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Peptic Ulcer Disease and Its Implications

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Abstract

Peptic ulcer disease (PUD) is one of the commonest diseases seen throughout the world. Peptic ulcers are open sores that develop on the inside lining of your stomach and the upper portion of your small intestine. The most common symptom of a peptic ulcer is stomach pain. There are various risk factors for the development of peptic ulcer disease, but the most important ones are *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drugs (NSAIDs). Patients generally present with dyspepsia or peptic ulcer bleeding. Acid suppressant therapy, *H. pylori* eradication, and avoidance of nonsteroidal anti-inflammatory drugs are the cornerstones of treatment of peptic ulcer disease. Peptic ulcer bleeding could be life-threatening. It is managed by appropriate supportive care, intravenous proton pump inhibitor therapy, and endoscopic homeostasis. Trans arterial embolization (TAE), Herbal treated and surgery are rarely required if endoscopic therapy fails.

Keywords: *Peptic, Ulcer, Disease, Implications, anti-inflammatory, drugs*

Introduction

Peptic ulcer disease (PUD) is a lesion or an erosion in the lining of digestive tract [1]. It is a common disease, and because of this, it represents a significant social and economic factor. Effective prevention and treatment depend heavily on further understanding of the nature of the disease and a more precise understanding of the variations between various types of ulcers. Although recent research has suggested a decrease in the incidence, rates of hospital admissions, and death rate linked with this condition, the predicted prevalence of peptic ulcer disease in the general population is 5–10% (Lanas *et al*., 2015; Sonnenberg, 2013) [2, 3]. Due to pepsin or gastric acid secretion, peptic ulcer disease is characterized by discontinuity in the GI tract's inner lining. It penetrates the stomach epithelium's muscularispropria layer. The stomach and proximal duodenum are where it frequently happens. It could affect the distal duodenum, jejunum, or lower oesophagus [4]. The use of nonsteroidal anti-inflammatory medicines (NSAIDs) and a chronic *Helicobacter pylori* infection (Hp) are the two most frequent etiological causes [5]. Peptic ulcer disease symptoms can range from minor stomach discomfort to severe bleeding and perforation. Although one of the most widespread medical conditions in the world, peptic ulcers are reportedly now treatable. Since a *Helicobacter pylori* infection is what causes peptic ulcers, treatment often aims to accomplish the following objectives:

- eliminating the bacteria
- lowering acid production in the digestive tract by relieving discomfort, and
- accelerating the healing of peptic ulcers.

Proton Pump Inhibitors (PPIs) and histamine-2 (H2) receptor antagonists, two commonly used therapies for peptic ulcers, have demonstrated negative side effects, relapses, and a variety of medication interactions. However, medicinal plants and their chemical constituents can also be used to cure and prevent Peptic Ulcer Diseases [6].

Definition and Etiology of Peptic Ulcer Disease

A peptic ulcer is described as an extreme loss of substance that affects the mucosa of the stomach

and/or duodenum and extends past the muscularis mucosa, primarily to the muscle layer, as a result of the ambient discharge of gastric acid. The use of nonsteroidal anti-inflammatory medicines (NSAIDs), especially Acetylsalicylic Acid (ASA), and chronic *Helicobacter pylori* infection (Hp) are the two most frequent etiological causes. When all possible causes of peptic ulcers (PU) are taken into account, they account for fewer than 5% of cases. One of these neuroendocrine tumors, called a gastrinoma or Zollinger-Ellison syndrome, is hyperactive and secretory of the gastrin and typically found at the head of the pancreas or on the wall of the duodenum. It has been determined that O blood type and tobacco abuse are risk factors for the development of ulcer disease. There may be some instances of familial aggregation, although the presence of genetic components is unknown. Smoking makes ulcer healing more difficult and encourages their recurrence, especially in patients who are Hp (+) or who regularly take NSAIDs. The digestive and extra-digestive diseases, most frequently associated with peptic ulcer, among which are included the concomitant presence of chronic gastro esophageal reflux disease (GERD), Barrett's esophagus, chronic obstructive pulmonary disease (COPD), liver cirrhosis, chronic renal failure, while in other clinical situations, their presence is lower, as in the atrophic gastritis, Addison's disease, autoimmune thyroiditis and hyperparathyroidism [7].

Epidemiology of peptic ulcer disease

Although it has a pretty global spread and affects people of many races, the disease is fairly heterogeneous. Over the course of a lifetime, it affects 5–10% of the general population on average. The prevalence of *Helicobacter pylori* is inversely related to the level of economic population, the degree of development, and the level of hygienic social environment. This represents roughly 10–20% of people infected globally, with significant variations between different races and countries of the world having been confirmed. Peptic ulcers occur on average 1% of the time each year in people with HP infection. For both sexes, the prevalence is comparable. Some experts "estimate the average age for development of gastric and duodenal ulcer" based on the adjusted incidence in proportion to age. While the average age of duodenal ulcer beginning is around 45 years old, the peak incidence of stomach ulcer occurs between the ages of 55 and 65 [2]. Worldwide, there are considerable epidemiological variations. As a result, the prevalence of *H. pylori* infection is substantially higher (two to five times higher) in underdeveloped countries than in industrialized ones, most likely as a result of the poorest dietary and hygienic practices that exist today. Additionally, there are obvious disparities in how antibiotics and NSAIDs are used. This explains why the prevalence of negative HP peptic ulcers is significantly lower in developing nations than it is in industrialized ones [8]. The duodenal side of the body is better known than the stomach side for the processes through which the Hp favours the development of PU. This bacterium causes an inflammatory and immunological response at the level of the stomach and duodenal mucosa in infected patients, which is followed by the release of several pro-inflammatory cytokines such IL-8, IL-1 β, and TNF-α. As a result, both acute and chronic gastritis develop, which in turn causes the mucus layer's quality and thickness to decline. Because the density of the antral D cells declines in Hp-infected patients, less somatostatin is secreted, which results in the loss of the inhibitory stimulus and gastric hypersecretion. The ensuing hypergastrinemia activates the gastric parietal cells, increasing acid secretion and lowering pH in the duodenal and stomach lumens. This process also continuously controls the degree to which duodenal gastric metaplasia manifests. As a result, the duodenal mucosa loses some of its ability to segregate bicarbonate, which promotes the development of duodenitis and, ultimately, duodenal ulcer. The levels of gastrin revert to normal following the elimination of Hp. The ability of various Hp strains to produce the cytotoxic protein (CagA) and the so-called vacuolating protein influences how ulcerogenic they are (Vac A). The second most typical reason for ulcers is the use of NSAIDs. Once Hp has been reliably ruled out, this group of medications accounts for 70–85% of cases where they are the cause. They are thought to be responsible for 20–30% of gastric ulcers and up to 10% of duodenal ulcers overall. According to estimates, up to 50% of people who take chronic NSAIDs have few clinically significant erosive lesions, up to 30% of them ulcers, of which only 1% annually are complicated. NSAIDs harm the gastric and duodenal mucosa primarily through two mechanisms. On the one hand, these medications have the properties of mild non-ionized acids, which can easily enter the epithelial cells and the mucus layer. The ability of cyclooxygenase inhibitory enzyme to lower the intracellular concentration of prostaglandins is another and most significant consequence. These are crucial for preserving the health of the gastroduodenal mucosa because they have an intramucosal vasodilator effect that keeps

the blood flow unhindered and, secondarily, stimulate local mucus and bicarbonate secretion, which promotes cell turnover and epithelization [9].

