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Original Article

Body Mass Index and Other Risk Factors Effects on Colon Cancer Prognosis in Pakistan

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Abstract

Introduction: Asian developing countries share the burden of colorectal cancer (CRC) with rising mortality rates. This prospective study aims to apprehend the clinical relevance of age, gender, lifestyle choices (dietary habits and addiction) and body mass index (BMI) to the occurrence and progression of colon cancer (CC). **Methods:** A cohort of non-cancer (NC) and CC patients of South-Central Asian origin registered for screening colonoscopy or surgery at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH and RC), Lahore, Pakistan, from 2015 to 2020 was identified. BMI (Kg/m^2) was classified according to the World Health Organization criteria as underweight (<18.5 Kg/m^2), normal weight (18.5–24.9 Kg/m^2) and overweight (≥25 Kg/m^2). **Results:** Among 236 participants, 99 (41.9%) belonged to the NC group, and 137 (58.1 %) participants had CC Overall, participants included 74 women and 162 men aged 20–85 years (mean ± SD; 49.9 ± 14.9). Notably, 46.0% of cancer patients had a family history of cancer. There was a direct relationship between CC with abnormal BMI (underweight and overweight), positive smoking history and positive family history of cancer. **Conclusion:** Being underweight or overweight is a potential risk factor for CC patients. The overall survival in patients with CC is clinically associated with lifestyle choices before CC diagnosis. A balanced diet, walking and other forms of exercise should be strongly recommended to the community and those undergoing screening colonoscopy.

Keywords: Balanced diet, body mass index, colon cancer, lifestyle choices, risk factors

Introduction

Globally colorectal cancer (CRC) is the 2nd most common gastrointestinal malignancy in men and 3rd in women, with the rising mortality rates in Asian countries which may partly reflect underlying incidence trends and changing distribution of risk factors, possibly linked to a more modern lifestyle, in combination with limited access to effective treatment.[1] Pakistan is a lower-middle-income country (LMIC) with an estimated population of 216 million in 2019 with no established Nationwide Cancer Registry except for the separately operated Karachi Cancer Registry,[2] Pakistan Atomic Energy Commission Cancer Registry[3] and Punjab Cancer Registry of 24 collaborating centres.[4] Age and non-modifiable risk factors such as personal or family history of polyps or cancer, inflammatory bowel disease, inherited syndromes and type 2 diabetes have been linked with colon cancer (CC).[5]

Body mass index (BMI), body composition and risk of cancer have been reported with supporting results.[6] A survey of 451 participants in Pakistan concluded that a total of 29% were overweight according to the South Asian cutoff (BMI 23.1–27.5 kg/m^2), and 21% (BMI >27.5 kg/m^2) were found to be obese among the participants.[7] The possibility of having CC increased by over 7% for each 2 Kg/m^2 gain in BMI.[8] A remarkable increase in BMI is a prominent cause of CRC. However, some age groups are also significantly associated with the risk of neoplasms and mortality rate.[9] Obesity results in increased colon inflammation and oxidative stress, which may cause genomic damage and contribute to CRC.[10] The increased risk of CRC associated with a high BMI (5 kg/m^2 increments) might be primarily restricted to tumours that display the more common microsatellite-stable phenotype.[11] The current single-centre prospective study aimed to investigate potential risk factors BMI and lifestyle choices (dietary habits and addiction) in addition to the gender and age affecting the occurrence and aggressiveness of CC.

Materials and Methods

Patient selection

Ethical approval for this prospective study (Study ID: 1RB-14-03) was obtained from the Institutional Review Board (registered with Office for Human Research Protections, USA; IORG0004939) at SKMCH and RC, Lahore, Pakistan. Patients undergoing screening colonoscopy or invasive surgery were enrolled after obtaining written informed consent from 19 March 2015 to 25 March 2020. For the current analysis, non-cancer (NC) patients (n=99) and new cancer patients (n=137) aged 18 years or more were enrolled. Patients who reported a previous cancer diagnosis at their baseline interviews were excluded from the study. Cancer patients with previous treatments (chemotherapy and/or radiation therapy) were also excluded. Stage IV patients were excluded as the risk factors do not play any role in terminally advanced disease. An age cutoff was used to enrol the cancer patients; hence, this study cohort has a smaller number of participants older than 70 years of age.

