Medicare Churning
International Journal of Medical Science, Healthcare & Research Innovations
(Multidisciplinary, Double-Blind Peer-Reviewed, Refereed & Open Access Publication)
www.medicare.educarepublication.com
Volume 1 Issue 1 January-April 2026

Peptic Ulcer Disease: An In-Depth Analysis of Pathophysiology, Symptoms, Diagnosis, and Cutting-Edge Treatments

Gazi Musaib Ul Islam*, Dr. Tanya Sharma*, Mr. Obaid Ahmad Lone, Mr. Pankaj Chasta, Dr. Gaurav Sharma.
Department of Pharmaceutical Sciences, Mewar University, Chittorgarh, Rajasthan
***Corresponding Author**
Email Id: gazimusaib502@gmail.com
DOI NUMBER: 10.5281/zenodo.20437366

Abstract

Peptic Ulcer Disease (PUD) is a common stomach condition where ulcers form in the stomach lining or the upper part of the small intestine. It is mainly caused by a bacteria called Helicobacter pylori (H-pylori). H-pylori infection and long-term use of NSAIDs can cause this condition. This detailed study looks at the causes, symptoms, risks, signs, ways to diagnose, and treatments for PUD. The sickness is characterized by symptoms like pain in the upper abdomen, pain after eating, pain at night, and feeling better after eating or taking antacids. Less common symptoms of stomach ulcers may include anaemia from bleeding in the stomach, weight loss due to loss of appetite, and vomiting from complications like pyloric stenosis. The diagnosis of stomach ulcers often requires endoscopy to directly see and take samples of ulcers to rule out cancer and confirm H. pylori infection. H-pylori infection. Advances in medical tests have made it easier to detect stomach ulcers. Treatment options include medicines like proton pump inhibitors (PPIs) and antibiotics for H. pylori. Treatment for H-pylori infection to eliminate the bacteria and lifestyle changes to prevent ulcers from coming back. Even with these improvements, there are still problems, especially with the increasing levels of bacteria that are resistant to antibiotics. Ulcers caused by H-pylori bacteria and NSAIDs need to be managed. This study shows how important it is to diagnose correctly and treat effectively to avoid problems like bleeding, perforation, and gastric outlet obstruction. Continuous research is important to tackle new problems with antibiotic resistance and to create better ways to manage Peptic Ulcer Disease. This will help lessen its impact on health and healthcare systems worldwide.

1. Introduction

Peptic Ulcer Disease (PUD) is a prevalent digestive system issue marked by the formation of open sores on the inner wall of the stomach or the initial section of the small intestine (duodenum). These sores are caused by an unevenness in the aggressive elements such as stomach acid and pepsin, and the body's protective systems like the mucus and bicarbonate barrier. The main causes of PUD are the presence of Helicobacter pylori (H. pylori) infection. H. pylori bacteria) and long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs). It is believed that these factors are responsible for more than 90% of peptic ulcer disease cases worldwide, including H. pylori infection, NSAID use, and smoking. H pylori by itself causes large part (Lanas & Chan, 2017). H pylori infection weakens the protective layer of the stomach by making enzymes and toxins that cause swelling and harm, leaving the stomach lining open to acidic digestive juices (Malfertheiner, Chan, & McColl,2009). NSAIDs prevent the creation of prostaglandins, which are substances that support the protection of the stomach lining. Long-term use of these drugs can weaken the mucosal defence and raise the possibility of developing ulcers (Sung, Kuipers, & El-Serag, 2009).
The occurrences decreased in numerous advanced nations because of better cleanliness, widespread use of PPIs, and effective treatment for H. pylori. H. pylori infections. However, it continues to be a major health issue in underdeveloped areas where H. The prevalence of H. pylori is high and people have limited access to healthcare (Sung, Kuipers, & El-Serag, 2009). The chances of developing peptic ulcer in a lifetime is approximately 10%, which means it is one of the most common gastrointestinal diseases globally (Lanas & Chan, 2017). Accurate identification and treatment are important for preventing problems like bleeding, puncture, and blockage in the stomach opening.

Advancements in diagnostic equipment, like endoscopy and non-invasive exams for H. pylori, have improved the ability to detect and treat digestive system issues. The discovery and treatment of PUD have greatly improved thanks to the identification of H. pylori (Malfertheiner, Chan, & McColl, 2009). Despite these enhancements, the increasing usage and the expanding issue of antibiotic-resistant H. Different H. pylori types show that more research and new treatment plans are necessary to lessen the impact of the disease. For over 100 years, peptic ulcer disease was mainly treated with surgery, which led to high rates of sickness and death. The successful medical reduction of stomach acid production started with the development of histamine H2-receptor antagonists (H2RAs) in the 1970s, and this led to a significant improvement in patient outcomes. During the 1980s, voluntary surgery for peptic ulcers decreased by 85%, mostly because of the use of the H2RAs cimetidine and ranitidine. (Lanas, A., & Chan, F. K. 2017) The creation of proton-pump inhibitors (PPIs) also enhanced the ability to stop the secretion of stomach acid, and

the lack of tachyphylaxis to PPI therapy ensures very high rates of healing for duodenal and gastric ulcers. (Sung, J. J., Kuipers, E. J., & El-Serag, H. B. 2009 It has been over 20 years since the arrival of the ‘H. pylori eradication’ strategy for peptic ulcer disease.

