Original Article

Risk Factors for Colorectal Cancer in Goa, India: A Hospital-based Case–Control Study

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Abstract

Introduction: Colorectal cancer is the third most common cancer in men and the second in women worldwide. The objective of the present study was to determine and quantify important modifiable risk factors attributable to colorectal cancer, in order to explore the ways to reduce the incidence of colorectal cancer in this region. **Materials and Methods:** A case–control study was conducted at a tertiary care hospital in Goa, India. The study subjects were group matched for age and sex so as to include 110 cases and 110 controls. Only incident cases of colorectal cancer were recruited in the study. Predesigned structured questionnaire was utilized for data collection, while anthropometric measurements and laboratory investigations were conducted. Statistical analysis was conducted using SPSS software package. The study was approved by the Institutional Ethics Committee of the institute. Informed written consent was obtained from the study participants. **Results:** Smoking, smokeless tobacco use, alcohol consumption, red meat consumption, high body mass index (BMI), and the presence of Type 2 diabetes mellitus were found to be the risk factors for colorectal cancer on univariate analysis, while fruit and vegetable consumption were found to be the protective factors. Multiple logistic regression analysis identified Type 2 diabetes mellitus and high BMI as risk factors for colorectal cancer and consumption of fruits and vegetables as protective factors. **Conclusion:** Identification of risk factors for colorectal cancer would help in setting of colorectal cancer screening guidelines as well as for creating awareness regarding prevention of colorectal cancer among the general population.

Keywords: Case–control study, colorectal cancer, risk factors

Introduction

Colon cancer has been defined as malignancy affecting cecum, ascending, tranverse, descending, and sigmoid colon, while rectal cancer affects the last several inches of the large intestine.[1] Colorectal cancer is one of the major causes of mortality and morbidity worldwide.[2] Colorectal cancer is the third most common cancer in men and the second in women worldwide.[3]

Within Asia, the incidence rates of colorectal cancer vary widely but are uniformly low in all South Asian countries and high in all developed Asian countries.[3,4] Compared to the Western world, the incidence rates of colorectal cancer are low in India; for colon cancer, they vary from 0.7–3.7/100,000 men to 0.4–3/100,000 among women and for rectal cancer from 1.6–5.5/100,000 men to 0–2.8/100,000 women.[5] In the 2013 report of the Indian Council of Medical Research[6] based on population cancer registries, the highest "Age Adjusted Ratio" in men for colorectal cancer was recorded in Thiruvananthapuram (4.1), followed by Bangalore (3.9) and Mumbai (3.7). As far as women are concerned the highest age-adjusted ratio was recorded in Nagaland (5.2), followed by Mizoram (4.5).

There are several risk factors for colorectal cancer. These risk factors can be broadly divided into genetic and environmental or lifestyle-related factors. Temporal trend and migrant studies have indicated that etiology of colorectal cancer is predominantly environmental hence modifiable.[7] Established

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nondietary factors of colon cancer include smoking tobacco, chronic use of nonsteroidal anti-inflammatory drugs, and genetic predisposition.[8]

In order to reduce the incidence of colorectal cancer in this region, it was therefore of interest to investigate specific risk factors related especially to lifestyle and diet. The objective of the present study, therefore, was to determine and quantify important modifiable risk factors attributable to colorectal cancer.

Materials and Methods

The study was conducted at a tertiary care hospital in Goa, India. A case–control study design was utilized for the study. The study subjects were group matched for age and sex in a case: control ratio of 1:1. The study was conducted for a duration of 24 months from January 2014 to December 2016.

Sample size was calculated using the tables for hypothesis tests for an odds ratio (OR) developed by Lwanga and Lemeshow.[9] Level of significance was set at 5% and power at 80% for a two-sided test, and for these values of Type I and Type II errors, the values of power of detecting these errors are as under; $Z\ 1-\alpha/2 = 1.96$ and $Z1-\beta = 0.84$. Considering proportion of red meat consumption at 20% among controls and anticipated OR of 2.25, the minimum sample size was calculated to be 105/group. Considering nonresponse, it was decided to include 110 cases and 110 controls in the study.

A case of colorectal cancer is defined as one who is newly detected, having symptoms suggestive of colorectal cancer and confirmed using both a radiological or colonoscopy and histopathology report. Only incident cases diagnosed for the first time during the study period and admitted in the tertiary care hospital were recruited in the study. Patients admitted during the same period for medical conditions other than colorectal cancer in the same tertiary hospital were recruited as controls.

