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Epidemiological factors associated with colorectal cancer in north-east India: A hospital-based descriptive cross-sectional study

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Ethics Committee Approval
Institutional human ethics committee of the concerned tertiary care setting approved the study protocol, and all participants gave written informed consent before the study started (B.12018/1/13-CH(A)/IEC/72, Date:12-09-2016: Institutional ethics committee, civil hospital, Aizawl. Mizoram).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Identifying the epidemiological factors associated with the causation and development of colorectal cancer may help gain a better understanding of the disease to assist in screening and assessing the prognosis. This study aimed to determine and analyze the clinical-epidemiological profile of colorectal cancer.

Methods: A cross-sectional study was conducted at a tertiary teaching hospital on 138 colorectal cancer patients for 1.6 years (June 2017 to December 2018). The participants were examined clinically, and detailed history regarding demographic features, adverse habits, occupation, and family history was taken using a structured pro forma. The tumor stage and site of cancer were considered the primary outcomes. Descriptive and inferential analyses were carried out using coGuide software, V.1.03, and the *P*-value was set at <0.05.

Results: The mean age was 54.52 (15.9) years, and 86 (62.30%) patients were males. Twenty-seven (19.60%) had hypertension, 20 (14.50%) had fissures piles and 17 (12.30%) had Diabetes Mellitus. Ninety-seven (70.28%) had a history of smoking and alcohol consumption. Carcinoma cases were more common among patients with a history of non-vegetarian dietary intake, but it was not statistically significant. In our study, smoking and comorbidities like (hypertension, fissure piles) proved to be associated with stages of tumor ($P<0.05$).

Conclusion: The associated risk factors in our study were age >50 years, smoking, and hypertension. If controlled, these can help reduce the overall incidence of CRC in the Indian population.

Keywords: Colorectal cancer, Epidemiology, Smoking, Signs, and symptoms, Lifestyle factors

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Introduction

The widely increasing number of cancer cases is perceived as an essential contributor to health ailments globally. Worldwide, approximately 13 million cancer cases are reported per year, among which almost 60% of patients die in developing countries. If not controlled, the number may increase to 10 million per year shortly [1]. According to the World Health Organization, colorectal cancer (CRC) is the third most common cancer diagnosed among men and the second most common in women [2]. Lung, prostate, colorectal, stomach, and liver cancers are the most common types of cancer in men, while breast, colorectal, lung, cervix, and stomach cancer are the most common among women (WHO, 2017) [3].

Over 1.8 million new colorectal cancer (CRC) cases and 881000 deaths were estimated to occur in 2018, accounting for approximately 1 in 10 cancer cases and deaths. Overall, CRC ranks third in terms of incidence but second in terms of mortality [4]. CRC incidence and mortality trends have evolved strikingly in recent decades. Despite significant declines in older populations, the incidence of CRC has nearly doubled among younger adults since the early 1990s [5]. In his systematic review (SR), Leddin [6] concluded that the risk of CRC increases in individuals with positive family history. The study showed that 3%-10% of subjects have one or more first-degree relatives (FDRs) diagnosed with CRC and 0.3%- 3% have two or more FDRs diagnosed with CRC.

The CRCs do not share similar driving mutations. They consist of a diversified group of a disease-driven array of modifications and mutagens. Hence, designing a "catch-all" molecular therapy for CRCs is troublesome. If CRC is diagnosed at an early stage, it can be treated surgically. Still, surgery remains ineffective if diagnosed in the advanced stage, as usually happens in 25% of cases where it has already metastasized to other areas. Drug resistance and cancer recurrence have restrained such patients for neoadjuvant and cytotoxic therapies. This deadly neoplasm can be prevented and treated when its development pattern, association with environmental and genetic factors, and molecular evolution are firmly understood by researchers and physicians [7].

CRCs' most crucial risk factors are industrialization and economic growth leading to a western dietary pattern, sedentary lifestyle, and increasing obesity [8]. In their study, Dos Santos Guedes MT et al. reported the interactions between lifestyle factors like tobacco usage and alcohol consumption, genetic factors, few environmental agents like ionizing radiation, chemical, and biological carcinogens as the possible factors for the development of most sporadic cancers [9]. Despite the awareness about CRC as a significant cause of mortality, the incidence of CRC is increasing. A review of the literature suggests a scarcity of data on factors associated with CRC. A previous study by Sharkas et al. [10] investigated the association between CRC and lifestyle factors. Based on the American Cancer Society (ACS, 2018), there is no proven way to prevent colorectal cancer. However, modifiable risk factors can be controlled to minimize the risk of developing the disease [11].