After learning a great deal about the "H. pylori era," we have now peaked in our knowledge of peptic ulcer disease, its diagnosis, and its treatment. There are still three main issues that need to be resolved. We must figure out how to get rid of H-pylori (Sung, J. J., Kuipers, E. J., & El-Serag, H. B. 2009 At a time when H. pylori eradication failure rates are increasing, we need to figure out the best strategy to prevent ulcers from forming and returning in NSAID users. The appropriate course of action for non-NSAID users who do not have H. pylori must also be determined. ulcers in the stomach caused by H. pylori. The prevalence of ulcers varies around the world; gastric ulcers are more common in Asia, especially Japan, and duodenal ulcers are more common in Western countries. About one in ten Americans still have peptic ulcer disease, despite the fact that its prevalence has declined in Western nations over the past century. It is estimated that the combined direct and indirect costs of peptic ulcer disease in the United States amount to $3.4 billion annually. The impact of peptic ulcer disease on human health and health economics is expected to be a major problem in the future due to its continued prevalence, particularly among the elderly. (Sung, J. J., Kuipers, E. J., & El-Serag, H. B. (2009).

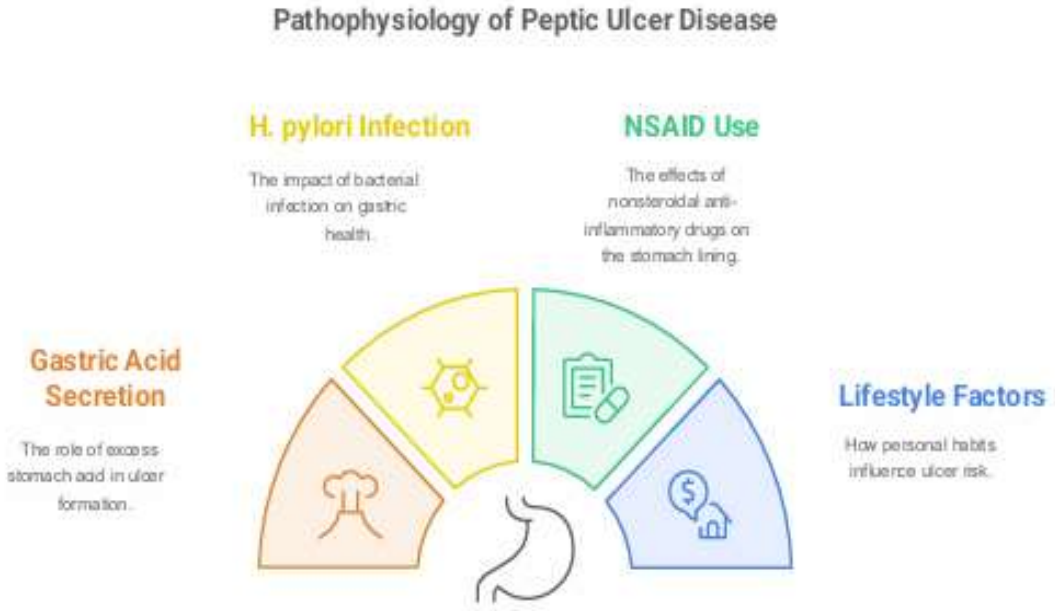
2. Epidemiology and Etiologic Factors

Peptic ulcer disease is a source of significant morbidity and mortality worldwide. Sequelae may range from abdominal pain and gastrointestinal bleeding to gastric outlet obstruction and perforation. The prevalence of peptic ulcer disease in the United States is estimated to be 8.4%. (Sonnenberg, A., Steinkamp, U., & Weise, A. 1986)Higher peptic ulcer disease incidence has been found to be associated with male sex, smoking, and chronic medical conditions.(Sonnenberg, A., Steinkamp, U., & Weise, A. 1986) .Peptic ulcer disease has also been found to be associated with increasing age. (Boey, J., Branicki, F. J., & Wong, J. 1982). Over time, a significant decrease in peptic ulcer disease diagnoses, as well as its associated complications, has been observed in both the United States and elsewhere in the world. (Boey, J., Branicki, F. J., & Wong, J. 1982). The majority of peptic ulcer disease cases are now known to be associated with H. pylori infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), or both. (Ramakrishnan, K., & Salinas, R. C. (2007). H-pylori is a Gram-negative bacterium that colonizes the gastric mucosa, progressing to gastritis and potentially peptic ulcer disease and gastric cancer. (Kurata, J. H., & Haile, B. M. (1984) H. pylori effects a large segment of the population; however, only a small subset will

develop clinical disease. (Ramakrishnan, K., & Salinas, R. C. 2007) NSAID use, including aspirin, is common and leads to an increased risk of gastrointestinal adverse events, including peptic ulcer disease. The relative risk of developing a symptomatic ulcer is 4.0 for non aspirin NSAID users and 2.9 for patients taking aspirin. (Garcia Rodriguez LA, Hernandez-Diaz S.2004) While H. pylori and NSAID use are the cause of the vast majority of peptic ulcers, other less common causes have been identified, including gastrinoma (eg, Zollinger Ellison syndrome) other medications (Garcia Rodriguez LA, Hernandez-Diaz S.2004).

