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Metabolic Syndrome, Insulin Resistance, and Age Are Associated with an increased Risk of Colorectal Cancer Among Yemeni Subjects

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Abstract

Background and objective: Colorectal cancer (CRC) and obesity are major global public health challenges. Colorectal cancer (CRC) is among the most common malignancies worldwide, and growing evidence suggests that obesity contributes to the initiation and progression of colorectal cancer. Therefore, this study aimed to investigate the association between CRC and age, metabolic syndrome (MetS) parameters, and insulin resistance.
Method: A case-control study was conducted between 2023 and 2025 from the endoscopy units of the Replication Teaching Hospital Authority and USTH hospital, including 214 Yemeni adults aged 20 to 90 years. The association between CRC and age, MetS parameters, and insulin resistance was analyzed using binary logistic regression analysis.
Results: CRC patients had a significantly higher age compared to controls. Age, fasting blood sugar (FBS), and HOMA-IR were positively correlated with CRC ($r = 0.49$, $p < 0.001$; $r = 0.24$, $p = 0.003$; and $r = 0.19$, $p = 0.02$, respectively), whereas high-density lipoprotein cholesterol showed a significant negative correlation ($r = -0.30$, $p < 0.001$). Logistic regression analysis demonstrated that older age, elevated FBS, increased HOMA-IR, and reduced HDL-C were independent risk factors for CRC (OR = 5.7, 95% CI: 2.7–11.9, $p < 0.001$; OR = 4.6, 95% CI: 1.5–13.5, $p = 0.006$; OR = 2.5, 95% CI: 1.1–5.8, $p = 0.04$; and OR = 3.2, 95% CI: 1.2–8.1, $p = 0.016$, respectively).
Conclusion: This study demonstrates that age, elevated blood glucose, increased HOMA-IR, and reduced HDL-cholesterol are significantly associated with colorectal cancer (CRC) and may contribute to its development, particularly in older individuals.

Article Info

Keywords:
Colorectal cancer, HOMA-IR, Fasting blood sugar, High-density lipoprotein-cholesterol, Low-density lipoprotein-cholesterol , Body mass index, Metabolic syndrome, Insulin, Total cholesterol, Triglyceride.

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1. INTRODUCTION

Colorectal cancer (CRC) is the most frequent cancer in men [1] and the second most common cause of cancer-related deaths worldwide [2]. Colorectal cancer (CRC) is an invasive malignant neoplasm that originates in the mucosa of the colon and rectum. It begins as colorectal polyps [3] and progresses to adenocarcinoma through genetic and epigenetic events that induce chromosomal instability, oncogene activation, and progressive silencing of tumor suppressor genes [4].

Recent studies have identified aging, eating habits, lifestyle, smoking, alcohol intake, and physical environmental variables as risk factors for tumor development. Increased chronic inflammation and alterations in the immune population are important links between obesity and malignancies [5].

The CRC is linked to MetS, the physical inactivity, cigarette smoking, dietary imbalance (e.g., low consumption of fruits and vegetables and high consumption of red/processed meats) [6], advanced age, gender, genetic predisposition, family history of CRC, radiation, personal

history of inflammatory bowel diseases (IBD)[7], obesity[8], intestinal microbiota, diabetes mellitus, a history of colon polyps, and cholecystectomy are risk factors for the development of colorectal cancer (CRC)[9]. Obesity has been linked to an increased risk of acquiring different types of cancer, according to numerous studies, in which MetS and CRC have a strong clinical correlation [10]. This could be connected to the overexpression of the MetS core gene IL6, which can increase the aggressiveness of colorectal cancer. One important risk factor for colorectal cancer (CRC) is metastasis (Mets) [11].

Numerous factors, such as dysregulation of sex hormones and adipokines, hyperinsulinemia, and chronic inflammation, have been linked to obesity and cancer [10]**.** High BMI, particularly those more than 30 kg/m2, is significantly associated with cancer in studies on obesity and cancer [12]**.**

According to O'Sullivan et al., male sex, ethnicity, a first-degree relative's history of colorectal cancer, hyperlipidemia, obesity, and alcohol use seem to be risk factors for CRC onset [13]. Obesity imposes carcinogenic vulnerability through peroxidation pathways and dysregulated metabolism, including altered glucose metabolism, increased insulin production, and chronic inflammation. Chronic inflammation increases the release of signaling cytokines involved in the development, spread, and metastasis of colorectal cancer (CRC). Hyperinsulinism functions as a mitogen, promoting tumor growth, while obesity stimulates cellular development pathways and encourages neoplastic transformation[14].