The final sample size for analysis was 236 participants with 99 (41.9%) NC (non-malignant colon pathology but an underlying problem including altered bowel habits, abdominal pain, long-standing ulcerating colitis, bleeding per rectum, anaemia, non-malignant colon polyps, weight loss and strong family history of cancer) and 137 (58.1%) CC (adenocarcinoma) patients (case: control ratio of 1:1.4). At study entry (baseline), participants attended clinics where demographic and disease information was collected. Overall, 74 women and 162 men were enrolled in the study. They aged between 20 and 85 years (mean ± SD; 49.9 ± 14.9). Notably, 46.0% of cancer patients had a family history (at least one blood relative) of cancer.

Data preparation

We used the STROBE case–control reporting guidelines.[12] Participants at the baseline filled out a structured questionnaire to obtain demographics, alcohol intake, smoking, dietary and exercise

habits, comorbidity (diabetes mellitus [DM]) and family history. Height was measured at baseline with a stadiometer and weight was measured (kilograms) using electronic scales. BMI was calculated as body mass (kg) divided by height (m) squared.[13]

The cancer patients included in the cohort were diagnosed with malignant neoplasm of the colon (ICD-O-3 Topography code for Colon: C18). The American Joint Committee on Cancer (AJCC, 8th Edition) staging system was used to categorise tumours: Stage I (T1-2, N0 and M0), Stage II (T3-4, N0 and M0) and Stage III (T any, N1-2 and M0/x). The degree of tumour differentiation was classified as well (G1), moderately (G2), poorly (G3) differentiated and (G4) undifferentiated. Tumour anatomic site, stage and degree of differentiation were obtained from histopathology report in the electronic hospital information system (eHIS) after approval from the IRB. Stage I and II cancers are restricted to the primary site (colon) with no positive nodes (pN^-) and were referred to as non-metastatic (77/137; 56.2%). In the case of Stage III, regional lymph nodes showed positivity for the presence of malignant cells, confirming the disease spread. In contrast, in Stage IV, distant metastases exist. No such cases were included in this study. Nonetheless, in the present study, Stage III (pN^+) was referred to as metastatic (CC M: 60/137; 43.8%). Tissues from all cancer patients were taken from the primary tumours in the colon.

Normal colon lining tissue site for the NC patients was noted at the time of its collection during the screening colonoscopy procedure. The cancer status of the patients was confirmed by a histopathology study of H&E slides by two pathologists. NC patients were selected as a control group for comparison with cancer patients.

The independent variable categories or responses to each question were coded. BMI normal weight (NW) was defined as 18.5–24.9; underweight <18.5; overweight, 25–29.9 and obese, 30 or above.[13,14] Diet responses comprised 'mixed diet, prefers meat or vegetables and fruits' were grouped as a balanced diet and 'poor inconsistent, mixed diet' as non-balanced diet (categorical: Balanced diet: 1 and non-balanced diet: 2). All multivariate models were adjusted for age at diagnosis of CC (categorical: <50, 50–59, 60–69 and >70 years), ethnicity within Pakistan (Balochi/Kashmiri/Pathan/Punjabi/Urdu speaking), AJCC stage (categorical: Stage I, Stage II and Stage III), degree of differentiation (categorical: Well, moderately, poorly differentiated and undifferentiated) and anatomic site (categorical: Ascending colon, transverse colon and descending colon). The dependent variable was encoded as NC: 0 and cancer: 1 for the survival analysis (Kaplan–Meier).

Analysis time began at the date of diagnosis for each patient. It ended at his/her death or 9 September 2020 (the date follow-up was completed), whichever came first. Individuals were excluded for CC-specific survival when the cause of death was anything other than CC or no information was available on the cause of death. Categorical variables were described in frequencies and percentages. Chi-square test or Fisher's exact test was used for the significance of categorical variables. Univariate and multivariate logistic regression analyses were performed to identify risk factors. Kaplan–Meier method was used to estimate overall survival. Survival differences were scrutinised by the Breslow generalised or Wilcoxon test. Two-tailed $P < 0.05$ was considered statistically significant. All the patients' data were analysed using statistical software IBM SPSS version 20.0 for Windows (Armonk, NY: IBM Corp).

Results

The main goal of this study was to report the important biological roles of age, gender, BMI and lifestyle choices (dietary habits and addictions) in colon carcinogenesis that could further be evaluated for the prognosis.

