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Original article

Exploring the Relation Between Lifestyle Choices and the Occurrence of Colorectal Cancer Disease

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Abstract

Colorectal cancer is among the leading causes of cancer mortality worldwide. The occurrence of CRC has been associated with various lifestyle risk behaviors about major modifiable risk factors, which include dietary patterns, physical activity, smoking status, and alcohol intake. This study aimed to investigate the association of these parameters of lifestyle with the incidence of CRC. In this case-control study, a total of 140 individuals were enrolled: 70 subjects diagnosed with CRC and 70 controls (1st degree relative). The data were obtained by structured questionnaires and medical records, and analyzed by chi-square tests and logistic regression methods. The results indicated that, compared with their counterparts, physical inactivity, low exercise, smoking, and alcohol drinking are significantly associated with an increased risk for CRC. Besides, other dietary habits, such as high consumption of processed meat and low intake of vegetables and fruits, were major characteristics of the cases of CRC. It has been estimated that promoting healthy lifestyle choices could reduce excess CRC risk by more than 70%. This study underscores the critical role of lifestyle modifications in preventing CRC.

Keywords: ***Colorectal Cancer (CRC), Lifestyle Risk Factors, Physical Activity, Smoking Status, Dietary Habits, Alcohol Consumption, Case-Control Study.s***

1. Introduction

Colorectal cancer is the third most common cancer and ranks among the major causes of cancer mortality worldwide. Over time, a steady increase in CRC incidence has been registered worldwide, although with major differences by region. Already, this large variation can implicate environmental exposures, and more specifically lifestyle and diet factors, as having an etiologic role. Historical evidence from migrant studies and extensive epidemiological research has documented the strong influence of changes in diet and lifestyle on CRC incidence [1-3].

Physical inactivity, obesity, smoking, and alcohol drinking have also been reported as modifiable risk factors for CRC [4]. Red and processed meat, fat, and foods with added sugar, but low in dietary fibre, fruits, and vegetables, are associated with raised CRC risk [5]. While sedentary lifestyle and bad eating habits are related to an increased risk of CRC, on the other hand, it has been observed that healthy lifestyle habits such as regular physical activity and a balanced diet a diet high in whole grains, vegetables, and fruits are inversely associated with CRC risk. The mechanistic insights into the ways lifestyle factors influence risk for CRC suggest metabolic dysfunction, inflammation, oxidative stress, bacterial dysbiosis, and disruption of gut barrier integrity. For instance, obesity and a sedentary lifestyle allow for high levels of insulin and related growth factors-insulin-like growth factor, which drives proliferation in cancer cells. Smokers and alcohol drinkers induce carcinogenic chemicals and chronic inflammation [6-8].

In light of these findings, understanding the role of lifestyle factors in CRC risk forms a platform for devising some effective preventive measures. The present study consequently explores the relationships between lifestyle risk factors and the incidence of CRC, illustrating how CRC risk may be lessened by changes in lifestyle. This study aims to identify those major lifestyle factors that have a bearing on CRC, for the purpose of informing public health strategies and promoting those very lifestyle modifications which reduce the risk of CRC [9,10].

The main goal of this study is the identification of important individual and combined lifestyle risk factors for colorectal cancer. This review identifies major lifestyle variables in relation to CRC, providing important information that could inform public health policy and motivate lifestyle behavior changes toward reducing CRC risk. Notably, our investigation points out that both the cases and the controls are first-degree relatives, which puts them in a similar circle of genetic risk due to CRC. This genetic predisposition becomes an important consideration when interpreting the results, as it underlines the potential role of lifestyle modification in mitigating the elevated risk due to genetic factors.

2. Methods

This was a case-control study that involved 140 participants. Of the 70 cases of CRC, the 70 controls were first-degree relatives, while the cases were obtained from a cancer registry at the Oncology Teaching Hospital. Information was collected using structured questionnaires and medical records. Questionnaires were used to get broad data on demographics, lifestyle factors, and dietary habits. Medical records were analyzed to confirm the diagnosis with colorectal cancer but for further clinical data.

Descriptive statistics were used to summarize the basic demographic and lifestyle characteristics of the participants. Continuous variables such as age and BMI were summarized using means and standard deviations, while frequencies and percentages were used for categorical variables. Chi-square tests were used to test the associations between categorical lifestyle factors (for instance, exercise, and smoking) and CRC. Logistic regression analysis was performed to evaluate the independent effects of multiple lifestyle factors on CRC risk, taking into account potential confounding variables.

Schematic: Research Procedure and Statistical Analysis

Participant Selection

- CRC Cases (n=70)
- Controls (n=70)

Data Collection

- Structured Questionnaires
  - Demographic Information
  - Lifestyle Factors
  - Dietary Habits
- Medical Records Review

Data Analysis

- Descriptive Statistics
  - Means and Standard Deviations
  - Frequencies and Percentages
- Chi-square Tests
  - Associations between Categorical Variables
- T-tests
  - Comparison of Means
- Logistic Regression
- Adjusted Effects of Lifestyle Factors

3. Results

This study examined the relationship between various lifestyle choices and the incidence of colorectal cancer (CRC) among participants. The results provided valuable insights into the associations between CRC risk and lifestyle factors, including dietary habits. The demographic and lifestyle characteristics of the study population are presented in Table 1, highlighting significant differences between CRC cases and controls.

