WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A REVIEW ON: CARCINOMA OF STOMACH

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ABSTRACT

Stomach carcinoma is still secondary the leading cause of cancer deaths worldwide, though incidence and death dropped significantly over 50 years in most districts. Gastric episode cancer varies in different parts of the world and in the middle different nations. Despite the progress of the diagnosis and treatment, a survival rate of 5 years of pregnancy cancer is only 20 percent. Stomach cancer can vary-divided into intestinal tract and spread on the basis of the epidemic miological and clinical pathological features. The etiology for stomach cancer is multifactorial and covers both dietary and nondietary features. Great food related risk factors involved in the development of gastric cancer they include high nitrate content and high salt content.Numerous evidence has touched on the role of Helicobacter pylori (H. pylori) infection in pathogenesis stomach cancer. Development of stomach cancer a complex, multi-step process involving many genes and epigenetic mutations of oncogenes,genes, genes for DNA repair, cell cycle controls, and signaling molecules. Sound sensory system cancer prevention involves eating a balanced diet containing fruits and vegetables, improved sanitation and hygiene, testing and treatment of H. pylori to infection, and follow-up of malignant lesions. True that food plays an important role in gas etiology-Tric cancer provides a wide range of chemoprevention nutrition. Animal models have been widely used in analysis the gradual emergence of gastric carcinogenesis and this check chemopreventive food agents. Development of many prevention and treatment strategies Stomach cancer is a major challenge for the future.

Keywords*: Chemoprevention, Diet epidemiology, gastric cancer, Helicobacter pylori , Genetic alterations*

1. INTRODUCTION

In India, the rate of gastric detection rate is very low compared to western countries, and the number of new cases of stomach cancer is estimated at 34,000, with an increase in men (male and female ratio, 2: 1) The American Cancer Society's estimates of stomach cancer (also known as stomach cancer) in the United States by 2022 are: Approximately 26,380 new cases of stomach cancer (15,900 men and 10,480 women) About 11,090 deaths from this type of cancer (men) 6,690 women and 4,400 women)The incidence of stomach cancer in India is low compared to developed countries, although there are some local areas (the southern part and the northeastern regions of the country) where the incidence is similar to the world with the highest incidence. Abdominal adenocarcinoma, the leading cause of can-Death on earth is the second and fourth most common cancer in men and women respectively . Globe-ally, stomach cancer is estimated at 989 600 new cases too738,000 die each year. Stomach mortality rate cancer is higher than common diseases such as colon, breast, and prostate cancers. Despite the progress in diagnosis, the disease is usually diagnosed after an attack muscularis propria, because many patients experience it vague and indirect symptoms in the early stages as well the old triad of anaemia, weight loss, and rejection of meat-based diets are only seen in advanced stages. Wool-in addition, surgery and chemotherapy are of limited value in advanced diseases and there is a shortage of cellssymptoms of targeted treatment. As stom- cancer Ach has a very bad condition and a survival rate of 5 years by only about 20 percent, the new look of the results of epidemiological studies and screening are essential for develop key prevention strategies. This is updated discusses what is currently known about pathology,epidemiology, etiology, genetic and epigenetic mutations,and chemoprevention of stomach cancer[Sharma A,et al.,20l1]Living in the same place; African-American people, Hispanics and Native Americans are more affected than Caucasians in the United States. The high frequency of stomach cancer has written in Maoris of New Zealand . However, the spread of gastric cancer area is not possible only racial differences are listed. For example,The countries of Japan and China living in Singapore are very highrates than its counterparts in Hawaii. In addition,migrants from high-risk areas such AS Japan to destinations such as the United Statesfound to reduce the risk of stomach cancer .

Stomach cancer also called gastric cancer - cancer cells grow uncontrollably in stomach. Cancer can build anywhere in stomach. In the U.S., most cases stomach cancer include abnormal cell growth in the area where your stomach meets your esophagus (gastroesophageal congestion). In some countries, where stomach cancer is most common, cancer usually occurs in the main part of your stomach.About 95% of cases, stomach cancer starts in the gastrointestinal tract and progresses slowly. If left untreated, it can form a tumor and grow deep into the walls of your stomach.[Sharma A,et al.,2011] The tumor can spread to nearby organs such as your liver and pancreas. Stomach cancer occurs when there is a genetic mutation (mutation) in the DNA of your stomach cells. DNA code tells the cells when they grow and die. As a result of mutations, cells grow rapidly and eventually form a tumor instead of dying. Cancer cells out perfor healthy cells and can spread to other parts of your body(metastasize).Researchers do not know what causes the changes. However, certain factors appear to increase the risk of stomach . Stomach cancer is one of the most common cancers in the world

but is less common in the US Only about 1.5 percent of stomach cancers are diagnosed annually in the US, with cases steadily declining over the past 10 years.

Causes of Stomach cancer occurs when there is a genetic mutation (mutation) in the DNA of your stomach cells. DNA code tells the cells when they grow and die. As a result of mutations, cells grow rapidly and eventually form a tumor instead of dying. Cancer cells outperform healthy cells and can spread to other parts of your body (metastasize).Researchers do not know what causes the changes. However, certain factors appear to increase the risk of stomach cancer.

- Family history of stomach cancer.
- Infection with Helicobacter pylori (H. pylori).
- Gastroesophageal Reflux Disease (GERD).
- Gastritis.
- Epstein-Barr virus infection.
- History of stomach ulcers or stomach polyps.
- Fatty, salty, smoked or soaked foods.
- Foods that do not include many fruits and vegetables.
- Frequent exposure to materials such as coal, metal and rubber.
- Smoking, spraying or chewing tobacco.
- Excessive alcohol consumption.