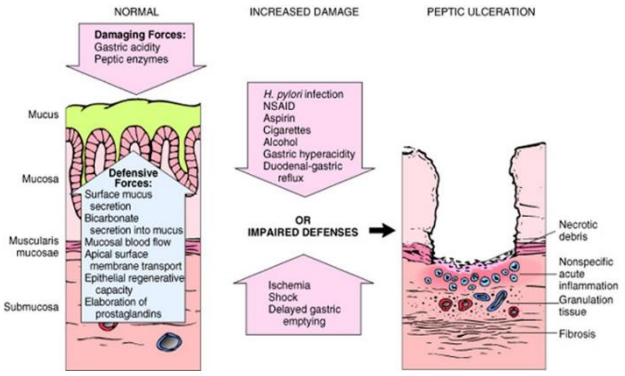

Fig 1: Pathogenesis of Peptic Ulcer Disease

Causes of peptic ulcer disease

Helicobacter pylori

Most patients with peptic ulcer disease have *H. pylori* as an etiologic factor, and it may increase a person's risk of developing stomach cancer. Human stomachs become colonized with *H. pylori* (Figure 2). Although the exact mode of *H. pylori* transmission is unknown, it appears to be a fecal-oral route of person-to-person transmission. Adult *H. pylori* prevalence appears to be negatively correlated with socioeconomic level. Additionally, it is believed that *H. pylori* transmission can occur in bodies of water [10].

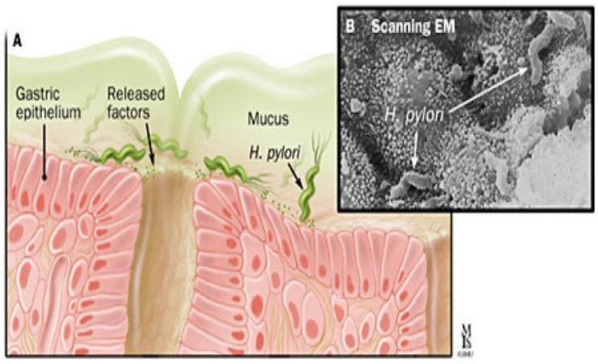

Fig 2: A, *H. pylori* resident on the gastric epithelium; **B**, electron micrograph.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDS)

Adverse gastrointestinal events linked to NSAID use occur in a small but significant proportion of patients, leading to significant morbidity and mortality. Advanced age, a history of previous ulcer illness, concurrent use of corticosteroids and anticoagulants, larger dosages of NSAIDs, and major systemic problems are all risk factors for the development of NSAID-associated gastric and duodenal ulcers. From the idea of topical injury to notions including various processes, the concept of gastroduodenal mucosal injury has evolved. By being acidic, NSAIDs cause mucosal damage topically. Endogenous gastric acid and pepsin may harm the surface epithelium by reducing the hydrophobicity of gastric mucus. The reduced synthesis of mucosal prostaglandins seems to be the primary mechanism via which NSAID systemic effects are prominent. The two cyclooxygenase isoenzymes, cyclo-oxygenase-1 and cyclo-oxygenase-2, catalyze the conversion of arachidonic acid into prostaglandins. The housekeeping enzyme cyclo-gene oxygenase-1's keeps organ homeostasis in check. The inflammatory enzyme cyclo-oxygenase-2 is induced. Only the gene for cyclo-oxygenase-2 has a corticosteroid-responsive repressor element, despite the fact that NSAIDs can block both processes. According to the literature, NSAIDs' anti-inflammatory effects are mediated by inhibiting cyclo-oxygenase-2, and their negative side effects, such as gastric and duodenal ulcers, are brought about by their effects on the constitutively expressed cyclo-oxygenase-1.

Between 22 and 63% of people using NSAIDs had *H. pylori*. The majority of research do not find a significant difference between NSAID users and nonusers in the prevalence of *H. pylori*. In contrast to medication use, underlying *H. pylori* appears to be the cause of gastroenteritis in patients receiving NSAID therapy. NSAID use is most likely the cause of the reduced prevalence of *H. pylori* in individuals with gastric ulcers compared to those with duodenal ulcers. Duodenal ulcers are less common from NSAID use than stomach ulcers. Based on the inhibition of prostaglandin synthesis, NSAIDs seem to cause ulcers by a mechanism unrelated to *H. pylori* [11].

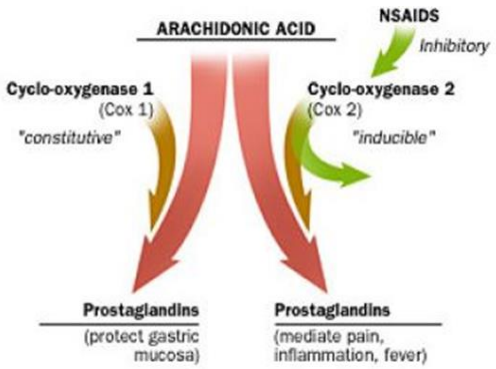

Fig 3: Prostaglandin synthesis and mechanism of action Cox-2 inhibitors

Gastrinoma (Zollinger-Ellison Syndrome)

The classic triad of Zollinger-Ellison syndrome involves peptic ulcers in unusual locations (i.e., the jejunum), massive gastric acid hypersecretion, and a gastrin producing islet cell tumor of the pancreas

(gastrinoma).

About 50% of patients develop gastrinoma in the pancreas. 20% of individuals also have it in their duodenum, while other people have it in their stomach, liver, ovary, stomach mesentery, peripancreatic lymph nodes, or small bowel mesentery. The prevalence of Zollinger-Ellison syndrome in duodenal ulcer disease is 0.1%. As one of the many neoplasia syndromes, this syndrome affects one-fourth of individuals [11].

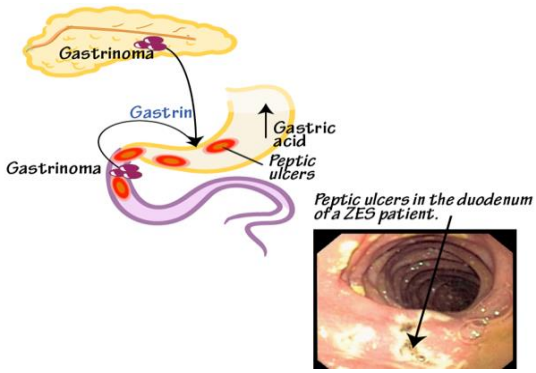

Fig 4: Gastrinoma (Zollinger-Ellison Syndrome)

Type I (MEN I)

Gastrinoma patients may develop inoperable ulcer disease. Endoscopy or x-ray may show enlargement of the gastric rugae because gastrin is trophic to the gastric mucosa. Additionally, patients may have gastroesophageal reflux and diarrhea, including steatorrhea from the inactivation of lipase by acid. 75% of individuals have sporadic episodes of these symptoms [11].