The first step in understanding cancer is to evaluate its local epidemiology. Identifying the epidemiological factors associated with the causation and development of the disease may help gain a better understanding of the disease to assist in screening and assessing the prognosis of the patients. Literature regarding the epidemiological factors associated with CRC in India is limited. Hence, we aimed to determine and analyze the clinical-epidemiological profile of colorectal cancer in East India.

Materials and methods

Study design: Descriptive cross-sectional study.

Study site: This study was conducted in the general surgery department at a tertiary care teaching hospital.

Source population: Subjects attending the department of general surgery at a tertiary care teaching hospital.

Study population: All the subjects diagnosed with colorectal cancer by either imaging or histopathological examination in the study setting were considered.

Sample size

The sample size was calculated assuming the expected proportion of colorectal cancer as 10% as per a previously published study by Bhattacharya et al. [12] with a 95% confidence level and 9% absolute precision. As recommended by Daniel et al. [13] for prevalence studies, the following formula was used for sample size calculation:

$n=Z2(1-P)/d2$

Where n = size of the sample

Z = level of confidence for Z

P = prevalence expected of proportion (If the expected prevalence is 36.53%, then P=0.365), and

d = Precision (If the precision is 9%, then d=0.09).

As per the parameters mentioned above, the required sample size would be 110.

To account for a non-participation rate of about 20%, a total of 132 subjects were needed for the study. One hundred and thirty-eight patients were recruited.

Sampling method: All study subjects were recruited sequentially by a convenient sampling method until the sample size was reached.

Study Duration: The data were collected between June 2017 and December 2018.

Inclusion criteria

Both genders, aged 18 years and above

Patients undergoing colorectal endoscopic biopsy during the study period for various clinical indications.

Exclusion criteria: Critically ill patients.

Ethical and informed consent: Institutional human ethics committee of the concerned tertiary care setting approved the study protocol, and all participants gave written informed consent before the study started (B.12018/1/13-CH(A)/IEC/72, Date:12-09-2016: Institutional ethics committee, civil hospital, Aizawl. Mizoram). The risks and benefits involved in the study were explained before obtaining consent. The confidentiality of the study participants was maintained throughout.

Epidemiological factors studied

Familial and hereditary factors: Relation- first-degree relative / cannot specify (second-degree relative)

Host factors: Age, gender, education, socioeconomic status, comorbidities

Lifestyle-related factors: Nutritional factors (a diet history), alcohol consumption, tobacco use in any form, etc.

Data collection

A detailed history was taken from the study participants using a structured pro forma, and data regarding demographic features, adverse habits, occupation, and family history were collected. All participants were clinically examined to document the relevant physical findings, and investigations like ultrasonography, CT abdomen, colonoscopy, etc., were performed. Biopsy of the identified lesions was done, and the tissue samples were sent for histopathology for the type and staging of colorectal cancer.

Statistical analysis

Tumor stage and site of cancer were considered as the primary outcomes. Other study variables were demographic parameters like age, gender, socioeconomic status, religion, education, comorbidity, surgical history, smoking and alcohol consumption, diet history, and signs and symptoms. Descriptive analyses were conducted by mean and standard deviation for quantitative variables like age and duration of tobacco usage and frequency and proportion for categorical variables like gender, comorbidities, adverse habits, family, and dietary history, etc. The chi-square test was used to compare demographic parameters and other relevant variables with stages of the tumor. *P*-value was set at <0.05 for significance. Data will be analyzed by using coGuide software, V.1.03 [14].

Results

A total of 138 subjects were included in the final analysis. In seven cases, the biopsy samples were inadequate and excluded from the study.

Table 1 shows the various demographic variables of colorectal cancer. There is an increased risk of colorectal carcinoma (CRC) with increasing age in our study population. The mean age was 54.52 (15.9) years, and 36 (26.10%) belonged to the age group of 41-50 years, and 27 (19.60%) belonged to above 60 years. There was an increased risk of colorectal carcinoma in males, as 86 (62.30%) were males, and the remaining 52 (37.70%) were females.