Several genetic conditions are associated with an increased risk of stomach cancer, including

- Peutz-Jeghers syndrome.
- Li-Fraumeni syndrome.
- Family adenomatous polyposis.
- Genetic cancer.
- The variable immunodeficiency

2. EPIDEMIOLOGY

Age, sex and site distribution

Stomach cancer incidence is known to increase with age with the peak incidence occurring at 60-80 years. Cases in patients younger than 30 years are very rare[4,5]. In India, the age range for stomach cancer is 35-55 years in the South and 45-55 years in the North. The disease shows a male preponderance in almost all countries, with rates two to four times higher among males than females[3,6]. Gastric cancer can develop both in the proximal and the distal region. Distal gastric cancers predominate in developing countries, among blacks, and in the lower socio-economic groups. Dietary factors and Helicobacter pylori (H. pylori) infection are major risk factors for the development of distal tumors. Proximal tumors are more common in developed countries, among whites, and in higher socio-economic classes.[Fock KM,et al., 2010]The major risk factors for proximal cancers are gastroesophageal reflux disease and obesity. Distal tumors continue to predominate in Japan in contrast to the increasing prevalence of proximal tu-mors in the rest of the world.

3. GEOGRAPHIC DISTRIBUTION

Continued declines of fatalities and deaths Stomach cancer in many rich countries has been caused by changes in diet, food storage, and infection control H. pylori. Gastric episode cancer varies in different parts of the world and is very high Incidence rates listed in Eastern Asia, Eastern Europe-rope, and South America, while North America and African shows low recorded values . Stomach cancer the fifth most common cancer in Europe in 159 900 new cases and 118 200 deaths were reported in 2006 . the population of Linxian, China is known to have one of them high rates of esophageal cancer / gastric cardia in earth . In India, a case of gastric carcinoma is higher in the southern and northeastern countries with Mizoram records a rate adjusted for 50.6 and 23.3 years for men and women respectively . Recent tests-A total of 556,400 people died of cancer in India in 2010 based on a nationwide study find that12.6% stomach cancer with a mortality rate and the most common fatal cancer .Significant changes in gastric can-cer have been observed among different nationsliving in the same place; African-American people, Hispanicsand Native Americans are more affected than Caucasians in the United States. The high frequency of stomach cancer has written in Maoris of New Zealand . However, the distribution of gastric cancer site is not possible only racial differences are listed. For example,The countries of Japan and China living in Singapore are very high rates than its counterparts in Hawaii. In addition,migrants from high-risk areas such as Japan to destinations such as the United States has been found to reduce the risk of stomach cancer .

Types H. pylori from different parts of the world are associated with a clear phylogeographic division; therefore, the genetic comparison of H. pylori can serve as a sign of human migration. Indeed, the number of studies in which H. pylori is used there as a symbol of the origin of the various races

published .[Fock KM,et al.,2010] It is now widely believed that people acquired H pylori early in their history, long before modern migration from Africa Some people with high incidence of H infection. pylori, like those in East Asian countries, have a higher incidence of stomach cancer, while some more infected people, such as Africans (African enigmas) and South Asian (Asian enigmas), do so. no. These mysteries can be explained by the H variants. pylori genotypes, especially cagA and vacA, circulate in different parts of the world.

4. PATHOLOGY

Stomach cancer refers to any malignant neoplasm from the region from the middle of the gastro-esophageal junction and pylorus. Probably 95% of abdominal tumors are from the epithelial and is classified as adenocarcinomas. Adenosquamous,squamous, and isolated carcinomasrare.World Health Organization and Lauren The sification system described two types of histological clinically and epidemiologically different parts - intestines and spreads. Well different -a type of interstitial intestine, consisting of neoplastic joint cells, which form regular tubular-like particles Ulceate and a separate type is characterized by the penetration and intensity of belly wall ("skin bottle look") outside of the formation of different piles.[Hofman p,et al.,2004]

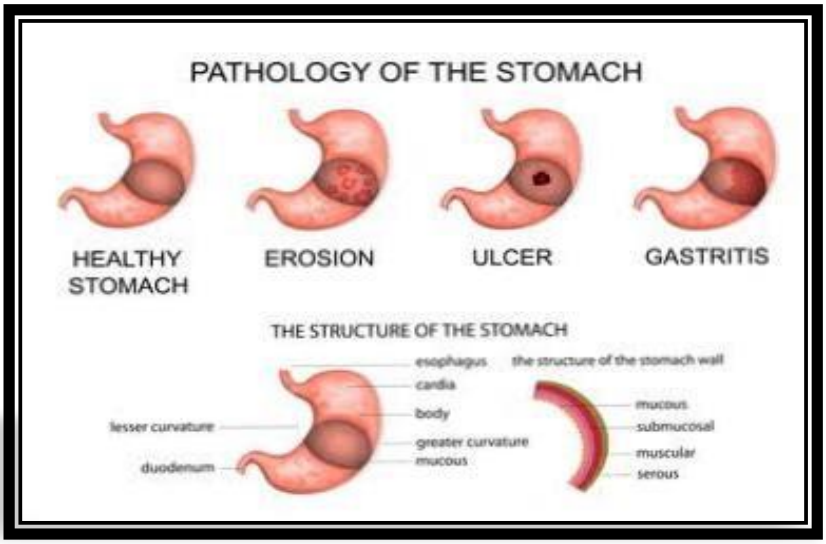

Diagram: Pathology of stomach

Intestinal type, more common in men, adults in high-risk areas, and African-American people, they are a pandemic and they can bet-ter prognosis. Such precancerous ulcers appear gastric atrophy and intestinal metaplasia, and are affected with natural materials such as H. pylori infection, which was-condition, and dietary factors. The diffuse type represents a large form of histological in permanent habitats, is very common in women and young patients, and is associated with blood group A, indicating genetic predisposition. Mixed gastric carcinomas that form in the intestines and spread components have also been identified .Development of invasive gastric carcinoma includes slow-moving evolution using a series of precan-cerous lesions. Consequential histopathological changes take place area in the abdominal mucosa including atrophic gastritis with loss of parietal cell mass, intestinal metaplasia, and dysplasia eventually leading to carcinoma. Meta-Sequence of plasia / dysplasia / carcinoma is very important for gastrointestinal cancer from an additional series of genetic mutations similar to those in it colorectal cancer.