The same investigator interviewed the cases and controls for almost the same duration of time using the same predesigned structured questionnaire. The questionnaire consisted of sections on sociodemographic variables, risk variables, and general examination including anthropometry and laboratory investigations. Data on possible risk factors such as alcohol use, smoking, red meat, processed meat, fish, eggs, dairy products, and vegetable and fruit consumption was collected. For dietary assessment, both quantity (serving size) and frequency of consumption (number of servings) were elicited.

Statistical analysis was conducted using IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Statistical analysis included calculation of OR with 95% confidence interval, Chi-square test of significance, and multiple logistic regression to examine the independent effects of different risk factors. The study was approved by the Institutional Ethics Committee of the tertiary care hospital. Informed written consent was obtained from the study participants.

Results

The hospital-based group-matched case–control study, matched for age and sex included 60% of males and 40% of females. As regards association of demographic factors with colorectal cancer, marital status ($P = 0.014$) and educational status ($P = 0.006$) were found to be statistically significant. Unmarried individuals (including separated and widowed) were more likely to have colorectal cancer compared to married individuals (OR = 2.41, 95% CI: 1.23–4.72), whereas those who were illiterate were at four times more likely to have colorectal cancer compared to those educated from 12th standard and above (OR = 4.47, 95% CI: 1.78–11.26)

As regards risk factors for colorectal cancer were concerned, ever smokers were 2.8 times more likely to have colorectal cancer compared to nonsmokers (OR = 2.79, 95% CI: 1.36–5.71). When we disaggregated the smoking history data into current smokers, past smokers, and nonsmokers, the odds for current smokers (OR = 2.77, 95% CI: 1.08–7.06) and past smokers (OR = 2.82 95% CI: 1.03–7.69 were found to be similar [Table 1]. We found similar elevated risk for colorectal cancer among users of smokeless tobacco (OR = 2.66, 95% CI: 1.27–7.12). The risk of developing colorectal cancer increased with increasing duration of smoking (χ^2 for trend 8.79, $P = 0.003$) but not with increasing duration of smokeless tobacco use (χ^2 for trend 1.14, $P = 0.284$).

We found that those who reported alcohol use were 2.23 times more likely to have colorectal cancer compared to those not consuming alcohol (OR = 2.23, 95% CI: 1.21–4.14). As far as quantity of alcohol consumed was concerned, those consuming more than four standard drinks per day were almost five times as likely to have colorectal cancer compared to those not consuming alcohol (OR = 4.94, 95% CI: 1.34–18.19). The risk of colorectal cancer for those consuming one to four standard drinks was 2.33 times (OR = 2.33, 95% CI: 0.98–5.54) and 1.23 times (OR = 1.23, 95% CI: 0.46–3.27) for those consuming <1 standard drink compared to those not consuming alcohol. In addition, the risk of colorectal cancer increased with increasing duration of alcohol use (χ^2 for trend 11.15, $P = 0.0008$). Those consuming red meat were 2.52 times more likely to have colorectal cancer compared to those not consuming (OR = 2.52, 95% CI: 1.38–4.58) [Table 1]. This risk of having colorectal cancer was found to increase with increasing frequency of consumption of red meat (χ^2 for trend 10.88, $P = 0.0009$). We found similar risk for those consuming processed meats (OR = 2.10, 95% CI: 1.17–3.78) as well.

Consumption of fruits and vegetables was found to be protective against colorectal cancer. The protective effect increased with increase in frequency of consumption of fruits and vegetables. Those consuming vegetables daily were 0.06 times less likely to have colorectal cancer compared

to those who had vegetable only once a week or less, while those consuming fruits daily were 0.61 times less likely to have colorectal cancer compared to who had fruits rarely. This protective association was found to be statistically significant [Table 2].

Body mass index (BMI) was significantly associated with colorectal cancer ($P = 0.003$). Similarly, those having diabetes mellitus were 2.51 times more likely to have colorectal cancer compared to nondiabetics and this association was statistically significant ($P = 0.006$) [Table 3].

Table 4 describes the results of the multiple logistic regression analysis for risk factors of colorectal cancer using forward method. The model yielded a $R^2 = 0.49$. The presence of diabetes mellitus and high BMI were the significant risk factors