Pathophysiology

The pathogenesis of peptic ulcers is now better understood thanks to recent advancements. The imbalance between the protective systems in place to prevent mucosal digestion and the digestive activity of pepsin and acid is a fundamental paradigm for ulcer development. Despite the fact that ulcer patients have numerous disruptions in the normal physiology of the stomach and duodenum, it is still unclear which anomalies are most significant. (Garcia Rodriguez LA, Hernandez-Diaz S.2004) Individual differences may exist in the key flaw, or the final common denominator of ulceration may be caused by a combination of faults. Three etiologic types of peptic ulcers can be distinguished: those caused by nonsteroidal anti-inflammatory medicines (NSAIDs); those linked to Helicobacter pylori infection; and those resulting from major acid peptic hypersecretion in Zollinger-Ellison syndrome. This article will focus on H. pylori-related ulcers, which make up the biggest and least known component of ulcer illness. (Peterson WL, Barnett CC, Evans DJ Jr, et al1993).

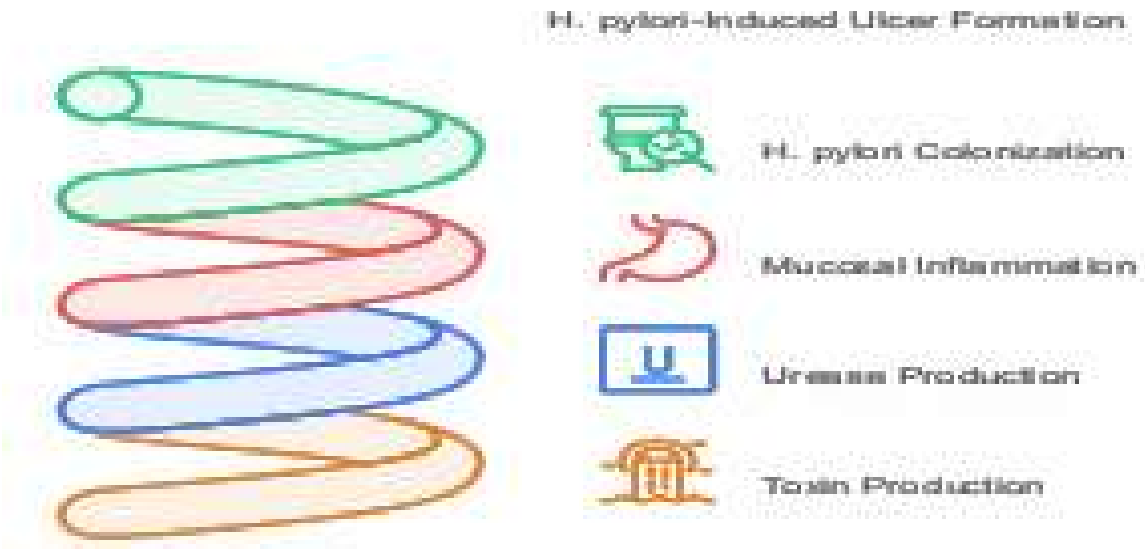


1. Role of Gastric Acid and Pepsin

Although pepsin and stomach acid are necessary for digestion, they can harm the stomach lining if the protective barriers are broken. In reaction to stimuli like food intake, gastrin, and vagal activation, the parietal cells in the stomach release gastric acid. Proteins are broken down into peptides by the proteolytic enzyme pepsin, which is active at acidic pH values. These invasive chemicals infiltrate the epithelial cells and produce inflammation and cell damage, which are the initial stages of ulceration, if the mucosal layer is compromised (Peterson, 1991).

2. Helicobacter pylori Infection

Globally, H. pylori infection is the primary cause of PUD. By generating urease, an enzyme that hydrolyzes urea into ammonia and carbon dioxide, this bacterium has adapted to live in the stomach's acidic environment. The bacteria can flourish in the small microenvironment created by the ammonia's neutralization of the surrounding gastric acid (Suerbaum & Michetti, 2002). A persistent inflammatory response is triggered by H. pylori and is mediated by a number of virulence factors: Cytotoxin-associated gene A (CagA): A type IV secretion mechanism is used to deliver this protein into gastric epithelial cells. Once inside, it interferes with regular cellular communication, which causes inflammation and epithelial structural alterations that aid in the development of ulcers (Hatakeyama, 2004). Vacuolating cytotoxin A (VacA): This toxin damages the stomach mucosa by causing the creation of huge vacuoles in epithelial cells, interfering with mitochondrial activity, and increasing apoptosis (Ruggiero, 2010). Cytokines including interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α) are released during the inflammatory response and draw immune cells like neutrophils and macrophages. These cells emit proteases and reactive oxygen species (ROS), which worsen the mucosal lining's damage and increase its vulnerability to acid attack.

