

Risk Factors of Colorectal Cancer Other than Genetic Factors at Jinnah Post Graduate Medical Center

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ABSTRACT

Objective: To determine the association of different risk factors other than genetic factors in patients having colorectal carcinoma.

Study Design: Case control study.

Place and Duration of Study: Medical Oncology Department, Jinnah Postgraduate Medical Center, Karachi Pakistan, from Jan 2019 to Jan 2020.

Methodology: A total of 200 patients of age more than 10 years of either gender were included in the study. Hundred were cases of newly diagnosed colorectal cancer and 100 were healthy controls. The data regarding socio-demographics and risk factors other than genetic risk factors was collected through pre-designed questionnaire.

Results: The mean age of the cases was 42.76±15.02 & the controls were 39.42±14.03 years. After adjusting odds in multivariate analysis, physically inactive (OR=0.40; 95% CI: 0.16-0.98, $p<0.05$), low fruits and vegetable intake (OR=0.42; 95% CI: 0.22-0.82, $p<0.05$), processed meat intake (OR=2.00; 95% CI: 1.01-3.96, $p<0.05$) and fats intake (OR=5.12; 95% CI: 2.68-9.76, $p<0.05$) remained positively associated with colorectal carcinoma.

Conclusion: Higher risk of developing colorectal carcinoma is associated with obesity, low fruits and vegetables intake, high red meat consumption, processed meat consumption, fats intake, physical inactivity and working during night. The initiative for screening would be helpful in determining the colorectal carcinoma at an early stage. Early diagnosis will increase the survival rate and help increasing long term prognosis of the colorectal carcinoma.

Keywords: Colorectal carcinoma, Dietary habits, Genetic risk factors, Obesity, Physically inactive.

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INTRODUCTION

According to global statistics, colorectal cancer is reported as 4th most common cancer occurring in Pakistan and 3rd most common in the USA. The mortality associated with colorectal cancer is reported as almost 4% that makes total 3903 cases out of 11917 cases reported in the year 2012.^{1,2} Usually, colorectal cancer is a disease more prevalent in western countries like New Zealand, Australia and Europe however the incidence is less in Asian, African and South Asian populations.¹ The worldwide prevalence rate suggests that males are more likely to develop colorectal cancer. The survival rate of a colorectal cancer patient is approximately 5-years in an American man.³ The cancerous abnormal growth of cells in colon and rectum simultaneously is known as colorectal cancer (CRC). There are four types of colorectal cancer namely gastrointestinal stromal tumors, adenocarcinomas, gastrointestinal lymphoma and carcinoid tumors.

The symptoms of colorectal cancer include bleeding per rectum, hematochezia, pain in abdomen and weight loss. The survival rate in CRC is increased and mortality rate is decreased with initial screening.⁴

Screening helps in detecting early, asymptomatic, benign or malignant polyps. Early detection leads to early complete treatment and hence better survival. The etiology of colorectal cancer is quite versatile. Major etiological factor is inflammatory bowel disease. However, geographically there are multiple causes for the disease to occur and familial factor is one of the major causes. There is two to four fold increased risk of developing CRC in individual who had positive family history of CRC as compare to who does not have any family history.^{5,6} The other causes include factors that can be modified. Approximately 70% of CRC occurred due to environmental factors and the recognition of these factors could help in preventing progression of CRC.⁷ Obesity, consumption of red meat, smoking, diet, sedentary lifestyle, diabetes, crohn's disease, ulcerative colitis, increase triglycerides in the blood, age over 50 years are all the factors that increase the risk of developing CRC.^{8,9}

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Modifiable factors that have been related with a diminished danger of CRC include strenuous exercise, postmenopausal hormone treatment, non-steroidal anti-inflammatory drugs, aspirin, young age, vegetable intake, calcium, folate and vitamin supplements and the utilization of yogurt are protect factors for CRC.¹⁰ Females with high proportion of vegetables in diet had 20% lower risk for colon malignant growth than females who didn't have intake of vegetables. Life style modification, increasing physical activity and diet high in fiber is essential way of reducing chance of colorectal disease. Hence, the purpose of the study is to determine the association of different risk factors other than genetic factors in patients having colorectal carcinoma.

METHODOLOGY

The case-control study was conducted at the Medical oncology department of Jinnah Postgraduate Medical Center, Karachi Pakistan, from January 2019 to January 2020. The study was approved by Institutional Review Board (NO.F.2-81-IRB/2019-GENL/10262/JPMC) and verbal informed consent was attained from all the eligible participants before data collection. Sample size was estimated using online Open Epi sample size calculator taking statistics for beef consumption (2-3 times per week) among patients with colorectal cancer as 4% and 18% among controls,¹¹ power of test 80% and 95% confidence level. The calculated sample size was 79 cases and 79 controls. About 100 cases and 100 controls were included in the study in order to increase the adequacy of results.

Inclusion Criteria: All the patients of age 15-80 years of either gender were included using non-probability consecutive sampling technique. Cases were newly diagnosed patients of histologically confirmed adenocarcinoma of colorectal cancer presenting to hospital OPD. Controls were healthy individuals presenting at the same hospital for routine check-ups and who were free from cancer or chronic diseases.

