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Gastric Cancer: A Comprehensive Review

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Abstract: The terrible effects of gastric cancer on health around the world are always there. Even though cancer rates are going down overall, stomach cancer is still the second most common cancer-related death and the fourth most common disease in general. This review aims to look at the disease's global frequency and downward trend, group the different types of pathology into subtypes based on immunohistochemical staining patterns and genetic signatures, and investigate the role of the H. pylori virus in the development of tumours, talk about how the disease is becoming more common among young people in the West, and explain how biological agents are used to treat the disease.

Keywords: Helicobacter Pylori, Type of Intestine, Stomach Cancer, Biologic-Focused Treatment

INTRODUCTION

A lot of people around the world die from stomach cancer. Even though cancer rates are going down overall, stomach cancer is still the second most common cancer-related death and the fourth most common disease in general. There is less of this disease because of better diets, improved food storage, greater protection, faster detection, and treatment, but the outlook is still not good. Most of the time, stomach cancer has already spread a lot by the time it is found. Surgery to remove the cancer is the main part of the treatment. If needed, chemo or radiation therapy is added on top of that. Survival rates have gone up because of this plan. Patients with metastatic stomach cancer still have a typical overall survival (OS) of less than a year because they are not getting good care. Because stomach cancer is a complicated disease, doctors are always looking for new ways to find it early and make treatments better [1].

The fact that stomach cancer is found in very different places around the world shows that many things affect how common it is, how many people survive it, and how many die from it. The vast majority of cases come from Asian countries. Only about 25% of cases are linked to the Americas and Europe together. In the US, people of colour and people from lower-income families are more likely to live in places that have been hit hard [2].

Lauren explained the difference between the two main types of the disease based on their histology: the intestinal type and the generalised type. What makes these groups different is their behaviour, biology, and understanding of how diseases spread and start. Over the last few decades, the number of cases of stomach cancer has been going down in a lot of different groups and subtypes. Electric cooling and other improvements in food storage technology, the ability to get fresh produce all year, reduced salt intake, fewer cigarettes, and the end of Helicobacter pylori disease in places where it was common could all be to blame for the drop. Even though the general rate of stomach cancer has gone down, the number of tumours in the stomach cardia and near the gastro-oesophageal joint has gone up. Also on the rise is noncardia stomach cancer in white people in the US and other Western countries aged 25 to 39 [3].

Foods and environmental factors have been linked to the disease in some studies. People who eat a lot of salt, salt-cured foods, nitrates, and smoked or pickled foods are more likely to get stomach cancer. Some studies have found a link between salt and food preservation, but most have used indirect methods and examined temporal patterns to reach their conclusions. Helicobacter pylori is a Class I human carcinogen that causes chronic mucosal infections. These infections are clearly linked to stomach cancers that don't affect the heart. However, gastro-oesophageal reflux is also linked to cancers of the heart and the gastro-oesophageal junction. The goals of this review are to look at the disease's decreasing trend in frequency and its spread around the world; describe the different clinical subtypes using immunohistochemical staining patterns and genetic signatures; and look at the role of the H. pylori bacteria has been linked to the growth of tumours; talk about how the disease is becoming more common among young people in the West; and describe the role of biological agents in treating diseases [4].

Global Impact

Over half of all cases of stomach cancer in the world are found in China, and 73% of those cases are found in Asia. The Americas account for 7% of the world's total, while the European Union accounts for 15% more. Different people in different parts of the world are affected in very different ways. As people age, guys get it twice as often as women do. Even in the same place, sickness rates are very different between race and ethnic groups. Minorities, Native Americans, and Hispanics all feel the effects of the problem, but white Americans feel them the most. Socioeconomic status, which strongly influences illness frequency, should not be considered separately from a person's ethnic background [5].

The type of gastric cancer found can be grouped by its location in the stomach. Cancers that begin in the cardia, or close by, are different from those that begin in the noncardia, or far away. It is very important to distinguish between cardia and noncardia diseases, as they appear to have different causes. Gastric cardia cancer and cancers of the gastro-oesophageal junction are becoming more common. Young people in the West are also getting more cases that aren't related to the heart.

Most of the time, stomach cancer rates are lower in wealthy countries than in less developed ones. In every place where stomach cancer that isn't caused by a heart problem is widespread, the poor are more likely to get it [6].

