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A REVIEW OF THE EPIDEMIOLOGY, AETIOLOGY, PATHOGENESIS, DIAGNOSIS, AND CURRENT THERAPIES RELATED TO COLORECTAL CANCER

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Abstract

Colorectal cancer (CCR), the third most frequent cancer in the world in both men and women, is the main reason why gastrointestinal cancers result in death. It also comes in second on the list of common causes of cancer-related deaths. The following conditions increase the risk of this cancer: smoking, bad diet, ageing, intestinal inflammatory illnesses, polyps, and heredity. Ninety percent of those who have colorectal cancer are over 50 years old, with a median age of 64. Those with early diagnosis, however, experience a more aggressive course of the illness. About 49,700 fatalities were attributed to it in 2015, according to the American Cancer Association. Reducing the death rate is the aim of early identification and therapy. The prognosis of the patient is currently determined by their survival rate. The immunochemical stool test, guaiac test, sigmoidoscopy, colonoscopy, and barium enema are a few techniques used to diagnose colorectal cancer. To guide future tactics in controlling the disease's burden through population-based preventative programs, more research on colorectal cancer and global advancements is essential.

Introduction

In the world, it is the third most frequent cancer and the third largest cause of cancer-related mortality. Frequent eating of red and processed meat, together with alcohol, increases the risk of colorectal cancer (CRC). The Westernization of lifestyle refers to the change in eating habits brought about by the advancement of development and economic development, even while socioeconomic conditions improve. This means consuming more processed meats, refined grains, animal fats, refined sugars, fruits, and vegetables, as well as less dietary Fiber and physical activity. A lifestyle like this frequently leads to overweight or obesity. Early-onset CRC, or EO-CRC, is a kind of colorectal cancer that was formerly thought to only affect the elderly (1). However, its prevalence is rising. The authors conduct a thorough evaluation of the body of information, taking into account treatment, overall survival (OS), clinical, molecular, and genetic features, as well as epidemiology and risk factors, in light of the lack of agreement (2). Since EO-CRC has become a major worldwide health issue, it is imperative that awareness be raised in order to reduce the diagnostic threshold for young individuals exhibiting symptoms.

1. Epidemiology

One of the top three most common malignancies globally, colorectal cancer (CRC) will account for 10% of all cancer cases and 9.4% of all cancer-related deaths in 2020. In this case, screening programs have been essential in assembling the identification and excision of adenomatous polyps, so stopping the adenoma-carcinoma sequence. During the 1990s, there has been a discernible decline in the incidence of colorectal cancer (CRC) in numerous nations as colonoscopy has become more widely used for screening average-risk CRC patients6. Geographically, the highest incidences are observed in China, the United States of America, and Japan. Because of increased exposure to CRC risk factors, incidence rates are rising in developing nations while stable or dropping in developed countries (3,4).

There has been a noticeable change in the epidemiology of colorectal cancer (CRC), especially in terms of a higher prevalence among younger patients. One problem, though, is that there isn't a single, accepted definition for patients

with early-onset colorectal cancer (EO- CRC). Some define EO-CRC as those who start at age 40, while others set the age at 50, in line with the Amsterdam criteria for determining who has a hereditary predisposition to colorectal cancer8. Additionally, most screening programs for the general population at risk begin at this age. There is no discernible variation in the gender distribution of CRC, and the prevalence of EO-CRC is likewise shown to be gender-neutral (5).

The observed birth-cohort effect is another factor impacting the incidence of EO-CRC [fig1], as opposed to a period effect where the incidence varies simultaneously across all generations. A study that covered 36 nations on five continents revealed that the incidence of EO-CRC was stable in 14 of those nations, declining in three (Lithuania, Austria, and Italy), and rising in 19 of them. According to projections, the incidence rates of EO-CRC will double by 2030, whereas the incidence rates of older patients will probably decrease by more than one-third. As a result, there will likely be a considerable increase in the percentage of colon and rectal cancer diagnoses among younger patients. These patterns highlight how important EO-CRC is becoming too public health's (6).