Two major types of GC have been described by Laurén both intestinal and peripheral that exhibit different clinical and pathogenetic profiles, cellular pathogenesis and biological behavior, which often occur in different epidemiologic settings. Intestinal GC occurs mostly in the elderly, male patients; Diffuse GC is more common in younger patients, women. Both subspecies share natural risk factors; However, propagated GC pathogenesis is poorly understood and genes. [Hofman p,et.al.,2004]According to the World Health Organization (WHO), five major types of GC are known: tubular, papillary malignancies (with or without signet-ring cells) and mixed and mucinous . Tubular and papillary carcinomas are more likely to be associated with Laurén intestinal type and carcinomas that are not closely related. Improved Gastric carcinomas can show a wide variety of malignancies. Borrmann classification is still the most widely used method and classifies stomach cancer into four distinct types: polypoid carcinoma (type I), fungating carcinoma (type II), ulceated carcinoma (type III), and infiltrative carcinoma (type IV). Wound tumors can vary in malignant lesions with an irregular border with raised margins and stiff, uneven, and attached to the surrounding mucosa. The ulcer base is crotic, shaggy, and usually nodular. The mucosal folds that come out of the crater are rare and often show a thick, convex convection. Harmful wounds are usually larger than their good counterparts. However, most fatal lesions do not have these common features, therefore, endoscopic appearance is not a reliable enough diagnostic indicator and should be accompanied by systemic biopsies.

5. ETIOLOGY

Although the etiology of stomach cancer is multi factorial, more than 80% of cases are said to be caused by H. Pylori infection. In addition, diet, lifestyle, genetics, socio eco-common and other factors contribute to gastric carcinogen-**esi.**

6. H PYLORI

H. pylori, Gram-negative microaerophilic, spiral bacterium found in the gastric mucosa in patients with severe gastritis and chronic atrophic gastritis, has been recognized as an important risk factor for stomach cancer . Results for Several meta-analyzes concluded that H infection. pylori isassociated with increased risk of doubling of having stomach cancer. In future research which included 1526 Japanese patients who had duodenal Stomach ulcers, stomach ulcers, stomach polyps or non-ulcer dyspepsia,2.9% of H-positive patients. pylori grew later Stomach cancer when there is not a single uninfected patient mature plants. In 1994, the International Agency for Cancer research classified H. pylori as "Group human carcinogen "based on multidisciplinary studies .Currently, about 50 percent of the worlds population infected H. pylori. The spread of H infection. pylori varies significantly from country to country in Asia with high seroprevalence levels in development countries rather than industrial, in developed countries.Identification of H. pylori as a gas hazard-Tric carcinogenesis has encouraged extensive research on methods H. pylori by carcinogen-esi. A combination of harmful, permissive organisms environment, and genetic predisposition is considered-red is important for H-cancer of the stomach. pylori. H. pyloriit has been suggested that it launch a series of eventsto promote the continuous continuation of the normal abdomen epithelium through atrophic gastritis, intestinal metapla-sia, and dysplasia to carcinoma . Bacteria of produces several products that cause gastric mucosal damage such as urease, protease, phospholipase, ammonia, and acetaldehyde.[Suzuki H,et al.,2012]pylori disrupts the contraceptive function with urease-mediated myosin Ⅱ activity .Generation of oxidative stress is seen as virallence factor in H-infected hosts. pylori. H. pylori infection promotes the production of active oxygen and nitrogen and suppresses antioxidant defenses methods, leading to DNA oxidative damage. How-ever, H. pylori, given a variety of combat-Oxidant enzymes are released from oxidative stress as well Injury is limited only to the abdominal mucosa affected host [30]. H. pylori though not directly genic, suggested to favor the formation of mu-tagenic substances through burning mediators or with disrupting the process of correcting differences showed that H infection. pylori improves gastric acidity carcinogenesis by increasing endogenous DNA damage while reducing repair and seduction activities for muta-Changes in mitochondrial and nuclear DNA. Aberrant DNA methylation caused by H infection. pylori has been has been found to be a major risk factor for stomach cancer

7. DIETARY FACTORS

Literature research on the role of food in the pathogen- Stomach cancer is using PubMed as a search engine revealed more than 2000 epidemiological and experimental lessons. There are four people at high risk for stomach cancer it has been shown to eat starchy and poor foods protein level, and tend to eat fresh fruit as well vegetables. Both high starchy and low protein foods are possible allow acid-catalyzed nitrosation in the stomach and cause mechanical damage to the gastric mucosa . Using environmental method, Park et al found aso-a link between the use of a refrigerator, fruit intake, and stomach cancer deaths and good associations between salt /sodium intake and gastric cancer death and incidence Korea.Both epidemiological and experimental studies strongly support the role of overeating in the stomach carcinogenesis. D'Elia reported a direct relationship-differences between dietary salt intake and risk of stomach cancer with a risk that grows slowly throughout the use levels based on meta analysis of future studies.Consumption of large amounts of salted fish, soy sauce,vegetables soaked in salted water, cured meat and other salted foods diet improves H. pylori colonization, and increases risk of stomach cancer with direct gas injury-tric mucosa that causes gastritis. Salt is also known cause hypergastrinemia and endogenous mutations, Epithelial cell proliferation eventually lead son parietal cell loss and progression of gastric cancer .

Reports from this laboratory and other staff show that sodium chloride is full(S-NaCl) promotes the development of N-methyl-N'-Stomach of mice induced by nitro-N-nitrosoguanidine (MNNG).cancer [Young ZM,et al.,2012]Dietary nitrates are found naturally in food such as cabbage, cauliflower, carrot, legumes, seedlings, beets,and spinach or added during storage. In addition the nitrate content in fertilizer, soil, and water also affects respect for dietary nitrate. Nitrate, nitrate, and nitrosating agents can be automatically integrated with the response mediates viruses and / or activated macrophages. Ni-modification of the number of naturally occurring guanidines and L-arginine-containing polypeptides producing mu-tagenic compounds. Dietary nitrate is converted into motor-Cinogenic N-nitroso compounds (NNC) with stomach acidthus increasing the risk of stomach cancer. Minimum amount Pre-built NNC nitrosamine may be presentin other foods including processed meat, dried milk, immediatelysoups, and coffee dried on a direct fire. In addition to certain dietary components, cer-dirty recipes are also associated with an increase risk of stomach cancer.

