Western Diet and its Effect on Colon Cancer

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The rise in colon cancer incidence overall and more so in the younger population is concerning among the western world. Diet plays an important role in gut health and the Western diet and associated lifestyles are being adopted worldwide due to globalization. This article aims to provide an updated review of the effects of Western diet on colon cancer. Dietary habits vary based on geography, climate and culture. The cross talk of Western dietary components and genetics and gut health has been the focus of this study to further our understanding. Through search engines, appropriate articles published on Western diet and colon cancer among both developed and developing nations have been reviewed. Gut microbiome and the role of fiber in colon cancer development have been highlighted through available evidence. Through this article the reader will hopefully gain understanding to consider making appropriate dietary and lifestyle adjustments to reduce colon cancer risk. Keywords: Western Diet; Colon Cancer; Processed Foods; Sedentary Lifestyle; Diet; Fiber; Fat; Gut Microbiome; Genetics

Introduction

Colorectal cancer is the third most prevalent cancer globally, and ranks second among cancer-related mortality worldwide. It accounts for about 10% of all existing cancer cases [1]. In 2022, over 1.9 million cases of colon cancer were diagnosed globally [2]. In the U.S., colon cancer is the second most common cause of cancer-related mortality [3]. Approximately 107,320 cases of colon cancer are anticipated to be diagnosed in 2025 with 52,900 mortalities expected in the U.S. [3]. Recent studies show colon cancer as the leading cause of cancer-related mortality among men under the age of 50 along with an increasing trend in incidence [4]. Colorectal carcinogenesis, the development of colorectal cancer, is a multifaceted process influenced by both genetic and environmental factors [5].

Methodology

A comprehensive search strategy was executed across multiple electronic databases to identify relevant studies. The databases searched included: PubMed, Google Scholar, and the Multidisciplinary Digital Publishing Institute (MDPI). The search was conducted including articles from 1992 to 2024. Only articles published in English were considered. The following search string was used: (”Western Diet” OR ”Processed Foods” OR ”Sedentary Lifestyle” OR Diet OR Fiber OR Fat OR ”Gut Microbiome” OR Genetics) AND (”Colon Cancer” OR ”Colorectal Cancer”). Additionally, reference lists of included studies were hand-searched for potentially relevant articles not found by database searches.

Development and Mechanisms of Colon Cancer

The development of colon cancer is dependent on the mutations of specific genes, including KRAS, BRAF, APC, and TP53. KRAS and BRAF, known as protooncogenes and tumor suppressors, promote cellular growth, while APC and TP53, acting as tumor suppressors, regulate cellular growth and proliferation within colon cells [6]. A major contributor to sporadic colorectal cancers is mutations in the APC gene, a tumor suppressor. This gene normally regulates the Wnt signaling pathway by controlling levels of -catenin, which in turn influences inflammatory, cell cycle, and proliferative pathways. When APC is mutated, -catenin accumulates, leading to uncontrolled cell growth and polyp formation [5]. Apoptosis is a programmed cell death where certain genes such as K-RAS cause the cell to break down molecularly in steps. Mutations of the K-RAS gene result in dysfunctional apoptosis, promoting cancer growth [7]. Figure 1 shows the development of colon cancer and the stages at which each protooncogene and tumor suppressor are involved in each stage [8]. When a colon cell transitions to an early adenoma, the APC gene is normally mutated. Once the K-RAS and B-RAF genes are mutated, the early adenoma transforms into a late adenoma. The late adenoma can transition into a carcinoma through additional gene mutations involving p53 signalling [8]. Figure 1 illustrates the stages of cancer development. In the first stage, a single gene mutation leads to increased cellular growth, resulting in the formation of an early adenoma. Subsequent gene mutations cause further cellular abnormalities, leading to the development of a late adenoma. Finally, additional gene mutations can transform the late adenoma into a carcinoma, or the malignant stage of cancer [8].

