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Gastrointestinal Cancer

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Abstract

Cancer or carcinoma is abnormal and excessive growth of respective tissues or parts of the body, which begins with nodules and latter formation extends to the nearby areas of the affected organ through metastasis. It affects the vast population of the world, including Asia. Various studies and data show increasing incidence and prevalence of gastrointestinal carcinoma globally. This article reviews gastrointestinal carcinoma's prevalence, clinical features, and risk factors.

Keywords: Gastrointestinal Carcinoma; Oral Cancer; Esophageal Cancer; Gastric Cancer

Introduction

The gastrointestinal tract is the most common site of cancer in Homosapiens. There is wide variation in incidences of the sites from mouth to anus, and the prognosis also depends upon the site of the tumor. The ratio for the invasive squamous cell carcinoma of the gastrointestinal tract in both males and females from 1983 to 1987 was 2.7:1, and of adenocarcinoma was more than 7:1.The incidence for the squamous cell carcinoma of the esophagus for blacks was four times higher than for whites. While adenocarcinoma was 3 times highest in white males than black males [1]. According to Bakkila BF, et al. [2], in the US, the majority of patients in surgical care GI (83.3%) were from the white population. According to the World Health Organization, cancer is the second principal reason of death worldwide and is accountable for an expected 9.6 million deaths in 2018. Globally, around 1 in 6 demises are due to cancer. Just about 70% of fatalities from cancer occur in low and middle earnings nations. While according to global cancer facts and figures, by the end of the year 2040, the global load is likely to increase up to 27.5 million fresh cancer cases and 16.3 million deaths by cancer basically due to the expansion and aging of the people. The overall yearly economic expenditure of cancer in 2010 was projected at approximately 1.16 trillion US$. Gastrointestinal carcinoma (oral, esophageal, gastric, liver, and colorectal) is common worldwide and is one of the leading causes of death globally. The prevalence and risk factors of carcinoma in the gastrointestinal tract and its morbidity were discussed one by one in this article, which is as follows:

Oral Cancer

Globally, 405,000 new cases of oral carcinoma are estimated each year, and the countries with the maximum rates are India, Bangladesh, Pakistan, Sri Lanka, France, and Hungary [3,4]. Tobacco and alcohol seem to have

a synergistic outcome in the development of oral and oropharyngeal Squamous cell carcinoma [5]. Other causes may include poor oral hygiene [6], exposure to wood and ash dust [7], deficiencies of certain things in diet [8], over-salted meat or red meat overconsumption have been accounted as causative factors [9]. Many types of cancers occur in the oral cavity, amongst which 90% of these are squamous cell carcinoma. The most common associated factor with oral carcinoma is tobacco. The most common signs and symptoms of oral cancer are: mass in the neck or the maxillary region, Difficulty in speaking, canker sores, bleeding and ulceration in the mouth, cellular growth can be found in the hard palate, soft palate, or in lips, pain may found in the areas that have similar nerve supply such as the ear.

The treatment and prognosis of oral carcinoma depend upon the location, size, and stage of the cancer. However, the worldwide statistics estimated 263900 new cases with 128000 deaths found per year globally. 58% of cases of oral cancer were found in South Asia [10]. Oral cancer is amongst the 10th most common cancers globally, and in underdeveloped countries, it is the 3rd most common cancer in men and the fourth most common cancer in women. Tobacco, paan, naswaar, and betel nuts are extensively used in Pakistan and are the potent causes of oral squamous cell carcinoma. Nearly 40% of men in Pakistan above 15 years of age smoke cigarettes. According to a study that had been performed, the most common site for oral cancer was the buccal mucosa and tongue in approximately 50% of the cases.

Esophageal Carcinoma

Carcinoma of the esophagus is the 2ndmostusualcancer and the 6th leading cause of cancer-associated death worldwide [11]. From 2016 to 2023, the GI cancer rate increased 4 times [12]. Its incidence is three times more in men than women, and around 80% of cases are found in underdeveloped countries. It has been estimated globally that the annual incidence of esophageal carcinoma is 456,000. According to an evaluation, every year 17,290 cases of esophageal carcinoma are diagnosed in the United States, among which nearly 16000 deaths are expected from cancer [13]. Concerning a report presented by cancer research centers in Pakistan, esophageal carcinoma accounted for almost 2 %of overall cancers recorded or detected from 1994 to 2004 at hospitals. Amongst those 335 cases chosen for this survey, 54.9 %were males, and 45.1% were females. In contrast, 77.6% of cases were diagnosed with squamous cell carcinoma and 22.4% with adenocarcinoma of the esophagus. According to various studies that have been conducted in Pakistan, chewing paan, eating naswaar, and inhaling snuff are high-risk factors in patients with esophageal carcinoma [14].