8. LIFESTYLE

Alcohol, gastric irritant is an important risk factor stomach cancer. Zaridze et al reported an increase risk of stomach cancer in men and women who live regularly use strong alcohol. Direct relationship identified between drinking alcohol and bacco and community-based stomach cancer risk group study Research from this laboratory-The story has shown a positive relationship between alcohol use and smoking of tobacco with blood lipidbprofile in patients with stomach cancer European Pro-Specific Cancer and Nutrition (EPIC)the project found an important link between the purpose-the place and time of smoking and stomach cancer accident A history of smoking has been found to be important an independent factor that is at risk of dying from stomach cancer in patients undergoing surgical resection Smoking is known to lower prostaglandin as well maintain the integrity of the gastric mucosal Cigarette smoke has reportedly made a preliminary improvement stomach ulcers such as gastritis, ulcer, and intestines metaplasia. Smokers are more likely to have a higher incidence of this H. pylori infection and gastroduodenal inflammation than non-smoker.

9. FAMILY HISTORY

Stomach cancer is a well-known manifestation of can-cer predisposition syndromes similar to hereditary nonpol-yposis colon cancer and Li-Fraumeni syndrome. Agreement-at the OMIM website, 90 percent of stomach cancers they occur occasionally, and 10 percent are genetic. First a written report of the family's tendency to gastric cancer was described by Napoleon Bonaparte's family(OMIM_192090) and Napoleon, father, grandfather,my brother, and three sisters, all dying of stomach cancer years younger compared Scandinavian twins learn from Swedish, Danish, and Finnish twins have been found increased risk of stomach cancer in af- twinsdeceased person .Family members often share similarities environment and

have the same socio-economic status.These risk factors work independently or collectively genetics thus increasing the risk of cancer. The importance of family history as a risk factor for stomach cancer is easily assessed using a case-control method. We reviewed 15 family history and gastrointestinal cancer control studies (Table 2); six studies were from Europe, seven from East Asia, one from India and one from the United States.[Young ZM,et al.,2004]In these studies, the odds ratios (OR) of stomach cancer were calculated with reference to one or more of the first or second degree types of stomach cancer, but the definition of a good family history varied between the studies.

10. OCCUPATION

Jobs A good relationship has been seen in the middle increased risk of stomach cancer and the number of stay-which includes mining, farming, refining, and fishing and workers repairing rubber, logs and asbes-drops. Exposure to work in dusty, hot climates-peature places such as cooks, wood process-plant operators, food processor and related products operators are associated with greater risk of diffuse cancer of the diffuse subtype . German study by a group of uranium miners however found positive results statistically the non-essential relationship between the abdomen cancer deaths and work exposure to arsenic dust, fine dust, and limited volume from α and low-linear radiation transmission. There is a significant regional variation between high-risk areas. Migration from high-risk and low-risk areas reduces risk in the second or third generation, providing accepted participatory eating habits.5 This adds weight to the hypothesis that natural features work early in life.21 Discovery Helicobacter pylori has added fuel to the search for the cause of stomach cancer.

Role of smoking and alcohol habits:

There is a significant regional variation between high-risk areas.Migration from high-risk and low-risk areas reduces risk in the second or third generation, providing accepted participatory eating habits.5 This adds weight to the hypothesis that natural features work early in life.Discovery Helicobacter pylori has added fuel to the search for the cause of stomach cancer.

Smokers showed an 80% increase in the risk of stomach cancer (HR = 1.81, 95% CI 1.36-2.41) among non-drinkers. In contrast, heavy drinkers showed a significant increase in the risk of stomach cancer (HR = 1.46, 95% CI 1.05-2.04) between all subjects and an 80% increase in risk among smokers . In a study of a group of 7,150 men in Lithuania over a 30-year period, 185 cases of stomach cancer were found. High wine intake> 0.5 liters at a time compared to low drinking was associated with a higher risk of stomach cancer with HR of 2.95 men (95% CI 1.30-6.68)

Genetic & epigenetic alterations in stomach cancer:

The development of gastric cancer is a complex, mul-tistep process involving multiple genetic and epigenetic alterations in oncogenes, tumor suppressor genes, DNA repair genes, cell cycle regulators, and signaling mol-ecules. The catalogue of gene alterations in gastric cancer is expanding rapidly.An average of 4.18 genomic alterations has been suggested to be necessary for the development of gastric cancer. Gastric carcinoma is characterized by genomic instability that could be either microsatellite instability (MSI) or chromosomal instability

CIN:

CIN, which is considered a common instability abnormal abdominal plants, may be seen as a gain or loss complete chromosomes (aneuploidy) or chro-componentsmosomes [loss of heterozygosity (LOH), transfer,and enhancement . Comparison of genomic hybridiza-the analysis reveals a number of copies of the DNA copy beneficial variation in chromosomal regions 6p21, 9p34,11q23, 17p13, 19p13, and 22q13, especially for minors patients . Using laser microdissection, showed variability in the number of copies of the DNA in the abdomen cancer patients with a high frequency of 20q13 chromo-another benefit and genetic control of 114 people in growth zones, and 11 reductions genes in removal regions. LOH on chromosomes1p, 2q, 3p, 4p, 5q, 6p, 7p, 7q, 8p, 9p, 11q, 12q, 13q, 14q,17p, 18q, 21q, and 22q which are potential plant areasstress genes are believed to play a key role in electricitytric carcinogenesis.A high frequency of LOH was detected in adenomatous polyposis coli (APC), p53, nm23 and Rb loci [Park B ,et al.,2011]A few features have been suggested participation in CIN in patients with stomach cancer including disruption of chromosome division, DNA damage

MSI:

MSI, caused by errors in DNA duplication is evident in 15-20 Percent of stomach cancer with *high* frequency in family situations. High frequency MSI associated with advanced stomach cancer, invasive, with intestinal cancer suggested to be due to epigenetic dysfunction genetic malformation of hMLH1, while mutations have occurred converting the growth factor-β (TGF-β) RII, which is similar to insulin growth factor Ⅱ (IGFⅡ) R, and BAX gene over time Abdominal tumors with MSI show a reduced tendency for invasion and nodal metastasis Cytosine-adenine repeating instability, LOH of the APC, and removed from the colony

The genes of the cancer have been carefully classified plants.