The connection between gene regulation and colorectal can-

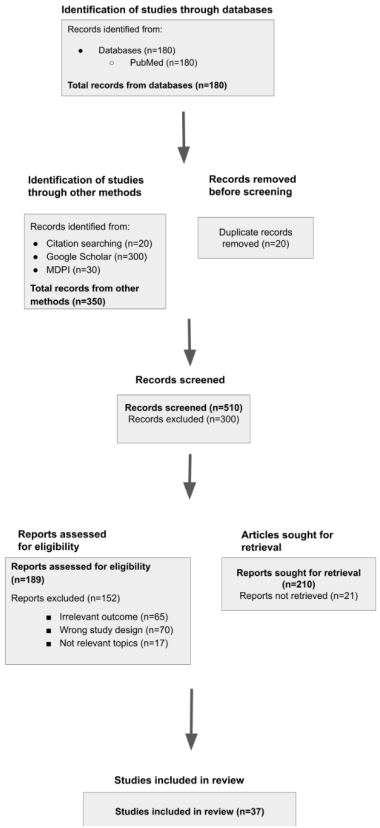

Fig. 1

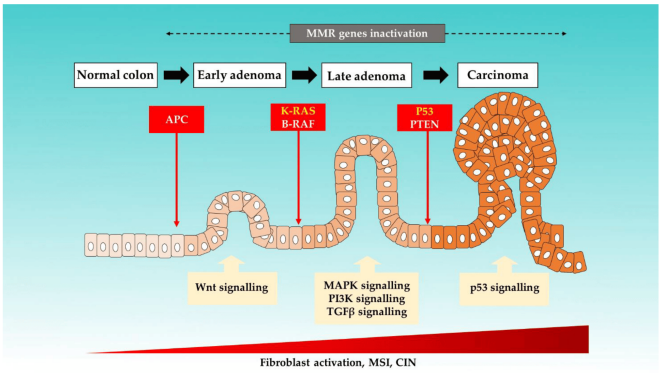

Fig. 2

cer (CRC) has gained significant attention, with several nutrients influencing gene expression through mechanisms like transcription factor binding and post-translational modifications such as acetylation and methylation. Diets high in red and processed meats can promote intestinal carcinogenesis via epigenetic modifications, as evidenced by a high red meat diet activating the Nucleosome Remodeling and Deacetylase complex, which is involved in methylation-mediated gene silencing[9]. Western dietary patterns are associated with an increased risk of CRC, particularly distal colon and rectal tumors. Western dietary patterns also appear more strongly associated with tumors that are KRAS wildtype, BRAF wildtype, have no or a low CpG island methylator phenotype, and microsatellite stability[10].

Dietary Factors

The Western diet started following the Industrial Revolution and is characterized by high fat content, low fiber, high carbohydrate consumption, processed meats, additives, excessive sugar intake, and unhealthy beverages as shown in Figure 3[11].

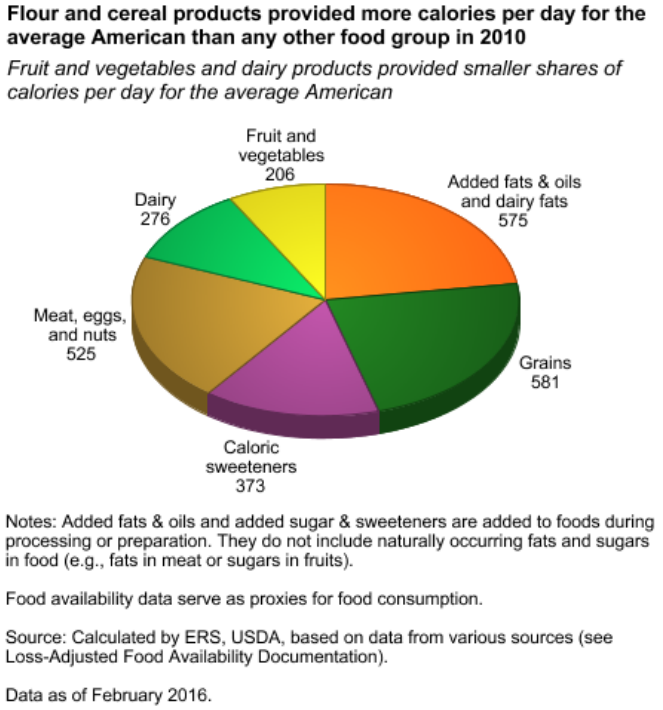

Fig. 3

Figure 3 The chart shows the total calorie consumption per food category within an American diet. Fats and oils compose approximately 25% of the daily caloric intake, providing 575 calories. Meat, eggs, and nuts provide 525 calories, whole grain products provide 581 calories. In contrast, fruits and vegetables contribute only 206 calories, and dairy products provide 276 calories. The data in this chart comes from the USDAs Loss-Adjusted Food Availability (LAFA) data. This data is an enhanced version of raw food supply data that provides a more realistic estimate of per capita food consumption in the U.S. Unlike basic availability figures, LAFA accounts for inedible portions, spoilage, and consumer waste, offering a refined measure of the edible food actually available for intake[11].