The distribution of patients according to BMI range and the cancer stage is shown in [Table 1]. Most cancer patients (n = 61 out of 137) were in the NW BMI group.

Table 1: Distribution of non-cancer and cancer participants according to the body mass index (BMI)

Patient groups	BMI range (Kg/m²)	Non-cancer	Cancer			
		(*n*=99)	(*n*=137)			
		Total controls	Total cases	Stage I	Stage II	Stage III
Underweight	≤18.5	9	8	0	1	7
Normal weight	18.5–24.9	34	61	6	31	24
Overweight	25.0–29.9	34	47	3	16	28
Obese	≥30.0	22	21	0	7	14

For gender, a significant difference was noted between the male and female groups. The age group of <50 years had the most participants with CC. Furthermore, there were more males (*n* = 58/74) in this age group than females. The younger populations, especially males, were found at the highest incidence rate compared to all other categories of age distribution. Gender and age groups showed a non-significant variation in the incidence rate [Figure 1].

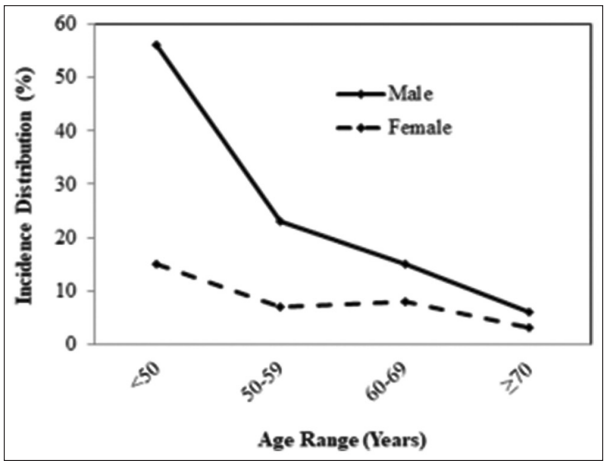

Figure 1: Gender distribution according to age categories. The age group of <50 years with the most colon cancer participants, especially males, was found at the highest incidence rate

The age range in the CC group was 20–85 years and the mean age was 49.9 ± 14.9. BMI, smoking, drinking alcohol, physical activities and fuel sources were associated with increased CC risk.

Most of our participants were from the Punjab province. The mean BMI (Kg/m²) of the study cohort was 26.2 ± 10.7. The results indicated that the overall study population was predominantly of the NW BMI (Kg/m²) category [Table 2]. The association between fuel source for household cooking and CC was 88% (44/50). On the contrary, this association was 12% (6/50) with the NC group. Gender, fuel source, eating behaviour and physical activity showed statistical significance ($P \leq 0.05$) with the presence of cancer in the bivariate analysis [Table 2]. The ascending colon was the prevalent site of the tumour in 103 of 137 (75.2%) CC group participants [Table 3].

In multivariate logistic regression model, four variables were identified as significant independent risk factors for CC: Female versus male (adjusted odds ratio [AOR] 2.31; 95% confidence interval [CI] 1.20–4.60, P = 0.02) and fuel source (wood vs. natural gas) (AOR 6.50; 95% CI [2.50–16.93], P = 0.001).

Furthermore, eating behaviour (balanced diet vs. non-balanced diet); (AOR 0.50; 95% CI [0.27–0.94], P = 0.03) and physical activity (walking vs. no physical activity); (AOR 0.41; 95% CI [0.20–0.85], P = 0.02), exercise versus no physical activity; (AOR 0.37; 95% CI [0.14–0.95], P = 0.04) and both (walk and exercise vs. no physical activity); (AOR 0.18; 95% CI [0.04–0.75], P = 0.02) were also significant independent risk factors [Table 4].