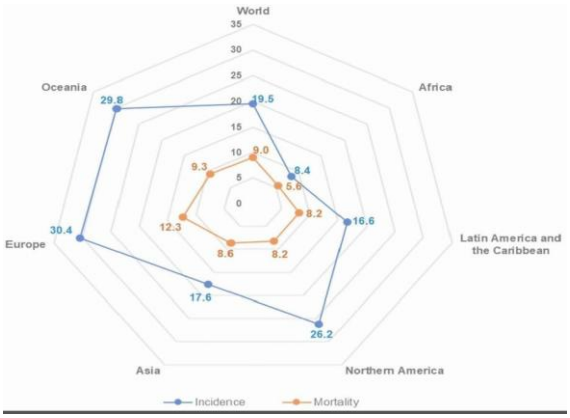

Figure 1; Standardized incidence and mortality rates for CRC

2. Intestinal Anatomy and Physiology of Colorectal cancer

The gut is composed of three layers. Two smooth muscular bands that are perpendicular to one another comprise the outer layer. In the area between these muscle layers lies a nerve plexus that regulates peristaltic action. The layers of muscle are surrounded by varying thicknesses of adipose and connective tissues. The length of the intestine is mostly covered by the peritoneum. The next layer within is called the sub mucosa, and it contains vital immune system components like Peyer's patches as well as blood, lymphatic, and connective tissue. The mucosa, which is situated above the sub mucosa, is where most intestinal processes occur [fig 2]. The colon only contains crypts, and the flat spaces between crypts serve as a substitute for the folds and invaginations known as villi that the mucosa of the small intestine produces (7).

The intestinal surface area and absorptive capacity are significantly increased by this micro-anatomical arrangement. Specialized cells within the villi and crypts perform certain functions. Paneth cells are found at the base of the crypts and release several peptides that have antibacterial properties. All of the cell's lineages present in the intestinal epithelium are

produced by the intestinal stem cells, which are located above the Paneth cells (8). Enterocytes, the predominant cell type in the villi, are primarily in charge of aiding in the absorption of nutrients.

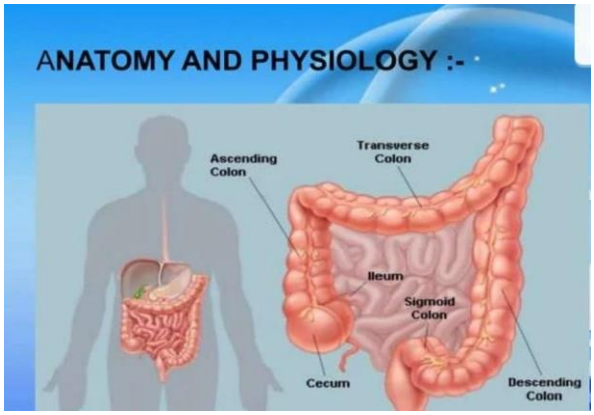

Figure: -2 Anatomy and Physiology of colorectal cancer

3. Risk factors

A multitude of factors have been associated with the development of colorectal cancer. Studies have indicated that a person's history of colon polyps, diabetes mellitus, inflammatory bowel diseases, or cancer itself is associated with an increased risk of colorectal cancer (CRC). Furthermore, lifestyle factors play a significant role in the development of CRC (9). Studies show that obesity, being overweight or obese, not exercising, smoking, drinking alcohol, and having an unhealthy diet high in red and processed meat and low in fruits, vegetables, fiber, calcium, and other nutrients all raise the risk of colorectal cancer (CRC).