Fats

Diets high in saturated fats, trans fats, and cholesterol have been directly associated with an increased incidence of colon cancer [12]. Fats are a class of nutrients essential for the bodys energy metabolism, nerve tissue, and hormones. The three primary types of fats are saturated, unsaturated, and trans fats. High-fat diets promote colon cancer by altering bile acid metabolism and impacting the gut microbiota. Excess dietary fat increases bile acid synthesis and these bile acids are then modified by gut bacteria, leading to a shift in their composition. This is observed in populations with higher CRC rates, who consume high-fat diets and have different bile acid profiles. Secondary bile acids stimulate CRC cell proliferation through various signaling pathways, including catenin, ERK1/2, AP1, c-Myc, and NF-B. The farnesoid X receptor (FXR) signaling pathway is also crucial. FXR deficiency, often seen in precancerous lesions and CRC, promotes colonic epithelial cell proliferation, and high-fat diets can disrupt FXR activity [13]. A recent study investigated the link between a high-fat Western diet (HFWD), obesity, and human colon cancer growth using mice. They wanted to see if insulin resistance induced by the HFWD would accelerate tumor growth. Mice were fed either an HFWD or a low-fat Western diet (LFWD), and human colon cancer xenografts were implanted subcutaneously or orthotopically. The HFWD successfully induced obesity and insulin resistance in the mice, leading to significantly increased tumor weight in the HT-29 xenograft models compared to the LFWD group. The study revealed that the HFWD-fed mice with HT-29 tumors had higher body weight, plasma glucose, and serum leptin, alongside increased insulin resistance. Molecular analysis of these tumors indicated elevated c-Jun N-terminal kinase (JNK) activation and increased monocyte chemoattractant protein 1 (MCP1) expression in adipose tissue, along with a reduction in apoptosis markers in tumors from the HFWD group. Surprisingly, a negative correlation was observed between leptin levels and tumor size. Overall, the study concluded that obesity and its metabolic consequences, driven by an HFWD, accelerate human colon cancer growth by influencing various cellular signaling pathways and inflammatory responses [14]. However, the influence of fat consumption on colon cancer risk includes controversy in animal models. The role of dietary fat is not straightforward. Some studies suggest that the type of fat rather than the amount is important. Some reviews of animal studies have indicated that high-fat diets containing certain types of fats such as coconut oil, olive oil, or fish oil had no colon tumor-enhancing effect compared to lower-fat diets in rats [15].

Sugars

Sugary beverages such as soda are extremely popular in the Western diet and make up almost half of the total sugar intake, accounting to more than 13% daily calorie intake [16]. High levels of sucrose, a type of sugar, have been associated with an elevated risk of colon cancer primarily by increasing plasma glucose levels which has been shown to have a positive effect in tumor growth [16]. In a 3-week study investigating the effects of a sucrose-rich diet on rats found that while food intake, energy intake, carbohydrate intake, weight gain, and final body weight remained similar between the control and experimental groups, significant changes were observed in the colon. The researchers concluded that a sucrose-rich diet led to mutations in the rat colon epithelium. This was accompanied by a decrease in colon I-compounds, a finding that was inversely correlated with the observed increase in mutations. Notably, the study did not find any significant effects of sugar on the liver. The authors also noted that the relatively short 3-week feeding period might have masked some details, suggesting longer studies could reveal further effects [12].Although many studies explore mechanisms through which sugar may promote cancer, rat studies directly demonstrating a lack of such influence are less highlighted. Another chemical commonly found in ultra-processed products is high fructose corn syrup (HFCS) [12]. HFCS serves as an artificial sweetener in both carbonated and non-carbonated beverages as well as processed foods. Furthermore, HFCS is utilized in preservation, reducing freezing points, retaining moisture, enhancing flavors, and facilitating fermentation. HFCS is typically a combination of fructose and glucose, usually in a ratio of 11:9 respectively. High-fructose corn syrup (HFCS) is a significant contributor to obesity in the United States, leading to substantial increases in body weight, blood sugar levels, and increasing the risk of sugar-related diseases such as diabetes mellitus.

