IX of Cancer Incidence in Five Continents (CI5) (Waterhouse et al, 1976; Waterhouse et al, 1982; Muir et al, 1987; Parkin et al, 1992; Parkin et al, 1997; Parkin et al, 2002; Curado et al, 2007). The CI5 included incidence data reported by the Indian Population-Based Cancer Registries (PBCRs) covering areas Ahmadabad, Bangalore, Chennai, Delhi, Mumbai, Nagpur, Pune, Thiruvananthapuram (Trivandrum) and Karunagapalli. Volumes III-IX generally provided data for 5-year time periods 1968-72, 1973-77, 1978-82, 1983-87, 1988-92, 1993-97 and 1998-02 respectively. The Bangalore data for 1998-02 and for registries such as Bangalore, Mumbai, Bhopal, Barshi, New-Delhi, Chennai data for 2004-05; Kolkata 2005; North Eastern registries, 2005-06; Ahmadabad-rural 2005, Nagpur, Pune and Aurangabad for 2001 were obtained from the individual registry reports or from the reports of the National Cancer Registry Programme (NCRP) of Indian Council of Medical Research (ICMR) (NCRP, 2008; Indian Cancer Society, 2007; Kidwai Memorial Institute of Oncology, 2004, 2005).

A uniform pattern of recording is being followed by all the registries and the information is collected on a standard proforma at each of the registries. The registries routinely undertake various exercises to ensure that the data they gather and the process is of high quality. The coordinating unit of the registries undertakes an extensive check for duplicates. The commonly used indices which are employed are: proportion of cases with microscopic verification of diagnosis, proportion of cases based on death certificate only and the mortality:incidence ratio. The microscopic verification of diagnosis has been generally good in all the Indian PBCRs during all the time periods (Waterhouse et al., 1976; Waterhouse et al., 1982; Muir et al., 1987; Parkin et al., 1992; Parkin et al., 1997; Parkin et al., 2002; Curado et al., 2007). As per the published report of 2008 of the PBCRs, the proportion of cancer cases based on microscopic verification ranged from 79 to 88.3% in various registries used for trend analysis, while the diagnosis based on X ray examination varied from 0.6-12.5% (NCRP, 2008). In all the Indian registries, cases are coded according to International Classification of Diseases for Oncology (WHO, 2000).

Data from 1968 to 2002 was available only for Bombay (Mumbai) registry. The Bangalore and Chennai registries which were established during the year 1982 provided data for four successive five-year calendar periods from 1983 to 2002. Limited data was available from Ahmadabad registry. Although the Nagpur and Pune registries had data for a long term, data was missing for some in-between 5 year periods. Delhi registry provided data for three successive 5-year periods.

The trend component was studied by calculating (i) mean annual percentage change in the crude, age-standardized and age-specific incidence rates and (ii) through regression modelling of data. The regression analysis was done using SAS version 8.1.while the rest of the analysis was carried out employing Microsoft Excel.

(i) Mean annual percentage change using crude, age-standardized or age-specific incidence rates: In this approach, the trend component has been isolated according to (i) 5-year calendar period and by (ii) considering age of both genders along with the calendar period. Data for Bangalore and Chennai relate to periods 1983-87 and 1998-2002; for Mumbai from 1968-72 and 1998-2002; Nagpur 1980-82 and 1998-2002; Pune 1973-77 and 1998-2002; Ahmadabad 1983-87 and 1993-97; and Delhi 1988-92 and 1998-2002. Karunagapalli and Thiruvananthapuram (Trivandrum) registries were not considered for trend analysis as data were available for only two consecutive five-year periods.