Helicobacter pylori infections are more common in areas with high population density, poor sanitation, and crowded conditions. It is true that income and education are linked in a good way for cardia stomach cancer, but not for noncardia tumours. When conducting these kinds of studies, keep in mind that other risk factors, such as Helicobacter pylori infection, smoking, or poor eating habits, may affect the results of the social class analysis. It's clear that environmental factors are important because first-generation migrants from countries with high incidence rates still face the risks of their home country even after moving to countries with low incidence rates. Because of the effects of early life experiences, the recurrence rate decreases with each generation [7].

Subtypes and Characteristics of Gastric Cancer

There are other ways to group stomach cancers, but the Lauren method is most commonly used. Based on the Lauren classification, there are two main histologic subtypes: intestinal and diffuse. There are different clinical and demographic traits found in each group. Gastric carcinomas may fall into any of these histopathological types. [8].

When intercellular adhesion molecules are lost, diffuse stomach cancer differs from intestinal-type cancer, which tends to remain localized. It's likely that both types produce proteins that can be targeted, such as the HER2 receptor.

One common way genes change in stomach cancer is by duplicating them. Immunohistochemistry (IHC) can identify proteins that are overexpressed. Amplification of HER2 has been linked to a lot of different types of cancer, like those in the lungs, liver, stomach, and intestines. 7–34% of stomach cancer tumours have too much HER2. This is especially true for tumours near the gastro-oesophageal junction or intestinal lesions [9].

People with stomach cancer who have too much of the EGFR gene are less likely to get better. A higher amount of vascular endothelial growth factors A (VEGFA) expression is linked to a worse outcome and the disease getting worse in about 40% of stomach cancer cases. The effects of the above proteins on life have been studied, and they could all be used as targets for biological treatments. We will discuss the specifics of the therapy studies later in this study. New measures for targeted treatments are being explored right now. The FGFR, the mammalian target of rapamycin, and the hepatocyte growth factor receptor are a few of them. Clinical studies are now looking into a number of new areas [10].

Intestinal Subtype

The most common tissue types found in people at high risk are intestinal subtypes, which tend to form spontaneously rather than being inherited from a parent. It mostly happens to older people; men are more likely than women to get it, and the lumps usually look like sores on the skin. A Helicobacter pylori infection is linked to a higher chance of getting cancer. The gastric form has been linked to a drop in stomach cancer cases around the world over the last few decades.

Changes in histology caused by a long-term infection with Helicobacter pylori ultimately lead to the development of a cancerous tumour. The first sign of a long-term H is gastritis without atrophy. pylori strain. After that, there is gastritis with widespread atrophy but no metaplasia, followed by intestinal metaplasia and dysplasia [11].

Long-Term H. Some people who develop an H. pylori infection may develop stomach atrophy, meaning they lose glandular cells, including parietal and chief cells. The illness causes the stomach to swell constantly and

damages the epithelium. The gastric epithelium can form in different parts of the stomach, but the small curve of the stomach is where intestinal metaplasia most often occurs. Metaplasia can lead to the growth of dysplastic sites. In Western medicine, dysplastic areas are thought of as aggressive cancers because they can spread to the lamina propria. In Japan, major nuclear and building problems that don't spread are thought to be cancer. Multiple oncogenes are overexpressed in gut tumours, but none have been reliably detected across different stages of the disease [12].

A gene called c-met is linked to 20% of stomach and intestinal cancers, and higher levels of c-met mRNA are associated with later stages of the disease. Some dangerous H. pylori strains produce an effector protein that appears to alter how c-Met receptors send and receive signals. This protein may affect how cancer starts and grows. Some changes in the K-ras gene have been linked to metaplasia, dysplasia, and invasive carcinomas in the gut [13].

In many stomach cancers, changes are found in genes that stop tumours from growing. The TP53 gene, which prevents tumour growth, is a key driver of the cell cycle. TP53 is lost or changed in a way that stops it from working in about 60% of invasive stomach tumours. Changes in TP53 expression have been observed in people with recurrent gastritis, metaplasia, and dysplasia linked to H. pylori; however, it is still unclear exactly how the two interact. Adenomatous polyposis coli gene changes have been linked to the development, spread, and progression of gastric cancer. These mutations have also been seen in gastrointestinal and diffuse stomach cancers. Microsatellites and hypermethylation are used in more situations [14].