Red Meat

Heme iron, which is abundant in red meat, is converted into cytotoxic heme factor (CHF) in the colon, damaging epithelial cells and promoting their excessive growth. This damage is worsened by reactive oxygen species (ROS) produced by heme iron, which oxidizes DNA, lipids, and proteins. Heme also inhibits colonocyte apoptosis, further contributing to carcinogenesis [17]. Heme, present in red meat, can suppress genes like Wif1 and BMP2 (which normally antagonize Wnt signaling and promote cell differentiation) and bind to transcription factors such as Bach1, leading to histone deacetylation and repression of p53 target genes involved in cellular senescence, also affecting chromosome alignment during mitosis [9]. Heme iron increases the production of N-nitroso compounds (NOCs). Nitrosamines, synthesized by the intestinal microbiota from the nitrites, are particularly active carcinogenic compounds [17]. Research in rat models shows that dietary heme increases colonic cytotoxicity. In a study investigating the effects of a heme diet on colonic epithelial cells, five sets of rats were maintained on purified diets for a period of 14 days. Following this dietary routine, the rats were euthanized through CO2 suffocation after a 2-hour

interval. The colons were then removed, opened longitudinally, and their contents removed by rinsing with 154 mM KCl. The colonic mucosa was carefully scraped off, homogenized in 1 ml of 154 mM KCl, and the resulting scrapings were analyzed. To assess for cytotoxic substances, fecal water was prepared by reconstituting freeze-dried feces with double-distilled water to a 30% dry weight, revealing a high level of cytotoxicity. Given the sensitivity of the colonic epithelium to diet-induced luminal changes, the proliferation of colonic epithelial cells was analyzed. The results indicated that a heme diet significantly increased cell proliferation compared to a control diet, while other dietary treatments had no notable effect on proliferation. Notably, DNA and protein content remained consistent across all experimental groups[17]. This effect was observed regardless of fat intake, although it was less pronounced in rats on a low-fat diet. Furthermore, dietary heme was found to boost colonic epithelial proliferation across fat levels, increasing the rate of colon cell division. Although many studies argue that there may be a correlation between the consumption of red meat, sugar, and fat and the incidence of colon cancer, others argue the opposite. For instance, some rat studies suggest that the preparation of red meat, rather than the meat itself, may be more influential in colon carcinogenesis. High-temperature cooking methods can generate carcinogenic heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), which are compounds known to damage DNA and potentially contribute to carcinogenesis. However, one study in rats found that a diet containing beef did not promote the growth of early markers of colon cancer and a bacon-based diet appeared to protect against carcinogenesis[18].

Processed and Ultra processed Items and Cooking style

The Western diet contains an excessive amount of processed and ultra-processed items.

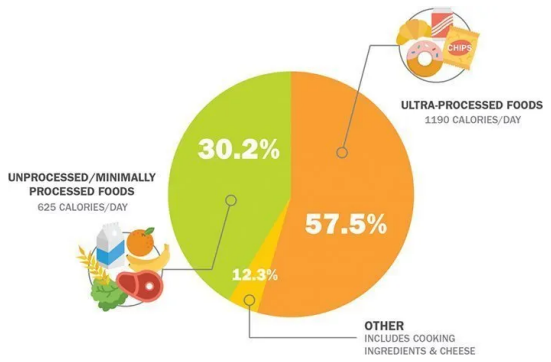

Fig. 4

The chart shows an estimate of the portions of each product in the Western diet as extracted from NHANES 2009-2010[19]. More than half of the products consumed in one day are ultra-processed and processed foods. These foods make up the bulk of the Western diet and include foods such as cereals, chips, and meat products. Less than a third of the daily diet is composed of unprocessed or minimally processed items, including milk, fruits, and vegetables. 12.3% of the daily items consumed in the Western diet includes cooking ingredients such as baking soda.

Figure 4 shows the estimated daily content of an Americans diet. About 57.5% of all foods consumed in a day are either processed or ultra-processed items while 30.2% are unprocessed or minimally processed foods. Only 12.3% includes natural products and home-cooked items[19]. Ultra-processed foods contain harmful substances that may increase the risk of colon cancer. For example, titanium dioxide, a chemical that was commonly found in Skittles, has been linked to cancer in multiple animal studies[20]. Western diet preparation style, such as grilling and smoking food along with eating preservative-rich packaged foods, promotes a higher risk of colon cancer by increasing exposure to carcinogens[21]. Smoked foods, such as barbecued meats, increase the intake of carcinogens, particularly black carbon. The packaging and storage of food also contribute to the risk of colon cancer. The primary packaging chemicals associated with colon cancer are nitrites and nitrates. These chemicals are commonly found in the preservatives used in meat, poultry, fish, and certain dairy products[22].