Hypercalcemia

The stomach acid hypersecretory state seen in people with MEN I and Zollinger-Ellison syndrome has a clear relationship with hypercalcemia. An intravenous calcium infusion causes an increase in stomach acid production in healthy individuals. Additionally, calcium has been shown to directly induce gastrin secretion from gastrinomas both in vivo and in vitro. In fasting gastrinoma patients and those with MEN I, resolution of hypercalcemia (by parathyroidectomy) decreases basal acid output and serum gastrin concentration, indicating that resolution of hypercalcemia is crucial to the treatment of this patient subgroup.

Genetic Factors

Pathogenesis of ulcer disease involves genetic factors. First-degree relatives of ulcer sufferers have a lifetime risk of having the condition that is around three times higher than that of the general population. A family history of duodenal ulcer is reported by 20–50% of patients; clusters of relatives with gastric ulcers are often reported by patients [11].

Smoking

The prevalence of ulcer disease, mortality, complications, recurrences, and rates of delayed healing are all strongly positively correlated with cigarette smoking, according to the research. Compared to nonsmokers, smokers have a roughly two-fold increased risk of developing ulcer disease. Both *H. pylori* and cigarette smoking contribute to the development of peptic ulcer disease. Both patients with and without peptic ulcers have a substantial correlation between *H. pylori* infection and cigarette smoking. Smoking cigarettes may make people more susceptible, reduce the stomach mucosal protective factors, or create an environment that is more conducive to *H. pylori* infection [11].

Stress

Regarding the part played by psychological elements in the pathogenesis and natural history of peptic ulcer disease, numerous researches has produced contradictory results. The significance of psychological elements is still far from clear. Acute stress causes increase in heart rate, blood pressure, and anxiety, but it only causes basal acid secretion to rise significantly in patients with duodenal ulcers. Nobody has a distinct "ulcer-type" personality. The psychological makeup of ulcer sufferers is largely similar to that of the general population, but they appear to be more sensitive to stress. Furthermore, there is little proof that certain employment characteristics affect the prevalence of ulcer disease [12].

Alcohol and Diet

Despite the fact that alcohol has been demonstrated to harm the gastrointestinal mucosa in animals, this damage appears to be connected to the absolute ethanol used (200 proof). Pure ethanol causes clear, immediate mucosal injury because it is lipid soluble. It is unlikely that mucosal damage occurs at ethanol concentrations of less than 10% because the majority of people do not consume absolute ethanol (20 proof). Low quantities of ethanol (5%), however, may only moderately promote the release of gastric acid; larger concentrations inhibit acid secretion. Although physically intriguing, this has no bearing on the development or treatment of ulcers. According to reports, some foods and drinks can lead to dyspepsia. There isn't any solid proof that a particular diet causes ulcer disease. Caffeinated, decaffeinated, or cola-type drinks, beer, or milk have not been linked in epidemiologic research to a higher risk of ulcer disease. In ulcer sufferers, dietary

modification is not necessary beyond avoiding things that make you feel pain [11].

Clinical Manifestations

The presence of burning or corrosive pain, primarily in the epigastrium, is the most common symptom of an uncomplicated peptic ulcer. It can occasionally be described as amorphous stomach pain, nausea, vomiting, generalized discomfort, or as a pressure or feeling of abdominal fullness or hunger. Epigastric discomfort typically manifests in duodenal ulcer patients while they are fasting, one to three hours after meals, or at night. It may also happen in connection with stressful circumstances. Eating any type of meal or taking antacids relieves this epigastric pain within a few minutes, but it returns cyclically within two hours. For numerous days, weeks, or months, symptoms may last. Due to the rarity of experiencing discomfort upon awakening in the morning, two-thirds of duodenal ulcer patients report that the pain wakes them at night. Anorexia and/or weight loss are uncommonly present in these patients. Contrarily, the majority of them frequently display hyperphagia and weight gain, likely because the pain typically goes away after eating. This is the well-known "pain/ingestion of food/alleviation" three-step process [13]. Even if the pain loses its characteristic three-step progression and instead becomes continuous and strong, there are instances when it radiates to the back or right upper quadrant, suggesting the development of an ulcer with a likely localization at the posterior surface of the duodenal bulb.

The pancreas can thus be thought to have a penetrating problem. The pain from a stomach ulcer typically subsides with food intake and/or antacids in the postprandial phase and manifests earlier than with a duodenal ulcer. Due to a concurrent delayed stomach emptying, only one-third of patients awaken at night from pain, and up to 50% may have anorexia and weight loss. Only 50–70% of duodenal ulcers and less than 50% of stomach ulcers exhibit the three-step traditional clinical pattern, which has a low sensitivity. Additionally, it lacks specificity because GERD and dyspepsia patients may have experienced symptoms that were quite similar. The most frequent finding during a clinical examination is the sensation of pain near the epigastrium. The initial sign of an ulcer, particularly in older individuals taking NSAIDs, may be connected to the occurrence of one ulcer-associated complication. However, ulcers can be asymptomatic in many people. NSAIDs have been suggested to be able to conceal ulcer discomfort [14]. Multiple entities, such as functional dyspepsia, gastroesophageal reflux disease, gastric cancer, gallbladder or pancreatic disease, should be considered in the differential diagnosis. When symptoms are consistent with a peptic ulcer, objective proof is required to support the diagnosis. Recurrences are frequently noted after the symptoms get better. Concomitant *H. pylori* infection that has not been completely eliminated and regular use of NSAIDs are the two most significant causes causing ulcer recurrence. The natural history of PUD has been drastically altered by the elimination of *H. pylori*, avoiding their recurrence. Additionally, stopping the use of NSAIDs clearly affects how the disease develops and, in some circumstances, causes the peptic ulcer to completely heal.

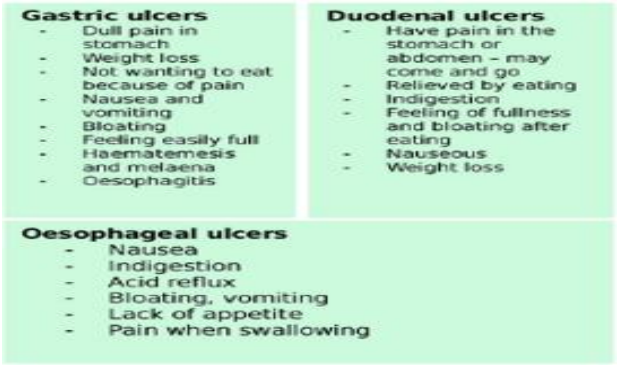

Fig 5: Clinical Manifestation diagram

Biochemistry of peptic ulcer disease

When *Helicobacter pylori* penetrates the stomach of the host, four steps are crucial for the bacteria to achieve successful colonization, chronic infection, and disease pathogenesis; this complicated interaction between the host, environmental variables, and the virulence factor of the bacteria. These steps include:

1. Survival in the acidic stomach
2. Motility mediated by flagella that is directed toward epithelia cells.
3. Attachment to host cell by adhensin/receptors interactions
4. Causing tissue damage by toxin release

It is not fully understood how *H. pylori* causes the different types of lesions to form in the gastroduodenal mucosa. The kind of peptic ulcer is determined by the hypo- or hyperchlorhydria caused by *H. pylori* infection. Cytokines that inhibit parietal cell secretion are the principal mediators of *H. pylori* infection. However, *H. pylori* can also directly impact the H+/K+ ATPase α-subunit, activate Calcitonin Gene-Related Peptide (CGRP) sensory neurons linked to somatostatin, or limit gastrin formation [15]. Although hyposecretion is linked to the

development of gastric ulcers, 10-15% of *H. pylori* infection patients experience enhanced gastric secretion due to hypergastrinemia and decreased antral somatostatin levels. This causes a rise in histamine release, which in turn causes the parietal and stomach cells to secrete more acid or pepsin.