3.1 Family and personal medical history

3.1.1 Family history and genetics

The chance of getting colorectal cancer was greatly raised by a family history of the disease. Both inherited genetic susceptibility and behavioural influences are shared by this phenomenon. Among other things, the following data are pertinent to the possibility of colorectal cancer in the future:

(i) The generational distance of the relatives to the individuals at risk

(ii) The ages at which the first-degree relatives developed colorectal cancer

(iii) The number of family members diagnosed with colorectal cancer

(iv) Family co-occurrence of other neoplasms (e.g., endometrial, ovarian and urinary tract, pancreatic)

(v) Personal history of cancer

3.1.2 Inflammatory bowel disease (Cohn's Disease; Ulcerative colitis)

Inflammatory bowel disease (IBD) is the third-highest

risk factor for the development of colorectal cancer, after FAP and HNPCC. IBD is a group of chronic, incurable diseases that affect the immune system of the gastrointestinal tract, which in turn leads to the growth of uncontrollably high levels of inflammation. Cohn's disease and ulcerative colitis are the two

main types of IBD. IBD is believed to be the outcome of interplay between immunological, genetic, and environmental variables, while its precise origin is unknown. IBD patients have a two to six time's higher risk of developing colorectal cancer (CRC) than the general population because chronic inflammation speeds up the growth and development of tumours. The likelihood of CRC increases with the duration of IBD.

3.1.3 Colon polyps

A colon polyp is a precancerous neoplastic lesion that is defined as an abnormal growth of tissue that protrudes from the colon's mucous membrane. Histologically, they can be divided into two main groups: non-neoplastic (hamartoma Tous, hyperplastic, and inflammatory polyps) and malignant (adenomatous). Adenomatous polyps are very significant because of their propensity to become malignant. Adenomatous polyps are expected to be the cause of 95% of occurrences of colorectal cancer9. Although adenomas are the cause of almost all malignancies, only about 5 percent of polyps are thought to progress to colorectal cancer [fig4].

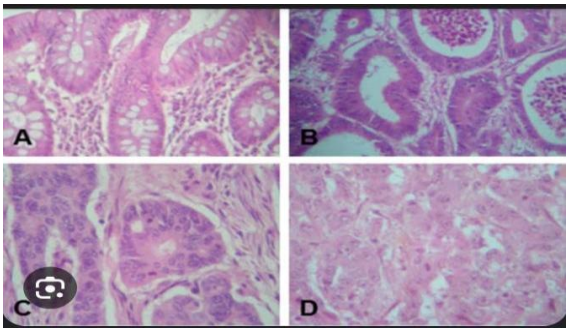

Fig 3: Representative histopathological appearance of adenomatous [A,B] and serrated [C,D] changes in the Colon

3.1.4 Diabetes mellitus

Diabetes is an independent risk factor for several gastrointestinal malignancies, including colorectal cancer, according to epidemiological research. People with type 2 diabetes are approximately two to three times more likely to develop colorectal cancer than people without the disease. The metabolic disease chronic hyperglycaemia, which is caused by abnormalities in insulin secretion and/or action, is a hallmark of diabetes mellitus. The estimated number of people worldwide with diabetes is 460 million, and this number is expected to rise. Hyperinsulinemia stimulates colonic cell proliferation and raises levels of insulin-like growth factor 1 (IGF-1) which may play a direct or indirect role in the oogenesis of colorectal cancer.IGF-1 is a mitogenic factor that promotes cell division and reduces apoptosis (10).

4.1.5. Cholecystectomy

The exact causative relationship between the cholecystectomy—the surgical removal of the gallbladder from the body—and the ensuing prevalence of colorectal cancer is still unclear. While some studies found no elevated risk, others suggested a potential correlation between cholecystectomy and a higher risk of colorectal cancer. Changes in the content and secretion of bile acids after cholecystectomy may result in an increased risk of colorectal cancer (CRC).Periodically, in response to eating, bile acid is normally secreted (11).