Other Risk Factors and Colon Cancer

The Western diet has been linked to other diseases such as stroke, heart disease, extreme obesity, and type 2 diabetes likely due to pro-inflammatory activity. The American Diabetes Association reports that approximately 1.2 million cases of diabetes mellitus are diagnosed annually[23]. Diabetes mellitus has been commonly associated with the rising obesity rates along with colon cancer in the U.S. In a prospective study by Yin Cao , young adults who consumed sugar-sweetened beverages were diagnosed with higher risk of early onset colon cancer[24]. Similarly in a study at MD Anderson on mutated mice without obesity or metabolic syndrome fed on HFCS led to rapid and large tumor development. The human small intestine lacks the ability to fully absorb all the sugars present in HFCS.

Consequently, the remaining sugars are pushed to the colon and large intestine. The glucose is absorbed by blood vessels, and fructose is directly absorbed into the colon. Once within existing tumor cells, these sugars start a process known as lipid synthesis, contributing to tumor growth[25]. However, its important to acknowledge that a sedentary lifestyle is another significant factor associated with the Western diet and the development of colon cancer. Obese individuals, who often face limitations in physical activity due to their weight, tend to adopt sedentary lifestyles. This combination of obesity and sedentary behavior has been linked to an elevated risk of colon cancer. Physical inactivity can indirectly lead to the accumulation of potential

carcinogens in the body. Physical inactivity reduces the bodys natural ability to eliminate carcinogens and slows metabolism, decreases the number of carcinogenic materials excreted from the body, and raises the risk of colorectal cancer[26]. This could possibly be one of the factors contributing towards the increasing incidence of colon cancer among rural areas in the U.S. due to the adoption of sedentary lifestyles despite access to naturally harvested foods and lower prevalence of consuming harmful preservatives and excessive processed foods[25].

Processed and fortified meats and grains, often with added sugars, can contribute to central obesity due to the rapid absorption of sugar and fats into the body. Central obesity thereby triggers chronic inflammation in the visceral fat by releasing inflammatory chemicals which promote cell growth and DNA damage, leading to the development of colon cancer[27]. Another theory is that obesity increases the insulin levels in the body along with other related hormones, potentially causing colon cancer[28].

Numerous case-control studies conducted in Siberia and Greece have established a correlation between elevated sodium intakes and colon cancer. However, studies conducted in Australia and Japan failed to discover any significant association between sodium intake and colon cancer. Conversely, a cross-sectional study in Oman found that the participants eating food high in salt had an increased risk factor for stomach and colon cancer[29]. Notably, urban environments tend to have higher sodium consumption due to the higher prevalence of processed foods. To further explore the effects of processed foods on gut health, researchers in a laboratory study conducted on animals observed that food preservatives and emulsifiers significantly impacted the gut microbiome ecosystem in mice. Common dietary emulsifiers prevalent in the Western diet include lecithin, carrageenan, glycerol monostearate, xanthan gum, and guar gum. Scientists at Georgia State University administered mice low quantities of these emulsifiers. They observed that mice fed on emulsifiers exhibited an altered gut microbiota ecosystem and a diminished mucus lining within the colon. This mucus layer plays a crucial role in preventing harmful acids and substances present in the digestive tract from damaging the colon. However, dietary emulsifiers reduced the mucus layer of the colon in mice, leading to inflammation. This inflammation subsequently increases the risk of cancer by causing genetic mutations over extended periods[30].

According to the latest World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) report on diet, nutrition, physical activity, and CRC from 2018, there is strong evidence for a protective effect of whole grains, dietary fibre, dairy products, and calcium intake and a detrimental effect of processed and red meat and alcohol consumption on CRC incidence[31]. The Spanish cohort of the European Prospective Investigation into Cancer and Nutrition study showed the association between adherence to Western, Prudent and Mediterranean diets and colorectal cancer risk. They saw detrimental effects of Western diet for rectal cancer among females and protective effect of Mediterranean diet against distal colon cancer among males and no effect with Prudent diet in first 10 year follow up[32].