On Histological Grounds, Esophageal Carcinoma has Two Subtypes

Esophageal adenocarcinoma and (2) esophageal squamous cell carcinoma [15]. Though squamous cell carcinoma has been the most frequent type of esophageal cancer for an extended time, and there is a stable rise in the incidence of adenocarcinoma, especially in industrial or developed countries [16]. Local rates of occurrence are low in regions such as Africa, Asia, and South America, where the frequency of squamous cell carcinoma is elevated for both types of subtype; as it's already mentioned above, esophageal carcinoma is higher in males than in females, with atypical squamous cell carcinoma and adenocarcinoma ratio of 2.5 and 4.4, correspondingly [17]. The frequency of squamous cell carcinoma in China is considerably higher than in other Asian countries [18].

The occurrence of adenocarcinoma esophagus (AC) in several Western countries is getting noticeably higher due to amplified risk factors, such as obesity. In contrast, the frequency of squamous cell cancer (SCC) in these countries is progressively diminishing due to reduced consumption of alcohol and tobacco. However, the incidence of squamous cell carcinoma in definite Asian countries is possibly to rise due to amplified alcohol and tobacco consumption [19].

Risk Factors of Esophageal Carcinoma

For Squamous Cell Carcinoma of the Esophagus

In underprivileged countries, the risk of developing squamous cell carcinoma is high because they take hot beverages more frequently [20], they lack certain vitamins, minerals, and antioxidants in their body consequential from little consumption of fruits and vegetables, findings from several studies demonstrate that there is a considerable relationship between reduction of squamous cell carcinoma risk and increased consumption of diet rich in all essential vitamins and minerals [21,22]. Furthermore, excess consumption of tobacco, areca nut, and alcohol are other well-known risk factors in the development of squamous cell carcinoma of the esophagus [23], as smokers are 5 times more prone to develop squamous cell esophageal carcinoma in comparison with nonsmokers [24].

Another possible source of carcinogen that inclines people towards squamous cell carcinoma of the esophagus is acetaldehyde, which is an organic compound usually established in cheese, bread, coffee, yogurt, ripe fruits, alcoholic beverages, and tobacco smoke [25] alcoholic drinks such as distilled alcohols contain particularly increased quantity of acetaldehyde, and everyday consumption of these drinks is linked with an augmented risk of squamous

cell carcinoma of the esophagus. It can also be produced in the oral cavity of individuals by microorganisms such as bacteria and yeasts. Hence, acetaldehyde either from foods, oral commensals, and alcoholic drinks, could provide a prospective basis for carcinogens that predispose people to squamous cell carcinoma of the esophagus [26,27].

Furthermore, a relationship between the development of esophageal carcinoma and Human Papillomavirus infection has been established in a few regions alongside China; moreover, its exposure rates are highest in Africa and China. Human papillomavirus may be infected in the etiology of squamous cell carcinoma in synergism with other aspects but not alone [28]. The only known viral cause of esophageal carcinoma is the human papillomavirus. More than the past 20 years, lots of studies have been carried out using different methods. Several serological research established a positive relationship between genotype 16 of human papillomavirus and squamous cell carcinoma [29,30].

Howell-Evans syndrome, also known as tylosis, is a rare disorder that is usually associated with hyperkeratosis of heels and palms, and hyperkeratosis, especially its hereditary type, increases the risk of squamous cell carcinoma [31].

For Adenocarcinoma of the Esophagus

The incidence of esophageal adenocarcinoma has been increasing over the past few years and is seen more in white males. Barrett's esophagus, gastroesophageal reflux disease, and obesity are the most common risk factors for developing adenocarcinoma of the esophagus. The frequency of GERD in Western people is approximately 10%, and millions suffer from it in the United States. As the stomach contains highly acidic content, recurrent reflux of that content can harm the esophagus and make it complicated to gulp down the bolus of food. In further severe conditions, gastroesophageal reflux disease causes the development or growth of irregular cells that can further lead to unnecessary esophageal carcinoma cells [32]; its symptoms are frequently insignificant, which is why it is overlooked, however, if the inflammation of the esophagus is chronic then it can lead to irreversible complication. Among these, one of the most severe problems is (BE). In the case of Barrett's esophagus, the typical covering of the esophagus demonstrates adaptive responses and transforms into the membrane, which resembles an intestinal membranous cover. Over the past 30 years, an increase in the frequency of Barrett's esophagus has been associated with a rise in the incidence of adenocarcinoma over a similar period [33].