3.2 .Life Style

3.2.1 Dietary patterns

❖ Diet high in red and processed meat

Red meat and processed meat were categorized by the International Agency for Research on Cancer Group as possibly carcinogenic to people (Group 2A) and carcinogenic to humans (Group 1), respectively. The meat from the muscles of farm animals is known as red meat, and it includes cow, lamb, game, and hog. Meat that has been preserved by curing, salting, smoking, adding a chemical preservative, or undergoing other techniques to enhance flavor or increase shelf life is referred to as processed meat. According to estimates, there may be a 17% increase in the risk of colorectal cancer (CRC) for every 100 grams of red meat consumed. Many molecules, such as N-nitroso compounds (NOCs), polycyclic aromatic hydrocarbons (PAHs), and heterocyclic amines (HACs), are thought to have an impact on the development of cancer (12).

❖ Diet low in fiber, fruits and vegetables

Research suggests that eating a high-fibre diet can lower your risk of colon cancer by as much as 50%. Nevertheless, the information that is now available from epidemiologic research does not offer compelling proof of fiber's ability to prevent colorectal cancer, and the specific mechanisms by which fiber functions as an anticancer agent remain unclear (13). Eating fiber may work through the following putative methods to inhibit the development of colorectal cancer (CRC):

(i) A reduction in the transit time of stool throughout the colon, which may reduce the amount of contact between potentially carcinogenic substances and colonic epithelium;

(ii) An increase in the amount of water in fecal content, which may dilute carcinogens and procarcinogens present in feces;

(iii) Binding sterols and bile acid metabolites, which may be implicated in carcinogenesis;

(iv) Stimulation the expansion of the good bacteria in the gut, which then ferments fiber and produces short-chain fatty acids.

❖ Diet low in calcium, vitamin D and dairy products

High consumption of dairy products, particularly milk, is likely associated with a lower risk of colorectal cancer, according to the World Cancer Research Fund/American Institute for Cancer Research. The potential preventative effect of dairy products has been frequently attributed to

their high calcium content. It has been demonstrated that calcium binds secondary bile acids and fatty acids, decreasing their ability to modify intestinal mucosa and, thus, their carcinogenic potential (14).

Moreover, it has been found that calcium suppresses the growth and death of tumor cells as well as particular patterns of mutation in the proto-oncogene KRAS. In addition to calcium, vitamin D, another ingredient in milk, may also prevent the development of colorectal cancer. A number of genes involved in the regulation of epithelial cell growth, proliferation, differentiation, and death are altered in expression by vitamin D. Moreover, it inhibits angiogenesis and has improved immune response and anti-inflammatory qualities (15).

❖ Overweight and obesity

Unusual or excessive fat accumulation is a hallmark of obesity and overweight, and it is a major risk factor for colon cancer. Obese or overweight men and women had a 50% and 20% increased risk of colorectal cancer, respectively, compared to those of normal weight. An essential part of the endocrine system, adipose tissue controls both the inflammatory response and calorie intake. It was discovered that adipose tissue releases of hormones and cytokines vary in response to aberrant or excessive fat accumulation (16).

Overweight and obese individuals' adipose tissue releases more factors (such as resisting, TNF-α, IL-1, IL-6, IL-7, and IL-8) that are known to exhibit mitogenic effects on epithelial

cells, inhibit cell apoptosis, promote oxidative stress, suppress immune response, and reduce IGF-1 axis activity. These factors have also been linked to the onset and progression of cancer.

❖ Physical inactivity

Based on epidemiological data, a sedentary lifestyle may be contributing to the rising incidence of colorectal cancer in both industrialized and developing nations. Compared to those who are physically active, those who are physically inactive are thought to have a 50% increased risk of colorectal cancer. Frequent physical activity has been demonstrated to enhance immune system performance, lower stress and inflammation, optimize metabolic rate, help control hormone levels, avoid obesity, and optimize metabolic rate. These benefits may help prevent the development of cancer (17).

❖ Cigarette smoking

The well-established fact is that breathing in tobacco smoke raises the risk of various malignancies, including colorectal cancer. The results of the study indicate that the risk of colorectal cancer (CRC) increases with exposure levels and duration, with smokers having a 2-

3 times higher risk than non-smokers. Moreover, it's thought that smoking cigarettes contributes to up to 12% of colorectal cancer deaths (18).