Table 1: Summary of demographic parameters (n=138)

Parameter	Summary
Age (Mean (SD))	54.52 (15.9)
Age group (in years)	
Less than 40 years	26(18.80%)
41 to 50 years	36 (26.10%)
51 to 60 years	23 (16.70%)
61 to 70 years	27 (19.60%)
71 to 80 years	20 (14.50%)
81 and above	6 (4.30%)
Gender	
Male	86 (62.30%)
Female	52 (37.70%)
Socioeconomic Status	
Low	36(26.10%)
Medium	80 (58.00%)
High	22 (15.90%)
Education	
Illiterate	5(3.60%)
Primary	26 (18.80%)
Secondary	46 (33.30%)
Diploma	30 (21.70%)
Graduate	20 (14.50%)
Postgraduate	11(8.00%)

Table 2 shows the associated comorbidities and past and adverse history. Among the study population, 27 (19.60%), had hypertension, 20 (14.50%) had fissure piles and 17 (12.30%) had diabetes mellitus. Ninety-seven (70.28%) had a positive history of smoking and alcohol consumption. The mean duration of tobacco use was 27.21 years in the study population.

Table 2: Summary of comorbidity, surgical history, and smoking and alcohol consumption (n=138)

Parameter	Summary (%)
Comorbidity	
Diabetes mellitus	17(12.30%)
Hypertension	27(19.60%)
Fusser piles	20(14.50%)
Tuberculosis	3(2.20%)
Asthma COPD	4(2.90%)
Chronic renal disease	3(2.20%)
Ulcerative Colitis	1(0.70%)
Surgical history	
Cholecystectomy	10(7.20%)
Ileal Resection	2(1.40%)
Smoking, using tobacco product	
Are you currently smoking	97(70.28%)
Using any other tobacco product	94(68.00%)
Type of tobacco product used	
Betel Nut	44(31.90%)
Khaine	24(17.40%)
Tuibur	12(8.70%)
No	58(42.00%)
Duration of smoking	27.21 (10.55) (range: 7 to 50)
Tobacco products usage	27.33 (9.66) (range: 6 to 52)
Alcohol consumption	
Males: Females	70:30

Table 3 shows the cancer site and family history. Fifty-six (40.57%) had a positive family history of cancer, and colorectal cancer was the most common site in 22 (15.94%) patients' family members. This was followed by seven (5.07%) lung cancers and six (4.35%) stomach cancer cases.

Table 3: Summary of the site of cancer and family history (n=138)

Parameter	Summary (%)
Cancer in family	56(40.57%)
Site of cancer	
Colorectal cancer	22(15.94%)
CA lung cancer	7(5.07%)
CA stomach cancer	6(4.35%)
CA breast cancer	5(3.62%)
Ovarian Cancer	4(2.90%)
CA Cervical cancer	3(2.17%)
Lymphoma cancer	3(2.17%)
Testicular cancer	2(1.45%)
Medullary ca thyroid	2(1.45%)
CA brain tumor	1(0.72%)
Bladder Cancer	1(0.72%)
No	82(59%)
Family history	
First-degree relative	
Brother	3(2.17%)
Sister	2(1.45%)
Father	3(2.17%)
Mom	4(2.90%)
No	126(91.30%)
Cannot specify (second-degree relative)	
Uncle	6(4.35%)
Aunty	7(5.07%)
Grandmother	8(5.80%)
Grandfather	9(6.52%)
Others	14(10.14%)
No	94(68.12%)

Diet history and signs and symptoms, and stages of cancer were reported in Table 4. Most patients (n=128, 92.80%) had a history of non-vegetarian dietary intake, followed by (n=108, 78.30%) smoked food intake. Out of 138 participants, 104 (75.04%) complained of occult blood per rectum as the main sign and symptom, followed by 71 (51.40%) who reported anorexia and weight loss. Diarrhea was reported in 36 (26.10%), and 36 (26.10%) complained of abdominal pain. Sixty-two (44.90%) had second-stage tumors, 39 (28.30%) had stage 1, 17 (12.30%) had stage 3 and the remaining 20 (14.50%) had stage 4 tumors.