Table 1: Association between some key risk factors and colorectal cancer

Risk variable	Cases (n=110), n (%)	Controls (n=110), n (%)	OR (95% CI)	P
Smoking status				
Current smoker	16 (14.5)	7 (6.4)	2.77 (1.08-7.06)	0.01
Past smoker	14 (12.7)	6 (5.5)	2.82 (1.03-7.69)	
Nonsmoker	80 (72.3)	97 (88.2)	1 (reference)	
Alcohol use				
Present	38 (34.5)	21 (19.1)	2.23 (1.21-4.14)	0.01
Absent	72 (65.5)	89 (80.9)	1 (reference)	
Frequency of red meat consumption (at least one serving)				
Do not consume	66 (60)	87 (79.1)	1 (reference)	0.012
Less than once per month	9 (8.2)	8 (7.3)	1.4 (0.54-4.05)	
1-3 times a month	10 (9.1)	5 (4.5)	2.63 (0.86-8.08)	
Once or more than once per week	25 (22.7)	10 (9.1)	3.29 (1.48-7.33)	
Processed meat consumption				
Present	42 (38.2)	25 (22.7)	2.10 (1.17-3.78)	0.013
Absent	68 (61.8)	85 (77.3)	1 (reference)	

OR: Odds ratio, CI: Confidence interval

Table 2: Association of some protective factors with colorectal cancer

Risk variable	Cases (n=110), n (%)	Controls (n=110), n (%)	OR (95% CI)	P
Consuming at least one serving of vegetables				
1 day in a week or less	9 (8.2)	1 (0.9)	1 (reference)	0.000
2-3 days in a week	22 (20.0)	3 (2.7)	0.81 (0.07-8.91)	
4-6 days in a week	26 (23.6)	12 (10.9)	0.24 (0.03-2.12)	
Daily	53 (48.2)	94 (85.5)	0.06 (0.01-0.51)	
Consuming at least one serving of fruit				
Rarely	36 (32.7)	13 (11.8)	1 (reference)	0.000
1-3 days per month	8 (7.3)	4 (3.6)	0.72 (0.18-2.80)	
Once a week	21 (19.1)	6 (5.4)	1.26 (0.41-3.82)	
2-3 days in a week	22 (20)	16 (14.5)	0.49 (0.20-1.22)	
4-6 days in a week	19 (23.6)	29 (26.4)	0.43 (0.1-0.55)	
Daily	4 (3.6)	42 (38.2)	0.61 (0.01-0.11)	

OR: Odds ratio, CI: Confidence interval

Table 3: Association of body mass index and diabetes mellitus with colorectal cancer

Risk variable	Cases (n=110), n (%)	Controls (n=110), n (%)	OR (95% CI)	P
BMI				
Under weight	21 (19.1)	14 (12.7)	1 (reference)	0.003
Normal weight	39 (35.5)	65 (59.1)	0.40 (0.18-0.88)	
Overweight	20 (18.2)	17 (15.5)	0.78 (0.31-2.0)	
Obese	30 (27.3)	14 (12.7)	1.43 (0.57-3.61)	
Diabetes mellitus				
Present	33 (30)	16 (14.5)	2.51 (1.28-4.91)	0.006
Absent	77 (70)	94 (85.5)	1 (reference)	

BMI: Body mass index, OR: Odds ratio, CI: Confidence interval

Table 4: Multiple logistic regression analysis for risk factors of colorectal cancer by forward Wald method

Risk factor	β coefficient	SE	Wald	*P*	Adjusted OR (95% CI)
Diabetes mellitus					
Present	0.997	0.431	5.35	0.021	2.71 (1.16-6.30)
Absent					1 (reference)
Consumption of at least one serving of fruits					
Rarely					1 (reference)
1-3 days per month	−0.246	0.775	0.101	0.751	0.78 (0.17-3.57)
Once a week	0.178	0.627	0.081	0.776	1.19 (0.35-4.08)
2-3 days in a week	−0.772	0.529	2.130	0.144	0.46 (0.16-1.30)
4-6 days in a week	−1.158	0.490	5.581	0.018	0.31 (0.12-0.82)
Daily	−3.207	0.713	20.23	0.000	0.04 (0.01-0.16)
Consumption of at least one serving of vegetables					
1 day in a week or less					1 (reference)
2-3 days in a week	−0.462	1.380	0.112	0.775	0.66 (0.04-10.67)
4-6 days in a week	−1.764	1.274	1.917	0.137	0.14 (0.01-1.85)
Daily	−2.741	1.226	5.00	0.027	0.061 (0.005-0.73)
BMI					
Underweight					1 (reference)
Normal weight	−0.187	0.500		0.708	0.82 (0.31-2.21)
Overweight	0.487	0.586		0.406	3.20 (0.51-5.12)
Obese	1.164	0.601		0.050	2.71 (1.16-6.3)

BMI: Body mass index, SE: Standard error, OR: Odds ratio, CI: Confidence interval

for colorectal cancer identified by multiple logistic regression analysis, whereas consumption of fruits and vegetables were found to be the protective factors.