Similar to most cancers, colorectal cancer (CRC) is more common in men than in women, and its risk increases with age. Racial and ethnic risk factors show that non-Hispanic blacks have the highest incidence and mortality of colorectal cancer (CRC), followed by Americans, Indians, Alaska Natives, and Asians/Pacific Islanders. CRC is more common among those with a family history of the disease, particularly among those with a first-degree relative [15, 16]**.**

2. MATERIALS AND METHODS

Data collection: Questionnaires were used to collect demographic data, including age, sex, height, and weight. The body mass index was calculated by dividing the weight in kilograms by the height in meters squared.

Inclusion and Exclusion Criteria: This study included CRC patients diagnosed by endoscopy and histopathology. Participants with polyps, those undergoing chemotherapy or radiation, and those with cancers other than CRC were excluded from this study. The current study excluded patients with renal failure, liver cirrhosis, cardiac diseases, and protein-losing enteropathies. Additionally, subjects in the control group with DM and MetS were excluded. These conditions can affect the excretion and metabolism of serum Dip2C protein.

Blood Sample Collection and processing: The blood specimens (5 ml) from 214 Yemeni participants were separated within 30 minutes after sample collection and stored at -80°C to evaluate fasting insulin, FBS, serum total cholesterol, serum triglycerides, serum LDL-cholesterol, and serum HDL-cholesterol. A fully automated clinical chemistry Cobas C 311 analyzer was used to test fasting blood sugar, serum triglyceride, total cholesterol, HDL cholesterol, and LDL cholesterol levels. Electrochemiluminescence Immuno Assay (CLIA) on a Cobas® 411 analyzer was used to evaluate fasting plasma insulin levels. The samples were examined at the Department of Biochemistry, National Center of Public Health Laboratories, Sana'a City.

HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was used to measure insulin resistance using the following formula: HOMA–IR = fasting glucose × fasting insulin/405 (fasting glucose in mg/dL, fasting insulin in μU/ml) [17].

According to the American Association of Clinical Endocrinology (AACE) definition, MetS was identified when three or more of the following criteria were met: body mass index (BMI) $\geq$25 kg/m^2, FBG $\geq$110 mg/dL, and/or people with diagnosed and treated diabetes, hypertension (SBP/DBP $\geq$130/85 mm Hg), fasting TGs $\geq$150 mg/dL, and/or fasting blood HDL-C < 40 mg/dL for men and 50 mg/dL for women[18, 19]. A body mass index (BMI) $\geq$ 30 kg/m^2 is considered obese, BMI 25–29.9 kg/m^2 is considered overweight, and BMI 18.5–24.9 kg/m^2 is considered normal [10, 20].

Statistical analysis

The data were divided into four groups based on CRC and MetS status: control, non-CRC/MetS, CRC/non-MetS, and CRC/MetS groups. Data were analyzed using IBM SPSS Statistics version 23(IBM Corp., Armonk, NY, USA), and normality was assessed using the Kolmogorov-Smirnov test. Normally distributed variables are displayed as mean ± SD, but anomalous continuous distributed variables were transformed to a normal distribution using an inversion function and reported as geometric mean with 95% CI. Quantitative variables were compared using ANOVA. The association between CRC and age, MetS parameters, and insulin resistance was analyzed using binary logistic regression. Statistical significance was set at P < 0.05.

3. RESULTS

This study included 214 Yemeni participants aged 20–90 years old. Of the 214 Yemeni participants, 71 exhibited MetS according to biochemical tests. Conversely, 73 participants had CRC, which was first diagnosed by endoscopy and confirmed by histological analysis. However, 70 healthy subjects (normal without CRC and MetS) who underwent endoscopy were included in the control group of this study. Throughout the study, the ages of the

Table 1. Demographic parameters of study groups, including control, non-CRC/MetS, and CRC/non-MetS and CRC/MetS groups.