Dietary Patterns and Colon Cancer

Western dietary patterns are associated with an increased risk of CRC, particularly distal colon and rectal tumors. Western dietary patterns also appear more strongly associated with tumors that are KRAS wildtype, BRAF wildtype, have no or a low CpG island methylator phenotype, and microsatellite stability. In contrast, prudent dietary patterns are associated with a lower risk of CRC that does not vary according to anatomic subsite or molecular subtype. Since dietary patterns vary across regions, the difference in the quality of diet consumed would be interesting to explore, especially between higher and lesser developed countries as showcased using AHEI dietary quality index below in Figure 5[33].

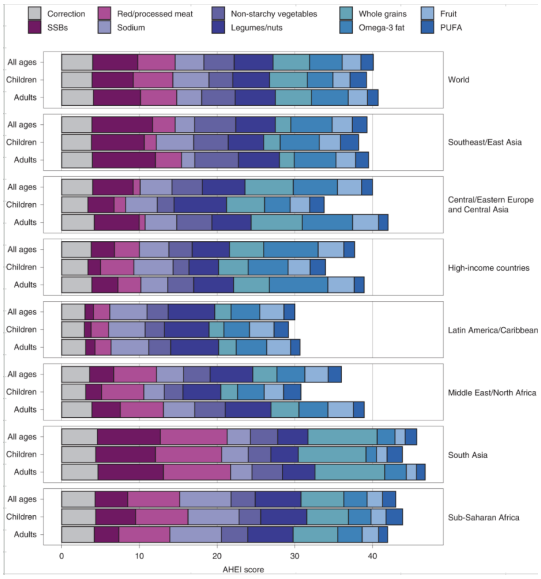

Fig. 5

Figure 5 shows the (AHEI) scores for Southeast/East Asia, Central/Eastern Europe, Latin America/Carribean. High Income countries, Middle East/ North Africa, South Asia, and Sub-Saharan Africa. The AHEI scoring is a system used to measure dietary quality with higher scores representing a healthier diet. The range for AHEI scoring is 0 to 110 with 110 indicating perfect adherence to healthy dietary recommendations. Figure 5 shows South Asia and Sub-Saharan Africa to have the highest scores compared to the rest of the regions shown. In particular, these two lesser developed regions have a higher AHEI score than high income countries and higher industrialized regions

such as Southeast/East Asia[33]. In the nested case control study from EPIC-Italy cohort the Protective effects against CRC was seen with the Mediterranean diet, mediated by DNA methylation of RUNX3. Other nutrients like n-3 polyunsaturated fatty acids, fibers (directly or via SCFAs), polyphenols, vitamins, and minerals also offer protection through methylation of apoptosis-related genes[34].

Surprisingly, when we look at the Age-Standardized Rates of colon cancer in the world from Figure 6, and AHEI dietary quality index below in Figure 6, there seems to be higher colon cancer rates among regions of lower dietary quality index pointing to potential areas for further exploration in local diet quality[25,33].

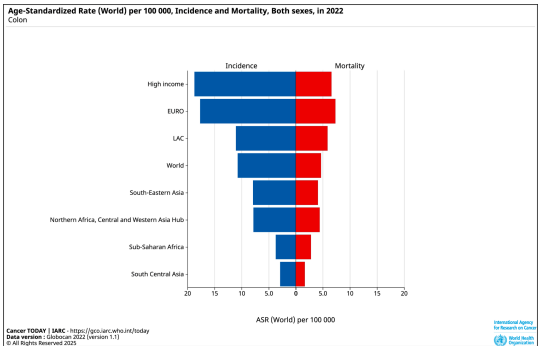

Fig. 6

Figure 6 shows the Age-Standardized Rates for High Income countries, Europe (EURO), Latin America and the Caribbean (LAC), South-Eastern Asia, South Central Asia, Sub-Saharan Africa, Northern Africa, Central and Western Asia Hub, and the world. It shows that high income countries have the highest incidence of colon cancer with an ASR of 18.7 with Europe, LAC, and the world following after. It is also observed that South Central Asia, which includes India, Bhutan, and Nepal, has the lowest incidence and mortality rates for colon cancer with an incidence of 2.9. SubSaharan Africa follows after with an ASR incidence of 3.7. South-Eastern Asia and Northern Africa, Central and Western Asia Hub have similar rates for incidence[35].