As shown in Table 1, there was a significantly higher proportion of males in the CRC group (57.1%) compared to the control group (40.0%), with a p-value of 0.042. This finding suggests a possible sex-based difference in CRC risk, potentially linked to lifestyle or biological factors. Exercise habits also differed markedly between the two groups, with 87.1% of the CRC cases not engaging in any exercise, compared to 50% of the control population ($p < 0.001$). In this study, lower physical activity levels were observed in CRC cases, with 72.9% reporting low activity compared to 52.9% in controls ($p = 0.049$). The smoking status was higher among CRC cases (37.1%) than controls (17.1%), with a p-value of 0.008. Alcohol consumption was reported in 10.0% of CRC cases, while none of the controls reported alcohol intake ($p = 0.013$).

Table 2 outlines the dietary factors associated with CRC. The mean consumption of red meat was significantly higher in CRC cases (29±16 servings per week) compared to controls (20±18 servings per week), with a p-value of 0.002. Processed meat consumption was notably higher in CRC cases (3.0 ± 1.1 servings per week) than in controls (1.3 ± 1.0 servings per week), with a p-value of <0.001. Conversely, seafood intake was significantly lower in CRC cases (2.0 ± 1.4 servings per week) compared to controls (5.5 ± 2.8 servings per week), with a p-value of <0.001. The mean consumption of fast food per week was also higher in CRC cases (5.1 ± 2.4 servings) than in controls (1.9 ± 1.6 servings), with a p-value of <0.001. Moreover, the intake of vegetables (7.0 ± 0.9 servings per week in CRC cases vs. 10.9 ± 3.6 servings per week in controls, $p < 0.001$) and fruits (3.7 ± 2.7 servings per week in CRC cases vs. 9.3 ± 6.5 servings per week in controls, $p < 0.001$) was significantly lower in CRC cases. Milk consumption was also significantly lower in CRC cases (5.5 ± 2.6 servings per week) compared to controls (7.9 ± 4.7 servings per week), with a p-value of <0.001.

In addition to the above dietary factors, as shown in Fig. 6, the consumption of soft drinks, pastries, and cream cheese was also higher among CRC cases compared to controls. CRC cases reported a mean soft drink intake of 6.5 ± 2.2 servings per week compared to 3.0 ± 1.5 servings per week in controls, and a mean pastry/cream cheese intake of 3.2 ± 1.7 servings per week compared to 1.8 ± 1.0 in controls.

Fig. 1 shows that education levels were generally lower among CRC cases compared to controls. For example, 45.7% of CRC cases had only a basic level of education compared to 28.6% of controls.
Fig. 2 compares exercise frequency between CRC cases and controls, showing that only 12.9% of CRC cases engaged in regular exercise, compared to 50.0% of controls.
Fig. 3 further details the different levels of physical activity (PA) between participants, showing that a higher percentage of controls (25.7%) engaged in high levels of PA compared to CRC cases (15.7%).
As indicated in Fig. 4, smoking was more prevalent among CRC cases (37.1%) than among controls (17.1%).
Fig. 5 illustrates that 10.0% of CRC cases consumed alcohol, while none of the controls reported alcohol consumption.

Finally, Fig. 6 shows significant differences in dietary intake between CRC cases and controls, with CRC cases consuming more red meat and processed meat (mean of 3.0 servings per week) and less seafood (mean of 2.0 servings per week), vegetables, and fruits.

Table 1: Demographic and Lifestyle Factors Characteristics of Study Population (n=140)

Characteristics	Cases (n=70)	Controls (n=70)	p-value
Sex			0.042*
Male	40 (57.1%)	28 (40.0%)	
Female	30 (42.9%)	42 (60.0%)	
Exercise			<0.001*

No	61 (87.1%)	35 (50.0%)	
Yes	9 (12.9%)	35 (50.0%)	
Physical Activity			0.049*
Low	51 (72.9%)	37 (52.9%)	
Medium	8 (11.4%)	15 (21.4%)	
High	11 (15.7%)	18 (25.7%)	
Smoking			0.008*
No	44 (62.9%)	58 (82.9%)	
Yes	26 (37.1%)	12 (17.1%)	
Alcohol Consumption			0.013*
No	63 (90.0%)	70 (100.0%)	
Yes	7 (10.0%)	0 (0.0%)	

Table 2: Dietary Factors Associated with CRC (n=140)

Dietary Factor	Cases (n=70)	Controls (n=70)	p-value
Meat Consumption			0.002*
Mean ± SD	2.9 ± 1.6	2.0 ± 1.8	
Processed Meat			<0.001*
Mean ± SD	3.0 ± 1.1	1.3 ± 1.0	
Seafood			<0.001*
Mean ± SD	2.0 ± 1.4	5.5 ± 2.8	
Fast Food			<0.001*
Mean ± SD	5.1 ± 2.4	1.9 ± 1.6	
Vegetables			<0.001*
Mean ± SD	7.0 ± 0.9	10.9 ± 3.6	
Fruits			<0.001*
Mean ± SD	3.7 ± 2.7	9.3 ± 6.5	
Milk			<0.001*
Mean ± SD	5.5 ± 2.6	7.9 ± 4.7	