Parameters	Control (n=70)	Non-CRC/MetS (n=71)	CRC/non-MetS (n=48)	CRC/MetS (n=25)
Age (yrs) **95% CI** **p-value**	38.2 (34.4- 42.0)	47.2 (43.8- 50.5) **[a] 4.2×10^{-4}, [d]0 0.02**	54.3 (50.5- 58.7) [a] **1.5×10^{-8}**, [b]**0.008**	55.2 (49.3- 61.1) **[a]2.0×10^{-6},** [c] 0.87
Weight(kg) **Mean ± SD** **p-value**	59.4 ± 12.7	78.7 ± 15.32 **[a] 4.8×10^{-15}, [d]0.002**	57.6 ± 10.2 [a] 0.49, **[b] 1.2×10^{-14}**	69.8 ± 14.4 **[a]0.001 [c]3×10^{-4}**
Height(m) **Mean ± SD** **p-value**	1.62 ± 0.08	1.63 ± 0.071 [a]0.9, [d]0.5	1.63 ± 0.047 [a]0.94, [b]1.0	1.65 ± 0.054 [a] 0.13 [c]0.36
BMI(kg/m^2) **Mean ± SD** **p-value**	22.5 ± 4.0	29.4 ± 5.0 **[a] 1.6×10^{-17}, [d] 1.2×10^{-4}**	21.6 ± 3.3 [a]0.3, **[b]3.6×10^{-18}**	25.4 ± 5.2 **[a]0.005 [c] 4.9×10^{-4}**

Data presented as Mean ± SD for all parameters except for age, presented as geometric means (95% confidence interval), [a]vs control group: [b]vs non-CRC/MetS group: [c]vs CRC/non-MetS, [d]vs CRC/MetS, which was evaluated by ANOVA. Blot values are significant. MetS, metabolic syndrome; BMI, body mass index. P-value significant at $\leq$ 0.05.

CRC/non-MetS and CRC/MetS groups were considerably older than those of the control group. Tables 1 and 2 display the participants' biochemical data and demographics for the study groups. The three target groups (non-CRC/MetS, CRC/non-MetS, and CRC/MetS) were significantly older than the control group.

The non-CRC/MetS and CRC/MetS groups had significantly higher weight and BMI than the control and CRC/non-MetS groups, but no significant difference was observed between the CRC/non-MetS and control groups. Additionally, the CRC/non-MetS group had significantly lower weight and BMI than the CRC/MetS group.

As shown in Table 2, serum triglyceride (TG), serum LDL-cholesterol, and fasting insulin levels were significantly higher in non-CRC/MetS subjects in our study than in the non-MetS groups (control and CRC/non-MetS), but there were no significant differences between the CRC groups and CRC/non-MetS when compared to the control and to each other. According to our research, the control group's serum total cholesterol did not differ substantially from any of the other study groups; the non-CRC/MetS group's serum total cholesterol was only significantly higher than that of the CRC/non-MetS group. In contrast, serum HDL cholesterol levels were significantly lower in all three target groups (non-CRC/MetS, CRC/non-MetS, and CRC/MetS) than in the control group. However, HDL levels were the lowest in the CRC/MetS group. Compared to the control and CRC/non-MetS groups, fasting blood sugar (FBS) and insulin resistance (HOMA-IR) were considerably greater in the MetS groups (non-CRC/MetS and CRC/MetS); however, there was no significant difference between the CRC/non-MetS and control groups.

Bivariate correlation of colorectal cancer with metabolic syndrome parameters and age:

The results of the bivariate correlation analysis are presented in Table 3. Age, FBS, low serum HDL cholesterol, and HOMA-IR were all highly correlated with CRC, whereas serum LDL cholesterol, serum total cholesterol (TC), serum triglycerides, and fasting insulin levels did not seem to be related.

The association between age and MetS parameters (FBS, HOMA-IR, and low HDL cholesterol) with CRC, adjusting for covariate gender for age, while MetS parameters were adjusted for age and gender, was revealed by a binary logistic regression analysis between MetS parameters and CRC on one hand and CRC with age on the other hand (Table 3).