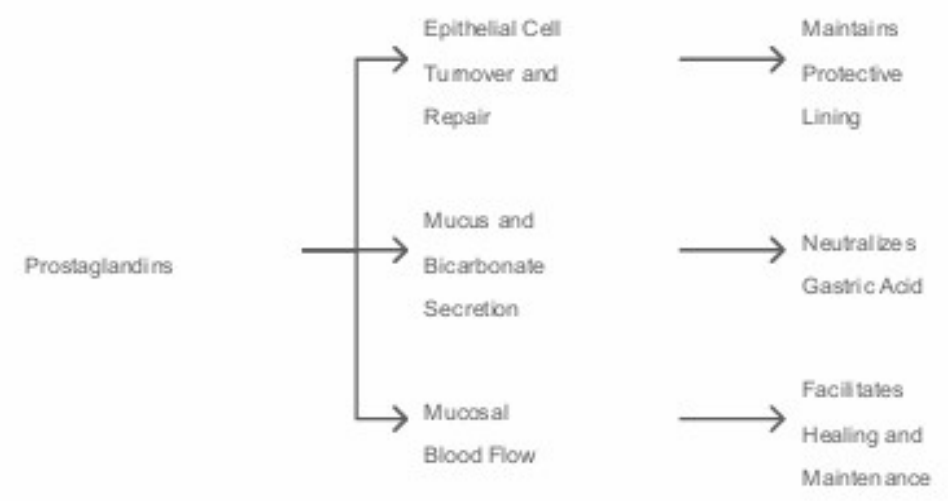


3. NSAID-Induced Mucosal Injury

Although NSAIDs, such as aspirin, ibuprofen, and naproxen, are frequently used to treat pain, they have serious adverse effects on the digestive system. The cyclooxygenase (COX) enzymes (COX-1 and COX-2) that produce prostaglandins are inhibited by these medications. Specifically, COX-1 generates prostaglandins that support the turnover and repair of epithelial cells, increase mucus and bicarbonate secretion, and promote mucosal blood flow, all of which contribute to the integrity of the gastric mucosa. Wallace (2008). The protective mucus barrier is weakened when NSAIDs inhibit COX-1, which lowers prostaglandin levels. Furthermore, through topical irritation, NSAIDs have the potential to directly harm the stomach epithelial cells. Because NSAIDs are weak acids, they do not ionize in the stomach's acidic environment, which makes it easy for them to pass through the membranes of epithelial cells. They ionize and release protons inside the cells, causing apoptosis and cellular destruction.

4. The Effect of Additional Risk Elements

A number of environmental and lifestyle factors can make the pathophysiological mechanisms of PUD worse, including: Smoking: Nicotine affects the mucosal barrier and raises the risk of ulcers by increasing the secretion of stomach acid and decreasing the generation of bicarbonate (Ko et al., 1996). Alcohol: By lowering the formation of protective mucus and increasing the emission of stomach acid, alcohol might damage the mucosal barrier. Additionally, it has the potential to directly harm epithelial cells, increasing the mucosa's susceptibility to ulceration (Bode & Bode, 1997). Stress: Stress-related mucosal disease (SRMD) can result from physiological stress, especially in people who are very sick. Hypoxia, poor epithelial cell repair, and heightened vulnerability to acid-induced injury result from reduced blood supply to the stomach mucosa.



5. Development of Ulcers

The loss of mucosal integrity, which results in epithelial erosion and exposes the underlying tissue to pepsin and stomach acid, is the last frequent pathway for ulcer formation. An ulcer crater forms as a result of this exposure, along with further injury and inflammation. (Boey, J., Branicki, F. J., & Wong, J. 1982) Untreated ulcers have the potential to worsen, impacting blood vessels and resulting in consequences like bleeding, perforation, and obstruction of the stomach outlet. Because PUD is chronic, there may be intervals of symptom relief interspersed with flare-ups, especially if the underlying causes such as an H. pylori infection or NSAID use are not treated. Knowing this intricate pathophysiology aids in the development of targeted treatment strategies, such as eradicating *H. pylori* with antibiotics and reducing gastric acid production with proton pump inhibitors (PPIs) or H2-receptor antagonists. (Boey, J., Branicki, F. J., & Wong, J. 1982).

6. Burning or gnawing pain in the epigastrium

The primary symptom of PUD is epigastric pain, which patients report as an aching, burning, or gnawing feeling in the upper abdomen. Because there is less food in the stomach, gastric acid can directly irritate the ulcer, which is why the pain usually happens during the night or in between meals. Usually, eating, using antacids, or taking drugs that lower stomach acid can briefly relieve it (Sonnenberg, 1985). Because eating increases the formation of acid in the stomach, gastric ulcers often cause pain soon after eating. But when the acidic chyme enters the duodenum, duodenal ulcers frequently cause pain a few hours after eating. Eating can ease this pain since food and pancreatic secretions neutralize the duodenum's acid (Kurata & Haile, 1984). Patients with PUD may present with a range of symptoms, which include:

Early Satiety and Bloating

Bloating, a sense of fullness, and early satiety are all possible symptoms for PUD patients. The mucosal lining's oedema, inflammation, and decreased gastric motility are the causes of these symptoms, which might delay the emptying of the stomach. Patients may experience discomfort due to this delayed digestion, which makes it challenging for them to eat meals of a typical size (Ramakrishnan & Salinas, 2007).

Vomiting and Nausea

Especially in individuals with severe ulcers or consequences such gastric outlet obstruction, nausea and vomiting are common symptoms. Food cannot flow from the stomach to the duodenum if a blockage results from an ulcer that affects the pyloric area. Gastric contents accumulate as a result, resulting in nausea, chronic vomiting, and occasionally even vomiting of undigested food (Borum, 1996). Hematemesis, which manifests as bright red or coffee-ground-like substance, is a condition in which individuals who have had bleeding may vomit blood.

Appetite Loss and Weight Loss

People who have stomach ulcers frequently experience hunger reduction and consequent weight loss. Over time, decreasing food consumption and malnutrition may result from eating discomfort brought on by greater pain after eating. Chronic nausea and vomiting can sometimes lead to substantial weight loss as well (Fischbach et al., 2002).