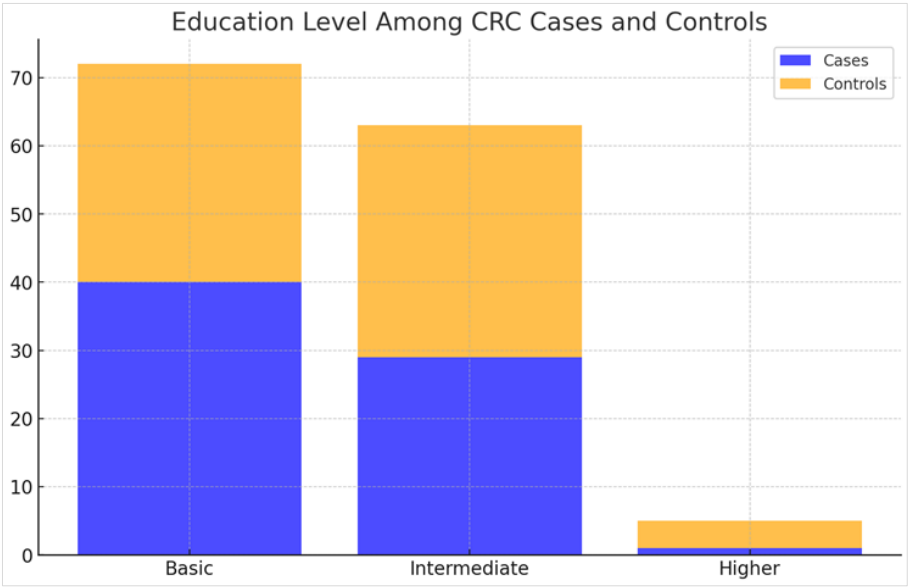

Figure 1: Education Level Among CRC Cases and Controls

Caption: Comparison of education levels between CRC cases and controls, indicating the distribution of basic, intermediate, secondary, and higher education.

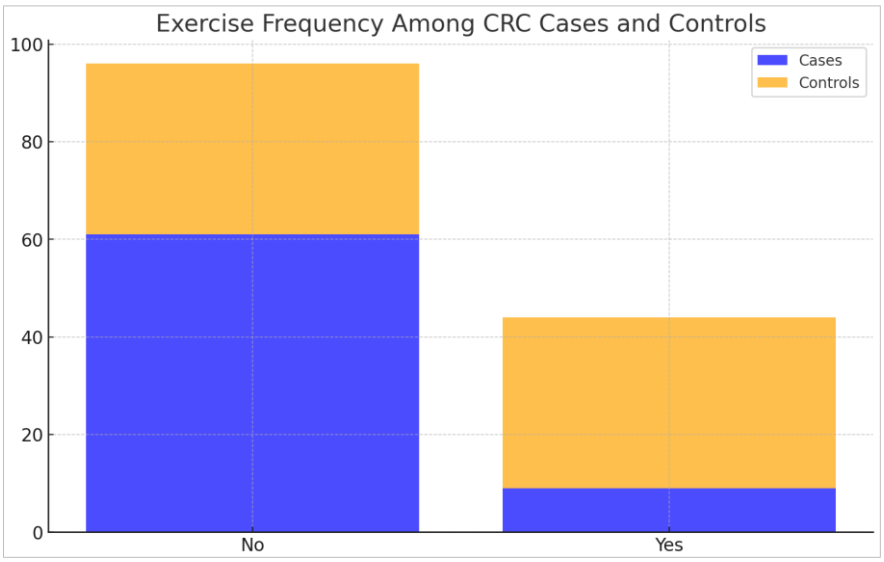

Figure 2: Exercise Frequency Among CRC Cases and Controls

Caption: Comparison of exercise habits between CRC cases and controls, demonstrating the lower frequency of exercise among CRC cases.