Ontogenes:

Flexible activation and / or several enhancements to cogenes have been implicated in stomach cancer. K-ras oncogene was found to be altered (codon-12) in the intestine-nal-type cancer and pre-existing ulcers, intestinal meta-plasia, and adenoma, but not in advanced cancer .Excessive exposure to c-erbB2 cell surface receptor the tyrosine kinase family is most common in the intestinal tract Stomach cancer, and different types of stomach cancer,increasing c-met, transmembrane tyrosine kinase receptor, and deviation in FGFR2 / ErbB3 / PI3 the kinase method has been documented

several times .High correlation detected between EZH2 the hu-man homolog of Drosophila protein '' Enhancer of Zeste '', with colon cancer and the risk of remotenessmetastasis .

Tumor suppressor genes:

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Cell cycle regulators, growth factors and cytokines:

Genetic abnormalities and reverse exposure to the cell cycle regulators play a key role in gas pathogenesis-tric cancer. Excessive exposure to cyclin E and CDK together with improper expression of p53 and reduction of p27,a common occurrence in stomach cancer, associated with increased anger and negative ppredictio. Meta-cell proliferation analysis-related genetic polymor-phisms have posed a very high risk of the type spreading of stomach cancer in people with TP5372Propolymorphisms.[Park B,et al.,2011] Immunohistochemistry and TUNEL contamination caused by tissue series slides containing 293 Examples of gastric carcinoma have shown good correla interaction between cyclin expression D1, p21, or p27 with early stages of pTNM, tumor cell proliferation and positiveprognosis, but the opposite of the lymph node me-tastasis. However,the expression p27 is associated with the opposite ofindicator of apoptosis showing that tell cycle controls-tors may act as markers of molecular molecules prematurely gastric carcinoma. Many growth factors and cytokines are produced by the gastric tumor microenvironment regulates secretion,activation, as well as the survival of many cell types. Wide changes in the expression profile of parts of TGF-β signature method and its targets downstream occur during consecutive continuous normalization epithelium through chronic atrophic gastritis and dys-plasia to carcinoma. These changes include continuous increase in expression of TGFB1 / 2, TGFBR1, MYCand TP53, enhanced expression of SMAD4, CDKN1A,SMAD1 / 2/3, SMAD2 / 3 and CDKN1B in dysplasia a decrease in carcinoma, as well as improved exposureTGFBR2, SMAD7, RELAX, and CDC25A both in dyspla-sia and carcinoma . Systematic reviews and meta-anal-Interleukin (IL) -1B sysis is a collection of genetic polymorphisms impositions' -511, -31, and +3954 and receptor IL-1RN variable number tandem repeat (VNTR) polymorphisms revealed that IL-1B -511 T allele and IL-1 RN 2 VNTRare strongly associated with the increasing risk of development of gastric carcinoma especially non-cardia or intestinal type and in the Caucasus .

Invasion and angiogenesis:

Mutable dysfunction and reduced genetic control encoding cell-adhesion molecules that act as a tumor sppressors are labeled for stomach cancer. By activation of E-cadherin, a genetic product of CDH1 suggested to play a significant role in cell motil-growth, and attack of stomach cancer . Rare genetics changes in IQ motif containing GTPase-activating Protein 1 gene, also called p195 (locus 15q26), is negative cell adhesion control at adherens junction was has been found to occur in stomach cancer .Manifestations of proangiogenic vascular endothelial growth factor (VEGF) was shown to be related poor health in patients with stomach cancer[Wang XQ,et al.,2009]VEGF-Afound to be an important sign of the existence of tumor cells in the bone marrow, VEGF-D is auseful predictor of lymphatic proliferation of tumor cells in patients with metastatic cancer of the abdomen The spread of stomach cancer can be determined, in part, by profile of VEGF family members revealed in A major tumor in patients with stomach cancer . Using hu-examples of human stomach cancer, in vitro cell tests,and in vivo animal experiments, Lee et a demonstrated that AKT-HIF-independent hypoxia promotion The 1α-VEGF method contributes to stomach cancer genesis and angiogenesis.

Microribonucleic acids(miRs)

miRNAs are found within LOH regions, enlargement,weak areas, and other genomic associated with cancer regions control a number of important biological factors Conditions associated with carcinogenesis include proliferation,apoptosis, contrast, angiogenesis, metastasis, and The immune system also acts as both oncogenes and gene suppression of the tumor. MiR dysregulation plays a role an important role in the pathogenesis of gastric cancer. Read-Ies have shown that miRs act as oncogenes, such as miR-21, miR-106a and miR-17, were controlled,and miRs act as tumor suppressors, in including miR-101, miR-181, miR-449, miR-486, let-7a,control of stomach cancer . [Suzuki H,et al.,2005]In addition, genes polymorphism of miR-196a-2 that disrupts or-incorrect binding with mRN A targeted as a homeobox gene cluster and annexin A1 were strongly associated with a increased risk of stomach cancer . H. pylori infection was shown to cause cancer-associations Combined miRNAs include oncogenic (miR-106b) and tumor suppressor (let-7) miRNAs with hypermethylation of tumor suppressor miRNAs miR-124a-1, miR-124a-2 and miR-124a-3

Gene and protein expression profiling:

The advent of genomics, proteomics, and transcriptomic smake it a complete success molecular changes that occur during neoplastic trans-formation of gastric mucosa. In Japan, the genome comprehensive linking research has identified chromosome 2q33-35 as potentially at risk of proximal gastric can-cer . Data analysis of microarray gene-expression of 54 colorectal cancer and nearby cancer-free gas-tric tissue has identified genetic signals of different stages and various stages of stomach cancer. In the 19-gene period a signature that is separated between the upper and lower extremities Stomach cancer, an extended panel of 198 genes allowed breakdown of cancer into four stages and control once 10- and 9-gene signature enabled for pre-classification and advanced cancer respectively .. ana-patterns of genetic expression and their authenticity roles in gastric carcinogenesis using high-throughput tis-sue microarray technique. The results showed that in time p53 was useful in classifying low-grade dysplasia from high-grade dysplasia, to high levels of cyclin E may be an indication of a dangerous change dysplasia.[Suzuki H,et al.,2005] Affymetrix Gene expression profiles technology and quantitative polymerase chain reaction and in situ hybridization in exposed microarrays of exposed tissuet hat many

changes related to original gas-tric cancer stored in advanced stomach cancer, with additional genetic expression mutations in the corresponding AGC with a progressive model of gastric carcinogenesis. Mo-lecular manifestations of 8 primary gastric carcinomas,accompanying xenografts, and 2 novel gastric carcinoma cell lines reveal comparative histological features as well manifestation of a few symptoms as revealed by immunohis-tochemistry, copy number, and hypermethylation of upto 38 genes .