Diffuse Subtype

This makes the idea that the gut type of stomach cancer is not as dangerous as the widespread type more likely. When it comes to younger people seeing it, there is no gender bias. There have been no precancerous cells found, and while it has been linked to H. E-cadherin levels drop most often when you have an H. pylori infection. If a stomach cancer doesn't come from a gland, it's likely metastasized, which means it's spread to other parts of the digestive system. Linitis plastica is a condition that can sometimes cause the stomach wall to become infected throughout its thickness. It is very uncommon for this group to have signet ring cell histology [15].

In widespread stomach tumours, a unique process that leads to cancer is marked by bad intercellular binding. Usually, this happens because the production of the cell adhesion protein E-cadherin decreases. The E-cadherin (CDH1) gene encodes a transmembrane protein that forms homodimers and helps cells adhere to one another. This gene can only be turned off by a "two-hit" method because it stops tumours from growing. Based on the information we have, inherited diffuse gastric cancer (HDGC) seems to follow an autosomal dominant trend. Because this disease starts early in life, a person's chance of getting stomach cancer has gone up by more than 80% by the time they are 80 years old. It can be hard to get the right diagnosis for some people with HDGC because they have multiple cancers hidden under a healthy mucus layer. People who have a history of stomach cancer in their family or who have CDH1 genetic mutations should get a preventive gastric gastrectomy. Diffuse stomach cancers have sometimes been linked to changes in CDH1. Different types of diffuse gastric cancers show promoter changes, mutations, and loss of CDH1 heterozygosity [16].

Helicobacter Pylori

One very rare type of cancer, stomach cancer, is linked to a spreading bacterium. Health risks to people are called class I. Helicobacter pylori is a spiral Gram-negative bacterium that affects half of the world's people. It causes stomach lymphomas, non-cardia adenocarcinomas, gastric lymphomas, and chronic gastritis. A Helicobacter pylori infection is the most well-known thing that can make you more likely to get stomach cancer, but not many people who get this infection actually get the disease. Cancers of the stomach and intestines are more likely to be linked to H. pylori. People with the diffuse form of stomach cancer are more likely to have H. pylori infections, but illnesses with this bacterium can cause either type of cancer. About 80% of cases of distal gastric cancer are thought to be caused by bacteria, but there isn't much of a link between bacteria and cardia gastric carcinoma [17].

The signs often start in childhood and can persist for a person's whole life if left untreated. Infections often cause long-lasting inflammation. Inflammation creates reactive oxygen species (ROS), which can damage DNA. Helicobacter pylori may cause hypermethylation, especially on CpG islands, which can turn off genes that stop tumours from growing. There is a wide range in the number of cancer-causing germs. Some of the most deadly types have the cancer protein coded by the cytotoxic-associated gene A (CagA). Type IV release of this protein into cells that line the stomach may start a chain of molecular events that lead to breast cancer. CagA appears to contribute to cancer development by disrupting epithelial polarity, promoting cell growth, reducing cell death, and disrupting intracellular connections. Because of the high number of CagA-positive types, cancer is more common in East Asia and the Colombian Andes, which are both high-risk places. One example of a virulence factor is the vacA protein, which signals epithelial cells to form more intracellular compartments and membrane channels [18].

Getting rid of H. pylori is a technical challenge because the cancer it causes takes decades to develop. This study examined how precancerous tumours grow and shrink after an infection resolves. A study that tracked patients for 15 years found that those who took medicine to treat H. stomach cancer was much less likely to happen in people who had H. pylori. At some point in the development of stomach cancer linked to H. pylori, treatment no longer lowers the risk for H. pylori, as clear analysis of the elimination studies shows. For now, we don't know what the exact effects of getting rid of the

germs will be. Paradoxically, the number of people getting gastric cancer has gone up in the global population [19].