❖ Alcohol consumption

One of the main factors contributing to the development of colorectal cancer is alcohol consumption. Drinking two to three drinks a day is thought to increase the risk of CRC by approximately 20%, whereas consuming more than three drinks is thought to increase the risk by approximately 40%. Those who regularly consume four or more drinks each day may be upto 52% more likely to get colorectal cancer. Various mechanisms have been proposed thus far for how alcohol may induce carcinogenesis (19).

These include the following: inactivation of the tumour suppressor genes; reduction in folate concentration; impairment of retinoic acid metabolism as well as retinoic acid metabolism deficiency; production of mutagenic acetaldehyde (the first metabolite of ethanol); and production of reactive oxygen species and nitrogen species (during the oxidative metabolism of ethanol).

3.3 Others

3.3.1 Gut microbiota

Recent studies have revealed a growing amount of evidence suggesting the gut microbiota may be crucial in the emergence of several disease processes, including cancer. The gut microbiota, also referred to as the microbiome, is the enormous population of diverse microorganisms (bacteria, viruses, fungi, and protozoa) that reside in the human gastrointestinal tract. The microbiota affects nutrition absorption and metabolism, xenobiotic clearance, and drug metabolism in healthy people. Moreover, a robust intestinal barrier, protection against infections, and immunomodulation are all facilitated by a healthy gut microbiota. The formation, promotion, and spread of colorectal cancer may be facilitated by modifications in the functionality and composition of the normal gut microbiota, according to recent research that examined the microbiomes of patients with the disease (20).

3.3.2 Age

Given that over 90% of new cases of colorectal cancer occur in those over 50, being older is considered to be one of the most significant risk factors for developing the disease. Based on estimations, individuals over 65 have a three times higher risk of developing colorectal cancer compared to those between the ages of 50 and 64, and a nearly thirty times higher risk than those between the ages of 25 and 49. The average age at diagnosis is 72 years old for womenand 68 years old for males. It is particularly evident that colorectal cancer is associated with age in the developed countries with the highest prevalence of the disease.

3.3.3 Gender and race

According to the American Cancer Society, men have a 30% higher risk of developing colorectal cancer than women do. Men also have a worse prognosis and a death rate from colorectal cancer that is over 40% higher than that of women. On the other hand, right-sided colon cancer, which is more common in women, looks to be more aggressive than left-sided tumors and is typically detected at a later stage. The exact causes of sex

discrepancy are unknown, although theories include differences in dietary patterns, sex hormones, and exposure to risk factors (such alcohol and tobacco). Additionally, there were notable racial disparities in colorectal cancer incidence. Black individuals that are non-Hispanic have one ofthe highest incidence rates.

Additionally, there were notable racial disparities in colorectal cancer incidence. Non-HispanicBlack individuals have one of the highest incidence rates of any racial group. The incidence of colorectal cancer in non-Hispanic Blacks is estimated to be 20% higher than in non-Hispanic Whites and about 50% higher than in Asians and Pacific Islanders.

4 .3.4 Socioeconomics factors

It is believed that those with low socioeconomic level (SES) have a higher risk of developing cancer compared to people with high SES. The low socioeconomic class population's unhealthy eating, smoking, and sedentary lifestyle, together with their limited access to high-quality treatment resources and medical facilities, may account for some of this. However, it should be highlighted that there is conflicting information regarding the link between SES and the incidence of colorectal cancer. In North America, the prevalence of colorectal cancer was higher in those with low socioeconomic status (SES) than in those with high SES16. On the

other hand, high SES groups often show a greater prevalence of colorectal cancer in Europe when determining how socioeconomic status affects the incidence of colorectal cancer. Thus, it is essential to carry conducting additional investigation to ascertain.