Exclusion Criteria: Individuals who had hyperlipidemia, hypertension, liver, cardiac and renal diseases, mentally disability, lactating and pregnant females were excluded from the study.

The data regarding socio-demographics and risk factors was collected through pre-designed questionnaire. The risk factors for colorectal cancer other than genetic factors were consider as alcohol consumption (more than 2 packs per day for males and more than 1 pack per day for females from last six months), no

physical activity, obesity (BMI>27.5 kg/m²), constipation (frequency of stools 2 times per week), previous history of treatment for certain cancer, night shift work, history of inflammatory bowel disease and presence of diabetes mellitus. The dietary risk factors were low fruits and vegetable intake (2-3 times per week), high red meat consumption (more than 3 times per week), high processed meat consumption (2-3 times per week) and high fats intake (more than 4 days per week).

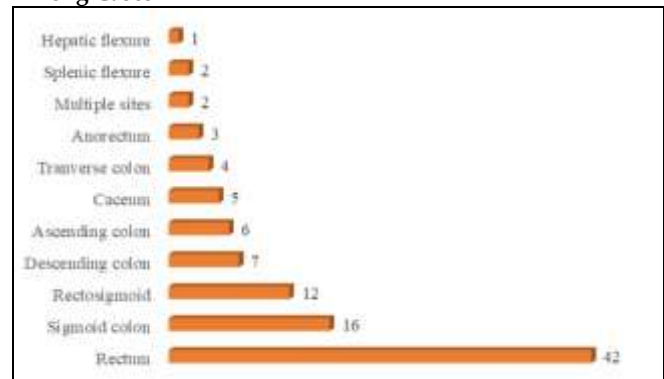
SPSS version 23 was used to analyze data. Numeric variables were represented as mean and SD. Categorical/binary variables were represented as frequencies & percentages. Univariate logistic regression was applied and odd ratios were calculated to assess association between variables and colorectal cancer. The variables associated with cases/controls in univariate logistic regression models with $p < 0.25$ were included in a single multivariate logistic regression model. p -value less than and equal to 0.05 was taken as statistically significant for multivariate model and OR >1 showed positive association.

RESULTS

Total of 100 cases and 100 controls were included in the study. The mean age of the cases was 42.76 ± 15.02 & the controls was 39.42 ± 14.03 years. Majority of patients were males ($n=113$, 56.5%), out of which 48(48%) were in controls and 65(65%) were in cases, further the relationship was statistically significant between gender and groups ($p=0.015$). The religion also showed statistical significant relationship with the cases and controls ($p=0.043$).

In patients with colorectal cancer, the rectum was the most frequent anatomical site of tumor 42(42%), followed by sigmoid colon 16(16%) and rectosigmoid 12(12%) as shown in Figure-1.

Figure: Frequency Distribution of Anatomical Sites of Tumor Among Cases



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In univariate analysis, odds of obesity, low fruits and vegetables intake, high red meat consumption, processed meat consumption, fats intake, physical inactivity and working at night shifts among colorectal cancer was 2.12(95% CI:1.31-3.98), 1.96(95% CI:1.08-3.55), 2.23(95% CI:1.07-4.67), 5.19(95% CI:2.84-9.48), 3.22(95% CI:1.65-6.29), 2.63(95% CI:1.41-4.54) and 2.84(95% CI:0.49-13.62) times higher as compared to same odds among controls ($p<0.05$) (Table-II).

Table-I: Baseline Characteristics of Cases and Controls (n=200)

	Cases (n=100)	Control (n=100)	p-value
Age in years (Mean±SD)	42.76±15.02	39.42±14.03	0.106
Gender			
Male	65(65%)	48(48%)	0.015
Female	35(35%)	52(52%)	
Ethnicity			
Sindhi	37(37%)	30(30%)	0.415
Punjabi	8(8%)	8(8%)	
Pakhtun	20(20%)	15(15%)	
Balochi	6(6%)	10(10%)	
Urdu speaking	29(29%)	35(35%)	
Others	0	2(2%)	
Religion			
Muslim	96(96%)	100(100%)	0.043
Non-Muslim	4(4%)	0	
Marital status			
Married	84(84%)	76(76%)	0.157
Unmarried	16(16%)	24(24%)	
Residence			
Rural	45 (45%)	40(40%)	0.474
Urban	55(55%)	60(60%)	
Education			
Illiterate	38(38%)	50(50%)	0.131
Primary	30(30%)	20(20%)	
Matric	18(18%)	24(24%)	
Intermediate	8(8%)	4(4%)	
Graduate	4(4%)	2(2%)	
Post graduate	2(2%)	0	
Monthly income			
<15,000 rupees	41(41%)	44(44%)	0.156
15,000-30,000 rupees	53(53%)	55(55%)	
>30000 rupees	6(6%)	1(1%)	

After adjusting odds in multivariate analysis, physical inactivity (OR=0.40; 95% CI: 0.16-0.98, $p<0.05$), low fruits and vegetable intake(OR=0.42; 95% CI: 0.22-0.82, $p<0.05$), processed meat intake(OR=2.00; 95% CI: 1.01-3.96, $p<0.05$) and fats intake(OR=5.12; 95% CI: 2.68-9.76, $p<0.05$) remained positively associated with colorectal carcinoma (Table-III).