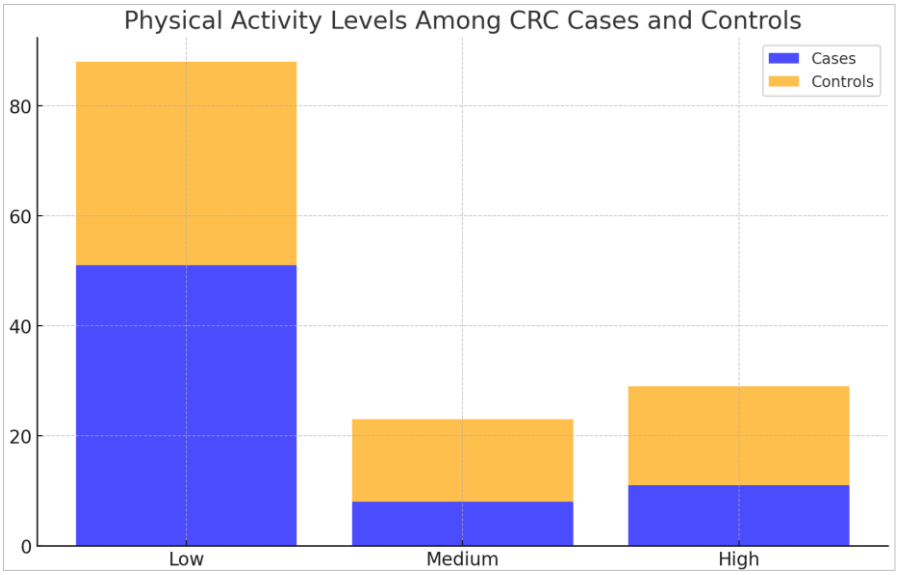

Figure 3: Physical Activity Levels Among CRC Cases and Controls

Caption: Comparison of physical activity levels (low, medium, high) between CRC cases and controls, showing lower activity levels among CRC cases.

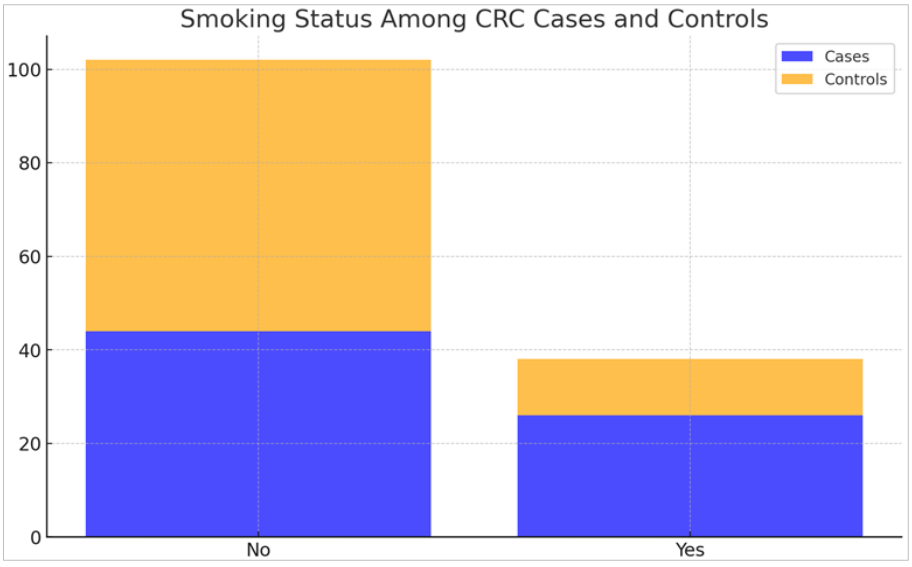

Figure 4: Smoking Status Among CRC Cases and Controls

Caption: Comparison of smoking status between CRC cases and controls, highlighting the higher proportion of smokers among CRC cases.

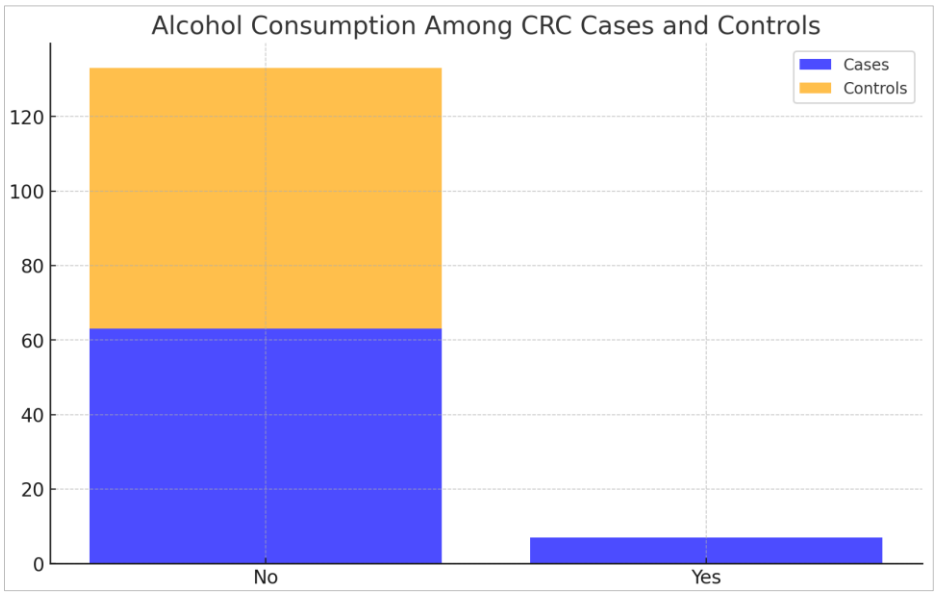

Figure 5: Alcohol Consumption Among CRC Cases and Controls

Comparison of alcohol consumption between CRC cases and controls, illustrating the presence of alcohol consumption among CRC cases and its absence in controls.