4.3.5 Development factors

The steps of initiation, promotion, and progression make up the formation of CRC. Beginning with irreversible genetic damage, the impacted epithelial cells of the intestinal mucosa are more vulnerable to later neoplastic transformation. The started cells proliferate during the promotion phase, leading to aberrant growth (cancer) [fig 4].

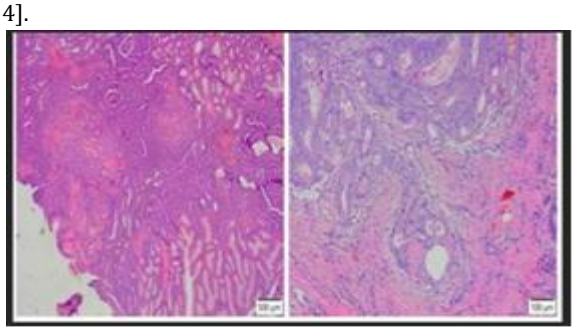

Figure no: - 4 Representative histopathological appearance of adenocarcinoma in the colon

Selected endoscopic images of adenomas and CRC at different stages

A. Tubular Adenoma

B. Tubulo-villous Adenoma

C. Sedentary Serrated Adenoma (SSA) without Dysplasia

D. Tubular Adenocarcinoma, Grade-1

E. Tubular Adenocarcinoma, Grade-2 5.Etiology and Pathogenesis

The genesis of colorectal cancer (CRC) is the colon, the rectum, and the epithelial cells lining the gastrointestinal tract. Vogelstein was the first to propose a model explaining the interplay between oncogenes and tumour suppressor genes over the course of colorectal cancer formation19.

Consequently, it has been established that the adenoma-carcinoma sequence of colorectal cancer is directly caused by the oncogenes K-RAS and NRAS as well as the tumour suppressor genes APC, DCC (deleted in colon cancer), p53, and MCC (mutated in colon cancer). The most common mutations in CRC occur in the want-signalling pathway. The intestinal crypt stem cell may experience the inherited mutations. The most often mutated gene in all colorectal malignancies is the Adenomatous Polyposis Coli, or APC, gene. The APC protein is encoded by this gene20. In the absence of APC, β-catenin accumulates to high concentrations, enters the nucleus, binds to DNA, and initiates the transcription of genes that are frequently essential forstem cell growth, differentiation, and renewal. Therefore, APC serves as a "brake" on the accumulation of β-catenin protein.

6. Diagnosis

6.1 Diagnostic methods

The current screening methods that target populations at moderate risk who are 50 years of ageor older are the focal occult blood test (TSOH) with high sensitivity based on the Guaiac or immunologic test (Tshi) with an annual periodicity, sigmoidoscopy every 5 years with TSOHevery 3 years, or colonoscopy every 10 years11. Most diagnostic procedures are based on the patient's expected life span; however, some procedures, such as the use of focal occult blood, may yield false-positive results if the subject eats a lot of fruits, vegetables, and red meat—all of which may contain peroxidase—in comparison to individuals who do not have bleeding disorders and who take vitamin C1221.

By carrying out a specific test, it is possible to detect biological genetic markers and further the goal of identifying mutations in specific genes associated with colorectal cancer. Unfortunately, around 50% of advanced adenomas (>1 cm) and proximal colon cancer are missed by this approach. While the colon is the only way that is examined, the cost, risk, and level of pain for the patient are higher with this diagnostic and therapeutic care than with othertests22

Diagnosis by location

37% of tumor localizations occur in the rectum, with less common locations including the hepatic angle (4%), splenic angle (2%), cecum (8%), ascending colon (9%), descending colon (5%), transverse colon (4%), and sigmoidal tumors (31%). Elevated serum levels of carcinoma

embryonic antigen (ACE) are associated with a recurrence of the disease in 60–70% of cases,and this is likely to be related with a worse prognosis for the patient.

However, ACE's value is still noteworthy, especially in stadium TNM II15.