Even though the number of cases of stomach cancer has gone down around the world in the last 30 years, a new tracking study from the SEER Program shows that the number of cases of noncardia, gut-type stomach cancer has gone up among white US people ages 25 to 39 during that time. In Europe, Spain is one of six places where this trend has been seen. There is no clear reason for this trend. People affected are very young, so it's unlikely this is the cause. However, the regular and possibly dangerous use of proton pump inhibitors and H2 blockers has been identified as a factor. One likely reason is the worrisome rise in the use of antibiotics by children. To prevent the worsening of disease numbers, more statistical studies are needed on this worrying trend [20].

Other Therapeutic Options

Surgically removing the growth is the best way to treat it. A full or partial gastrectomy may be part of this, based on the size and location of the tumour. You can test chemotherapies in three different situations: before, during, and after cancer spreads. To be more specific, the SWOG 9008 study examined what happened when chemoradiation was given after surgery for stomach or gastro-oesophageal joint cancers. The person could either wait it out or get radiation therapy with 5-FU/leucovorin up to 45 Gy. During the ten-year follow-up, the treatment group had a much higher total survival rate. However, this group often had a hard time handling chemotherapy after surgery. The MAGIC study looked at what happened to people who had cancer of the gastro-oesophageal junction or lower stomach after receiving treatment with epirubicin, cisplatin, and 5-FU (ECF) [21].

The treatment group had much better overall survival (OS) and progression-free survival (PFS) than the group that only had surgery. You can choose from other options besides combination chemotherapy for spread or return, such as ideal supporting care, ECF, DCF, or FOLFIRI. The US has approved only two specific drugs after they passed clinical trials, even though many others have undergone clinical trials. Many types of cancer have been studied as possible targeted treatments by blocking HER2. The monoclonal antibody trastuzumab binds only to HER2 and prevents it from sending signals or from activating its external domain. The TOGA trial was a Phase III international study evaluating trastuzumab with either cisplatin and 5-FU or capecitabine. Patients were grouped based on the degree of HER2 overexpression [22].

Patients who were going to get chemotherapy along with trastuzumab lived longer than those whose plans did not include the drug. As of now, the Food and Drug Administration has approved ramucirumab, a monoclonal antibody that targets vascular endothelial growth factor receptor 2. It is the first biologic therapy to show a survival benefit in patients with advanced gastric or gastro-oesophageal cancer who have progressed after first-line treatment. The AVAGAST study found that administering the monoclonal antibody bevacizumab with cisplatin and capecitabine improved total response rate and progression-free survival in patients with stomach cancer. Because it didn't make a big difference in total life, bevacizumab may not be useful for treating stomach cancer. In the EXPAND and REAL3 studies, adding the anti-EGFR monoclonal antibodies cetuximab and panitumumab to treatment did not prolong survival in people with advanced stomach cancer. Survival rates dropped everywhere because of the change. If you have stomach cancer and want to try nimotuzumab as a second-line treatment, a clinical study is now being done to see how well it works when added to irinotecan [23].

A Look at Future Endeavours

It is very important to protect everyone from getting stomach cancer. Even though the number of recorded cases of disease has decreased over the last few decades, there is still significant room for improvement in early detection, treatment, prevention, and drugs that increase life expectancy. People who are more likely to get stomach cancer, like those with CDH1 genes or a family history of the disease, must follow certain screening and treatment plans. Whether all high-risk places should regularly check for and treat the contagious and cancer-causing H. pylori bacteria is still a question. There are no clear guidelines for assessing atrophic or dysplastic changes in people living in high-risk areas without symptoms. Changes in the gut lining that are dysplastic or atrophic raise the chance of invasive cancer. People in this group should have an endoscopy. Endoscopic removal of visible cancers has led to a 5-year mortality rate of 90% or higher in Japan. Positive findings from observational studies conducted in Japan form the basis for developing screening guidelines for high-risk groups worldwide [24].

REFERENCE

[1] Siegel, R.L. *et al.* "Cancer statistics, 2023." *CA Cancer J Clin*, vol. 73, no. , 2023, pp. 17–48.

[2] International Agency for Research on Cancer "Cancer today." *International Agency for Research on Cancer*, 2024.

[3] Bray, F. *et al.* "Global cancer statistics 2022: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries." *CA Cancer J Clin*, vol. 74, no. , 2024, pp. 229–263.