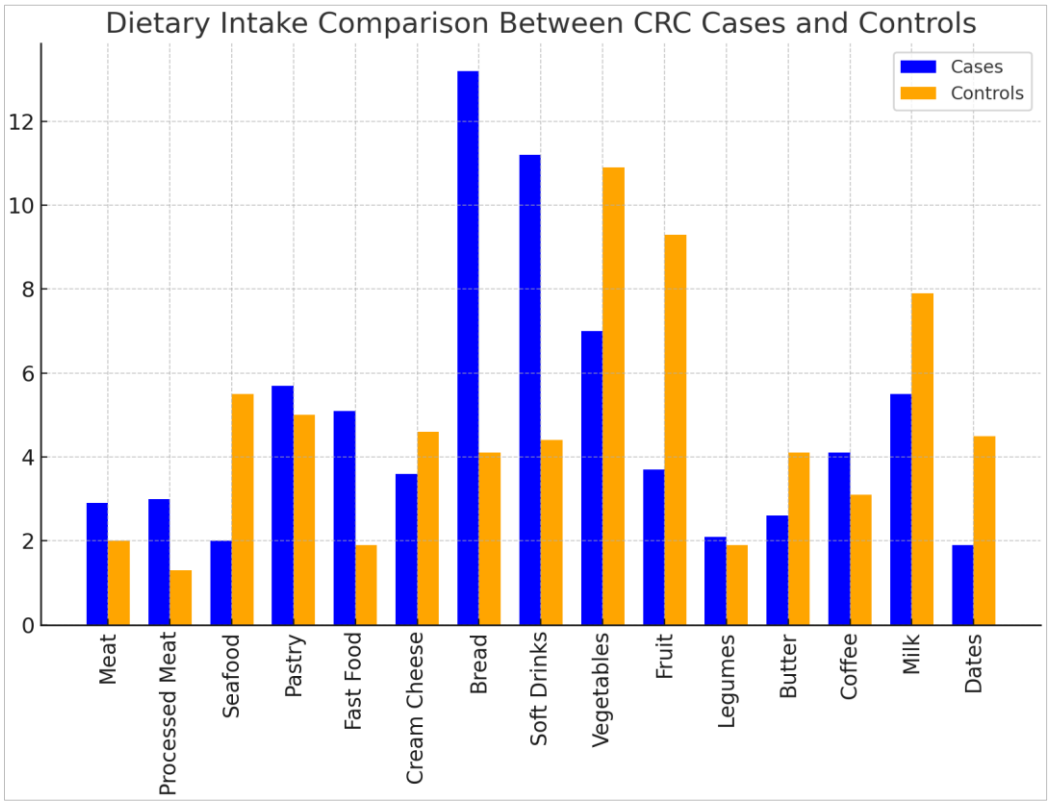

Figure 6: Dietary Intake Comparison Between CRC Cases and Controls

Comparison of dietary intake (meat, processed meat, seafood, fast food, vegetables, fruits, milk, etc.) between CRC cases and controls, showing significant differences in diet patterns.

4. Discussion

The results of this study contribute to the understanding of the relationship between various lifestyle factors and the risk of developing colorectal cancer. Principal risk factors identified include lack of physical activity, sedentariness, tobacco smoking, and alcohol intake. In addition, dietary patterns-low intake of fruits and vegetables, high intake of processed meat, and low intake of seafood-play an important role in determining the risk of CRC. Notably, seafood consumption, though more often less discussed, also influences CRC risk. Seafood in general, and especially fish high in omega-3 fatty acids, has been associated with a reduced risk of many cancers, including CRC. Omega-3 fatty acids have anti-inflammatory properties that may help offset the inflammation associated with carcinogenesis. Moreover, seafood serves as an important source of nutrients like vitamin D and selenium, which play important roles in cancer prevention. We found in our study that seafood consumption was lower for CRC cases compared to controls, indicating a diet devoid of seafood may not be able to avail these protective effects [4].

These findings are in accordance with the literature on the role of different lifestyle factors in CRC risk and may therefore encourage a healthy lifestyle behavior to reduce the burden of this disease. For instance, a detailed review by Gingras et. al and Harriss et. al. [6,10] highlights the impact of lifestyle and dietary factors on CRC susceptibility, showing that physical inactivity, obesity, and the consumption of red and processed meats are positively related to CRC, while a high intake of dietary fiber, fruits, vegetables, and seafood is inversely associated with CRC risk [1]. Dietary fiber is protective against CRC as it provides for regular passage of bowel movements, thereby reducing the time during which putative carcinogens can interact with the colonic mucosa. In addition, gut microbiota metabolize fiber to produce short-chain fatty acids such as butyrate, providing anti-inflammatory and anticancer effects that help maintain the gut at an optimal level of function. These observations are further supported by ours, as we observed higher consumption of red meat and processed meat and lower intake of vegetables, fruits, and seafood in CRC cases. Several key mechanisms drive the association between red and processed meat and the risk of CRC. Cooking red meat to high temperatures, such as grilling or frying, leads to the formation of heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), both carcinogens that can damage DNA and promote the development of cancer. Other mechanisms in processed meats include nitrates and nitrites, which the body can convert into nitrosamines - also known carcinogens. Besides that, red and processed meats encourage inflammation and oxidative stress, which are factors that contribute to cancer growth through cell proliferation and inhibition of apoptosis as well as a change in gut microbiota that favors carcinogenesis [11,12]. Adding seafood to a healthy diet might offset some of these risks, reinforcing the importance of a diverse diet rich in positive nutrients.