Overall survival by three age groups was plotted by Kaplan–Meier survival analysis for underweight (BMI <18.5 Kg/m²), NW (BMI 18.5–24.9 Kg/m²) and overweight (BMI ≥25 Kg/m²). Clinically, this

Table 2: Breakdown of clinical characteristics of the study population

Participants	Total (%) 236 (100)	Non-cancer (%) 99 (41.9)	Cancer (%) 137 (58.1)	*P*-value
Age at the time of diagnosis (years)				
Mean±SD	49.9±14.9	50.4±16.9	49.0±13.3	
Body mass index (Kg/m^2)				
Mean±SD	26.2±10.7	26.3±6.4	26.2±12.8	
Underweight	17 (7.2)	9 (9.1)	8 (5.8)	0.281
Normal weight	95 (40.3)	34 (34.3)	61 (43.8)	
Overweight	81 (34.3)	34 (34.3)	47 (34.3)	
Obese	43 (18.2)	22 (22.2)	21 (15.3)	
Gender				
Male	162 (68.6)	59 (59.6)	103 (75.2)	*0.011
Female	74 (31.4)	40 (40.4)	34 (24.8)	
Ethnicity				
Balochi	3 (1.3)	-	3 (2.2)	*0.001
Kashmiri	15 (6.4)	6 (6.1)	9 (6.6)	
Pathan	62 (26.3)	6 (6.1)	56 (40.9)	
Punjabi	144 (61.0)	80 (80.8)	64 (46.7)	
Urdu speaking	12 (5.1)	7 (7.1)	5 (3.6)	
Smoking				
Yes	81 (34.3)	30 (30.3)	51 (37.2)	0.269
No	155 (65.7)	69 (69.7)	86 (62.8)	
Passive exposure				
Yes	79 (33.5)	36 (36.4)	43 (31.4)	0.424
No	157 (66.5)	63 (63.6)	94 (68.6)	
Alcohol use				
Yes	19 (8.1)	10 (10.1)	9 (6.6)	0.325
No	217 (91.9)	89 (89.9)	128 (93.4)	
Walk				
Yes	67 (28.4)	39 (39.4)	28 (20.4)	*0.001
No	169 (71.6)	60 (60.6)	109 (79.6)	
Exercise				
Yes	37 (15.7)	23 (23.2)	14 (10.2)	*0.007
No	199 (84.3)	76 (76.8)	123 (89.8)	
Fuel source				
Natural gas	186 (78.8)	93 (93.9)	93 (67.9)	*0.001
Wood	50 (21.2)	6 (6.1)	44 (32.1)	
Eating habits				
Balanced diet	149 (63.1)	75 (75.8)	74 (54.0)	*0.001
Non-balanced diet	87 (36.9)	24 (24.2)	63 (46.0)	
Diabetes mellitus				
Yes	37 (15.7)	15 (15.2)	22 (16.1)	0.85
No	199 (84.3)	84 (84.8)	115 (83.9)	
Family history				
Yes	115 (48.7)	52 (52.5)	63 (46.0)	0.321
No	121 (51.3)	47 (47.5)	74 (54.0)	

Table 3: Breakdown of the histopathological characteristics of the study population

Participants	Total (%) 236 (100)	Non-cancer (%) 99 (41.9)	Cancer (%) 137 (58.1)w	*P*-value
Histology				
Adenocarcinoma	137 (58.1)	-	137 (100)	*0.001
No significant pathology	99 (41.9)	99 (100)	0	
Pathological T stage (pT)				
pT2	10 (4.2)	-	10 (7.3)	*0.001
pT3	99 (41.9)	-	99 (72.2)	
pT4	3 (1.3)	-	3 (2.2)	
pT4a	18 (7.6)	-	18 (13.1)	
pT4b	7 (3.0)	-	7 (5.1)	
Pathological N stage (pN)				
pN0	77 (32.6)	-	77 (56.2)	*0.001
pN1	6 (2.5)	-	6 (4.4)	
pN1a	13 (5.5)	-	13 (9.5)	
pN1b	13 (5.5)	-	13 (9.5)	
pN2	4 (1.7)	-	4 (2.9)	
pN2a	9 (3.8)	-	9 (6.6)	
pN2b	15 (6.4)	-	15 (10.9)	
Pathological M stage (pM)				
pMx	137 (58.1)	-	137 (100)	*0.001
Stage (pTNM)				
I	8 (3.4)	-	8 (5.8)	*0.001
IIA	55 (23.3)	-	55 (40.1)	
IIB	10 (4.2)	-	10 (7.3)	
IIC	4 (1.7)	-	4 (2.9)	
IIIB	42 (17.8)	-	42 (30.7)	
IIIC	18 (7.6)	-	18 (13.1)	
Grade				
G1	2 (0.8)	-	2 (1.5)	*0.001
G1-G2	41 (17.4)	-	41 (29.9)	
G2	56 (23.7)	-	56 (40.9)	
G2-G3	4 (1.7)	-	4 (2.9)	
G3	23 (9.7)	-	23 (16.8)	
G3-G4	11 (4.7)	-	11 (8.0)	
Groups				
Non-cancer	99 (41.9)	99 (100)	0	*0.001
Non-metastatic cancer	77 (32.6)	-	77 (56.2)	
Metastatic cancer	60 (25.4)	-	60 (43.8)	
Tissue site				
Ascending colon	180 (76.3)	77 (77.8)	103 (75.2)	0.893
Descending colon	26 (11.0)	10 (10.1)	16 (11.7)	
Transverse colon	30 (12.7)	12 (12.1)	18 (13.1)	