Measures of trend over time have been estimated as overall or mean annual percentage change (MAPC %) in crude incidence rate (CR) age standardized incidence rate (ASR) and age-specific incidence rates (ASIR). Mathematically, it is expressed as: MAPC%= [(Incidence rate at latest time period t- Incidence rate at base-line period t_o)/ (Incidence rate at base-line period t_o * number of actual years covered between the two time periods)]*100. The pooled ASIR were estimated for the age groups 15-34, 35-44, 45-54, 55-64 and above 65+ years to have more stabilized incidence rates.

ii) Estimated annual percent change (EAPC) using regression model: Annual percent changes in incidence rates of cancer using CR and ASR were estimated by means of a log-linear regression model. The logarithm of the respective incidence rates on the midpoint of the five-year time period was considered. The mathematical expression was of the form:

i.e. $\log_e$ (incidence rate) = $\alpha_o + \alpha_1 a + \beta y$; where a: age, y: year of diagnosis, α_o is a constant, α_1 and β are regression coefficients. The coefficients including the average annual change in incidence rate was calculated from the maximum likelihood estimate of the parameter for the year of diagnosis (β). Further, estimation of annual percent change (EAPC) was done as EAPC= $100*(e^{\beta} -1)$. This change was regarded as statistically significant if the p-value was less than or equal to 0.05. For the purpose of uniformity and comparison, published data from Mumbai, Chennai and Bangalore was employed for the five periods from 1983-2002. Satisfactory fit in terms of a linear model was obtained with a Poisson error distribution for the number of incident cases. Separate analysis was performed with the age terms being retained in the model.

Results

Age-standardized incidence rates of rectal cancer in various registries

The ASR of rectal cancer during the period 2004-2005 in the urban registries of Bangalore, Mumbai, Bhopal, Delhi, Chennai, Kolkata ranged from 1.4-3.7 and 1.4-2.7 per 100,000 in males and females respectively. In both the rural registries of Ahmedabad and Barshi the ASR was 1.2 per 100,000 in males while in females it was found to be almost similar (1.0 and 0.8 per 100000) during the same period. In the north eastern registries covering both urban and rural areas located at Dibrugarh, Kamrup district, Silchar Town, Imphal West District, States of Mizoram and Sikkim) the ASR ranged from 0- 3.4 in males while in females it ranged from 1.3-5.0 per 100,000.

Table 1.Trends in Crude Rates (CR) and Age-standardized Rates (ASR) per 100,000 Person Years in Various Registries by Calendar Year and Mean Annual per-cent change (MAPC) Between the Earliest and Last Period

Period	Ahmadabad		Bangalore		Chennai		Mumbai		Nagpur		Pune		Delhi	
	CR	ASR	CR	ASR	CR	ASR	CR	ASR	CR	ASR	CR	ASR	CR	ASR
Males														
1968-72	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	2.01	4.22	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
1973-77	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.67	4.50	N.A.	N.A.	2.61	4.70	N.A.	N.A.
1978-82	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.85	4.50	2.54	4.40	2.51	4.70	N.A.	N.A.
1983-87	2.62	4.60	1.81	3.00	1.55	2.40	1.69	3.20	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
1988-92	N.A.	N.A.	1.65	2.56	1.89	2.83	1.52	2.95	N.A.	N.A.	N.A.	N.A.	1.3	2.1
1993-97	1.41	2.18	1.52	2.22	1.78	2.35	1.53	2.54	1.47	2.02	1.32	2.13	1.2	1.9
1998-02	N.A.	N.A.	2.00	3.00	2.80	3.30	1.80	2.60	2.10	2.60	1.70	2.40	1.3	2.0
MAPC %	-3.08	-3.51	0.53	0.00	4.04	1.88	-0.30	-1.10	-0.75	-1.78	-1.16	-1.63	0.00	-0.32
Females														
1968-72	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.16	2.55	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
1973-77	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.41	3.10	N.A.	N.A.	1.50	2.90	N.A.	N.A.
1978-82	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1.21	2.50	1.20	1.90	1.87	3.40	N.A.	N.A.
1983-87	1.49	2.50	1.56	2.70	1.33	1.90	1.40	2.50	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
1988-92	N.A.	N.A.	1.38	2.11	1.24	1.83	1.20	2.12	N.A.	N.A.	N.A.	N.A.	0.8	1.2
1993-97	0.93	1.40	1.35	2.01	1.35	1.70	1.17	1.83	0.96	1.44	1.12	1.76	1.0	1.4
1998-02	N.A.	N.A.	1.50	2.10	2.00	2.20	1.40	1.80	1.50	1.80	1.70	2.40	0.9	1.3
MAPC %	-2.52	-2.93	-0.20	-1.11	2.52	0.79	0.59	-0.84	1.09	-0.23	0.44	-0.57	0.83	0.56