The link between a high BMI, diet intake, and low physical activity (PA) is crucial in understanding the overall risk of malignancies, including colorectal cancer (CRC). Diet and physical activity are both key modifiable factors that influence BMI and, subsequently, cancer risk. A diet high in processed and red meats, refined sugars, and unhealthy fats but low in fiber, fruits, and vegetables is strongly associated with obesity and an increased risk of cancer. Processed and red meats contain carcinogenic compounds formed during cooking, while a low intake of fiber and plant-based foods reduces the body's natural protective effects against cancer.

Physical inactivity compounds these risks by contributing to weight gain and obesity, which are significant factors in the development of cancer. Regular physical activity plays a protective role by helping to maintain a healthy weight, reducing inflammation, improving insulin sensitivity, and balancing hormone levels. These mechanisms collectively reduce the overall risk of cancer, highlighting the importance of both a balanced diet and regular physical activity in mitigating the risks associated with high BMI and unhealthy lifestyle choices. Together, these factors create a comprehensive approach to cancer prevention, particularly in relation to CRC.

The above associations were supported by a current review of the literature relating to low levels of physical activity with an increased risk of CRC. Reviews have emphasized the positive influence of regular PA for reducing the incidence of CRC, possibly due to mechanisms such as lowering inflammation and improving insulin sensitivity, amongst others [13-15]. There was a significantly lower level of physical activity in cases with CRC compared to their controls, indicating the protective effect of PA on CRC risk. However, further discussion is required on the amount-intensity of physical activity needed for such a protective effect to be established. Further, different intensities of PA may differently impact CRC risk, and exploration regarding whether the protection offered is more significant by moderate or vigorous activities is warranted.

Our findings, in line with Botteri et al., emphasize the importance of maintaining a healthy weight in CRC prevention. The link between obesity and various cancers underscores the need for public health strategies that promote weight management, healthy eating, and physical activity. By targeting these modifiable risk factors, it may be possible to significantly reduce the incidence of CRC and other obesity-related malignancies [16].

Several studies have reported the effect of smoking on CRC risk. For instance, Jeon et al. developed CRC risk prediction models incorporating lifestyle and environmental features as well as genetic variants, identifying smoking as a potentially critical predictor of CRC risk [17]. In our study, a higher prevalence of smoking was noted among CRC cases compared to controls. Smoking introduces carcinogenic compounds into the body, which can damage deoxyribonucleic acid (DNA), promoting mutations and the development of cancer [18]. This further underscores the importance of health campaigns aimed at reducing smoking to lessen the incidence of CRC.

The relationship between smoking and colorectal cancer (CRC) is complex and sometimes contradictory. While smoking is a well-established risk factor for cancers like lung and bladder, its link to CRC varies. Research suggests smoking may be more strongly associated with proximal colon cancer than distal colon or rectal cancer. Additionally, the duration, intensity, and time since cessation influence CRC risk, with former heavy smokers still at a higher risk compared to never-smokers, though the risk decreases after quitting[19].

Contradictory findings have also emerged in some studies that did not find a significant association between smoking and CRC risk, especially when other lifestyle factors, such as diet and physical activity, were taken into account [20]. These inconsistencies may be due to differences in study design, populations studied, and the measurement of smoking exposure. These contradictions highlight the need for continued research to better understand the specific circumstances under which smoking may or may not influence CRC risk. Nevertheless, the overall body of evidence supports smoking as a significant risk factor for many cancers, including CRC, and reinforces the need for public health initiatives focused on smoking cessation to reduce the burden of cancer overall.

Alcohol consumption has been widely recognized as a significant risk factor for colorectal cancer (CRC). In the large European cohort study, higher alcohol intake was linked to an increased risk of CRC. Our findings support this, as alcohol use was higher among cases. Alcohol damages the colon and rectum linings, promoting carcinogenesis, and its toxic metabolite, acetaldehyde, causes DNA and protein damage. Additionally, alcohol can trigger oxidative stress and inflammation, which further drive cancerous mechanisms [19-20].

The exact threshold for risky alcohol consumption varies between studies, indicating the need for further research. Nonetheless, evidence consistently suggests that reducing alcohol intake should be part of cancer prevention strategies [21,22].

In conclusion, this study confirms the major associations between lifestyle choices such as physical activity, smoking status, alcohol consumption, and dietary habits and CRC risk. Our findings are in support of previously conducted research on this topic and further confirm that the promotion of healthy lifestyle behaviors should be pursued to reduce the incidence of CRC. Public health strategies should, therefore, focus on the need for regular physical

activity, healthy weight, avoidance of smoking, limited intake of alcohol, and balanced diets with plenty of fruits and vegetables to substantially lower the risk of CRC.