DISCUSSION

The present case control study measured the different risk factors of colorectal cancer other than

genetic factor. Due to increasing mortality rate of CRC patients, it has become important to explain risk factors to prevent mortality and improve quality of life. According to the current study results, gender and religion was statistically significant risk factors in developing CRC. Worldwide, male gender is at high risk of developing CRC. The gender as a risk factor is significant in CRC patients and validated by many studies.¹²⁻¹⁴ The significance of CRC with religion is because alcohol is one of the prohibitions in Islamic religion and evidence has supported the fact that drinking alcohol affects the colon and rectum. The ethanol in alcohol produces carcinogenic metabolites that causes CRC.^{15,16}

Table-II: Association of Risk Factors and Colorectal Cancer (n=200)

Risk factors	Cases	Control	O.R (95% CI)
Diabetes mellitus			
Yes	14(46.7%)	16(53.3%)	0.85(0.39-1.86)
No	86(50.6%)	84(49.4%)	
Obesity			
Yes	36(63.2%)	21(36.8%)	2.12(1.31-3.98)
No	64(44.8%)	79(55.2%)	
Constipation			
Yes	17(51.5%)	16(48.5%)	1.08(0.51-2.27)
No	83(49.7%)	84(50.3%)	
Alcohol consumption			
Yes	8(66.7%)	4(33.3%)	2.09(0.61-7.17)
No	92(48.9%)	96(51.1%)	
Physically inactive			
Yes	70(59.8%)	47(40.2%)	2.63(1.41-4.54)
No	30(36.1%)	53(63.9%)	
Low fruits and vegetables intake			
Yes	73(55.7%)	58(44.3%)	1.96(1.08-3.55)
No	27(39.1%)	42(60.9%)	
High red meat intake			
Yes	87(53.7%)	75(46.3%)	2.23(1.07-4.67)
No	13(34.2%)	25(65.8%)	
Processed meat intake			
Yes	69(69.7%)	30(30.3%)	5.19(2.84-9.48)
No	31(30.7%)	70(69.3%)	
Fats intake			
Yes	38(70.4%)	16(29.6%)	3.22(1.65-6.29)
No	62(42.4%)	84(57.5%)	
Previous treatment for certain cancer			
Yes	4(80%)	1(20%)	4.13(0.45-37.57)
No	96(49.2%)	99(50.8%)	
Night shift			
Yes	13(72.2%)	5(27.8%)	2.84(0.97-8.29)
No	87(47.8%)	95(52.2%)	
History of inflammatory bowel disease			
Yes	5(71.4%)	2(28.6%)	2.58(0.49-13.62)
No	95(49.2%)	98(50.8%)	

In the support of present study results with respect of nutrition, a recent study conducted by

Castelló A in 2019 to assess the reduce risk of CRC by adhering to Mediterranean diet.¹⁷ Consuming fruits and vegetable, nuts, olive oil, fish, avoiding red meat and legumes is associated with reduced risk of CRC.¹⁷ However, it was found that fried eggs, chicken, cheese, high fat products, processed and read meat, increase the risk of having CRC. Apart from nutritional status, raised BMI is associated with high visceral fat and abdominal obesity, which produces worst outcomes in patients with CRC and hence it found significant in increasing chance of CRC.^{18,19} According to another systemic review in 2019 regarding CRC and different risk factors, it was found that not only genetic factors but environmental factors, and dietary factors are equally important in increasing the risk of CRC.⁷ Supporting this evidence, another study found that socioeconomic status significantly increases the risk of CRC.²⁰ The study evaluated low socioeconomic status as a low education and found more CRC patients.²¹ Hence, the present study results are dissimilar to previous evidence. There is immense body of literature available in in this context. However, most of the literature belongs to western population. There is dearth of studies in Pakistan in this context. Screening should be initiated to for early detection, treatment, and subsequently better survival.

Table-III: Multivariate Binary Logistic Regression Analysis Between Cases & Controls (n=200)

Risk factors	p-value	Adjusted O.R	95% CI	
			Lower limit	Upper limit
Physically inactive	0.05	0.40	0.16	0.98
Low fruits and vegetable intake	0.01	0.42	0.22	0.82
Processed meat intake	0.05	2.00	1.01	3.96
Fats intake	0.01	5.12	2.68	9.76

CONCLUSION

The results showed that gender and religion showed statistically significant relationship with the cases and controls. The risk of developing colorectal cancer is higher with obesity, low fruits and vegetables intake, high red meat consumption, processed meat consumption, fats intake, physical inactive and working during night. The initiative for screening would be helpful in determining the CRC at an early stage.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MH & GH: Study design, data interpretation, critical review, approval of the final version to be published.

RR & SZ: Data acquisition, data analysis, approval of the final version to be published.

SA & PK: Concept, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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