Journal of Advances in Medical and Pharmaceutical Sciences

Volume 25, Issue 11, Page 14-27, 2023; Article no.JAMPS.109508
ISSN: 2394-1111

Peptic Ulcer Disease (PUD), Diagnosis, and Current Medication-Based Management Options: Schematic Overview

Yash Srivastav [a*], Vijay Kumar [a], Yashi Srivastava [b] and Madhaw Kumar [a]

[a] Department of Pharmacy, Goel Institute of Pharmacy and Sciences (GIPS), Lucknow, Uttar Pradesh, India.
[b] Department of Pharmacy, Amity University Lucknow Campus, Lucknow, Uttar Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2023/v25i11651

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/109508

Review Article

Received: 24/09/2023
Accepted: 29/11/2023
Published: 02/12/2023

ABSTRACT

A common condition in the world, Peptic Ulcer condition is sometimes referred to as stomach ulcers or peptic ulcers. PUD is caused by a defect in the mucosa of the stomach or duodenum that extends beyond the muscularis mucosa. PUD is the consequence of an imbalance between the aggressive and defensive elements impacting the mucosa, which occurs after gastric mucosal lesions. Peptic ulcer disease (PUD) is a widespread ailment affecting 5–10% of the world's population, with notable racial and regional variations. As a result of an imbalance between the aggressive and defensive elements impacting the mucosa, comes gastric mucosal injuries. The word "peptic" comes from the hormone pepsin, which is essential in causing mucosal breakdown.

**Corresponding author: E-mail: neelashsrv76@gmail.com;*

The most common cause of upper gastrointestinal bleeding in the Western world is bleeding from peptic ulcers (PUs). High rates of morbidity, mortality, and medical costs are linked to it. This review article covers the pathophysiology, aetiology, medical therapy, diagnosis, symptoms, and signs of Peptic Ulcer Disease (PUD).

Keywords: Peptic Ulcer Disease (PUD); history; epidemiology; etiology; pathophysiology; diagnosis and management.