5. Conclusion

These findings point to the great influence of lifestyle habits on CRC risk. Inactivity, sedentary behavior, smoking status, and alcohol intake were strongly found to have a higher risk for CRC. Poor dietary patterns, such as high processed meat consumption and low vegetable and fruit intake, were far more frequent in the cases compared with non-cases of CRC.

These findings agree with previously published literature that emphasizes the reality that modifiable lifestyle factors have much to contribute to CRC prevention. These include being active through regular exercise, staying at a healthy weight, not smoking, and not exceeding suggested limits for alcohol intake. Other than these, fruits, vegetables, and fiber-rich diet while limiting intake of red and processed meats alleviate CRC risk considerably.

Promotion of these healthy lifestyle choices warrants priority in public health strategies to most effectively reduce the incidence of CRC. Awareness campaigns and community-based interventions are undertaken to activate patients' interest in practicing healthier lifestyles. In this regard, primary care providers should, at all costs, become actively involved in counseling patients on the importance of lifestyle modifications against CRC prevention.

Study Limitations

1. **Selection Bias:** Since the controls were first-degree relatives of the CRC cases, there is a potential for selection bias. This could mean that both groups share similar genetic predispositions, confounding the observed associations between lifestyle factors and CRC risk.
2. **Recall Bias:** The study relied on self-reported data for lifestyle factors such as diet, physical activity, smoking, and alcohol consumption. This method is susceptible to recall bias, where participants may inaccurately remember or report their past behaviors, potentially leading to misclassification of exposure levels.
3. **Cross-Sectional Design:** The case-control design captures data at a single point in time, limiting the ability to establish causality or determine the temporal relationship between lifestyle factors and the development of CRC. As a result, it is unclear whether the observed lifestyle choices led to CRC or were influenced by the diagnosis.

These limitations highlight the need for cautious interpretation of the study findings and suggest that further research is necessary to validate these associations in broader populations and with more robust study designs.

List of Abbreviations

CRC: Colorectal Cancer
PA: Physical Activity
BMI: Body Mass Index
DNA: Deoxyribonucleic Acid
OR: Odds Ratio
CI: Confidence Interval
SD: Standard Deviation
HCAs: Heterocyclic Amines
PAHs: Polycyclic Aromatic Hydrocarbons
AKI: Acute Kidney Injury

Declarations

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the ethics committee of Al-Turath University, College of Pharmacy, Baghdad, Iraq. All participants provided informed consent prior to their inclusion in the study. The consent process ensured that participants were aware of the purpose, procedures, and potential risks of the study. Participation was voluntary, and confidentiality was maintained throughout.

Data Availability

The data that support the findings of this study are available from the corresponding author, Dr. Hayder G. Oufi, upon reasonable request. Due to privacy concerns, individual participant data cannot be shared publicly.

Conflicts of Interest

The authors declare that they have no conflicts of interest related to this study.

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Authors' Contributions

Ruaa E. Alabd: Conceptualization, data collection, writing - original draft preparation.
Hayder G. Oufi: Methodology, formal analysis, writing - review and editing, corresponding author.
Forat Yahya Mohsin: Investigation, data curation, interpretation of results.
Besmah M. Ali Ibrahim: Supervision, validation, writing - review and editing.

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References

[1] Murphy, N., Moreno, V., Hughes, D. J., Vodicka, L., Vodicka, P., Aglago, E. K., ... & Jenab, M. (2019). Lifestyle and dietary environmental factors in colorectal cancer susceptibility. *Mechanisms of Ageing and Development*, 185, 111-121. https://doi.org/10.1016/j.mam.2019.06.005

[2] Harriss, D. J., Atkinson, G., George, K., Cable, T. N., Reilly, T., Haboubi, N., ... & Renehan, A. G. (2009). Lifestyle factors and colorectal cancer risk (1): systematic review and meta-analysis of associations with body mass index. *Colorectal Disease*, 11(6), 547-563. https://doi.org/10.1111/j.1463-1318.2009.01766.x

[3] Jeon, J., Du, M., Schoen, R. E., Hoffmeister, M., Newcomb, P. A., Berndt, S. I., ... & Hsu, L. (2018). Determining Risk of Colorectal Cancer and Starting Age of Screening Based on Lifestyle, Environmental, and Genetic Factors. *Gastroenterology*, 154(3), 513-525. https://doi.org/10.1053/j.gastro.2018.02.021

[4] Aglago, E. K., Huybrechts, I., Murphy, N., Casagrande, C., Nicolas, G., Pischon, T., ... & Gunter, M. J. (2020). Consumption of fish and long-chain n-3 polyunsaturated fatty acids is associated with reduced risk of colorectal cancer in a large European cohort. *Clinical Gastroenterology and Hepatology*, *18*(3), 654-666.