Epigenetic changes:

Although the role of genetic mutations in stomach cancer It has long been known, global changes in epigenetic landscape with reference to DNA methylation, histone Methylation and histone acetylation have only been renewed.recently written. While global hypomethylation leads to activated oncogenes and genomic instability, promoter Hypermethylation is associated with written silence-mutations in TSGs and genes for DNA repair.Various CpG island methylator phenotypes have been identified stomach cancer that serves as a good predictor indicator .Meta-analysis revealed aberrant methylation of 77 genes in stomach cancer, which raises the number of potential clinicians of DNA methylation as a risk predictor as well prediction .[Wu Wk ,et al.,2010]Hypermethylation of gene developers involved in regulating cell cycle, an important metolism nutrients, as well as the production of inflammatory mediators, has described in H infection. pylori and stomach cancer In cadherin, a member of the APC method, once CDH4 (encoding R-cadherin), hypermethylated in tumors in the abdomen. In particular CDH4 methylation is ear-splitting diagnostic marker of intestinal tumorigenesis .Epigenetic dysfunction with RAS hypermethylation-related gene, RASSF1A isoform, negative effect of K-ras, and the oncogene activity of R-RAS by hypo-Methylation has been reported in gastric carcinomas .Histone acetylation and deacetylation by tone acetyltransferases and histone deacetylases (HDAC) play an important role in chromatin regeneration. Histone H4 acetylation in both promoter and code genetic regions of p21WAF1 / CIP1 in expressive cells dominant-negative p53 significantly reduced electricity-tric cancer cells express wild type p5. Epigenetic modification also plays an important role in miRNA de-control of stomach cancer .[Kim SH,et al.,2008]

11. PROGRESS IN THE TREATMENT APPROACHES OF GASTRIC CANCER

Surgery:

The surgical approach of gastric cancer has ranged from open surgery to laparoscopic resection; the surgical treatment of gastric cancer has witnessed a significant leap in terms of outcomes. From early-stage gastric cancer to advanced gastric cancer, the indications for laparoscopic surgery has notably expanded, with the confirmation of its efficacy and safety by the growing body of available evidence .

Robotic surgery has been acknowledged as a better surgical approach compared to laparoscopic resection in terms of avoiding the drawbacks of the later, as it provides the following advantages: seven degrees of freedom, a tremor-filtering system, the ability to scale motion, and a three-dimensional (3D) vision system that significantly impacts a surgeon's dexterity, particularly upon dealing with tissues in a narrow field of vision That being said, the mean operative time of robotic surgery has been reported to be longer compared to laparoscopic or open resection. Meanwhile, the only significant difference in favor of robotic surgery is the reduction in intra-operative blood loss Therefore, the current focus should be directed toward the development of a new direction in laparoscopic surgery related to the saving of human resources while increasing the precision of the surgical approach.

The use of single-port (SPLG) and reduced-port laparoscopic gastrectomy (RPLG) is now becoming more mature and is currently being investigated by clinical trials. The application of the minimally-invasive approach via SPLG and RPLG would minimize associated trauma. Such advances in single-site surgeries have enabled surgeons to perform RPLG and SPLG via the robotic approach, and therefore, eliminating the restrictions on the movement of the surgical instrument. In a single-arm, phase I/II clinical trial investigating the efficacy and safety of conducting RPLG by a single surgeon, it was found that among 19 patients who underwent RPLG, none of them required intra-operative conversion to laparoscopic or open surgery nor had major complications during RPLG surgery . Therefore, it is suggested that RPLG offers a safe and effective alternative in managing cases with early-stage gastric cancer. It is also suggested that this approach could be applied in high-advanced cases as well . SPLG is the reduced port technique on account of surgical approaches because the operation is performed through a single incision in the abdominal wall. It is an extremely minimally invasive method, theoretically providing less post-operative pain, improved cosmetic results and earlier recovery after surgery compared to conventional multiport laparoscopic gastrectomy.

Adjuvant Chemotherapy:

Adjuvant chemotherapy is recommended in completely-resected T2N0, T3, or T4 gastric adenocarcinoma, particularly in those who did not receive neoadjuvant therapy . The Japanese Adjuvant Chemotherapy Trial of TS-1 for Gastric Cancer (ACTS-GC) highlighted the benefits of S-1, an oral fluoropyrimidine, adjuvant therapy for 1 year . This trial included a total of 1,059 patients with stage II or III gastric cancer, who underwent D2 surgery, were randomly assigned to receive either S-1 (6-week cycles: 2 weeks without and 4 weeks with S-1 at a dose of 80–120 mg/m^2/day for 1 year) or surgery alone. The study showed significantly better 3-year survival in the S1 arm compared to surgery (80.1 vs. 70.1%), respectively.

The CLASSIC trial, which was conducted in South Korea, China, and Taiwan, included 1,035 patients with stage II, IIIA, or IIIB gastric cancer .Patients were randomly divided into two groups after D2 resection. One group received combined therapy of oral capecitabine of eight 3-week cycles (at a dose of 1,000 mg/m^2/twice a day on days 1–14 each cycle) and intravenous oxaliplatin (130 mg/m^2/on day 1 of each cycle for 6 months after surgery). Meanwhile, the other group received surgery only. Patients who received the combined adjuvant chemotherapy had significantly higher 3-year disease-free survival (DFS) of 74% compared to the 59% 3-year DFS in those who underwent surgery alone. This observation highlights the fact that XELOX (capecitabine plus oxaliplatin) adjuvant chemotherapy, when administered for 6 months, can significantly reduce the risk of post-operative recurrence while improving DFS in patients with gastric cancer. The results of this study further establish the status of the XELOX regimen as a standard chemotherapeutic agent for combined therapy in the population with gastric cancers of stages II or III.