Anaemia and Bleeding

A serious side effect of PUD is bleeding, which happens when the ulcer erodes blood vessels. It may appear as either. Overt bleeding, as evidenced by symptoms like melena (black, tarry stools from digested blood in the gastrointestinal tract) or hematemesis (blood in the vomit). Stool testing for concealed blood can identify occult bleeding, which may not be apparent. Iron-deficiency Anaemia, which manifests as exhaustion, pallor, and dyspnea, can result from prolonged blood loss (Sonnenberg et al., 1986).

Acute Abdomen and Perforation

An ulcer that erodes through the entire thickness of the stomach or duodenal wall and causes the stomach's contents to seep into the abdominal cavity is known as a perforation. This is a surgical emergency that causes abrupt, intense abdominal pain that is frequently compared to a "knife-like" sensation. According to (Boey et al. (1982), patients may exhibit fever, shock, and a stiff, board-like belly as symptoms of peritonitis.

Obstruction of the Gastric Outlet

Another serious consequence that can arise from persistent inflammation, scarring, or swelling close to the pylorus is gastric outlet obstruction. Symptoms include extreme bloating, early satiety, and continuous vomiting. A blockage in the distal stomach may also be indicated by the patient's

non-bilious vomiting of undigested food that was consumed hours or even days prior (Lanas & Chan, 2017).

7. Diagnosis

Epigastric discomfort, postprandial and nocturnal pain, pain that awakens a patient from sleep, and pain relieved by food or antacids are common indicators of peptic ulcer disease. Less common symptoms include Anaemia due to gastrointestinal bleeding, weight loss from reduced appetite caused by fear of pain, and vomiting associated with pyloric stenosis or gastric ulcers. (Graham DY et al. (1988)

However, the absence of pain does not exclude an ulcer, and the diagnosis can still be made without discomfort, especially in older patients who may have "silent" ulcers. No single symptom can differentiate between ulcers caused by H. pylori and NSAIDs; however, a detailed medical history can uncover NSAID misuse, and appropriate H. pylori testing can identify those infected. (Graham DY et al. (1988) Endoscopy is essential for an accurate diagnosis and to differentiate peptic ulcer disease from its complications (for instance, biopsying a gastric ulcer to exclude cancer or to obtain tissue for H. pylori testing). (Xia HH et al. 2001) Endoscopic healing is considered the gold standard for ulcer healing in clinical studies. Many individuals with dyspepsia symptoms can be screened and treated for H. pylori infection in primary care without endoscopy. This approach is recommended by guidelines for young people with dyspepsia without alarm symptoms because "test and treat" for H. pylori is more cost-effective than endoscopy for this demographic. Consequently, a small percentage of dyspeptic patients may have their ulcers treated without a formal diagnosis. (Xia HH et al. 2001)

Testing for H. pylori

Testing for the presence of H. pylori is multifaceted, with numerous methods available. Endoscopic techniques include histological and cultural analysis, the rapid urease test (RUT), and gastric polymerase chain reaction (PCR) on biopsy samples. Although PCR is highly sensitive, it may yield false-positive results. (Ford A et al. (2004). Non endoscopic tests include the 13C-urea or 14C-urea breath test (UBT), serology, and stool antigen analysis. The choice of the initial test for identifying H. pylori depends on the prevalence of infection in the population, as both the positive and negative predictive values of a test vary with the infection's prevalence. (Ford A et al. (2004) Tests can discern between past and current infections, with the UBT being the most effective for detecting active infections. However, in practice, when a patient undergoes

endoscopy for peptic ulcer disease, an RUT may be used as the initial test, followed by a secondary test if the RUT is negative. (Graham DY et al. (1988) Various factors must be considered for each test, including the impact of treatment, methodology, and technical aspects, to make the best selection for a specific clinical setting. For instance, serology tests, which rely on the presence of anti-H. pylori antibodies, do not indicate an active infection. The RUT and UBT are also affected by proton pump inhibitors (PPIs) and antibiotics, which inhibit urease activity and directly influence test sensitivity and specificity. (Graham DY et al. (1988) Post-treatment confirmation of infection eradication is essential, with non invasive testing via the UBT recommended 4–8 weeks after treatment completion. If the ulcer recurs, further follow-up is necessary. (Graham DY et al. (1988)

Treatment and Management

- **Role of Proton Pump Inhibitors in the Treatment of Peptic Ulcer Disease**

Proton pump inhibitors (PPIs) have significantly altered the management of peptic ulcer disease since they were first used in medicine in the late 1980s. PPIs continue to be the cornerstone of medical therapy for gastrointestinal bleeding related to peptic ulcers, and well-conducted systematic reviews support starting PPIs before endoscopic evaluation for acute upper gastrointestinal bleeding, even though there has not been any evidence of a clear mortality benefit. (Chey WD, Leontiadis GI, Howden CW, Moss SF.ACG 2004) The duration of PPI administration after a peptic ulcer diagnosis varies depending on the underlying ulcer etiology, location, and related complications. The ultimate goal of PPI therapy is to promote ulcer healing. While addressing the underlying cause of ulcers by suppressing acid production, patients with NSAID-induced ulcers should avoid the offending medications, and those testing positive for H. pylori are treated for the infection.