7. Protecting and developing factors of colorectal cancer

Numerous factors have been related, at least in some studies, to a lower risk of colorectal cancer (CRC). Some of these include a variety of dietary factors, consistent use of NSAIDs or aspirin, regular physical exercise, and hormone replacement therapy in postmenopausal females. At the moment, none of these factors are used to stratify CRC screening recommendations.

7.1 Resistant starch

When starches escape the small intestine's capacity to break them down and reach the colon, where they ferment and form short-chain fatty acids, they are referred to as "resistant starch". Butyrate, one of these fatty acids, has anti-tumor properties in the colon. Despite the initial excitement surrounding resistant starch's potential as a preventative medication against chemotherapy, a randomized trial involving resistant starch (Novelize, 30 g daily) failed to show any beneficial effects on the development of cancer or adenoma in individuals with Lynch syndrome. However, during the long-term follow-up of the experiment, resistant starch did show a delayed protective impact on all non-colorectal Lynch syndrome malignancies, especially those in the upper gastrointestinal tract.

7.2 Folic acid and folate

The vitamin, which is used in supplements and food fortification, is found in food both naturally as folate and artificially as folic acid. Depending on the metabolic pathways involved, the two may not be interchangeable and may have distinct in vitro effects. Studies conducted on humans and animals have demonstrated that folate inhibits the growth of cancer in several organs, including the colon22. However, it's unclear if folate and folic acid contribute

to the prevention of CRC. However, there's a probability that folic acid pills increase your riskof colon cancer.

7.3 Vitamin B6 (pyridoxine)

The available data suggests a slight association between higher vitamin B6 (pyridoxine) intakeand a decreased risk of colorectal cancer. In a meta-analysis of prospective trials, the pooled relative risks (RRs) of CRC for the highest vs. lowest categories of vitamin B6 consumption and blood levels of pyridoxal 5'-phosphate (the active form of vitamin B6) were 0.90 (95% CI0.75-1.07) and 0.52 (95% CI 0.38-0.71), respectively. The risk of colorectal cancer (CRC) was found to be considerably protected by higher versus lower vitamin B6 intake, with the exception of one research that greatly enhanced the heterogeneity in the vitamin B6 intake studies (pooled RR 0.80, 95% CI 0.69-0.92).

7.4 Calcium and dairy products

Increasing your calcium intake through food or supplements may offer an additional layer of protection. At least three controlled trials have evaluated the calcium supplementation'sefficacy in preventing the recurrence of colorectal adenomas23. A meta-analysis of these data, totalling 1485 participants, revealed that the recurrence risk was considerably lower for those randomized to calcium (RR 0.80, 95% CI 0.68-0.93). The following information is available:

- A review of combined data from the Health Professionals Follow-up Study and the Nurses' Health Study indicated that consuming more calcium could lower the risk of colorectal cancer. Every four years, the amount of calcium consumed was measured. Atotal calcium intake of ≥1400 mg/day, as opposed to <600 mg/day, was associated with a statistically significant reduction in the risk of colon cancer (multivariable RR 0.78, 95% CI 0.65-0.95).
- In the end, a post hoc analysis of a randomized controlled trial using calcium and vitamin D showed that the incidence of serrated polyps was higher in those assigned tocalcium (adjusted RR 2.65, 95% CI 1.43-4.91) and calcium + vitamin D (RR 3.81, 95% CI 1.25-11.64)23. There is inconsistent evidence from epidemiologic studies about the association between dairy products and colorectal cancer (CRC); some have reported no relationship at all between the incidence of CRC and consumption of milk, yogurt, and/or dairy products, while others have reported inverse relationships.