Table 4: Summary of diet, signs and symptoms, and tumor stage (n=138)

Parameter	Summary
Diet history	
Animal proteins	128(92.80%)
Green vegetables and fruits	18(13.00%)
Smoked foods	108(78.30%)
High salt intake	74(53.60%)
Complex carbohydrates	18(13.00%)
Signs and symptoms	
Abdominal pain	36(26.10%)
Nausea and vomiting	27(19.60%)
Anorexia and Weight Loss	71(51.40%)
Diarrhea	49(35.50%)
Constipation	36(26.10%)
Urinary Symptoms	22(15.90%)
Occult Blood Per Rectum	104(75.40%)
Tenesmus	36(26.10%)
Pelvic pain	35(25.40%)
Mass Per Abdomen	27(19.60%)
Tumor stage	
Stage 1	39 (28.30%)
Stage 2	62 (44.90%)
Stage 3	17 (12.30%)
Stage 4	20 (14.50%)

Table 5 compared the demographic parameters and other relevant variables with stages of the tumor. No significant differences were observed in demographic parameters, comorbidities, smoking, or its duration (P>0.05). Carcinoma cases were insignificantly more common among patients with a history of non-vegetarian dietary intake. In our study, comorbidities (hypertension, fissure piles) proved to be risk factors, which were significant with regards to tumor stage (P<0.05).

Table 5: Comparison of demographic parameters, comorbidities, adverse habits, and diet history with stages of tumor (n=138)

Parameter	Tumor				*P*-value
	Stage I	Stage II	Stage III	Stage IV	
Age (in years)	54.46 (6.44)	55.56(14.85)	50 (19.02)	56.75(11.63)	0.549*
Gender					
Male (n=86)	24 (27.91%)	43 (50%)	6 (6.98%)	13 (15.12%)	0.083†
Female (n=52)	15 (28.85%)	19 (36.54%)	11 (21.15%)	7 (13.46%)	
Comorbidities					
Diabetic(n=17)	6 (35.29%)	3 (17.65%)	4 (23.53%)	4 (23.53%)	0.085†
Hypertension(n=27)	7 (25.93%)	6 (22.22%)	7 (25.93%)	7 (25.93%)	0.007†
Fusser Piles(n=20)	6 (30%)	4 (20%)	4 (20%)	6 (30%)	0.041†
Tuberculosis(n=3)	0 (0%)	2 (66.67%)	0 (0%)	1 (33.33%)	‡
Asthma COPD(n=4)	1 (25%)	1 (25%)	1 (25%)	1 (25%)	0.746†
Chronic renal disease (n=3)	2 (66.67%)	1 (33.33%)	0 (0%)	0 (0%)	‡
Ulcerative Colitis(n=1)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	‡
Alcohol Consumption					
Males (n=70)	18 (25.71%)	37 (52.86%)	2 (2.86%)	13 (18.57%)	‡
Females (n=33)	8 (24.24%)	13 (39.39%)	7 (21.21%)	5 (15.15%)	
Smoking(n=97)	26 (26.8%)	45 (46.39%)	13 (13.4%)	13 (13.4%)	0.806†
Duration of smoking	27.51(11.53)	27.92(12.86)	29.35(13.1)	27.4(13.64)	0.961*
Tobacco product usage	25.92(11.88)	25.58(13.4)	29.71(10.2)	34.05(13.16)	0.051*
Diet history					
Animal Proteins(n=128)	37 (28.91%)	57 (44.53%)	16 (12.5%)	18 (14.06%)	0.898†
Green vegetables and fruits(n=18)	7 (38.89%)	7 (38.89%)	1 (5.56%)	3 (16.67%)	0.608†
Smoked Foods(n=108)	31 (28.7%)	47 (43.52%)	13 (12.04%)	17 (15.74%)	0.845†
High salt intake(n=74)	21 (28.38%)	30 (40.54%)	10 (13.51%)	13 (17.57%)	0.591†
Complex Carbohydrates(n=18)	7 (38.89%)	6 (33.33%)	3 (16.67%)	2 (11.11%)	0.588†

* One way ANOVA, † chi square test, ‡ No statistical test was applied- due to 0 subjects in the cells

Discussion

In the current cross-sectional study, 138 colorectal cancer patients were included. Our study population had an increased risk of colorectal carcinoma (CRC) due to increased age and male preponderance. Carcinoma cases were insignificantly more common among patients with a history of non-vegetarian dietary intake. In our study, smoking and comorbidities (hypertension, fissure piles) proved to be significantly related to tumor stage.