Low HDL-C levels, high HOMA-IR, high FBS, and advanced age were independent risk factors for colorectal cancer. (OR=5.7 (95% CI: 2.7-11.9, ***p=3.0×10-6***) for age after controlling for sex, (OR=4.6 (95% CI: 1.5-13.5), ***p=0.006***) for FBS, (OR=2.5 (95% CI: 1.1-5.8), ***p=0.04***) for HOMA-IR, and (OR=3.2 (95% CI: 1.2-8.1), ***p=0.016***) for HDL-cholesterol after controlling for age and sex in a binary logistic regression analysis.

In contrast, BMI, LDL-C, TGs, total cholesterol, and fasting insulin were not independent risk factors for colorectal cancer. (OR= (95% CI: 0.8 0.36-1.9, p=0.67) for BMI (OR=0.8 (95% CI: 0.28-2.1), p=0.6) for LDL cholesterol, (OR=0.7 (95% CI: 0.33-1.6), p=0.45) for TGs, (OR= 0.46(90%CI: 0.19-1.11) p value = 0,08) for total cholesterol, and (OR=8.9 (95% CI: 0.66-111.7),

Table 2. Biochemical parameters among normal, non-CRC/MetS, and CRC/non-MetS and CRC/MetS groups

Parameters	Control (n=70)	Non-CRC/ MetS (n=71)	CRC/non-MetS (n=48)	CRC/MetS (n=25)
TGs (mg/dl) **95% CI** **P value**	140.6 (121.7-159.4)	182.1 (166.6-197.6) [a]***0.005***, [d]0.27	139.9 (123.5-156.3) [a]1.0, [b]***0.002***	150.9 (123.1-178.8) [a] 0.99, [c]0.98
TC (mg/dl) **Mean ± SD** **P value**	177.1 ± 41.6	188.8 ± 41.0 [a] 0.096, [d]0.16	166.7 ± 39.7 [a] 0.18, [b]***0.005***	175.3 ± 44.8 [a] 0.85, [c]0.4
HDL-C(mg/dl) **95% CI** **P value**	42.1 (39.9-44.2)	37.5(35.4-39.6) [a]***0.002***, [d]0.13	37.4 (34.7-40.1) [a]***0.005***, [b]0.98	34.3 (31.1-37.5) [a]***0.0002,*** [c]0.16
LDL-C (mg/dl) **Mean ± SD** **P value**	102.7±31.1	114.5 ± 38.1 [a] ***0.04***, [d]0.38	101.7 ± 28.9 [a] 0.87, [b]***0.04***	107.6 ± 36.9 [a]0.54, [c]0.48
FBS (mg/dl) **95% CI** **P value**	84.1 (76.6- 91.5)	124.5 (115.1- 133.9) [a]2.8×10^{-9}, [d] 0.84	90.6 (79.6- 101.6) [a]0.9, [b] 4.6×10^{-5}	138.7 (114.1- 163.4) [a]***0.0009,*** [c]***0.005***
Insulin (μU/ml) **95% CI** **P value**	7.7 (4.4-10.9)	18.1 (14.0-22.3) [a] 1.1×10^{-9}, [d]0.14	10.3 (6.1-14.5) [a]*0.4*, [b]***0.008***	12.7 (5.2-20.3) [a]0.2, [c] 0.53
HOM-IR **95% CI** **P value**	1.2 (0.15-2.31)	5.8 (4.5-7.1) [a]2.3×10^{-7}, [d]0.5	2.2 (0.88-3.5) [a]0.3, [b] 2.0×10^{-4}	5.0 (2.5-7.6) [a]***0.002,*** [c]***0.03***

Data presented as geometric means (95% CI) for all parameters except for TC and LDL-C presented as Mean ± SD, [a]vs **control group**: [b]vs **non-CRC/MetS** group: [c]vs **CRC/non-MetS** group. The [d]vs **CRC/MetS** group was evaluated using ANOVA. The blot values were significant. MetS: metabolic syndrome. CRC, colorectal cancer; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TGs: Triglycerides; TC: Total cholesterol; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance. P-value significant at ≤ 0.05.

p=0.10) for fasting insulin after controlling for age and sex in a binary logistic regression analysis.