Additionally, the elimination of *H. pylori* results in a rise in somatostatin mRNA expression and a decrease in the expression of gastrin mRNA. The vast majority of individuals who still have stomach ulcers also have mucosal atrophy and hypochlorhydria. The systemic inhibition of constitutively expressed cyclooxygenase-1 (COX-1), which is responsible for prostaglandin synthesis and is linked to reduced mucosal blood flow, low mucus and bicarbonate secretion, and the inhibition of cell multiplication, is the primary mechanism of NSAID-associated damage to the gastroduodenal mucosa. NSAIDs, in a concentration-dependent pattern reversibly inhibit the enzyme activity. Exogenous prostaglandins and cyclooxygenase-2 (COX-2)-selective NSAID usage together lessen mucosal damage and ulcer risk [16]. However, the NSAIDs' varying physicochemical characteristics result in variations in their toxicity [17].

Mucosal injury is brought on by NSAIDs because they alter mucus phospholipids and cause mitochondrial oxidative phosphorylation to become decoupled. NSAIDs become protonated and pass lipid membranes to enter epithelial cells (pH 7.4), where they ionize and release H+ when exposed to acidic gastric juice (pH 2). In such state, NSAIDs are unable to penetrate the lipid barrier and become trapped inside epithelial cells. As a result, oxidative phosphorylation becomes decoupled, mitochondrial energy generation is lowered, cellular permeability is elevated, and cellular integrity is compromised. The risk of developing NSAID-induced ulcers is highest in patients with a history of peptic ulcers or hemorrhages, who are older than 65, who also use steroids or anticoagulants, and who take high dosages or combinations of NSAIDs [7].

Pathogenicity of peptic ulcer disease

The mechanisms involving the development of PU (favored by Hp) are better known in the duodenal than the gastric side. Patients with bacterial infections experience an inflammatory and immunological reaction at the level of the stomach and duodenal mucosa, as well as the release of several pro-inflammatory cytokines such as IL-8 and TNF-α. Thus, acute and chronic gastritis develop, which weakens the mucus layer's quality and thickness.

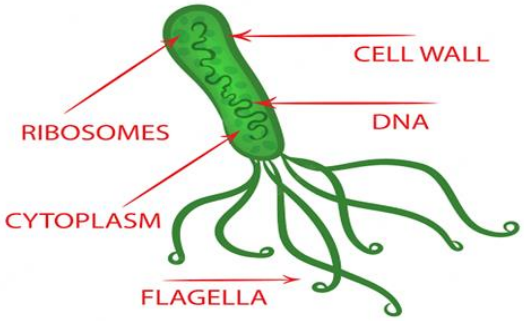

Fig 6: The structure of *Helicobacter pylori*

Because the number of the antra lD cells declines in Hp-infected patients, less somatostatin is secreted, which results in the loss of inhibitory stimulation and gastric hypersecretion. The ensuing hypergastrinemia activates the gastric parietal cells, increasing acid secretion and lowering pH in the duodenal and stomach lumens. This process also continuously controls the degree to which duodenal gastric metaplasia manifests. As a result, the duodenal mucosa loses some of its ability to segregate bicarbonate, which promotes the development of duodenitis and, ultimately, duodenal ulcer. The levels of gastrin revert to normal following the elimination of HP. The ability of various HP strains to produce the cytotoxic protein (CagA) and the so-called vacuolating protein (Vac A) determines how ulcerogenic they are [18]. The second most frequent cause of ulcers is the consumption of NSAIDs and/or ASA. Once HP is securely ruled out, both drug groups account for 70–85% of all cases of drug-related illness. They may contribute to up to 10% of duodenal and up to 20% of stomach ulcers, on average. According to estimates, up to 50% of long-term NSAID users have few clinically significant erosive lesions, ulcer prevalence can reach up to 30%, and only about 1% of complex ulcers per year [19]. NSAIDs harm the gastric and duodenal mucosa primarily through two mechanisms. On the one hand, these medications have the properties of mild non-ionized acids, which can easily enter the mucus layer and the inside of the epithelial cells. The ability of the cyclooxygenase inhibitory enzyme to lower the intracellular concentration of prostaglandins is another and most significant consequence. These are crucial for preserving the health of the gastroduodenal mucosa because they have an intramucosal vasodilator effect that keeps the blood flow unhindered and, secondarily, stimulates local mucus and bicarbonate secretion, which promotes cell turnover and epithelization [20].

Anatomy of peptic ulcer disease

The top portion of the abdomen, right behind the diaphragm, is where the stomach is situated. The size, shape, and position of the stomach can change depending on posture and content since it is distensible and has a free mesentery. When stuffed with food, an empty stomach, which is about the size of an open hand, can fill much of the upper abdomen and, when the person is upright, may sink into the lower abdomen or pelvis. The duodenum curves sharply and nearly in a circle from the pylorus to the ligament of Treitz. Its size, or 25 cm, is roughly equivalent in length to the width of 12 fingers. Its location is mostly stable and it is primarily retroperitoneal. In terms of both function and the development and presentation of disease, the duodenum and stomach are closely connected organs. There are seven main regions of the stomach. 1-2 cm distal to the esophagogastric junction is the heart section. The superior part of the stomach that is above a fictitious horizontal plane that crosses through the esophagogastric junction is referred to as the fundus. The smaller distal quarter to third of the stomach is the antrum. The pylorus is a 1-2 cm-wide canal that runs between the stomach and duodenum. The lesser curve is the stomach's medial shorter border, while the greater curve is the stomach's opposite surface. When peristalsis occurs, the angular, which is along the lesser curvature of the stomach where the body and antrum meet, is accentuated [11].

The duodenum is divided into four sections and curves in a circle from the pylorus to the ligament of Treitz. Beginning at the pylorus and running under the liver to the gallbladder neck, the superior portion is about 5 cm long. The duodenal bulb is the first 2 to 3 cm of the superior portion. Along the right side of the pancreatic head, the descending or second part of the duodenum descends in a sharp curve. At the major papilla, either individually or jointly, the common bile duct and the pancreatic duct enter the medial aspect of this section of the duodenum. The duodenum runs across the spinal column and inclines upward for 5-8 cm before making a medial turn to become the horizontal part. The ascending section starts at the left of the spinal column and ascends away from the aorta for a distance of 2 to 3 cm before coming to an end at the ligament of Treitz, where the intestine turns forward and downward to form the jejunum [11].

Therapy of peptic ulcer disease

If gastric acid production is adequately reduced, the majority of peptic ulcers will heal. There are two reasons why peptic ulcer disease should be treated. Both the lowering of hostile elements and the enhancement of protective variables are crucial.