It is recommended that patients with peptic ulcer disease who require ongoing NSAID therapy also continue proton pump inhibitor (PPI) co-therapy throughout their treatment. (Cochrane Database Syst Rev. 2006) Changes in prescribing practices and patient reluctance to seek treatment have arisen due to concerns about the long-term safety profile of PPIs. Chronic use of PPIs, leading to hypergastrinemia and gastric hypochlorhydria, may hinder the absorption of calcium, iron, magnesium, and vitamin B12, and increase infection risks. Some studies have associated PPI use with various diseases, including chronic kidney disease, Clostridium difficile infection, and community-acquired pneumonia. However, the causality remains uncertain due to

the low quality of available evidence. Physicians are advised to evaluate each patient individually to decide on the most appropriate treatment plan, the minimum effective PPI dose, and the optimal duration of therapy. (Cochrane Database Syst Rev. 2006)

H. Pylori Treatment

The Maastricht V/Florence Consensus Report, published in 2017, provides evidence-based recommendations for the diagnosis and treatment of H. pylori infection. This report cites several meta-analyses indicating that a 14-day triple therapy regimen has higher H. pylori eradication rates compared to shorter durations. The authors advocate for a 14-day treatment regimen that includes clarithromycin-based triple therapy and bismuth-containing quadruple therapy, pending confirmation of the efficacy of 10-day therapies at the local level. (Gisbert JP, Khorrami S, Carballo F, Calvet X, 2004) The report suggests that extending the treatment to 14 days may be less effective, but a longer course of antibiotics is recommended in areas with high metronidazole resistance. In addition, the American College of Gastroenterology released guidelines in 2017 for the detection and management of H. pylori infection, which also advise considering prior antibiotic exposure when selecting a treatment regimen for H. pylori. (Gisbert JP, Khorrami S, Carballo F, Calvet X, 2004).

In areas with low clarithromycin resistance (<15%), guidelines recommend 14 days of clarithromycin triple therapy, which includes a proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole. This is particularly advised for individuals who have never been exposed to macrolides. Additionally, bismuth quadruple therapy comprising tetracycline, bismuth, a PPI, and a nitroimidazole is recommended as an alternative first-line treatment for 10–14 days, especially for those with a penicillin allergy or prior exposure to macrolides. Tables 3 list common first-line and salvage therapies in accordance with the American College of Gastroenterology's (ACG) guidelines for H. pylori treatment. (Strand DS, Kim D, Peura DA 2017).

However, there is limited information on the efficacy of current H. pylori treatment regimens and the prevalence of antibiotic resistance in the United States, leading most guidelines to rely on data from studies conducted elsewhere. First-line treatments offer the highest likelihood of success, yet achieving eradication rates over 90% is improbable. Currently, there are no coordinated efforts in the United States to monitor H. pylori antibiotic resistance patterns. (Strand DS, Kim D, Peura DA 2017).

Management of Peptic Ulcer Disease Complications includes addressing bleeding, perforation, penetration, and gastric outlet obstruction. Unique patient risk factors such as NSAID use, aspirin, H. pylori infection, smoking, and acid hypersecretion contribute to the disease. Conditions like Zollinger-Ellison syndrome, chronic and refractory ulcers, location (e.g., pyloric channel), and size (≥1 cm) increase the risk of complications. Negative outcomes in complex cases may be linked to comorbid conditions, age, and poor physiological state at presentation, such as hypotensive shock, hypoalbuminemia, acute renal failure, metabolic acidosis, and delayed medical care. (Lai KC, Lam SK, Chu KM, et al.2002)

The most common upper gastrointestinal bleeding from peptic ulcer disease can lead to significant morbidity and healthcare costs. Upper endoscopy is the preferred initial test for suspected bleeding, serving both diagnostic and therapeutic purposes. Management strategies before, during, and after endoscopy are crucial. (Sreedharan A, Martin J, Leontiadis GI, et al.2010) Current endoscopic haemostasis treatments include mechanical, thermal, and injection methods, or a combination thereof, which have proven effective in achieving primary haemostasis, reducing re-bleeding, blood transfusion needs, emergency surgery, hospital stay, and mortality. High-dose intravenous PPIs are recommended for 72 hours post-endoscopic haemostasis, followed by oral PPI therapy. Patients with recurrent bleeding should consider repeat endoscopic procedures. (Sreedharan A, Martin J, Leontiadis GI, et al.2010). Patients presenting with sudden, generalized, or severe abdominal pain should be evaluated for an ulcer. The classic triad of sudden onset tachycardia, abdominal pain, and stiffness suggests a perforated peptic ulcer. Physical examination may reveal abdominal distension, guarding, tenderness, and rebound tenderness indicative of peritonitis. Leukocytosis and fever may also be present. (Laine L, Jensen DM 2012) Chest X-ray using an erect position may miss sub-diaphragmatic free air in up to 15% of cases of bowel perforation. Abdominal computed tomography is more sensitive, with a 98% sensitivity rate for detecting minute amounts of free air, making it the preferred imaging method for suspected peptic ulcer perforation. Initial management includes fluid resuscitation, nasogastric suction, and nil per os status. (Laine L, Jensen DM2012) Treatment may involve proton pump inhibitors, broad-spectrum antibiotics, and urgent surgical consultation. Prompt diagnosis and immediate surgical intervention are crucial for improving patient outcomes, as delays in surgery are associated with increased mortality. Peptic ulcer penetration is defined as an ulcer extending through the intestinal wall into an adjacent organ or anatomical structure without causing leakage of intestinal contents into the peritoneal cavity. Penetration is more common with ulcers in the antrum of the stomach and duodenum, potentially involving the pancreas, liver, omentum, biliary tract, and vascular structures, such as a fistula between the aorta and colon. Prepyloric peptic ulcers may penetrate the pyloric channel or duodenal bulb, forming a gastroduodenal fistula and resulting in an acquired

"double" pylorus. Complications from ulcer penetration can affect surrounding anatomical tissues. (Scarpignato C, Gatta L, Zullo A, et al 2016).