A Japanese, randomized controlled clinical trial (JACCROGC-7) was published in the American Society of Clinical Oncology (ASCO) conference in 2018 . Patients with stage III gastric cancer after radical gastrectomy (D2, R0) were randomly divided into two groups. The first group (experimental) received S-1 combined with Docetaxel, while the second group (control) received S-1 alone. The results of this study showed that the relapse-free survival (RFS) in the experimental group was significantly higher than that of the control group at 3 years (65.9 vs. 49.6%, $P = 0.0007$). The analysis also revealed that S-1 combined with docetaxel significantly reduced the risk of all types of recurrence, including hematogenous, lymphatic, and peritoneal

12. INTRAPERITONEAL HYPOTHERMIC CHEMOTHERAPY

The management approach of peritoneal metastasis from cancer of gastric-origin has improved dramatically with the use of cytoreductive surgery (CRS) and hypothermic intraperitoneal chemotherapy (HIPEC) However, this is only applicable to a certain subgroup of patients. In the same context, the value of the prophylactic use or the combined therapy with HIPEC in high-risk individuals or those with positive cytology is still to be confirmed by larger and more robust randomized controlled trials.

Since the application of HIPEC, researchers around the world had put tremendous efforts into improving this approach. Gastrectomy, combined with HIPEC, may lead to the prolongation of survival in patients with stage IIIB gastric cancer Recently, a meta-analysis reported that HIPEC may improve the OS of patients who undergo surgical resection for advanced gastric cancer, and may also help in the prevention of local peritoneal recurrence among cases with serosal invasion in gastric cancer .

13. MOLECULAR-TARGETED THERAPY AND IMMUNOTHERAPY

In the context of precision treatment, chemotherapy combined with targeted drugs to improve efficacy has been a research hotspot and clinical focus in recent yearsThe multicenter, randomized, phase III ToGA (Trastuzumab for Gastric Cancer) trial examined the comparative efficacy chemotherapy doublet regimens in the form of (capecitabine plus cisplatin) or (5-fluorouracil plus cisplatin), which were given every 3 weeks for a total of six cycles, and chemotherapy plus intravenous trastuzumab in a group of patients with HER-2 positive gastric cancer . Trastuzumab plus chemotherapy was noted to result in a significantly higher median overall survival compared to the chemotherapy-alone arm (13.8 vs. 11.1 months), respectively. In patients with high HER-2 expression, trastuzumab significantly improved their median overall survival to reach 16 months compared to the 11.8 months in those assigned to chemotherapy only.

In the setting of 2nd line treatment, ramucirumab resulted in a significant clinical improvement in previously-treated patients with gastric cancer both as stand-alone therapy and as an adjuvant to paclitaxel. The REGARD trial examined the efficacy of ramucirumab in patients with gastric adenocarcinoma . Patients received either intravenous ramucirumab (8 mg/kg) or placebo 2 weeks after progression following first-line chemotherapy. Ramucirumab resulted in a significantly longer median overall survival compared to placebo (5.2 vs. 3.8 months), with a 6-month PFS rate of 41.8 and 31.6%, respectively. This observation was also confirmed in the double-blinded randomized phase II RAINBOW trial, where patients with gastric adenocarcinoma received either (paclitaxel 80 mg/m^2/days 1, 8, 15 plus ramucirumab) or placebo (days 1 and 15) .The combined therapy of ramucirumab and paclitaxel resulted in significantly higher OS (9.63 vs. 7.26 months), with further improvement in PFS and RR as well.

However, in the setting of 1st line treatment, ramucirumab failed to result in the same efficacy observed in 2nd-line treatment trials. In a double-blinded phase II clinical trials involving patients with advanced gastric and esophageal cancer, patients were randomized to receive either (FOLFOX chemotherapy plus ramucirumab) or (FOLFOX plus placebo) Even though the combined therapy of FOLFOX and ramucirumab resulted in a significant improvement in disease control rate; however, the median PFS was insignificant to the placebo group (6.4 vs. 6.7 months, $P = 0.89$).

14. PREVENTION STARTERGIES

Proposed a portable system of prevention of stomach cancer including screening once H treatment. pylori infection, endoscopic and histolog-ic detection of malignant lesions, development of sanita-hygiene, dietary restriction, and diet a balanced diet consisting of rich fresh fruits and vegetables on antioxidants.Elimination of H infection. pylori is considered important mary chemoprevention strategy to reduce the incidence of stomach cancer . American and European guidelines recommend the termination of H. pylori in all patients with atro-phy and / or intestinal metaplasia and in all degree-degree rel-patients with gastric cancer more than endoscopic and histological observations. Asian Pacific Gastric The Cancer Consensus is recommended based on people diagnosis and treatment of H infection. pylori regions with annual cases of more than 20 / 100,000 stomach cancers to convert H. pylori-induced biochemical, genetic, andepigenetic mutations. In a few intervention trials, H. Pylori termination prevents precancer progression-ulcers. Intervention studies in Japan are demonic-significant prophylactic effects of H. pylori eradi-cation in the development of stomach cancer. Price for immediate termination of the treatment of stomach cancer development was also confirmed in animal models.Modification of dietary patterns and changes in cooking-Ing procedures are believed to significantly reduce diarrhea risk of cancer [108]. Freezing foods that prevent consumption salt as a barrier, reduces the chances of mold excessive growth in the diet, and provides nitrate conversion in the NNC it is more difficult to treat and soak in water .Several studies have shown a protective effect of a diet high in raw vegetables and fruits against risk of stomach cancer. A total EPIC study of 521,457 studies in 23 of the 10 European institutions countries have found good relations within taking dietary antioxidants and reduced risk of constipation cancer .[kabir S,et al.,2009]A review of the beneficial effects of the fruit as well vegetables in the conduct of EPIC research that European 477 312 studies covering 683 adenocarcinoma in the abdomen patients with 11 years of follow-up received that diet of fresh fruit and citrus fruits protected against risk of spreading and cardiac cancer of the abdomen respectively .The EPIC study also reported positive correlations between eating red meat and the risk of stomach cancer,while high plasma vitamin C, some carotenoids, retinol and α-tocopherol, a diet high in cereal fiber,Mediterranean cuisine exhibited inverse associa-episode . Dietary modification by reducing diet salt and salty foods, as well as dietary supplementation Fruit and vitamin C are therefore considered strat-egy to prevent stomach cancer . Both green and black drinking tea has been reported