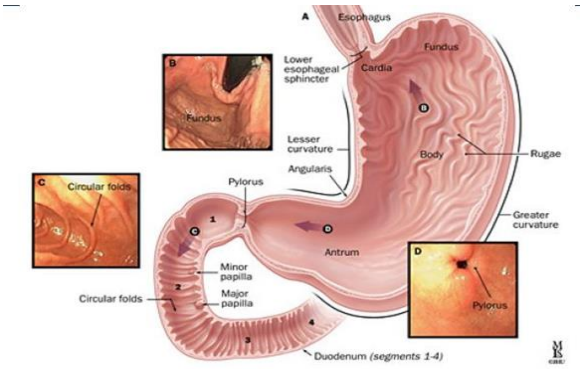

Fig 7: A, Normal anatomy of the stomach and duodenum; B-D, corresponding endoscopic images.

Surgery, Proton Pump Inhibitors (e.g., omeprazole, lansoprazole), H2-receptor antagonists for histamine, and antacids all work by neutralizing or reducing gastric acid. Mucosal protection is increased by prostaglandin and sucralfate drugs. Although the *H. pylori* infection is eradicated, unlike other treatments, it does not necessitate maintenance therapy to prevent ulcer recurrence. Patients should refrain from substances like NSAIDs and smoking that are known to aggravate peptic ulcer disease.

Medical Therapy

The purpose of treatment for peptic ulcer illness is to alleviate symptoms, heal craters, stop complications, and avoid recurrences. Drug therapy should be a part of medical therapy, and it should aim to do the following:

1) Reduce gastric acidity by mechanisms that inhibit or neutralize acid secretion,

2) Coat ulcer craters to prevent acid and pepsin from penetrating to the ulcer base,

3) Provide a prostaglandin analog,

4) Remove environmental factors such as NSAIDs and smoking, and

5) Reduce emotional stress (in a subset of patients).

In addition to treating gastric and duodenal ulcers more effectively than a placebo, antacids neutralize stomach acid. Antacids must be taken in relatively large dosages between one and three hours after meals and before bed, and they may have unwanted side effects. Diarrhea brought on by magnesium hydroxide is the main adverse effect of antacids containing magnesium.

By inhibiting the H2 receptor on the parietal cell, histamine H2-receptor antagonists lower the generation of stomach acid. Cimetidine, ranitidine,

famotidine, and nizatidine are a few examples of H2 blockers that can be used to treat gastric and duodenal ulcers. This class of substances successfully reduces acid output. In general, H2-receptor antagonists are secure. Cost, dose requirements, practicality, and potential drug interactions should all be taken into account while selecting a medication. The hydrogen-potassium ATPase enzyme found on the lumenal surface of parietal cells is rendered inactive by the class of medications known as proton pump inhibitors, or PPIs. The last common pathway in the secretion of hydrogen ions is made up of ATPase, which functions as a proton pump. In terms of medical treatment for peptic ulcer disease, this class of medications is currently regarded as the gold standard. Omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole are a few examples of PPIs that are on the market. Increasing the PPI dosage can cause achlorhydria by significantly decreasing acid output (unachievable by H2 blockade). When gastric hypersecretion is resistant to other treatments, proton pump inhibitors are the go-to treatment. A safe and efficient type of treatment, proton pump inhibitors have been found to prevent NSAID-associated gastroduodenal ulcers. Additionally, research has demonstrated that PPIs are superior than H2-receptor antagonists in the treatment of all forms of peptic ulcer disease. The aluminum salt of a sulfated disaccharide is sucralfate. The medication promotes prostaglandin synthesis, coats or forms a barrier over the ulcer crater, and binds to unpleasant substances like bile salts. Sucralfates appear to increase prostaglandins, which support enhanced mucosal integrity and accelerate epithelial regeneration, while the precise mechanism of action is unclear. Patients are less likely to adhere to a sucralfate regimen since it takes numerous doses per day, despite the fact that it has been found to be just as effective as an H2 blocker in treating both duodenal and stomach ulcers. Sucralfate's main notable negative effect is constipation and it is not absorbed systemically. A prostaglandin E1 analog called misoprostol boosts mucosal resistance and very slightly decreases acid output. Misoprostol has been recommended as a preventative measure against NSAID-induced mucosal damage. The medication is too expensive for the majority of people on long-term NSAIDs and has severe side effects, mostly mild to moderate diarrhea. Peptic ulcer healing is aided by the reduction of stomach acid production. Unfortunately, peptic ulcers frequently return if acid suppression medication is not continued. Since the elimination of *H. pylori* is necessary for the long-term treatment of peptic ulcers, all ulcers caused by this infection should be treated with the intention of eliminating the virus. Despite being susceptible to a number of medicines in vitro, *H. pylori* is challenging to treat because to its home beneath the stomach mucosa. Two weeks of triple therapy, which included bismuth, tetracycline or amoxicillin, and metronidazole, was the initial gold standard for treatment. The *H. pylori* cure rate is 90-95% or higher when adherence to this regimen can be ensured; nonetheless, 20% of these cases experience side effects. Treatment guidelines for *H. pylori* are continually developing, and newer, simpler regimens have been devised. A triple medicine combination that combines a PPI (such as omeprazole or lansoprazole) along with amoxicillin and a more recent antibiotic, clarithromycin, is currently the gold standard of treatment. For seven to fourteen days, all three medications must be taken twice daily (preferably 14 days). Patients with particular allergies or pharmaceutical intolerances may be given alternative medications. Patients with confirmed *H. pylori* infection and peptic ulcer disease should always have the option of curative therapy available. If a stomach ulcer does not heal after 8 weeks of standard medical treatment, it should be reevaluated by numerous endoscopic biopsies and cytology to rule for gastric cancer. If a biopsy reveals no cancer, vigorous therapy should be started for six weeks in order to eliminate *H. pylori* and restrict acid production with full doses of a proton pump inhibitor. Non-healing gastric ulcers should be surgically removed since they may indicate underlying cancer even with negative repeat biopsies following this second severe course of medical therapy.

Surgical Therapy

The necessity for surgery to treat peptic ulcer disease has decreased during the past few decades in the United States. The extensive use of H2 receptor antagonists and, more recently, proton pump inhibitors may be the main causes of this reduction. The main reasons for surgical intervention continue to be complications such gastrointestinal hemorrhage, perforation, or gastric outlet obstruction. The most frequent justification for surgical surgery in the treatment of benign gastric ulcers is the ulcer's incomplete healing following a sufficient trial of medicinal or endoscopic therapy. Before receiving a surgical consultation, patients typically receive a 6-month trial of anti-secretory medications. The significant danger of underlying cancers is the main worry with relation to ulcers that have not healed. Due to the benign nature of duodenal ulcers, doctors may

track their patients' symptoms to determine how they are responding to treatment plans. Surgery is typically one of three options for people with duodenal ulcers: vagotomy, vagotomy plus antrectomy, or subtotal gastrectomy. Truncal vagotomy with drainage, selective vagotomy with drainage, or proximal gastric vagotomy alone are all examples of vagotomy alone (without stomach resection) [21].