Table 3 Common First-Line Therapies for Treating Helicobacter Pylori Infection			
Treatment regimen Clarithromycin-based triple (if clarithromycin resistance <15%)	**Medication (dose)** PPI (standard or double dose) Clarithromycin (500 mg) Amoxicillin (1gm)	**Dosing frequency** Twice daily Twice daily Twice daily	**Duration of treatment** 14 Days
Clarithromycin-based triple (if clarithromycin resistance <15%, penicillin allergy)	PPI (standard or double dose) Clarithromycin (500 mg)	Twice daily Twice daily	Twice daily 14 days
	Metronidazole (500 mg)	Three times daily	
Bismuth-based quadruple	PPI (standard dose)	Twice daily	10-14 days
	Bismuth sub citrate (120−300 mg) or subsalicylate (300 mg) Tetracycline (500mg) Metronidazole (250 mg-500 mg)	Four times daily Four times daily 250 mg 4 times daily or 500 mg 3 times daily	
		Twice daily	
Concomitant (non-bismuth based quadruple)	PPI (standard dose) Clarithromycin (500 mg) Amoxicillin (1 gm) Metronidazole (500 mg) or Tinidazole (500 mg)	Twice daily Twice daily Twice daily	10-14 days
Sequential	PPI (standard dose) + Amoxicillin (1 gm)	Twice daily Twice daily	5-7 days
			5-7 days
	PPI (standard dose) + Clarithromycin (500 mg) +	Twice daily	

Conclusion

In conclusion, Peptic Ulcer Disease (PUD) is mainly caused by infection with Helicobacter pylori and the extended use of nonsteroidal anti-inflammatory drugs (NSAIDs), which together account for more than 90% of cases. The pathophysiology of PUD involves a fragile equilibrium between harmful factors like gastric acid and pepsin, and protective elements such as mucus production and bicarbonate buffering. Any disruption in this balance can result in mucosal damage, inflammation, and the formation of ulcers. Grasping these mechanisms is essential for creating effective treatment strategies. The epidemiological trends of PUD have changed significantly in recent decades. In developed countries, the prevalence has decreased due to better hygiene and the

widespread use of proton pump inhibitors (PPIs) for acid suppression. However, PUD continues to be a significant health concern in developing areas where healthcare access is limited. The lifetime risk of developing a peptic ulcer is about 10%, indicating its prevalence as a gastrointestinal issue. Additionally, the economic impact of PUD is considerable, with estimates indicating it costs the U.S. healthcare system around $3.4 billion each year. Improvements in diagnostic methods have greatly enhanced the early detection of PUD. Endoscopy and non-invasive tests for H. pylori have become routine in clinical practice, facilitating prompt treatment. The advent of PPIs has transformed treatment by effectively suppressing acid, resulting in high healing rates for both gastric and duodenal ulcers. Despite these advancements, challenges persist, particularly with the increasing rates of antibiotic resistance among H. pylori strains, which complicate eradication efforts. Furthermore, there is an urgent need for strategies to prevent ulcer recurrence in patients who require long-term NSAID use. Identifying alternative treatment options for patients who do not have H. pylori or are not NSAID users is also vital for comprehensive management.

References

Lanas, A., & Chan, F. K. (2017). Peptic ulcer disease. The Lancet, 390(10094), 613-624.

Lanas, A., & Chan, F. K. (2017). Peptic ulcer disease. The Lancet, 390(10094), 613-624.

Malfertheiner, P., Chan, F. K., & McColl, K. E. (2009). Peptic ulcer disease. The Lancet, 374(9699), 1449-1461.

Sung, J. J., Kuipers, E. J., & El-Serag, H. B. (2009). Systematic review: the global incidence and prevalence of peptic ulcer disease. Alimentary Pharmacology & Therapeutics, 29(9), 938-946.

Gustavsson S and Nyren O (1989) Time trends in peptic ulcer surgery, 1956 to 1986. A nation-wide survey in Sweden. Ann Surg 210: 704–709

Sach G (1997) Proton pump inhibitors and acid related diseases. Pharmacotherapy 17: 22–37

Sonnenberg A (1985) Geographic and temporal variations in the occurrence of peptic ulcer disease. Scand J Gastroenterol Suppl 110: 11–24

Sonnenberg A and Everhart JE (1996) The prevalence of self-reported peptic ulcer in the United States. Am J Public Health 86: 200–205

Sandler RS et al. (2002) The burden of selected digestive diseases in the United States. Gastroenterology 122: 1500–1511

Peterson, W. L. (1991). Helicobacter pylori and peptic ulcer disease. New England Journal of Medicine, 324(15), 1043-1048.

Garcia Rodriguez LA, Hernandez-Diaz S. Risk of uncomplicated peptic ulcer among users of aspirin and non aspirin nonsteroidal anti inflammatory drugs. Am J Epidemiol. 2004;159(1):23–31.

Suerbaum, S., & Michetti, P. (2002). Helicobacter pylori infection. New England Journal of Medicine, 347(15), 1175-1186.

Hatakeyama, M. (2004). Oncogenic mechanisms of the Helicobacter pylori CagA protein. Nature Reviews Cancer, 4(9), 688-694.

Ruggiero, P. (2010). Helicobacter pylori virulence factors. Current Opinion in Microbiology, 13(1), 44-49.