[4] Pabla, B.S. *et al.* "Increased incidence and mortality of gastric cancer in immigrant populations from high to low regions of incidence: a systematic review and meta-analysis." *Clin Gastroenterol Hepatol*, vol. 18, no. , 2020, pp. 34759.e5.

[5] Petrillo, A. and Smyth, E.C. "27 years of stomach cancer: painting a global picture." *Lancet Gastroenterol Hepatol*, vol. 5, 2020, pp. 5–6.

[6] Li, Y. *et al.* "Global burden of young-onset gastric cancer: a systematic trend analysis of the Global Burden of Disease Study 2019." *Gastric Cancer*, vol. 27, 2024, pp. 684–700.

[7] Arnold, M. *et al.* "Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035." *Gut*, vol. 69, 2020, pp. 823–829.

[8] Ben-Aharon, I. *et al.* "Early-onset cancer in the gastrointestinal tract is on the rise-evidence and implications." *Cancer Discov*, vol. 13, 2023, pp. 538–551.

[9] Lumish, M.A. *et al.* "Clinical and molecular characteristics of early-onset vs average-onset esophagogastric cancer." *J Natl Cancer Inst*, vol. 116, 2024, pp. 299–308.

[10] Qu, X. *et al.* "The clinicopathological characteristics of

early-onset gastric cancer and its evolutionary trends: a retrospective study." *Am J Cancer Res*, vol. 12, 2022, pp. 2757–2769.

[11] Cho, S.Y. *et al.* "Sporadic early-onset diffuse gastric cancers have a high frequency of somatic CDH1 alterations, but a low frequency of somatic RHOA mutations compared with late-onset cancers." *Gastroenterology*, vol. 153, 2017, pp. 536–549.e26.

[12] GBD 2017 Stomach Cancer Collaborators "The global, regional, and national burden of stomach cancer in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease study 2017." *Lancet Gastroenterol Hepatol*, vol. 5, 2020, pp. 42–54.

[13] Gertsen, E.C. *et al.* "18F-fludeoxyglucose-positron emission tomography/computed tomography and laparoscopy for staging of locally advanced gastric cancer: a multicenter prospective Dutch cohort study (plastic)." *JAMA Surg*, vol. 156, 2021, pp. e215340.

[14] Maron, S.B. *et al.* "Determinants of survival with combined HER2 and PD-1 blockade in metastatic esophagogastric cancer." *Clin Cancer Res*, vol. 29, 2023, pp. 3633–3640.

[15] Gwee, Y.X. *et al.* "Integration of genomic biology into therapeutic strategies of gastric cancer peritoneal metastasis." *J Clin Oncol*, vol. 40, 2022, pp. 2830.

[16] Mariette, C. *et al.* "Consensus on the pathological definition and classification of poorly cohesive gastric carcinoma." *Gastric Cancer*, vol. 22, 2019, pp. 1–9.

[17] Nagtegaal, I.D. *et al.* "The 2019 WHO classification of tumours of the digestive system." *Histopathology*, vol. 76, 2020, pp. 182–188.

[18] Cancer Genome Atlas Research Atlas "Comprehensive molecular characterization of gastric adenocarcinoma." *Nature*, vol. 513, 2014, pp. 202–209.

[19] Cristescu, R. *et al.* "Molecular analysis of gastric cancer identifies subtypes associated with distinct clinical outcomes." *Nat Med*, vol. 21, 2015, pp. 449–456.

[20] Correa, P. and Piazuelo, M.B. "The gastric precancerous cascade." *J Dig Dis*, vol. 13, 2012, pp. 2–9.

[21] Yeoh, K.G. and Tan, P. "Mapping the genomic diaspora of gastric cancer." *Nat Rev Cancer*, vol. 22, 2022, pp. 71–84.

[22] Polk, D.B. and Peek, R.M. "Helicobacter pylori: gastric cancer and beyond." *Nat Rev Cancer*, vol. 10, 2010, pp. 403–414.

[23] Chen, Y.C. *et al.* "Global prevalence of helicobacter pylori infection and incidence of gastric cancer between 1980 and 2022." *Gastroenterology*, vol. 166, 2024, pp. 605–619.

[24] Totoki, Y. *et al.* "Multiancestry genomic and transcriptomic analysis of gastric cancer." *Nat Genet*, vol. 55, 2023, pp. 581–594.