Table 4: Breakdown of risk factors of colon cancer using logistic regression models

Variables	Univariable logistic regression model odds ratio (95% confidence interval), *P* value	Multivariable logistic regression model odds ratio (95% confidence interval), *P* value
Gender		
Male	Reference	
Female	2.05 (1.17–3.60), 0.01	2.31 (1.20–4.60), *0.02
Body mass index (Kg/m^2)		
Normal weight	Reference	
Underweight	0.50 (0.19–1.43), 0.19	0.40 (0.11–1.42), 0.15
Overweight	0.70 (0.40–1.21), 0.20	1.10 (0.54–1.91), 0.95
Smoking status		
No	Reference	
Active smoker	1.40 (0.78–2.37), 0.27	1.10 (0.60–2.10), 0.82
Fuel use		
Natural	Reference	
Wood	7.33 (2.98–18.04), 0.001	6.50 (2.50–16.93), *0.001
Eating habits		
Non-balanced diet	Reference	
Balanced diet	0.38 (0.21–0.66), 0.001	0.50 (0.27–0.94), *0.03
Family history		
Absent	Reference	
Present	0.77 (0.46–1.30), 0.32	1.22 (0.66–2.25), 0.52
Physical activity		
No	Reference	
Walk	0.39 (0.21–0.74), 0.01	0.41 (0.20–0.85), *0.02
Exercise	0.36 (0.15–0.87), 0.02	0.37 (0.14–0.95), *0.04
Both (walk+exercise)	0.15 (0.04–0.60), 0.01	0.18 (0.04–0.75), *0.02

implies that NW CC patients have a better chance of survival than overweight patients [Figure 2].

Discussion

The main goal of this study was to report the roles of age, gender, BMI and lifestyle choices (dietary habits and addictions) in colon carcinogenesis that could further be evaluated for the prognosis.

With the increasing risk rate of CC worldwide, it is important to evaluate the clinical parameters for estimating and identifying CC risk for early precautions and detection. This single-centre study showed the clinical relevance of BMI with CC in the Pakistani-Asian population. The number of underweight, NW, overweight and obese patients in the total cohort was 17 (7.2%), 95 (40.3%), 81 (34.3%) and 43 (18.2%), respectively. NC patients were taken as a control group to analyse the cross-correlation of the risk of CC. Association of underweight with CC may not be cause and effect since many patients will become underweight due to cancer effects. It is hard to prove this is causative. Both cancer and control populations are from different socioeconomic groups. The Punjabi ethnic patients constituted a major group of the study cohort; however, the proportion of each ethnic group in the study does not reflect the national distribution of ethnic groups. The information on cancer statistics retrieved from the patient-based annual report 1994–2020 from Cancer Registry

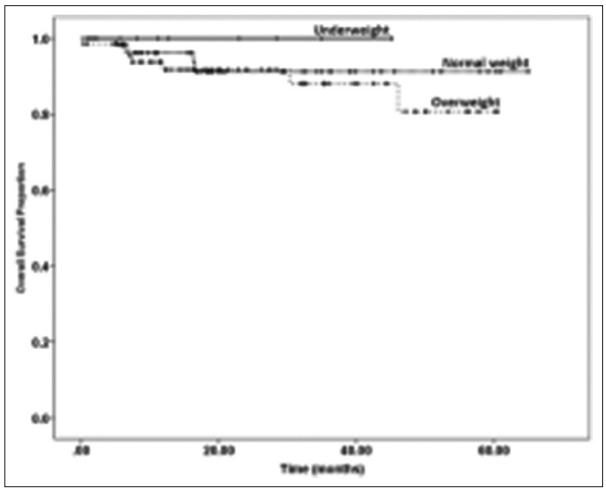

Figure 2: Kaplan–Meier survival analysis for the body mass index groups. Colon cancer patients with normal weight have a better chance of survival than overweight patients