Injection Therapy

Upper gastrointestinal hemorrhage can be treated cheaply, easily, and frequently using injection therapy. A tiny retractable needle-equipped sclerotherapy catheter is inserted into the endoscope's biopsy channel. The treatment for non-bleeding visible vessels involves the injection of a solution at three or four nearby sites that are 1-3 mm away from the vessel. The visible vessel is then inserted after that. When a vessel is bleeding, injections are given in the area until hemostasis is reached. The vessel is then injected after that. Endoscopic hemostasis has been accomplished with a variety of different sclerosant drugs, either alone or in combination. Adrenaline, hypertonic saline with adrenaline, adrenaline plus polidocanol, pure ethanol, or combinations of dextrose, thrombin, and sodium morrhuate have all been demonstrated to reduce mortality, rebleeding, and the requirement for emergency surgery. The use of combined injectable and thermal therapy to treat bleeding ulcers has theoretical benefits. Epinephrine injection causes vasoconstriction and promotes platelet coagulation, decreasing blood flow and amplifying the effects of heat therapy, which causes coaptive coagulation. Recent research has showed that patients with spurting bleeding responded better to combination therapy (epinephrine injection and heating probe) than patients with oozing bleeding.

Mechanical Therapy

Recently created endoscopic hemoclips have entered the world of endoscopic therapy for peptic ulcer disease. These tiny titanium clips, which measure 3–4 mm, can be opened and closed while being used through the endoscope's operating channel. They could be used to clip or pinch off a bleeding vessel. When completely extended, they hold tight to the vessel even after the patient's endoscope is taken away. Hemoclips should be utilized in the proper environment as emerging research have demonstrated that they are an efficient and secure way for treating some types of peptic ulcer disease [2].

Radiological Therapy

In the management of bleeding gastric and duodenal ulcers, angiography is a helpful diagnostic and therapeutic method. When endoscopy is ineffective as a diagnostic tool, angiography can locate the site of bleeding. In patients who are at high risk for surgical intervention, it should also be taken into account. Two distinct embolization methods are used in angiographic therapy to treat GI bleeding. Infusion of vasopressin intra-arterially results in vasoconstriction, which stops ulcer bleeding in 50% of instances. Through a catheter, emboli can be injected into the bleeding location, such as absorbable gelatin sponges, tissue adhesives, or other occlusion tools (such microcoils). Ischemia and perforation are two possible side effects of embolization therapy.

Complications and implications

Complications And Implications of Peptic Ulcer Disease in Human Health

If peptic ulcers are not treated, the patient may experience internal bleeding and develop open sores on the lining of the stomach or small intestine that may not heal until the lining is perforated, at which point peritonitis may result. Due to the swelling of the ulcer-affected area, which results in a sense of early satiety, frequent vomiting, and weight loss, peptic ulcers may also produce a blockage in the digestive tract.

Peptic ulcer disease patients may experience a number of consequences, regardless of the underlying cause. They are the primary causes of the high morbidity and mortality rates linked to this disease that have been discovered so far. In comparison to earlier decades, the incidence of *Helicobacter pylori* infection has dramatically decreased thanks to the frequent use of various gastro-protection techniques and eradication medications. They are more prevalent in chronic NSAID and frequent smokers [22]. Peptic ulcer disease has four main side effects: bleeding, perforation, penetration, and blockage.

Bleeding

Cases of bleeding had been the most frequent complication around 10–20% of patients, despite a slight drop in occurrence over the past few years. It frequently leads to admission in emergencies. NSAID-related ulcers are more likely to bleed than ulcers merely brought on by a persistent *H. pylori* infection. The elderly and those with underlying serious diseases, such as respiratory, cardiac, cerebrovascular, or renal issues, are the populations

most at risk. Around 40–50% of upper gastrointestinal hemorrhages result from peptic ulcer disease, and 80–90% of them are not due to variceal bleeding. There is a 5.5% average related mortality. The clinical signs can vary: 15% have melenas, 30% have hematemesis, 50% have both, and 5% or so have hematochezia brought on by really heavy bleeding. In some situations, ulcer bleeding may progress slowly and show up as iron deficiency anemia or positive fecal occult blood. Because NSAIDs and aspirin increase the risk of ulceration and block platelet aggregation, there is a direct relationship between using these medications and ulcer bleeding. Although it does not appear that using corticosteroids alone significantly increases the risk of ulcer bleeding, using these medications in combination with NSAIDs may run-up the risk to tenfold.

Perforation

This occurs in up to 5% of people with peptic ulcers and usually accounts for 40% of gastric ulcers, frequently impacting less curvature, and 60% of duodenal ulcer cases, the majority of which are found at the anterior wall of the duodenal bulb. The patient's life could be in danger if a duodenal or gastric ulcer perforated freely into the peritoneal cavity. It typically manifests as an abrupt, excruciating stomachache in the epigastrium that may spread to the back or become diffuse. The presence of acute shock and an accompanied acute shock suggest a complex ulcer perforation with peritonitis. The patient often doesn't move, with the flexed thighs creating the illusion of gravity on the abdomen. Upon inspection, a rigid, hard abdomen with rebound is discovered. Auscultation may first reveal more pronounced intestinal noises, which gradually fade away until they nearly vanish as the illness worsens. About 70% of cases had an apparent pneumoperitoneum on an abdominal plain radiograph. The cause of perforated duodenal ulcers is thought to be multifactorial and includes factors like alcohol, tobacco, *Helicobacter pylori*, and especially the use of NSAIDs, which are linked to up to 50% of perforations, especially in elderly patients and are occasionally the only acetylsalicylic acid NSAIDs taken, even in small doses. Chronic cocaine usage is a different factor, but one that is far less frequent. The etiology of a cocaine-induced duodenal ulcer is still unknown. There is a potential that a localized vasoconstriction or vascular thrombosis will cause perforation [23]. According to reports, the majority (40%) of these cases involve the juxta-pyloric region.

Penetration

This complication happens when an ulcer crosses the wall of the stomach or duodenum but burrows into a nearby organ rather than drilling freely into the peritoneal cavity. 15% of stomach ulcers and 25% of duodenal ulcers are affected by it. The pancreas, liver, or omentum are the adjacent organs that extend most frequently. Although the clinical appearance may resemble that of an uncomplicated ulcer, the pain is typically more intense and long-lasting [22]. Eating does not ease pain; in fact, it may make it worse and more frequently wakes the sufferer at night. When an ulcer has reached the pancreas or the right upper quadrant, pain frequently radiates to the back. This typically happens when the ulcer has reached the gastro hepaticomentum. Rarely, penetrating peptic ulcers can create fistulas between the colon (gastro-colic fistula) and stomach or between the duodenum and bile duct (choledoco-duodenal fistula).

Obstruction

It is a rare complication, accounting for only around 5% of ulcer-related complications. Peptic ulcers were the most frequent type of restriction to stomach emptying up until about 1970. Gastric cancers are now the most common cause of gastric outlet obstruction, as the prevalence of obstruction secondary to peptic ulcer has reduced in recent years. Obstruction-causing ulcers typically arise in the duodenal bulb or pyloric channel and are brought on by the edema and swelling that accompany active ulceration or by the ulcer's shrinking throughout the healing phase. Anorexia, early satiety, nausea, and vomiting are the main signs of blockage. Vomiting typically starts 30 to 60 minutes after meals, and patients frequently feel full for hours thereafter. On a clinical examination, they can exhibit signs of dehydration, thinning, and splashing caused by liquid and air held in the swollen stomach. Endoscopy should be used to confirm the diagnosis and rule out any stenosis with a potentially malignant cause. Clinical symptoms are mostly influenced by the size and location of lesions, complications, and links to surrounding organs; some symptoms and traits, however, may also be influenced by genetics. Last but not least, it is not without curiosity to discover whether there are any correlations between the various symptoms (Malfertheiner *et al*., 2007) [24].