4. DISCUSSION

The average age of the participants in this study was 38.2 years for normal participants, 47.2 years for non-CRC/MetS participants, 54.3 years for CRC/non-MetS participants, and 55.2 years for CRC/MetS participants, with the two CRC groups having the oldest ages. According to previous studies, 90% of colorectal cancer cases occur in people over 50 years of age [21], and its incidence increases with advanced age [22]. This is because advanced age has been linked to changes in bile acid production and composition, which impact colorectal carcinogenesis. Additionally, postmenopausal women have decreased estrogen secretion, which may increase secondary bile acid production and, consequently, the risk of colorectal cancer [23].

In this study, the weight and BMI of non-CRC/Mets and CRC/MetS individuals were significantly higher, while those of non-MetS individuals (control and CRC/non-MetS) were normal. This is consistent with the conclusion drawn from a substantial amount of epidemiological evidence, which states that MetS is a high risk factor for CRC and that CRC is one of the obesity-related diseases due to several adipocytokines secreted by adipose tissue, particularly visceral adipose tissue (VAT) in obese individuals, which can cause insulin resistance syndrome [11]. A high BMI and weight lead to hyperinsulinism and insulin resistance, which increase insulin-like growth factor-1 (IGF-1) levels. Obesity also causes insulin resistance, chronic inflammation, and adipokines, which may have sensitive roles in the intricate metabolic pathways of colorectal carcinogenesis [24]. Furthermore, hormones released by adipocytes, including resistin, leptin, and adiponectin [25, 26].

Although recent studies have revealed low blood HDL levels and elevated serum levels of total cholesterol (TC), triglycerides (TG), and LDL-c in colorectal cancer (CRC), as well as showing that low serum lipid levels reduce and protect against cancer incidence and death,

Table 3. Correlations of patient characteristics and serum lipid concentrations with colorectal cancer (CRC) and their odds ratios

Characteristic	r	P value	B	OR (95% CI)	P value
Age (Yrs)	**0.49**	***4.8×10^{-9}***	***1.5***	***5.7 (2.7-11.9)***	***3.0×10^{-6}***
BMI (Kg/m^2)	0.04	0.65	-0.18	0.8 (0.36-1.9)	0.67
FBS (mg/dl)	***0.24***	***0.003***	***1.5***	***4.6 (1.5-13.5)***	***0.006***
HDL-C (mg/dl)	**-0.30**	***2.7×10^{-4}***	***1.15***	***3.2 (1.2-8.1)***	***0.016***
LDL-C(mg/dl)	0.01	0.99	-0.25	0.8 (0.28-2.1)	0.6
TGs (mg/dl)	-0.02	0.81	-0.31	0.7 (0.33-1.6)	0.45
TC (mg/dl)	-0.09	0.25	-0.78	0.46 (0.19-1.11)	0.08
Insulin (μU/ml)	0.10	0.22	2.1	8.9 (0.66-111.7)	0.10
HOMA-IR	***0.19***	***0.02***	***0.91***	***2.5 (1.1-5.8)***	***0.04***

Correlations were performed by the Spearman correlation test, r; correlation coefficients, BMI: body mass index; FBS: fasting blood sugar; HDL-C: high density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol, TGs: Triglycerides; TC: Total cholesterol; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance) Odds ratios were determined by binary logistic regression analysis. Statistical significance was set at $P < 0.05$.