and Clinical Data Management shows that 104,960 malignancies were registered, of which 67.8% are from Punjab, 19.8% from Khyber Pakhtunkhwa and F.A.T.A, 3.4% from Sindh, 1.5% from Baluchistan, 1.2% from Federal Capital, 0.2% from Gilgit-Baltistan, 1.0% from Un-occupied Kashmir and 0.04% from other countries,[15] which may cover the population of Pakistan, but more frequently cover residential areas of Punjab, particularly underdeveloped areas and urban environments such as major villages. In our study, using the WHO BMI classification, being underweight or obese was related to cancer. Ascending part of the colon seems to be the preferred site of tumour formation. There was a significant correlation between cancer stage and gender ($P = 0.011$). There were relatively more male patients in all the age groups, with highest in the <50 years. Clinicopathological differences between younger and older patients may be explained by underlying different molecular patterns.[16] The aetiology of the gender differences is primarily unknown. However, the preventive effect of oestrogen and progestin,[17] less use of smoking, genetic differences,[18] differences in lifestyle and eating habits[19] and differences in screening rates[20] have been suggested as possible explanations. A study reported that a significantly higher risk of CC in female versus male patients in the obese group was observed than that in the NW group.[21] Our study showed that female patients were more likely (2 times) to have CC than male patients [Table 4].

In a study in Japan, BMI was also positively associated with CC risk for men. In contrast, the pattern for women was not clear.[22] Data from 8213 participants showed a statistically significant direct association between BMI and the odds of non-advanced adenomas ($P < 0.001$) and proximal neoplasia ($P < 0.001$), while the relation for advanced adenomas was of marginal significance ($P < 0.07$) and no relation for distal neoplasia ($P < 0.85$).[23] Individuals younger than 50, eating a balanced diet and BMI <25 Kg/m^2 with no metabolic condition are at a 15% lower risk of CRC.[24] In a Canadian study, alcohol was associated with a higher risk of CRC (OR: 2.2; 95% CI: 1.2–4.0) among obese participants (BMI ≥30) relative to the non-alcohol obese. However, no increased risk was observed in people without obesity.[25] Pre-diagnostic alcohol abstaining and heavy drinking were associated with poorer survival after a CRC diagnosis than light drinking.[26] Colon microbiota is a recently recognised mediating factor in colon carcinogenesis. It is heavily affected by metabolites of ethanol, so even moderate drinking of alcohol increases the risk of CC.[27] The majority of Pakistanis do not drink alcohol for religious reasons. However, the exact percentage of drinkers within the general population is unknown. Our study showed that 217 out of 236 (91.9%) participants did not drink alcohol. Smoking is strongly associated with cancer risk in organs such as the lungs, oral cavity, kidney, bladder, digestive and urinary tract. Total tobacco usage early in life may be a significant independent prognostic factor of cancer recurrences and mortality in patients with Stage III CC.[28] In a prospective study of older women, cigarette smoking was associated with the MSI-high, CpG island methylator phenotype (CIMP)-positive and *BRAF* mutation-positive CRC.[29] Based on the World Health Organization's 2017 age-standardised current estimate of smoking

prevalence, 34.6% of men, 6.8% of women and 20.7% of Pakistan's adult population use tobacco in one form or another.[30]

Three meals a day are a regular diet of the majority of the Pakistani population ranging from 2000 to 5000 calories/meal. There is a direct link between dietary choices and health outcomes. However, there are few studies on the dietary patterns in Pakistan,[31-33] so there is a knowledge gap in ethnic and regional dietary variations that might contribute to CC. The use of wood for cooking food seems to increase the likelihood of CC; hence, this could be a potential risk factor for CC [Table 4]. There is a great deal of variation in terms of fuel used for cooking the food from natural gas, animal and plant products producing hydrocarbon-rich soot that has been reported as a potential cancer risk factor.[34] Eating habits, high BMI and physical inactivity enhance the threat of CC. Multiple studies in Asia, Europe and the USA have shown the link between eating red or canned meat and a higher threat of CC in evaluating the male and female populations.[35] Incidence of CRC in a meta-analysis of 13 studies from different areas of Pakistan ranged from 4% to 6.8%, possibly due to genetic differences, environmental factors and dietary variations along multiethnic lines such as consumption of large quantities of fat and smoked meat.[36]