N.A.: Not available

Table 2. Estimated Annual Percentage Change (EAPC) in the Incidence Rates of Cancer of Rectum in Different Ages During the Years 1983-2002

Male	Mumbai		Chennai		Bangalore		Female	Mumbai		Chennai		Bangalore	
Age (in yrs)	EAPC	P value	EAPC	P value	EAPC	P value		EAPC	P value	EAPC	P value	EAPC	P value
35-39	3.1	0.12	-	-	-	-		-	-	-	-	-	-
40-44	1.8	0.29	-	-	-	-		1.7	0.35	-	-	-	-
45-49	1.4	0.41	-	-	-	-		0.4	0.83	-	-	-	-
50-54	-0.2	0.84	-	-	-	-		-0.3	0.84	-1.3	0.32	-2.4	0.24
55-59	-0.5	0.70	2.3	0.12	-0.6	0.73		-1.5	0.46	1.5	0.46	-5.3	0.01
60-64	-0.6	0.63	2.0	0.10	-	-		-0.4	0.70	1.0	0.61	0.6	0.8
65-69	-1.8	0.12	3.6	0.05	4.2	0.05		-0.6	0.73		-	-	-
70-74	1.2	0.36	4.6	0.03	2.3	0.36		-1.4	0.55	-	-	-	-
75+	2.3	0.09	2.7	0.18	-	-		-2.8	0.01	-	-	-	-
CR	1.5	0.00	4.0	0.00	2.1	0.00		1.1	0.00	-0.2	0.94	1.8	0.00
ASR	0.3	0.60	2.6	0.00	1.7	0.01		-0.9	0.04	-0.4	0.80	0.8	0.19

Time trends in occurrence of rectal cancer

Regarding period effects (Table 1), among males, excepting for the southern cities of Bangalore and Chennai, all other registries revealed a decreasing trend / no change in the incidence of rectal cancer both in CR and ASR. There has been an increase/ no change in MAPC amongst males in Bangalore (CR = 0.53%, ASR = 0.00%) and Chennai (CR = 4.04% and ASR = 1.88%). In females increase in MAPC in CR was noted in several registries namely Chennai (2.52 %), Mumbai (0.59%), Nagpur (1.09%), Pune (0.44%) and Delhi (0.83%). Similarly in the ASR, increase was noted for Chennai (0.79%) and Delhi (0.56%), while the other five registries revealed a decreasing trend ranging from 0.23% to 2.93%.

Age-specific incidence rates (ASIR) of rectal cancer

The ASIR for the latest five-year period of 1998-02 available for six of seven registries was considered for comparison. The incidence is comparatively very low in age groups below 35 years in all registries. ASIR was observed to be high after the age of 45 years, the highest being recorded in Bangalore in males and Pune in females. Observations revealed increasing incidence rates with increasing age groups in all PBCRs except for females in Delhi and Nagpur where a dip was noticed after 64 years.

Age and period-wise incidence rates

Only Chennai registry showed an increase in the MAPC in all age groups in males and females. Furthermore, the Chennai registry showed that the MAPC was the highest (6.71%) in males of the youngest age group of 15-34 years. Ahmadabad registry was the only one which had a decrease in the MAPC in both males and females in all age groups. In males, in Nagpur and Delhi, only the 15-34 year age group showed an increase, while in Bangalore all age groups showed a decrease except for the 65+ age group. In females, the MAPC was highest (5.31%) in the Pune registry in the 55-64 age group followed by Nagpur with 4.60% in the 15-34 age group. Further, the MAPC in females increased after 45 years in Delhi and in both the age groups of 15-34 and 45-54 in Nagpur.