especially in CRC [27], lipid imbalance contributes to the risk of colorectal cancer by causing oxidative stress, inflammation, insulin resistance, and changes in protein function [28]. However, the results of our study revealed that the CRC groups' serum levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-cholesterol) were not significantly different from those of the control group and were close to those of the control subjects. The pathophysiology of metabolic alterations and malnutrition in patients with colorectal cancer explains this. Tumor necrosis factor μ, interleukins, calcitonin gene-related peptide, and insulin-like growth factor-1 are examples of inflammatory molecules produced by all malignancies that disrupt appetite and satiety processes [29]. Furthermore, CRC is linked to weight loss, diarrhea, constipation, and appetite, all of which lead to malnutrition and low serum lipids [30]. These factors account for the significantly lower serum triglyceride levels in the CRC/MetS group compared to the non-CRC/MetS group and the significant difference with normal individuals in our study. These findings are consistent with earlier research that demonstrated elevated CPT1 (carnitine palmitoyl transferase 1) expression in cancer tissue and oxidation of fatty acids (FAs) stored as TG in lipid droplets, which may be the cause of the decline in TG. Additionally, low serum levels in CRC cells indicate that they are focused on cell membrane synthesis [31]. The metabolic, competitive, and rapid uptake of nutrients by cancer cells causes the serum levels of TG, TC, and LDL-C to decrease in patients with CRC [32]. Because HDL has reverse transport for cholesterol, anti-inflammatory, and antioxidant properties, low serum HDL-C levels have been linked to the development of colorectal cancer (CRC). This is consistent with the current study, which found that serum HDL levels were significantly lower in the CRC and non-CRC metastasis groups than in the control group [33]. Fasting blood sugar (FBS) and insulin resistance (HOMA-IR) were significantly higher among patients with CRC/MetS in the current study, which may have contributed to the development of CRC in this study group. These individuals also had significantly higher BMI and weights. These findings are consistent with earlier research showing that high weight, BMI, particularly obesity, hyperglycemia, and dyslipidemia in MetS can result in increased insulin levels, which in turn causes cellular proliferation, reduces apoptosis, and ultimately leads to the development of CRC [34, 35]. The present study found that non-CRC/Mets patients had significantly higher FBS and HOMA-IR levels.

These individuals also had significantly higher weight, BMI, hyperinsulinemia, insulin resistance (HOMA-IR), hyperglycemia, dyslipidemia, serum triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C) levels. These metabolic alterations are characteristics of MetS that have been identified in prior research as risk factors for the development of colorectal cancer (CRC), particularly HOMA-IR, which is more strongly associated with CRC risk [36]. However, FBS and HOMA-IR levels did not differ significantly in patients with CRC without MetS. This is due to the presence of other risk factors for CRC, such as advanced age, family history, unhealthy lifestyle choices such as smoking, and inflammatory bowel disease [37]. The present study revealed insignificant statistical differences in insulin levels in CRC patients, which is consistent with other studies that showed no alterations in insulin levels in CRC [35]. Growing tumors can quickly deplete blood glucose, resulting in low blood sugar levels and, consequently, reduced insulin secretion by the pancreas. Additionally, pancreatic involvement or dysfunction due to advanced cancer can affect insulin production, contributing to low insulin levels in patients with cachexia.

In the Yemeni population, old age was the most associated with CRC, and this study showed that the increased risk of CRC was in advanced age compared with other risk factors, followed by FSB, reduced HDL-cholesterol, and HOMA-IR, and there was a positive association between these risk factors and CRC incidence. The odds of CRC in older adults were 2.3, 1.9, and 1.2 times for HOMA-IR, reduced HDL- cholesterol, and FBS, respectively; these findings are consistent with those of previous studies. MetS components and obesity are associated with CRC, inducing insulin resistance, chronic inflammation, and alterations in adipokines, which are involved in complex metabolic pathways in colorectal carcinogenesis [24]. Advanced age is associated with insulin resistance [38], a gradual decline in insulin effectiveness [39], and metabolic alterations, which are risk factors for CRC [40].

In contrast, BMI, LDL-C, triglyceride, serum total cholesterol, and fasting insulin were not associated with CRC incidence, and their odds were not significantly different among Yemeni participants. These findings are consistent with those of previous studies that demonstrated no association between lipid levels, such as TG and LDL-cholesterol, and the risk of colorectal cancer. However, the relationship between lipids and colon cancer is controversial; some studies have found a positive correlation between hyperlipidemia and the development of colorectal cancer (CRC), while others have found a negative correlation [41, 42]. Lu P. et al. explained that the relationship between dyslipidemia and CRC carcinogenesis depends on overall health and disease stage, with advanced stages characterized by weight loss and a catabolic state, accompanied by lower serum TG levels [43].

CONCLUSION

This study found associations between CRC and risk factors, including age, blood sugar, reduced HDL cholesterol, and HOMA-IR, with the risk worsening in advanced age. Age was the most independent risk factor for colorectal cancer (CRC) was age, which was more strongly linked to the development of CRC in Yemeni patients with CRC. This study also showed that blood sugar and HOMA-IR were significantly positively correlated with CRC, and that HDL cholesterol protected against colorectal carcinogenesis.

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