Wallace, J. L. (2008). Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself? Physiological Reviews, 88(4), 1547-1565.

Ko, J. K., Cho, C. H., & Lam, S. K. (1996). Role of smoking, alcohol, and diet in the development of peptic ulcer disease: An update. Postgraduate Medical Journal, 72(843), 469-473.

Bode, C., & Bode, J. C. (1997). Alcohol's role in gastrointestinal tract disorders. Alcohol Health & Research World, 21(1), 76-83.

Sonnenberg, A. (1985). Dyspeptic symptoms and peptic ulcer disease: a comparative study. Gut, 26(11), 1133-1141.

Peterson WL, Barnett CC, Evans DJ Jr, et al. Acid secretion and serum gastrin in normal subjects and patients with duodenal ulcer: the role of Helicobacter pylori. Am J Gastroenterol 1993;88:2038-43)

Kurata, J. H., & Haile, B. M. (1984). Epidemiology of peptic ulcer disease. Clinics in Gastroenterology, 13(2), 289-307.

Ramakrishnan, K., & Salinas, R. C. (2007). Peptic ulcer disease. American Family Physician, 76(7), 1005-1012.

Borum, M. L. (1996). Peptic ulcer disease: a review of pathophysiology, diagnosis, and treatment. Digestive Diseases, 14(3), 142-148.

Fischbach, L., Evans, E. L., & Peppercorn, M. A. (2002). American Gastroenterological Association technical review on the management of Helicobacter pylori infection. Gastroenterology, 123(1), 179-190.

Sonnenberg, A., Steinkamp, U., & Weise, A. (1986). Clinical epidemiology of peptic ulcer disease: a 10-year study of admissions and mortality. Gastroenterology, 90(1), 167-173.

Boey, J., Branicki, F. J., & Wong, J. (1982). Perforated duodenal ulcers: an analysis of the prognostic factors. American Journal of Surgery, 144(1), 99-104.

Lanas, A., & Chan, F. K. (2017). Peptic ulcer disease. The Lancet, 390(10094), 613-624.

Graham DY et al. (1988) Effect of age on the frequency of active Campylobacter pylori infection diagnosed by the 13C urea breath test in normal subjects and patients with peptic ulcer disease. J Infect Dis 157: 777–78

Xia HH et al. (2001) Reduction of peptic ulcer disease and Helicobacter pylori infection but increase of reflux esophagitis in western Sydney between 1990 and 1998. Dig Dis Sci 46: 2716–2723 15 Perez-Aisa MA et al. (2005) Clinical trends in ulcer diagnosis in a population with high prevalence of Helicobacter pylori infection. Aliment Pharmacol Ther 21: 65–72

Ford A et al. (2004) Eradication therapy for peptic ulcer disease in Helicobacter pylori positive patients. The Cochrane Database of Systematic Reviews. Issue 4, Art. No. CD003840.pub2

Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology. 2005;129(5):1756–1780.

Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of Helicobacter pylori infection. Am J Gastroenterol. 2017;112(2):212–239.

Dorward S, Sreedharan A, Leontiadis GI, Howden CW, Moayyedi P, Forman D. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2006 [CD005415].

Sreedharan A, Martin J, Leontiadis GI, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010(7) [CD005415].

Gisbert JP, Khorrami S, Carballo F, Calvet X, Gene E, DominguezMunoz E. Meta-analysis: Helicobacter pylori eradication therapy vs. antisecretory non-eradication therapy for the prevention of recurrent bleeding from peptic ulcer. Aliment Pharmacol Ther. 2004;19(6):617– 629.

Lai KC, Lam SK, Chu KM, et al. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. N Engl J Med. 2002;346(26):2033–2038.

Scheiman JM, Yeomans ND, Talley NJ, et al. Prevention of ulcers by esomeprazole in at-risk patients using non-selective NSAIDs and COX-2 inhibitors. Am J Gastroenterol. 2006;101(4):701–710. 30. Lanza FL, Chan FK, Quigley EM. Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol. 2009;104 (3):728–738.

Strand DS, Kim D, Peura DA. 25 years of proton pump inhibitors: a comprehensive review. Gut Liver. 2017;11(1):27–37.

Scarpignato C, Gatta L, Zullo A, et al. Effective and safe proton pump inhibitor therapy in acid-related diseases - A position paper addressing benefits and potential harms of acid suppression. BMC Med. 2016;14 (1):179.

Sheen E, Triadafilopoulos G. Adverse effects of long-term proton pump inhibitor therapy. Dig Dis Sci. 2011;56(4):931–950.

Freedberg DE, Kim LS, Yang YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology. 2017;152(4):706–715.

Lambert AA, Lam JO, Paik JJ, Ugarte-Gil C, Drummond MB, Crowell TA. Risk of community-acquired pneumonia with outpatient protonpump inhibitor therapy: a systematic review and meta-analysis. PLoS One. 2015;10(6):e0128004.

Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut. 2017;66(1):6–30.

Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011;84 (2):102–113.

Gurusamy KS, Pallari E. Medical versus surgical treatment for refractory or recurrent peptic ulcer. Cochrane Database Syst Rev. 2016;3: CD011523.

Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015;47(10):a1

Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345–360 [quiz 361].

Lau JY, Barkun A, Fan DM, Kuipers EJ, Yang YS, Chan FK. Challenges in the management of acute peptic ulcer bleeding. Lancet. 2013;381(9882):2033–2.