Helicobacter pylori-associated peptic ulcer disease

Helicobacter pylori-negative

The main etiology is related to the use of NSAIDs, so withdrawing these treatments is an important step. A thorough investigation should be conducted to find

additional contributing factors, such as medical comorbidities, poor nutritional status, ischemia, and acid hyper-secretory diseases, in *H. pylori*-negative, NSAID-negative ulcers. The standard antisecretory therapy is the foundation for treating patients who are not infected (Fiedman *et al*., 2010). Histamine-2 receptor antagonists (H2RAs) and Proton Pump Inhibitors (PPIs) are the two categories of anti-secretory medications that are most frequently utilized in these circumstances. The stomach parietal cells' inhibition of acid secretion is the mechanism of action. The first medications worked by inhibiting the histamine H2 receptors on the basolateral membrane of the cell, but these are now hardly ever used and have largely been replaced by PPIS, which inhibits the hydrogen-potassium ATPase pump on the luminal surface of the cell membrane by irreversibly binding to it. In the therapy of PUD, all PPIs produce a comparable level of acid secretory inhibition and healing rates. When taken 30 to 60 minutes before meals, PPIs work best. Global ulcer healing rates are above 75%, however PPIs outperform H2RAs (near 100%) in terms of effectiveness. PPI usage is therefore advised whenever possible. It is advised to try twice-daily dose or switch to another PPI if a normal PPI therapy fails to heal a peptic ulcer. For 12 weeks, a double dose of PPI is advised for big ulcers (>2-3 cm). Other hypersecretory states, like the Zollinger-Ellison syndrome, require higher doses to regulate symptoms. Approximately 80% of ulcer recurrences with the traditional antisecretory medication occur within the first year of treatment. Because of this, it is advised that patients at increased risk have long-term maintenance therapy with a PPI. Patients at increased risk are those who have a history of problems, frequent recurrences, torpid evolution (refractory, gigantic, or fibrosed ulcers), or who cannot stop using NSAIDs. The use of COX-2 inhibitors as a substitute for this latter condition necessitates a careful individual assessment of the potential gastrointestinal and cardiovascular hazards. Although prolonged medication should be continued at least until ulcer healing is established or NSAIDs are stopped, there are no conclusive findings from controlled trials regarding the ideal period of prolonged therapy. For acute duodenal and stomach ulcers, respectively, the suggested schedule for each of these medications is the normal dose once day for four and six to eight weeks. H2RAs are effectively absorbed following oral administration and are not affected by concurrent food consumption. The incidence of side effects associated with H2RAs and PPIs is typically modest (4%). Most are treatable, and they primarily affect those over 50. In patients with renal failure, it is advisable to make a few dose changes for H2RAs. Ranitidine may prevent the excretion of other medications that are processed via the same metabolic pathway because it binds to the cytochrome P-450 (CYP) enzyme system. PPIs are remarkably safe medications that don't require dosage modifications for liver or renal impairment. The existence of hypergastrinemia brought on by the inhibition of acid secretion and the connection to gastric atrophy are the main worries with regard to the prolonged use of these drugs. However, no substantial clinical repercussions of these hazards have yet been observed. It's important to take into account any additional negative effects of long-term PPI use, such as the potential development of enteric infections (such as Clostridium difficile) and nutritional deficiencies (such as hypomagnesaemia, decreased calcium absorption and an increased risk of bone fractures, and vitamin B12 deficiency). PPIs are metabolized by cytochrome P450 enzymes, with CYP2C19 playing the primary role. Since various agents prefer different parts of this metabolic pathway, the interaction patterns may shift as a result. The lowest potential for P450 metabolism and medication interactions has been noted for pantoprazole in this context (Wedemeyer *et al*., 2014). One of the most pertinently characterized interactions is that between PPIs with clopidogrel. The possible clinical harm that some PPIs may have on the curative effects of clopidogrel, however, is still up for debate. PPIs with weaker CYP2C19 inhibition are preferable in combination with clopidogrel as opposed to those with higher inhibition, such as omeprazole, due to the conflicting findings [26].

Helicobacter pylori-positive PUD

The most recent consensus reports' compilation of scientific information serves as the foundation for the *H. pylori* infection eradication therapies [24]. It is feasible to think about the empiric eradication treatment in environments where *H. pylori* infection is highly prevalent and where NSAID use is not common. Amoxicillin, clarithromycin, metronidazole, tetracycline, and bismuth are medicines that have proven effective. According to the most recent statistics, the traditional triple therapy of PPI-clarithromycin, amoxicillin, and metronidazole has lost some of its effectiveness, mostly as a result of the rise in clarithromycin resistance seen in recent years. Due to this, only regions with low rates of resistance are now advised to use this conventional regimen as the first line of treatment. The rates of eradication are

increased when PPI is administered twice daily and for a total of 14 days. Quadruple therapy (also known as "concomitant" treatment), which combines PPIs, amoxicillin, clarithromycin, and metronidazole, is advised as the first-line empirical treatment in areas with high levels of clarithromycin resistance. Both a bismuth-containing quadruple therapy and a levofloxacin rescue treatment are advised if these combinations fail to eradicate the disease. It is better to refer the patient to a facility with more experience treating *H. pylori* that is multi-drug resistant after three unsuccessful regimens. In the absence of NSAID use, *H. pylori* eradication alone should be thought of as sufficient for small or moderate-sized ulcers and for compliant individuals with verified eradication. Patients who have complicated duodenal ulcers, gastric ulcers, or other signs of increased risk (such as giant ulcers, fibrosed lesions, or a history of relapse) need to continue taking antisecretory medications at least until the *H. pylori* infection has been completely eliminated and/or the ulcer has healed. If the infection persists, long-term therapy with a typical dose of PPIs is recommended in these high-risk populations. The rate of side effects is influenced by the antibiotics employed in the various treatment regimens, and the combination treatments are typically well tolerated. The most common side effects reported are candidiasis, diarrhea, and rash (amoxicillin); nausea, metallic taste, peripheral neuropathy, and an antabus-like effect with alcohol consumption (metronidazole); prolongation of QT interval and seizures can occur in patients who are predisposed for other reasons (fluoroquinolones); and in rare cases, transient tongue pigmentation and dark stools (bismuth).

Diagnosis of peptic ulcer disease

A thorough physical examination and a thorough clinical history must be performed in order to collect all the symptoms and signs of PUD. Additionally, it is crucial to record all previous medical conditions, the amount of alcohol consumed, NSAID use history, smoking history, and any potential peptic ulcer history. The diagnosis of a peptic ulcer involves two key factors. To ascertain the precise etiology of the ulcer and to determine whether the mentioned symptoms are not caused by functional dyspepsia.