7.5 Vitamin D

In a pooled analysis of 5706 CRC patients and 7107 control patients with varying amounts of circulating 25(OH)D, this connection was shown. Compared with 25(OH) D levels of 20 to

<25 mg/mL, lower levels of 25(OH) D (<12 mg/mL) were associated with a higher risk of CRC (RR 1.31, 95% CI 1.05-1.62). In model systems, the progression of colorectal cancer is suppressed by vitamin D and its metabolites through effects on both initiation and development24. The World Health Organization found that colon cancer was the form of cancermost directly associated with low vitamin D levels. Additionally, observational studies show a link between low vitamin D levels and an increased risk of colorectal cancer (CRC) and other cancers. A correlation has been shown between low vitamin D levels and the risk of several malignancies, including colorectal cancer (CRC), according to pooled research encompassing 5706 CRC patients and 7107 control patients with a range of circulating 25-Observational tests. There is contradictory evidence about the preventative effect of vitamin D intake on the development of colorectal neoplasia. We do not yet know if supplements can lessen the elevated risk of colorectal cancer (CRC) linked to vitamin D deficiency25.

7.6 Magnesium

Research on animals suggests that dietary magnesium may have an effect on the development of CRC. A population-based study conducted in Sweden found a negative relationship between the risk of colorectal cancer in females and the amount of magnesium they consume. Compared to females in the lowest quintile, the risk was reduced by almost 40% (RR 0.59, 95% CI 0.40-

0.87) in those with the highest quartile of intake. It has been demonstrated that rectal and coloncancer is inversely related.

7.7 Garlic

Consuming garlic has been associated with a decreased incidence of colonic adenomas in both laboratory and observational studies involving people with colorectal cancer. After analyzing the information, the US Food and Drug Administration (FDA) concluded that there was "very limited credible evidence for a relation between garlic consumption and reduced colon cancer risk." Garlic is categorized as a potential preventive factor by the American Institute of Cancer Research and the World Cancer Research Fund26.

7.8 Fish consumption

The usage of omega 3 fatty acids, mostly from fish oil, has been associated in certain observational studies with a decreased risk of colorectal neoplastic; however, the findings are not totally consistent. Individuals who eat more fish than others had a typically lower risk of colorectal cancer (CRC) (summary odds ratio [OR] 0.88, 95% CI 0.80-0.95), according to a meta-analysis comprising 22 prospective cohort and 19 case-control studies. Two grams of the free fatty acid eicosatetraenoic acid (EPA) improved the overall polyp burden in familial adenomatous polyposis (FAP) and decreased the number of adenomas by a net change of 22.4 percent when compared with placebo in a randomized controlled trial. Coffee intake Results on the association between coffee consumption and colorectal cancer risk have been varied in research based on observational studies. Twelve case-control studies found a correlation between high rates of coffee consumption and a lower risk of colorectal cancer (CRC), in addition to the population-based Molecular Epidemiology of Colorectal Cancer (MECC) study, the National Institutes of Health (NIH)-AARP Diet and Health Study, and a third analysis from Japan27. However, data from the Nurses' Health Study, the Health Professionals Follow-up Study, a meta-analysis of 12 prospective cohort studies, or a pooled analysis of data from 13 prospective cohort studies do not support this finding.

Conclusion

More clinical research is needed to understand the processes of carcinogenesis, the influence of lifestyle, behavioural, environmental, and genetic factors, or the synergistic action of the various components in order to improve preventive/treatment efficaciousness and patient survival with colorectal cancer. Additionally, scientists are still searching for new tumour markers that might be applied to primary and secondary care diagnosis; however, presently available data is insufficient, despite promising results. By 2030, it is expected that 14% of rectal cancers and over 10% of colon cancers will be diagnosed in those under 50. Studies show that EO-CRC differs from older-onset CRC in terms of its molecular profiles, aggressive behaviour, pathological abnormalities, and clinical aspects. Further research is necessary, even though they could account for variations in survival and treatment responses. A study found that over a 20-year period, risk factor adjustment could lower CRC-related death by about 12%. This study also aims to educate clinicians on the need of lowering the threshold of suspicion when paediatric patients present with troubling gastrointestinal symptoms.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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