[5] Green, J., Cairns, B. J., Casabonne, D., Wright, F. L., Reeves, G., Beral, V., & Million Women Study Collaborators. (2012). Height and cancer incidence in the Million Women Study: prospective cohort, and meta-analysis of prospective studies of height and total cancer risk. *The Lancet Oncology*, 13(8), 785-794. https://doi.org/10.1016/S1470-2045(12)70254-1

[6] Gingras, D., & Béliveau, R. (2011). Colorectal cancer prevention through dietary and lifestyle modifications. *Cancer microenvironment*, *4*, 133-139. Lichtenstein, P., Holm, N. V., Verkasalo, P. K., Iliadou, A., Kaprio, J., Koskenvuo, M., ... & Hemminki, K. (2000). Environmental and heritable factors in the causation of cancer--analyses of cohorts of twins from Sweden, Denmark, and Finland. *New England Journal of Medicine*, 343(2), 78-85. https://doi.org/10.1056/NEJM200007133430201

[7] Renehan, A. G., Tyson, M., Egger, M., Heller, R. F., & Zwahlen, M. (2008). Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *The Lancet*, 371(9612), 569-578. https://doi.org/10.1016/S0140-6736(08)60269-X

[8] Wolin, K. Y., Yan, Y., Colditz, G. A., & Lee, I. M. (2009). Physical activity and colon cancer prevention: a meta-analysis. *British Journal of Cancer*, 100(4), 611-616. https://doi.org/10.1038/sj.bjc.6604917

[9] Murphy, N., Moreno, V., Hughes, D. J., Vodicka, L., Vodicka, P., Aglago, E. K., ... & Jenab, M. (2019). Lifestyle and dietary environmental factors in colorectal cancer susceptibility. Mechanisms of Ageing and Development, 185, 111-121. https://doi.org/10.1016/j.mam.2019.06.005

[10] Harriss, D. J., Atkinson, G., George, K., Cable, T. N., Reilly, T., Haboubi, N., ... & Renehan, A. G. (2009). Lifestyle factors and colorectal cancer risk (1): systematic review and meta-analysis of associations with body mass index. Colorectal Disease, 11(6), 547-563. https://doi.org/10.1111/j.1463-1318.2009.01766.x

[11] Cross, A. J., & Sinha, R. (2004). Meat-related mutagens/carcinogens in the etiology of colorectal cancer. Environmental and Molecular Mutagenesis, 44(1), 44-55.

[12] Bouvard, V., Loomis, D., Guyton, K. Z., Grosse, Y., Ghissassi, F. E., Benbrahim-Tallaa, L., ... & Straif, K. (2015). Carcinogenicity of consumption of red and processed meat. The Lancet Oncology, 16(16), 1599-1600.

[13] Jeon, J., Du, M., Schoen, R. E., Hoffmeister, M., Newcomb, P. A., Berndt, S. I., ... & Hsu, L. (2018). Determining Risk of Colorectal Cancer and Starting Age of Screening Based on Lifestyle, Environmental, and Genetic Factors. Gastroenterology, 154(3), 513-525. https://doi.org/10.1053/j.gastro.2018.02.021

[14] Aleksandrova, K., Pischon, T., Jenab, M., Bueno-de-Mesquita, H. B., Fedirko, V., Norat, T., ... & Boeing, H. (2014). Combined impact of healthy lifestyle factors on colorectal cancer: a large European cohort study. BMC Medicine, 12(1), 168. https://doi.org/10.1186/s12916-014-0168-4

[15] Song, M., Chan, A. T., & Sun, J. (2020). Influence of the gut microbiome, diet, and environment on risk of colorectal cancer. Gastroenterology, 158(2), 322-340.

[16] Botteri, E., Borroni, E., Sloan, E. K., Bagnardi, V., Bosetti, C., Peveri, G., ... & Lugo, A. (2020). Smoking and colorectal cancer risk, overall and by molecular subtypes: a meta-analysis. *Official journal of the American College of Gastroenterology| ACG*, *115*(12), 1940-1949.

[17] Johnson, C. M., Wei, C., Ensor, J. E., Smolenski, D. J., Amos, C. I., Levin, B., & Berry, D. A. (2013). Meta-analyses of colorectal cancer risk factors. Cancer causes & control, 24, 1207-1222.

[18] Irigaray, P., Newby, J. A., Clapp, R., Hardell, L., Howard, V., Montagnier, L., ... & Belpomme, D. (2007). Lifestyle-related factors and environmental agents causing cancer: an overview. *Biomedicine & Pharmacotherapy*, *61*(10), 640-658.

[19] Tsoi, K. K., Pau, C. Y., Wu, W. K., Chan, F. K., Griffiths, S., & Sung, J. J. (2009). Cigarette smoking and the risk of colorectal cancer: a meta-analysis of prospective cohort studies. *Clinical Gastroenterology and Hepatology*, *7*(6), 682-688.

[20] Rossi, M., Jahanzaib Anwar, M., Usman, A., Keshavarzian, A., & Bishehsari, F. (2018). Colorectal cancer and alcohol consumption—populations to molecules. *Cancers*, *10*(2), 38.

[21] Klarich, D. S., Brasser, S. M., & Hong, M. Y. (2015). Moderate alcohol consumption and colorectal cancer risk. *Alcoholism: Clinical and Experimental Research*, *39*(8), 1280-1291.

[22] Tuan, J., & Chen, Y. X. (2016). Dietary and lifestyle factors associated with colorectal cancer risk and interactions with microbiota: fiber, red or processed meat and alcoholic drinks. *Gastrointestinal tumors*, *3*(1), 17-24.