Estimated EAPC in incidence through regression analysis

EAPC (see Table 2) was attempted between the period and incidence rates for (i) each of the 5 year age specific incidence rates (35-39, 40-44….>=75), (ii) CR and (iii)

ASR for the data of 3 PBCRs viz. Mumbai, Chennai and Bangalore for the period 1983-2002. Except for Mumbai, the analysis of EAPC could not be done for some five year age intervals due to the limited number of cases in these age groups. Results of the analysis of EAPC revealed that linear regression was found to be a satisfactory fit between period and incidence rate. In both males and females, statistically significant increase in EAPC was noted in CR in all registries except for females in Chennai. Similarly, ASR showed a statistically significant increase in EAPC in males in Chennai and Bangalore and in females only for Mumbai. The estimated EAPC in CR & ASR in males ranged from 1.45% to 3.987% and 0.26% to 2.573% and in females, EAPC in CR and ASR ranged from -0.22% to 1.765 % and -0.856% to 0.803%. No consistent pattern was noted when different five year age wise incidence rates were considered but the EAPC was found to be statistically significant in some age groups.

Discussion

The absolute number of new cancer patients in India is increasing rapidly due to an increase in the size of the population as well as an increase in the proportion of elderly persons due to improved life expectancy (Murthy et al., 2008). However, the incidence of rectal cancer has been found to vary to a great extent in different registries. The ASR of rectal cancer was lower in Western and Eastern India as compared to Southern and North-eastern states of India. The highest incidence rate in these geographical areas was observed in Mizoram State in females followed by Chennai in males. Most cancer registries in India have reported a higher ASR in males when compared to females; the male to female ratio ranging from 1.07 to 4.57. Male preponderance for rectal cancer has been reported to be 1- 1.5 times in the more developed regions of the world as well as in the SEAR countries (WCRF and AICR, 1997; Ferlay et al., 2010).

Reports of Indian registries for the period 2006-08 have revealed that rectal cancer among men is one among the ten leading sites of cancer in the Southern India (Bangalore, Chennai, Kollam and Thiruvananthapuram) and in the North Eastern registries (Dibrugarh District, Manipur State, Mizoram, Aizwal). Among women also, it is within the ten leading sites of cancer in the rural registry of Barshi (Western India), in the Southern registries of Chennai, Kollam and Thiruvananthapuram and the North eastern registries of Kamrup Urban District, Mizoram State and Aizwal (NCRP, 2010). Further studies are required to understand the geographical differences in the incidence of rectal cancer in the various registries.

It has been reported that the incidence of rectal cancer in India is considered moderate-to-low as compared to its incidence in the Western hemisphere (Deo et al., 2004). The projected incident number of rectal cancer in India for 2016 has been estimated to be 22,317 cases (Murthy, 2009). ASR of colorectal cancer in more developed regions of the world estimated for the year 2008 has been reported to be 37.7 and 24.3 per 100,000 males and females, respectively. In the South East Asian Region, the ASR was 5.6 and 7.4 in males and females respectively (Ferlay et al., 2010).

In the present analysis, time trends in the incidence of rectal cancer have been examined using the data published by CI5 for the Indian PBCRs existing in the country. It has been reported that the data collected by the other Indian PBCRs are both complete and reliable (NCRP, 2001; Parkin et al., 2005).

Many studies have included both colon and rectum together as a single entity since the dietary risk factors of cancer in these two sites may be similar and as such published data refer to colon and rectum as a single entity. It may also be possible that due to the anatomical continuity of colon and rectum there could be some amount of misclassification in the diagnosis of cancer in these two sites. Hence, as such, due to the non-availability of findings pertaining to rectal cancer separately, we could compare our findings with those of colorectal cancer studies.

Modeling of data through age, birth cohort and calendar time period are the appropriate techniques for analyzing trends in cancer. However, the above approach could not be adopted in the present analysis, as the data were not available for a sufficiently long period of time from registries other than Mumbai. Hence, MAPC using CR, ASR, and ASIR of rectal cancer was computed between the earliest and latest time periods to evaluate the changes over the time period. Additionally, EAPC through log-linear regression model was computed for CR, ASR and ASIR of rectal cancer from the data of three registries viz. Mumbai, Chennai and Bangalore.