Many African countries have diets composed of staple grains like corn, rice, or sorghum, varieties of vegetables and fruits, and a significant portion of legumes. Other developing countries such as Nepal and Bhutan have similar diets with dishes consisting of rice as a staple grain mixed with vegetables and dairy products. Many of these countries' diets are deficient in essential vitamins and minerals showing the similarity in diet among the developing countries[36–38].

Interestingly, colon cancer incidence is relatively low in developing countries like Africa, which researchers attribute to the prevalent habit of low-fat, high-fiber diet consumption due to its property to increase the excretion of toxic wastes and potential carcinogens and its protective antioxidative effects[16,39–41].

What are the Effects of Fiber on Colon Cancer?

Fiber, a type of carbohydrate exclusively found in plant-based foods as cellulose, hemicellulose, or pectin, is indigestible to the human body. Fiber can either be soluble or insoluble. Soluble fibers ferment faster than insoluble ones. Insoluble fibers are more beneficial in terms of colon cancer as they add more to fecal bulk, promoting healthy, faster bowel movements and limited contact with the colon. Both types of fibers are found in grains and vegetables such as wheat and seeds. Fiber offers a wide range of health benefits, including aiding digestion, promoting weight loss, stabilizing blood sugar and cholesterol levels, and fostering the growth of beneficial bacteria or probiotics[42]. Fibers found in vegetables contain antioxidants, promoting reduced cellular damage and lowered risk of colon cancer[43]. It was found that there was a 40% CRC risk reduction with the highest fiber intake, a finding further supported by the NIH-AARP Diet and Health Study, which showed a 16% lower CRC risk for those consuming the most whole grains. This latter study suggests that the protective effect is likely due to other constituents within whole grains (e.g., folate), rather than just the fiber content itself. However, the chemoprotective effect of fibers may vary with food source and the location of the colon[44]. Despite strong evidence from epidemiological, basic science, and animal studies, human study results remain conflicting and largely inconclusive[45].

Several mechanisms explain how dietary fiber reduces CRC risk. Non-fermentable fiber can dilute carcinogens in stool. Fermentation of fiber by gut microbiota reduces fecal pH, which in turn decreases the production of bacterial carcinogens from bile acid metabolism and shortens intestinal transit time, limiting carcinogen exposure. Patients with CRC typically exhibit a higher large bowel intraluminal pH[34]. Fiber also brings more health benefits by undergoing processes such as bile acid interaction. Bile acid interaction is a metabolic process in which fibers bind to bile acids, reducing their harmful effects and lowering the absorption of cholesterol. The fermentation of fiber by the gut bacteria produces short-chain fatty acids (SCFAs) like butyrate and acetate which reduces colon cancer risk by promoting healthy cellular proliferation. Butyrate, a key energy source for normal colonocytes, exhibits protective effects. It possesses anti-inflammatory properties, reduces proliferation, increases differentiation, and induces apoptosis in CRC cells, acting as a histone deacetylase inhibitor and activating the Fas receptor-mediated death pathway. Butyrate also promotes colonocyte apoptosis through the production of reactive oxygen species[34].

Interestingly, butyrate has differential effects on normal and cancerous colon cells: it promotes proliferation and growth in normal cells while arresting growth and inducing differentiation in cancer cells. Butyrate can also modulate micro-RNAs,

specifically reducing the expression of the MYC oncogene and subsequently the miRNA-17-92 cluster, which are involved in cellular proliferation, metastasis, and angiogenesis. Recent attention has focused on how different fiber types modulate microbiota composition and SCFA production[45]. Stephen OKeefe in his study pointed out the possible influence of the diet on the composition of microbiota and metabolic activity to higher risk of colon cancer in African Americans than in Native Africans by comparing the stool of age-sex matched Native Africans with African Americans and measured the differences in colon microbes and their metabolites. His study showed that the total bacteria and major butyrate-producing groups along with higher SCFAs were higher in Native Africans as compared to African Americans[46]. The effects of acetate are still being researched but the known effects on colon cancer are very minimal and insignificant. Propionate is more potent than acetate and has effects such as inhibiting cell growth and increasing apoptosis rates. Unfortunately, fiber is not a major component of the typical Western diet. Given that processed foods compose the majority of the Western diet, fiber intake is significantly reduced due to how it is stripped during food processing[16]. Fiber also takes part in microbiota modulation. Growth of beneficial bacteria is increased with the consumption of fiber, enhancing gut health while also lowering the amount of harmful bacteria as fiber is the primary food source of beneficial bacteria in the microbiome.