The initial reports about the likely relationship between esophageal adenocarcinoma and obesity were published in the 1990s [34]. This result was confirmed in research on huge populations; case studies in Australia, Europe, and the United States signify a strong association between the increased risk of EA and BMI [35]. Results from various epidemiological studies point towards the fact that obesity is among the main causes of adenocarcinoma. One of the main risk factors for adenocarcinoma of the esophagus is GERD, and people who are suffering from obesity experience symptoms of gastroesophageal reflux disease frequently [36,37].

Gastric Carcinoma

Though the incidence of stomach carcinoma or gastric carcinoma is waning in most of the globe, it is still considered as one of the major health concerns and one of the main sources of morbidity and death all over the world. It is the 4th most common cancer and 2nd leading cause of cancer-associated death worldwide; while it is the most frequent cancer in East Asia, its occurrence is 2 to 3 times more in males than females [38]. Males are more prone or have a high risk of developing gastric carcinoma of both types (noncardia or cardia) as compared to females. The rationale for such variations is unclear. However, ecological or job-related exposures may be part of the cause. For instance, traditionally, males are more prone to consume tobacco products; on the other hand, variations in sex may be a sign of physiological divergences. Female dominant hormone i.e. estrogen may give protection and guard against the growth of gastric carcinoma during the proliferative phase of a woman's life; however, its effects begin to reduce after cessation of the menstrual cycle, and that is the reason why the fertile and menstruating women have fewer chances to develop carcinoma of the stomach while the drugs that work against estrogen or have anti-estrogen properties such as tamoxifen may enhance the chances to develop gastric cancer [39]. It has been estimated that around 990,000 cases of gastric cancers are recorded per year, with around 738,000 fatalities from the diseases recorded worldwide. The incidence rates of gastric cancer seem highest in East Europe, Asian countries, and South America; however, in the northern region of America and most parts of Africa, the lowest incidence rates are observed [40]. While the whole world, Japan and Korea have the highest incidences of gastric carcinoma, boosting the highest incidence in East Asia [41].

Although increased awareness of people regarding the risk factors and causes of the disease, increased intake of fruits and vegetables, and increased use of anti-microbial to treat H. pylori infection, it still remained the 2nd leading cause of cancer-associated death worldwide. Usually, its incidence is seen more in low socio-economic groups as they overlook the symptoms more often. Increased incidence of the lesion at the cardiac end of the stomach has been associated with adenocarcinoma of the lower esophagus,

hyperacidity, reflux esophagitis, Barrett's esophagus, and obesity are common risk factors. Helicobacter pylorus is an important cause of the development of noncardiac gastric adenocarcinoma. Helicobacter pylori are gram-negative bacteria that form colonies in the stomach. Highest incidence of gastric cancer has been reported in Asia [42,43]. The most frequent type of gastric cancer is adenocarcinoma. Around 90% of gastric carcinoma is adenocarcinoma. According to Lauren's classification (the most frequently accepted classification for gastric cancer), there are two histological types of gastric carcinoma. This histological form is seen all over the world, while the intestinal form takes place in areas with a high occurrence of gastric carcinoma and follows an expected stepwise sequence for the development of cancer from metaplasia. Gastric carcinomas of intestinal type are frequently described by the existence of gland-forming mitotically dynamic columnar cells with distended, darkly marked nuclei, with buildup of mucin in the lumina of these invasive glands, exclusive of much intracellular mucin accumulation [44].

Diffused Type

It is due to endogenous host factors and genetic predisposition but is unintroduced by known precancerous factors. Its cells are smaller, more homogenous in shape, and have less cellular division activities [45].

Intestinal Type

Related to the exogenous factors and is introduced by prolonging the precancerous process. The global decline in gastric carcinoma appears to be due to decreased intestinal type incidence [46,47].

Clinical Features of Gastric Carcinoma

Symptoms of gastric carcinoma appear late, which is responsible for delay in diagnosis and treatment. According to a Scandinavian study, weight loss, epigastric pain (63.3%), and gastrointestinal hemorrhage due to ulceration (27.3%) are the crucial symptoms [48,49]. Other symptoms may include nausea, epigastric mass, vomiting, dysphagia due to involvement of the cardiac orifice of the stomach, bloating, and other signs of metastasis such as anorexia, jaundice, liver enlargement etc.