Multivariate analysis of BMI and clinical variables showed that the underweight group had a high risk for advanced stage cancer. A study on 31,756 patients (malignant neoplasm of the colon) using a Korean nationwide cohort showed the association of high BMI with CC and reported that the risk of advanced cancer stage (III) in the underweight group was 33% higher ($P < 0.001$).[21] The results of our study are in alignment with these findings. We collected the data on DM status in our study cohort to see if a sugar-associated disease is comorbid in CC patients. Only 37 out of 236 patients (15.7%) had DM with 15 (15.2%) NC and 22 (16.1%) cancer patients ($P = 0.85$) showing no association. In Pakistan, despite ethnic and regional dietary variations, high-calorie meals are generally consumed, which might lead to high BMI if a physically inactive lifestyle is opted. Literature shows that as BMI increases, the risk of some diseases, including cancer, will also increase.[13] Increased BMI (≥25 Kg/m^2) was identified as a potential risk factor for CC [Table 4]. Many risk factors can be associated with weight gain in a particular age window of a patient's lifespan. Advancement in screening protocol is an important factor in reducing the overall incident rate of CRC. It has been estimated that in 2030, the incidence rate of CC will increase by 90% in patients aged 20–34 years and 28% in patients aged 35–49 years.[37] Young-onset (age <50) CC in Asian regions follows a similar pattern of CRC as seen in Europe.[38] In the USA, 20% of CRC diagnosed individuals are younger than 55 years.[39] In Japan, CRC screening starts at 40 years.[40]

The lack of CRC screening programmes and socioeconomic hurdles, such as a significant out-of-pocket expense, is major problems in the developing countries such as Pakistan. CC is on the rise, but it has the potential to move down the rungs of the mortality ladder. Centers for Disease Control and Prevention recommends a battery of screening tests, including guaiac-based faecal occult blood test, antibody-based faecal immunochemical test (FIT), the FIT-DNA test, colonoscopy and virtual colonoscopy.[41] Implementing CRC screening at an earlier age will have a long-term, cost-effective impact in low-income developing countries in Asia.[40] Screening colonoscopy use was associated with a 65% reduction in risk of death in the right colon and a 75% reduction in risk of death for the left colon/rectal cancers.[42] In Asia, Japan, Korea and Taiwan are leading nationwide databases to record CRC endoscopy procedures performed, complications and outcomes.[43-45] When offered as a primary screening test, colonoscopy screening typically starts at age 50 or 55. It is repeated every 10 years after that up to age 75 or 79, with two or three examinations in total for one individual.[46-49] India has early detection programme/guidelines for three of four cancers (breast, cervix, colon

and childhood) and Nepal and Afghanistan are in the process of adapting a national level cancer screening programme.[50] Similar nationwide cancer screening models in developed countries could be adopted by LMICs such as Pakistan to reduce the cancer burden. The limitation of this study is the lack of quantified values for smoking in terms of pack year, exercise in terms of minutes per week and nutrition in terms of type and frequency.

Our single-centre preliminary study is one of the first studies investigating the clinical relevance of BMI with CC in Pakistani. New measures must be taken not only to avoid the onset of CC but also for general good living, such as screening programmes and recommending a balanced diet and physically active lifestyle to the community through awareness and education. Several distinctive results in our study offer future research possibilities in challenging environments such as ours found in the developing countries. In Pakistan, nationwide epidemiological studies should be conducted to gather information on their dietary habits, exercise routines, kind of fuel in use, specific amounts of addictive substances and more prevalent diseases (diabetes, hypo or hyper blood pressure) affecting their BMI and linking it to cancer burden identified by advanced methods in emerging sciences (bioinformatics, metabolomics and proteomics) at an appreciable pace. Launching a nationwide screening programme using a non-invasive test (e.g., occult blood measurement in stool) could reduce the number of patients with advanced stage cancer, giving a chance for disease management at an early stage.

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Data Availability

The deidentified dataset for this study is available on request.

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Authors' Contributions

Conceived and designed the analysis: SS. Collected the data: MZ, IA, AA, MT and SH. Contributed analysis tools: SS, MAB, SK, AAS, MTM, MH, AHA and MAY. Performed the analysis: MAB. Wrote the paper: All authors.