Gut Microbiome and Colon Cancer

The gut microbiota also plays a crucial role in colon cancer development. Disturbances in its composition, often by diet, can cause genetic alterations. On the other hand, beneficial microbial fermentation products, such as butyrate, and microbially-activated phytochemicals like polyphenols, exhibit antineoplastic effects. These compounds can counteract tumorigenic signaling pathways and activate epigenetic mechanisms, such as histone deacetylase inhibition, which promote apoptosis, suppress cell proliferation, and stop the progression of neoplastic transformation[5].

In our current understanding diet, gut microbiome and host genetics govern the human metabolome or health. Experimental studies in mice have demonstrated that a high fat diet stimulates intestinal stem cell numbers and promotes dysplasia and tumor development. Farnesoid X receptor signaling and oncogene mutations mediated by gut microbiota and bile acid and genotoxic E coli have been documented. High corn syrup enhanced intestinal tumor growth in mutant mice as well. Also the opposite effect of anti tumor and decrease in size of tumor with high fiber diet in mouse model has been shown through gut microbiome modification. The PREDICT trial shows that Western diet promotes decrease in density of gut microbiota leading to rise in systemic low-grade inflammation and chronic diseases[47].

The gut microbiota significantly influences colorectal cancer (CRC) development through various mechanisms. Microbes can produce toxic or carcinogenic metabolites, or their metabolic byproducts, like lactate, can indirectly fuel CRC cell growth. Bacterial toxins, such as those from Bacteroides fragilis, Fusobacterium nucleatum, and Escherichia coli, play a central role by activating pathways like -catenin signaling, cleaving E-cadherin, and inducing the NF-B pathway. While some bacterial metabolites like short-chain fatty acids (SCFAs) and niacin offer protective effects, the precise role of many metabolites remains unclear and can be context-dependent, as seen with succinate[34]. The production of these metabolites is complex, often involving interactions between multiple bacterial species, meaning the concentration at the colonic mucosa might not directly reflect individual species' production[34].

Diet is a crucial modulator, directly providing substances and altering the microbial community and its metabolic output, though these interactions are further complicated by individual metabolic and microbial variations[34]. Emerging evidence also suggests that probiotics may exert positive immunomodulatory effects and improve gut barrier activity. Overall, understanding the intricate crosstalk between the host, gut microbiome, and microbial metabolites is vital for developing tailored dietary interventions to prevent CRC[34].

Discussion

In conclusion, the Western diet composed of low fiber intake, excess sugars and saturated fats, processed meats and ultra processed preservative-rich fast foods plays an important role in the development of colon cancer. Lifestyle and traditional practices alongside gut microbiome interactions seem to be gaining importance in understanding colorectal cancer development. While dietary bioactive compounds clearly influence the epigenetic modification of CRC-related genes, more research, particularly beyond in vitro and animal studies, is needed to fully understand the mechanisms of action of these protective nutrients. Nutritional therapies leveraging epigenetically active nutrients are a promising area for future research[34].

The significance of this article is to synthesize all available information from previous and current available peer reviewed scientific data regarding the influence of Western Diet on colon cancer development especially to the younger population who seem to be at higher risk for early onset colorectal cancers. There are however limitations involving research studies focused in this field. One possible explanation for this lack of conclusive evidence may be that most studies focus on exploring the effect of individual foods and nutrients on the risk of colorectal cancer, even though foods and nutrients are not consumed individually under normal circumstances. This qualitative review is also subject to limitations such as not all experiments and articles are fully accessible online and the inconsistencies among studies.

These inconsistencies may be due to the fact that studies often have different procedures in determining their results and conducting their experiments and the often unchangeable factors of each experiment such as lifestyle habits and age. Moreover there are other factors such as non adherence to dietary practices alongside cultural beliefs that could affect the integrity of the study outcomes and reliability. This article primarily focuses on Western diet and does not take into consideration the various confounding factors attributed with colorectal cancer beyond the scope of this qualitative literature review. Further large population based studies adopting healthy dietary and lifestyle changes in the Western world are needed to help further our understanding.

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