Colorectal Carcinoma

Colon and rectum are ending parts of the gastrointestinal tract; usually, in combination, it is called the large intestine. It aids in the absorption of nutrients and the elimination of waste. The unusual growth of cells in the colon or rectum leads to the development of cancer. Colorectal carcinoma is one of the principal causes of death and diseases worldwide. It is the fourth leading cause of cancer-associated death globally. In the current era, there has been a considerable rise in the incidences of colorectal cancer, and the frequency of recently diagnosed cases has amplified to more than 1,361,000. Colorectal carcinoma usually begins as a polyp and gradually converts into true cancer after a period of around 10 to 20 years [50]. Not all polyps are converted into cancer, though all of them can potentially convert into cancer. However, the chance of a polyp converting into colorectal carcinoma depends upon a few factors, such as if it is larger than 1 cmor abnormal cellular growth found in the polyp's lining preceding the cancerous stage, etc. These polyps are also known as adenomas (precancerous stage). Approximately 96% of colorectal carcinomas are adenocarcinoma.

The American Cancer Society had estimated that about 148,810 people could be diagnosed with colorectal carcinoma in 2008, and 49,960 would die from it. According to the new estimate of 2018, the key statistics for new cases of colon cancer is 97,220, while new cases of rectal carcinoma are 43,030. From 1990 to 2012, the prevalence of colorectal carcinomas has increased by 2 Lac, and new cases are reported yearly. According to a study in Pakistan, colorectal carcinoma was seen more in the age of 40-60 years, and its male-to-female ratio was 2.54:1. According to the Pakistan Medical Research Council, it is the 6th most common cancer in males with the incidence of 5.7% and in females it ranked as 9th common cancer [51]. According to a study, the most common tumor site is lower than 1/3rd of the rectum 45%. The patients who are suffering from inflammatory bowel disease are more prone to develop colorectal carcinoma as the risk in patients with ulcerative colitis is increased by 3.7 %, while in the case of Crohn's disease, it is 2.5%. Colorectal carcinoma is 30% more common in men than women, while death rates are roughly 40% elevated. The cause of these sex differences is not entirely understood; however, sex hormones and persistent exposure to risk factors may play a role [52]. Anatomical site of the tumor, besides the gender and age of the patient, plays an important role in identifying the survival rate. If the tumor is in the proximal colon or on the right side of the colon, the patient has a lower chance of surviving for longer than those with tumors in the distal part of the colon and rectum. However, a tumor in the proximal colon is more common in women than men and occurs more in old age rather than young age [53]. 65% of sufferers of colorectal carcinoma have a chance to survive for 5 years.

Risk Factors of Colorectal Carcinoma

The known risk factors for colorectal carcinoma are family history being the first-degree relatives of any person who is suffering from colorectal carcinoma are 2 to 4 times more prone to develop the disease [54], people suffering from inflammatory bowel disease are nearly two times at

risk to develop colorectal cancer [55], physical inactivity as researches persistently demonstrates that the risk to develop tumors at both ends of the colon are 25% less in individuals who are physically active than those who are inactive [56], overweight, diabetes, smoking, deficiency of vitamin D, unhealthy diet or reduce intake of fruits and vegetables on the contrary excessive consumption of animal fat and meat, sedentary lifestyle, alcoholism etc. [57]. Majority of the studies found that consumption of calcium from dairy products and/or supplements is related to a declining risk of developing colorectal carcinomas and adenomas. It is extremely reasonable that dietary fiber minimizes the risk of colorectal carcinoma for lots of reasons, including a lesser amount of exposure to carcinogens due to increased volume of stool and earlier transit time [58,59]. Using processed or red meat enhances the risk of both rectal and colon cancer [60]. The International Agency for Research of Cancer classified red meat and processed meat as carcinogenic for humans principally based on the facts related to the risk of colorectal carcinoma in 2015 [61]. While in November 2009, the Agency stated that there is adequate data to conclude that smoking may cause colorectal carcinoma [62]. Moderate and intense use of alcohol [63]; however, not light consumption (i.e. p<12.5 grams for each day, about one drink) is related to enhanced risk of colorectal carcinoma [64]. According to Wong SH, et al. [65] relevant prevention is systematic supplementation of gut microbiota with lactic acid bacteria.