In the present study, 54.52 (15.9) years was the mean age. This finding is similar to a hospital-based analytical observational study by Bhattacharya et al. [12] where CRC was much more common in patients aged >50 years. CRCs are majorly diagnosed after 50 years of age in 90% of cases, and hence increasing age is considered the most significant factor associated with the risk of CRC development. In the United States, the incidence of CRC sharply increases after 40 years in males compared to females, as reported by Surveillance, Epidemiology and End Results Program from National Cancer Institute [15]. This gender difference could be attributed to varying levels of exposure to dietary and lifestyle risk factors. Our finding contrasts to a study by Siegel et al. [16] where subjects less than 50 years of age were diagnosed with CRC. In the mid-1990s, this was referred to as an early-onset disease. These young patients have multiple other challenges in continuing the cancer management as they are diagnosed at a very early stage with these rectal diseases compared to older patients.

In the present study, the majority, 56 (40.57%), had a positive family history of cancer, and colorectal cancer was the most common in 22 (15.94%) patients' family members. This finding is similar to the meta-analysis by Wong M et al. [17] conducted on 9.28 million individuals, reporting that the increase in the RR of CRC attributed to family history was higher in younger subjects. The possible explanations for family history related to CRC can be inherited risks, environmental factors, or a combination of both. Since aging is a global issue, the relationship between multimorbidity and CRC should not be ignored. The majority, 27 (19.60%), had hypertension as comorbidity, followed by 20 (14.50%) fissure pile and 17 (12.30%) diabetes mellitus patients. The finding is similar to a study by Shin CM et al. [18] where diabetes mellitus and hypertension were associated with the risk of CRC among men but not among women in Korea.

In the present study, 97 (70.28%) had a positive history of smoking. This finding was similar to an epidemiological analysis by Almatroudi et al. [19] They concluded that CRC cases among both genders in Saudi Arabia are mainly due to lifestyle factors such as the lack of physical exercise, increased BMI, and tobacco usage. The finding was in contrast to a case-control study by Mafiana et al. in Oman [20] that reported no significant association between smoking and the risk of CRC. In our study, 128 (92.80%) subjects had a history of non-vegetarian dietary intake, followed by 108 (78.30%) smoked food intake. This result is consistent with Sinha et al. [21] where fatty diet (60%), spicy food consumption (45%), and non-vegetarian diet (43%) were the most commonly observed lifestyle factors significantly affecting the disease and directly correlated with higher stage and tumor grade. A majority, 97 (70.00%), had a positive history of alcohol consumption. This finding is similar to a systematic review and meta-analysis by Chapelle et al. [22] where an increased incidence of CRC was observed with frequent alcohol or meat consumption. Stage II was the typical presentation of CRC in the majority 62 (44.90%), followed by 39 (28.30%) in stage I. This was in contrast to a study by Suryadevara et al. [23] where stage III was the most distinct presentation stage.

CRC has various risk factors, including age, sex, lifestyle, genetic factors, obesity, diabetes, gut microbiota status, and precancerous lesions. To restrict CRC, the preliminary step is limiting its incidence and mortality rates. To reduce the burden of CRC, public health officials should promote the prevention and management of modifiable risk factors through national policies. The increasing incidence and mortality rate of CRC

may be timely curbed by clarifying specific epidemiological characteristics, optimizing early screening strategies, and strictly implementing diagnosis and treatment guidelines [24].

Limitations

The study has some limitations: First, the study design is cross-sectional. The generalizability of the study findings to other settings is limited, as the profile and lifestyle practices of the study population appear to be completely different, with peculiar dietary patterns and a high prevalence of tobacco consumption. Obesity and physical activity, thought to be risk factors for CRC, were not reported in the present study, yielding biased results for modifiable risk factors. There is a need to conduct large-scale community-based, prospective longitudinal studies to understand the risk factors, their strength of association with colorectal cancer, and its outcomes to develop prevention strategies.

Conclusion

Hypertension, non-vegetarian diet, family history, and tobacco smoking are major contributing factors to CRC incidence in East India. Prevention is the primary strategy to reduce its incidence and mortality rates. Prevention can be achieved through lifestyle changes, a healthy diet, and early screening for high-risk individuals. Therefore, healthcare strategies should focus on enhancing prevention interventions and public health programs to reverse the increasing prevalence of CRC.

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