The present trend analysis over period as estimated through MAPC has revealed a decrease in the ASR of rectal cancer in five of the seven registries. However, the Southern registries of Bangalore and Chennai showed no increase / an annual increase of nearly 2% among males, while in females, Chennai and Delhi showed an increase in the ASR of less than 1%. Declining trends in colorectal cancer incidence in the USA over the past three decades have been reported (Ries et al., 2000; Cheng et al., 2011). The decline observed in the USA has been primarily attributed to more widespread screening for colorectal carcinoma (Garfinkel and Mushinski, 1999). In India, although no such screening programmes are in existence, further studies are required to explain the decreasing trend noted in many registries. Minimal change in colorectal cancer has also been reported in the Mumbai registry for the period 1970-1985 (Coleman et al., 1993).

The ASIR by period did not reveal any consistent pattern of the disease in many age groups. Excepting Mumbai, data for Chennai and Bangalore in each of the age groups was available for only four 5-year periods for EAPC analysis. Further, the frequency of cases in each time period was very low and hence the statistical computations could not be carried out for various five-year age intervals. Increase in MAPC was highest in the CR of the Chennai registry. Statistically significant increase in EAPC in CR was noted in all the registries from 1983 to 2002 except in females of Chennai. Statistically significant increase in EAPC in ASR was found in males in Chennai and Bangalore registries, while a significant decrease in females in Mumbai registry was observed. However, a

trend analysis carried out for the period 1986-2007 in Brunei, showed an increasing trend in the ASR from 10.4 (1986-90) to 24.3 per 100,000 (2006–07) (Chong et al., 2009).

Obesity has shown to be an important risk factor for development of colorectal cancer while adequate intake of fruits and vegetables have been shown to be a protective factor. Low intake of fresh fruits has been shown to be associated with an increased risk of rectal cancer (WCRF & AICR, 1997; Mathew et al., 2004; Murthy et al, 2009). It has been shown that cereals, vegetables, fruits, pulses, spice and other plant foods contain many micronutrients such as vitamins and minerals including phytochemicals, which have chemoprevention properties (WCRF & AICR, 1997; Mathew et al., 2004).

A case control study carried out in Italy to elicit the role of diet on rectal cancer has revealed an odds ratio of 1.74 for persons who consumed a starch rich pattern of diet. Inverse relationships were found between the consumption of vitamins and fibre pattern and rectal cancer (OR = 0.61) (Vrieling and Kampman, 2010). Similar findings have been reported from a case control study carried out at the National Naval Medical Centre, USA (Mathew et al, 2004). Besides dietary risk factors, nondietary risk factors associated with the development of colorectal cancers are genetic predisposition, ulcerative colitis and tobacco smoking.

Initiation of screening programmes, changing profile of risk factors in the population, changes in diagnostic methods, completeness and reliability of data, as well as better health awareness may bring about changing trends in the incidence of rectal cancer (Coleman et al., 1993). It has been suggested that the most effective means of maintaining the decreasing trend of this cancer or preventing it, are maintenance of body weight within recommended levels throughout life and consumption of diets high in fibres, vegetables, nonstarch polysaccharides and carotenoids and low in sugar, fat and eggs. Regular physical activity and low consumption alcohol, red and processed meat has also been recommended as effective means of preventing colorectal cancer (Ray et al., 2010). Dietary modification for weight control has met with variable success in developed countries. Implementing such a programme in a country like India is a big challenge. Further, as a chemoprevention measure, aspirin and other NSAIDs have been shown to decrease the risk of colorectal cancer (Ulrich et al., 2006).

In conclusion, in most of the Indian registries, male preponderance of rectal cancer was observed. Among males, excepting for the Southern cities of Bangalore and Chennai, all other registries revealed a decreasing trend / no change in the MAPC in incidence of rectal cancer both in CR and ASR. In females increase in MAPC in CR was noted in several registries. In both males and females, statistically significant increase in EAPC was noted in CR in all registries except for females in Chennai. Further analytical studies are required to understand these decreasing trends observed in colorectal cancer in some Indian registries. Considerable effort has to be made to increase the public awareness and interests on health issues associated with obesity, physical inactivity and diet.

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