Clinical Features of Colorectal Carcinoma

The symptoms associated with this carcinoma are bleeding per rectum (60%) as if the size of the tumor increases, there may be a chance of bleeding, excessive blood loss from the tumor can cause anemia and its associated symptoms such as dyspnea, fatigue, lethargy etc. Alteration of bowel habits or dark color stools (30%), intestinal obstruction (15%), and abdominal pain (30%) [66].

Hepatic Carcinoma

Hepatic carcinoma is the 6th most common cancer globally, with nearly 782,000 new cases identified in 2012 [67]. In contrast, it is the 3rd leading cause of cancer death worldwide. It occurs more in men than women. Nearly 90% of primary liver carcinoma in the United States is liver cell carcinoma, while the remaining 10% is cholangiocarcinoma. Liver cirrhosis and fibrosis that can be caused by alcohol, hepatitis B, and C infection may lead to hepatocellular carcinoma [68]. Amongst the reasons for deprived survival rates, one of the reasons is that hepatic cancer symptoms are not marked in the early phases of the disease, which indicates that the cancer is usually highly developed by the time it is diagnosed. In European countries, the population's standard 5 years survival rate after disease diagnosis is around 12%.

Additionally, the quantity of new cases is on the increase. WHO statistics demonstrate that around 626,162 fresh cases of hepatic cancer were identified in 2002, but by 2012, the number had risen to 782,451. This figure is expected to enhance by 70% to almost 1,341,344 cases by 2035 [69]. According to a study, hepatocellular carcinoma was seen more in cirrhotic than non-cirrhotic patients. According to the World Health Organization statistics of 2000, it has been evaluated that there are 565000 cases of liver cell carcinoma per year globally, amongst which 400000 were men and 165000 were women. It is a familiar cancer that is found among Asians and Africans. Its prognosis is not so good, and the patients who develop hepatocellular carcinoma die within 1 year [70]. Amongst Pakistani, the prevalence of hepatitis B and C is moderate. Recognizing the load of hepatitis B and C, it is expected that the incidence of hepatocellular carcinoma will increase in the future. The most common HCV genotype in Pakistan is genotype 3 [71].

Risk Factors of Hepatocellular Carcinoma

The majority of hepatocellular carcinoma is considered to be linked with either chronic hepatitis B virus or C virus infection [72]. In the United States of America, more than 3 million people are continually infected with the hepatitis C virus [73]. Long-standing infections with hepatitis B virus, a chief universal risk factor for hepatocellular carcinoma, are less frequent generally in the United States than hepatitis C virus infection is. Amongst a few ethnic groups in the United States, though, the hepatitis B virus is a more widespread risk factor than the hepatitis C virus. For example, a Los Angeles report found that around 74% of hepatocellular carcinoma amongst the Asian population was associated with hepatitis B virus infection, whereas 90% of hepatocellular carcinoma in whites was related to hepatitis C virus infection [74].

Clinical Features of Hepatic Carcinoma

In lots of patients, hepatocellular carcinoma is asymptomatic. When ailments are visible, they are generally associated with chronic diseases of the liver, such as skin and eyes turning yellow, pain in the right upper quadrant of the abdomen, inflammation of the abdomen, general weakness, weight loss, and fever [75]. Hepatomegaly and discomfort were found in the majority of the patients. While the frequency of pain was double in non-cirrhotic than in cirrhotic patients [76,77].

Conclusion

The prevalence and economic impact of gastrointestinal carcinomas is considerable and is rising worldwide due to increased intake of processed and canned foods. The increased occurrence of GI tumors can be linked to reduced

consumption of foods that contain vitamins, minerals, and antioxidants, which help the body boost and enhance the activities of the immunity system. While according to the World Health Organization, approximately one-third of demises from cancer are due to the five principal dietary and behavioral risks such as high BMI (as obesity has become a pandemic and most people are developing multiple complications of this malfunction), little consumption of vegetables and fruits, not having enough physical activity, increased use of tobacco(as tobacco is accountable for around 22% of cancer-related deaths) and alcohol. The measures should have to be taken as people should know and be aware of the risk factors, predisposing factors of all cancers and how they can manage and modify their way of living and decrease the prevalence and incidence of gastrointestinal carcinoma, especially in developing countries. Only 1 in 5 low- or middle-income countries have updated or crucial data to make cancer policies.

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