Discussion

We conducted a hospital-based group-matched case–control study to determine the risk factors for colorectal cancer at a tertiary care hospital in Goa, India. Univariate analysis was done to identify risk factors for colorectal cancer and unadjusted ORs were calculated. Statistically significant risk factors were then analyzed by multiple logistic regression analysis using forward method and adjusted ORs were calculated.

As far as association of demographic factors with colorectal cancer were concerned, we found that illiterate individuals were at the highest risk of colorectal cancer compared to those educated from 12th standard and above, while those who were unmarried (including divorced/widowed) were at more likely to have colorectal cancer compared to married individuals. Doubeni *et al*.[10] have also reported that overall incidence of colorectal cancer was significantly higher in those with low educational level. El-Haddad *et al*.[11] found that divorced or separated and never married or widowed had decreased odds of adherence with colorectal cancer screening guidelines compared with individuals who were married and unmarried couples and therefore potentially more at risk to develop colorectal cancer.

As far as risk factors for colorectal cancer were concerned, ever smokers were 2.8 times more likely to have colorectal cancer compared to nonsmokers (OR = 2.79, 95% CI: 1.36–5.71). Cross *et al*.[12] reported that self-reported current smoking was significantly associated with elevated colorectal cancer risk (OR = 1.90, 95% CI: 1.02–3.54). Bhattacharya *et al*.[13] also identified smoking as a risk factor for colorectal cancer (OR = 5.4, 95% CI: 1.6–8.7). However, a case–control study conducted by Ganesh *et al*.[14] found no such association between smoking and colorectal cancer. We found the risk of developing colorectal cancer to be increasing with increasing duration of smoking. Verla-Tebit *et al*.[15] found that those smoking for more than 30 years were at increased risk of colorectal cancer (OR = 1.25, 95% CI: 0.90–1.75).

Those using smokeless tobacco were 2.66 times more likely to have colorectal cancer compared to nonusers. Study conducted by Mohan and John[16] showed an increased risk of colorectal cancer due to chewing of tobacco; however, a study conducted by Ganesh *et al*.[14] showed no such association between smokeless tobacco use and colorectal cancer.

Those who were consuming alcohol were 2.23 times more likely to have colorectal cancer compared to those not consuming alcohol. Bhattacharya *et al*.[13] identified alcohol consumption as the risk factor for colorectal cancer (OR = 3.5, 95% CI: 1–11.6), while Ganesh *et al*.[14] did not find any significant association between alcohol consumption and colorectal cancer.

Those consuming red meat were 2.52 times more likely to have colorectal cancer compared to those not consuming, while those consuming processed meats were 2.1 times more likely to have colorectal cancer. The risk of having colorectal cancer was found to increase with increasing frequency of consumption of red meat and processed meat. Spencer *et al*.[17] and Pham *et al*.[18] reported the association

of red meat with colorectal cancer. Nashar and Almurshed *et al*.[19] and Alexander *et al*.[20] also reported positive association between consumption of processed meat and colorectal cancer.

Consumption of fruits and vegetables was found to be protective as far as colorectal cancer was concerned. The protective effect increased with increase in frequency of consumption of fruits and vegetables. Nayak *et al*.[21] reported that there was a strong inverse association between consumption of fruits and vegetables and colorectal cancer with more than 50% lower risk for daily consumption on univariate analysis.

BMI was significantly associated with colorectal cancer ($P = 0.003$). Campbell *et al*.[22] and Larsson and Wolk[23] reported a significant association of colorectal cancer and increase in BMI. Similarly, Bhattacharya *et al*.[13] reported that obesity was significantly associated with colorectal cancer (OR = 7.2, 95% CI: 1.3–40.2).

Those having diabetes mellitus were 2.51 times more likely to have colorectal cancer compared to nondiabetics. Yang *et al*.[24] observed that prior diagnosis of Type 2 diabetes was associated with modestly increased risk of colorectal cancer (OR = 1.42, 95% CI: 1.25–1.62).

The multiple logistic regression analysis for risk factors of colorectal cancer using forward method yielded a $R^2 = 0.49$. The presence of diabetes mellitus and high BMI were the significant risk factors for colorectal cancer identified by the multiple logistic regression analysis, whereas consumption of fruits and vegetables was found to be the protective factors.

Conclusion

Identification of risk factors for colorectal cancer would help in setting of colorectal cancer screening guidelines as well as for creating awareness regarding the prevention of colorectal cancer among the general population. Both these strategies would help in reducing the incidence of colorectal cancer as well as early detection of the disease.

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Conflicts of interest

There are no conflicts of interest.

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