to be associated with it reduce the risk of stomach cancer in epidemiological and experimental studies Results from epidemiological studies and experiments shows great influence of antioxidant properties on to prevent gastric carcinogenesis. Low plasma levels It contains vitamin E and ascorbic acid Lreported in high-risk areas . Lessons from this laboratories have shown that patients in the stomach cancer is easily absorbed by active oxygen-lipid peroxidation due to lipid deficiency,antioxidant capacity . In particular, vitamin C reported to inhibit the growth of stomach cancer by inhibition-nitrate conversion to NNC and delay implantation of the tumor in experimental animals . Ascorbic the acid has been shown to reduce mutagenicity the power of MNNG in S. typhimurium and gastric in-cosal cells Results from the intervention trials confirm the topicshigh risk of developing stomach cancer can be pro-tested by adding antioxidants. Findings to reduce cancer mortality in those who receive it Antioxidant ingredients in Linxian, China, were the first a large-scale intervention study that promoted basic researchthis place .Dietary antioxidants may have their own anti-inflammatory effects in gastric carcinogenesis by any other or combination the following methods- to prevent metabolic function procarcinogens, carcinogens that do not work, improve Methods of DNA repair, reducing protooncogene ex-pressure, activating genes to suppress the tumor, blocking the cell enlargement, angiogenesis and inflammation, which causes variability,ferntiation and apoptosis, stimulate the body's response,and to correct the elements of cross-writing and signing methods. [Khan N,et al.,2008]Results from epidemiological studies and experiments shows great influence of antioxidant properties on to prevent gastric carcinogenesis. Low plasma levels It contains vitamin E and ascorbic acid reported in high-risk areas. Lessons from this laboratories have shown that patients in the stomach cancer is easily absorbed by active oxygen- lipid peroxidation due to lipid deficiency,antioxidant capacity . In particular, vitamin C reported to inhibit the growth of stomach cancer by inhibition-nitrate conversion to NNC and delay implantation of the tumor in experimental animals . Ascorbicthe acid has been shown to reduce mutagenicity the power of MNNG in S. typhimurium and gastric in-cosal cells The results from the intervention trials confirm the topics high risk of developing stomach cancer can be pro-tested by adding antioxidants. Findings to reduce cancer mortality in those who receive it Antioxidant ingredients in Linxian, China, were the first a large-scale intervention study that promoted basic research this place

15. CLASSIFICATION OF GASTRIC CANCER

1) Sporadic gastric cancer:

Most GCs occur occasionally and mainly affect people over the age of 45. These carcinomas are called "sporadic gastric cancers" (SGCs) They are usually caused by a combination of many natural substances. They are 60-80 years old, and males are often affected twice. there are women, especially in high-risk countries.

2) Early onset of gastric cancer:

Most GCs occur occasionally and mainly affect people over the age of 45. These carcinomas are called "sporadic gastric cancers" (SGCs) They are usually caused by a combination of many natural substances. They are 60-80 years old, and males are often affected twice. there are women, especially in high-risk countries.

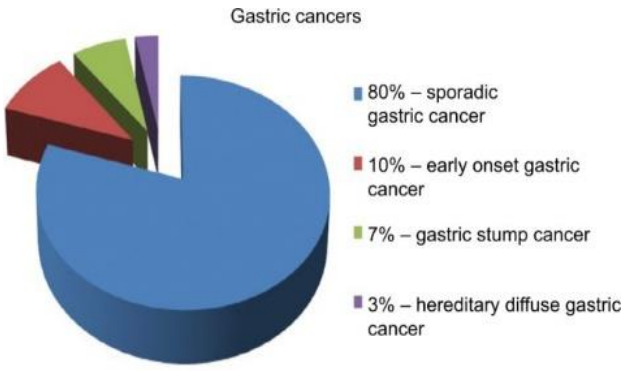

Fig : Classification of gastric cancer

3) Gastric stump cancer

Gastric stump cancer (GSC) is a separate subtype of GC, defined as a carcinoma that occurs in the gastric remnant at least 5 years after the surgery for peptic ulcer. GSC represents from 1.1% to 7% of all GCs , and males are more prone to them than woman. Gastrectomy is a well-established risk factor for GSC, even long time after the initial surgery. After 15 years from the gastrectomy, the risk of GSC is increased four- to sevenfold compared with the healthy population. EBV infection is more often in gastric remnants than in intact stomachs. The virus may interact with the p53 protein. In contrast, H. pylori infection in GSCs is less frequent. GSCs are commonly preceded by well-defined precursor lesions, mostly by dysplasia, and therefore, endoscopic surveillance with multiple biopsies of the gastroenterostoma is recommended.

4) Hereditary diffuse gastric cancer

Most cases of GCs appear sporadically, but in 5%–10% of cases, familial clustering is observed.44 HDGC concerns 1%–3% of all GCs (HDGCs) result from inherited syndromes, one of which are germline mutations in the CDH1 gene that encodes E-cadherin. These are autosomal

dominant conditions that cause diffuse, poorly differentiated GC, which infiltrates into stomach wall and causes thickening of the wall without forming a distinct mass.

16. CONCLUSION

Stomach cancer is a disease of complex etiology that includes- incorporation of many harmful substances and many genes and epigen-etic changes. Controlling H infection. pylori in ways termination or vaccination may be significant potentially preventing stomach cancer. In addition,changes in diet and lifestyle can be reduced stomach cancer especially at high levels places. Now there is evidence of price change genetic and genetic polymorphisms are associ- consumed with an increased risk of stomach cancer. Still the discovery of new drugs and types of organizations,the effect of treating stomach cancer is still negative.Information on various risk factors and cur-hiring genomic and proteomic technology can help identifying high-risk people, directed at the forerunner ulcers, development prevention strategies, and provision appropriate personal treatment. Strong, bigger balanced and controlled studies are required to genetic markers date. Pharmacogenomics can be i an attractive way to increase treatment once and for all reduce side effects. Targeted prevention and important strategies for treating stomach cancer the challenge of the future

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