Endoscopic findings

The most accurate PUD diagnostic test is an upper GI endoscopy. It provides details about the lesion's size and location. Additionally, mucosal biopsies may be carried out to aid in the differential diagnosis and endoscopic management of bleeding peptic ulcers. Additionally, a number of mucosal biopsies from the antrum and corpus must be performed in order to identify or rule out the presence of concurrent *H. pylori* infection. Regular mucosal folds surrounding the ulcer base and a fibrin deposit at the crater base are indicators of a benign etiology. Overhanging margins, uneven or thicker borders, and/or the presence of an ulcerated mass that protrudes into the lumen are characteristics that point to the existence of cancer. It is unusual for duodenal ulcers to be malignant. As a result, routine biopsy is not advised. Despite having a benign look, it is necessary to take multiple mucosal biopsies from the margins of any stomach ulcer. The mending process won't be finished until a subsequent endoscopy is done. Every patient who has a peptic ulcer has to get their *H. pylori* infection checked. The management has undergone significant change since its discovery in 1983. It is well known that there is no difference between men and women in the prevalence of the illness with age. Several tests are performed not only for diagnosis but also in the follow-up after the eradication treatment in order to confirm this one. Diagnostic testing for *H. pylori* is split into direct (depending upon the necessity for endoscopy) and indirect tests [27].

Radiology

Barium gastroduodenal examinations have been happily replaced by endoscopic explorations in normal diagnostic procedures, while they may still be helpful in a few individuals who refuse to undergo it or in situations where endoscopy is impossible due to esophageal stenosis. The radiologist's experience, the technique, the size of the lesion (if it is less than 0.5 cm in diameter, it can be difficult to detect), and the depth of the ulcer all affect the sensitivity and specificity of barium radiography tests. Regular edges and symmetrical mucosal folds, as well as a smooth translucent band or collar surrounding the ulcer crater suggesting edema and indentation of the opposing wall, are radiologic indicators of a benign nature. On the other hand, large ulcer size, uneven mucosal folds, lack of contrast, or irregular filling are indications of malignancy.

Treatment of peptic ulcer disease

The relationship between *H. pylori* and peptic ulcers has been discovered, and this has significantly altered how the condition is managed because it is now a treatable infectious disease. Other therapeutic options for the subset of patients with *H. pylori*-negative ulcers include the use of anti-secretory medications or the substitution of standard NSAIDs

with selective COX-2 inhibitors.

Treatment in special situations *H. pylori* infection in NSAIDs users

NSAID and low-dose aspirin users are more likely to develop gastroduodenal ulcers and their consequences if they have *H. pylori* infection [24]. The information offered aids in eliminating *H. pylori* prior to beginning NSAID treatment. Additionally, providing these patients with a PPI in addition to the eradication medication can lower their risk of developing problems from recurring ulcers.

Refractory ulcers

These are peptic ulcers that have not improved after receiving appropriate care for 12 weeks (Feldman *et al*., 2010). Investigating the following circumstances is necessary in this situation: persistent *H. pylori* infection or a false-negative first diagnosis, covert NSAID use, disregard for medical advice, large or fibrotic ulcers, ulcerated tumors, tobacco use, and hypersecretory acid conditions are some other factors. In this case, chronic ischemia brought on by celiac artery narrowing may also be taken into account. It is advised to demand that all other medical options be exhausted before suggesting surgery in the absence of all these risk concerns.

Pregnancy and lactation

The FDA lists omeprazole as a pregnancy class C drug, but all other PPIs and H2RAs, including cimetidine and ranitidine, are class B medications. The absence of data in humans prevents drawing firm conclusions about their safety, despite some analyses of prospective data showing that the overall risk is low in pregnancy with potential harm during lactation [33]. There are currently no recommendations for treating *H. pylori* infection when pregnant. It has been argued that postponing eradication during lactation and delivery [28].

Stress-related erosive syndrome

Intensive care unit patients who have serious systemic diseases like sepsis, major trauma, severe burn injuries, or multi organ failure are frequently afflicted by these lesions. According to this scenario's most significant risk factors for stress-related problems, mechanical breathing and coagulopathy [Feldman *et al*., 2010]. These lesions can be treated in a manner similar to how peptic ulcers are often treated. Only patients who have a high risk of bleeding from a stress ulcer are advised to receive routine prophylaxis. According to some research, PPIs are superior to H2RAs at preventing clinically significant and obvious upper gastrointestinal hemorrhage [29].

Treatment of complicated PUD

All patients with complicated peptic ulcer disease need the proper supportive care, which includes fluid replacement, the administration of acid-suppressing medication, the treatment of *H. pylori* infection, if present, and, if practical, stopping NSAIDs. Early care coordination between the medical, critical care unit, surgical, and radiology teams is particularly crucial because it enables teams to make informed decisions without risky delays.

Bleeding

In Western nations, peptic ulcer bleeding is a significant clinical issue in the emergency setting. Correcting fluid losses and regaining hemodynamic stability come first in patient care. Prior to an endoscopy, a high-dose intravenous PPI therapy (80 mg in a bolus followed by 8 mg/h in continuous infusion for 72 hours) is advised because it significantly lowers the incidence of ulcers with high-risk stigmata of recent hemorrhage, eliminates the need for endoscopic hemostasis, and encourages quick healing (Garza *et al*., 2014). For upper gastrointestinal bleeding, endoscopic therapy has typically been advised as the first line of treatment, and it should be carried out within 24 hours of the patient's admission. It has been demonstrated to decrease overall mortality (OR = 0.55; 95% CI, 0.40-0.76), the requirement for surgery (OR = 0.36; 95% CI, 0.28-0.45), and future bleeding (OR = 0.38; 95% CI, 0.32- 0.45). Endoscopic therapy can be split into mechanical methods using clips, thermal procedures using argon plasma coagulation and bipolar probes, and injectable therapy, which is the oldest approach and typically uses epinephrine with addition of a second drug. Only a small percentage of people with bleeding ulcers would need surgery. The failure of endoscopic treatments repeatedly, chronic hemodynamic instability despite resuscitation efforts, recurrent bleeding following a second attempt at endoscopic treatment, and ongoing high transfusion needs are among the reasons for emergency surgery. An angiography technique may be considered in individuals who are at high risk for surgery under certain circumstances and in some cases as an alternative to surgery. It is also useful for controlling post-operative bleeding that returns [30].

Perforation

Duodenal perforations are more common than stomach perforations (60 vs. 40%), mainly in elderly patients and those with a history of strong alcohol

use, heavy tobacco use, and/or NSAID usage. In these circumstances, surgical intervention is advised. However, in patients with penetrating ulcers, conservative medical treatment (including a nasogastric tube, intravenous fluids, parenteral nutrition, and broad-spectrum antibiotics) might be tried first with strict monitoring. If the patient's condition worsens, however, surgery must be done [31].

Gastrointestinal obstruction

Medical treatment methods should be used to control this problem at first (nasogastric tube for decompression, intravenous fluid, PPIs to decrease gastric secretion and promote ulcer healing, *H. pylori* eradication). By lowering the edema and spasm linked to the lesion, these therapies can frequently reverse the blockage. If the obstruction cannot be removed, if medication does not relieve the symptoms, and if the healing process has created a significant stenosis, endoscopic balloon dilation should be tried as soon as possible.32 Following the emergence of any clinical ulcer, surgery is the last option if no progress is seen with either pharmacological and/or endoscopic therapy [31].

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