1. INTRODUCTION

The condition known as peptic ulcer disease (PUD) is characterized by a significant loss of substance that affects the mucosa of the stomach and/or duodenum and typically extends across the muscularis mucosa to the muscle layer as a result of ambient gastric acid secretion. Peptic ulcer disease (PUD) is a common illness that affects 5–10% of people globally, with significant racial and regional differences. The use of non-steroidal anti-inflammatory medicines (NSAIDs) and a chronic Helicobacter pylori (Hp) infection are the two most common etiological causes [1]. The term "peptic ulcer disease" (PUD) refers to the upper gastrointestinal tract's mucosal breakage caused by acid peptic digestion, which leads to ulcers that penetrate the submucosa and go past the muscularis mucosae. It can also develop in the distal esophagus, distal duodenum, jejunum, and diverticulum of Meckel's with the heterotrophic gastric mucosa. The stomach and initial portion of the duodenum are the most typical places it occurs [2]. An imbalance between the stomach mucosa's endogenous protective factors (mucus and bicarbonate secretion, appropriate blood flow, prostaglandin E2, nitric oxide, sulfhydryl compounds, antioxidant enzymes, and others) and aggressive factors (acid and pepsin secretions) leads to peptic ulcer, a chronic disease. The genesis of stomach ulcers has also been linked to behavioral and environmental factors, including Helicobacter pylori infection, alcohol consumption, smoking, poor diet, and the use of non-steroidal anti-inflammatory medicines. A blister is an exposed lesion on the skin or mucous membrane that is characterized by the exfoliation of dead, inflammatory tissue. Lesions on the skin's surface or a mucous membrane that exhibit superficial tissue loss are called ulcers. Although they can occur practically anywhere, ulcers are most frequently found on the skin of the lower limbs and in the gastrointestinal tract. There are numerous varieties of ulcers, including vaginal, peptic, esophageal, and oral ulcers [3,4]. The stomach's hostile environment is home to the Gram-negative bacterium Helicobacter pylori, which is present between the mucous layer and the gastric epithelium. At first, Helicobacter pylorus is found in the antrum, but it eventually moves to the stomach's closer sections. One of the most common gastrointestinal conditions in the world, peptic ulcers impact 10% of the global population. The duodenum causes about 19 of every 20 peptic ulcers. An estimated 15,000 fatalities are attributed to peptic ulcers annually. Hemorrhage and perforation from peptic ulcers were estimated to occur annually in 19.4–57 and 3.8–14 cases per 100,000 people, respectively. The mean recurrence of bleeding within 7 days was 13.9%, while the mean recurrence of perforation over an extended period was 12.2%. The two Australian scientists discovered H. Pylori as the primary cause of stomach ulcers in 1982 [3,5]. Helicobacter pylori is the most frequent bacteria that causes stomach ulcers. Ulcers can also result from overusing nonsteroidal anti-inflammatory drugs (NSAIDs) such naproxen, ibuprofen, and aspirin, as well as painkillers like aspirin. The mucosal membrane of the gastrointestinal tract is destroyed in a Peptic Ulcer. Depending on where they are found, ulcers are referred to by different names (duodenal ulcers are found in the duodenum, whilst gastric ulcers are found in the stomach lining). In clinical practice, the primary cause of ulcers is often found to be a shortage of digestive enzymes [6,7]. The hazardous side effects of allopathic ulcer treatment have a negative impact on one's health. It prevents the organ that that membrane is a part of from carrying out its regular operations. It manifests in a variety of ways both inside and outside the human body. Different types of ulcers, including peptic ulcers, corneal ulcers, stomach ulcers, foot or leg ulcers, etc., are currently recognized in medicine [8]. The ulcer's dimensions range from 5 mm to several centimeters. However, erosions are only found in the mucosa, are superficial, and measure less than 5 mm. In our therapeutic practice, PUD is one of the most prevalent conditions that we see. The hormone pepsin, which is crucial in inducing mucosal breakage, is the source of the phrase "peptic." In the western

world, bleeding from peptic ulcers (PUs) is the most frequent cause of upper gastrointestinal bleeding. It is associated with high rates of morbidity, mortality, and healthcare expenses [9,10]. According to conventional wisdom, a hypersecretory acidic environment combined with dietary variables or stress is the cause of mucosal disruption in patients with acid peptic illness. Consumption of alcohol and tobacco, use of non-steroidal anti-inflammatory medicines (NSAIDs), Zollinger-Ellison syndrome, and H. pylori infection are risk factors for developing peptic ulcer. NSAID use and H. pylori infection are the primary risk factors for both stomach and duodenal ulcers [11,12].

2. TYPES OF PEPTIC ULCER DISEASE (PUD)

Stomach and duodenal ulcers are examples of the digestive tract ulcers covered by the general term "peptic ulcer." In the past, it was thought that eating spicy food and stress caused this kind of ulcer. Recent studies have demonstrated that these are merely the exacerbating circumstances. The infection brought on by the H. pylori bacteria or a reaction to specific medications, such as non-steroidal anti-inflammatory drugs, is the cause. Peptic ulcers can cause weight loss, bloating, nausea, vomiting, and dark feces, which are signs of internal bleeding in the gastrointestinal tract [13]. Mouth ulcers are sores that appear on the inside of the mouth lining. Mouth ulcers are frequent and typically result from trauma, such as loose or uncomfortable dentures, broken teeth, or fillings. Some common causes of mouth ulcers or sores include anemia, measles, viral infections, oral candidiasis, persistent infections, throat cancer, mouth cancer, and vitamin B deficiency. Among the most prevalent types of oral ulceration illnesses, aphathous minor is thought to afflict 15-20% of people globally. It is particularly frequent in North America, where reports of prevalences as high as 50–66% have been made. It has been discovered that smokers had a reduced incidence of aphthous ulcers than non-smokers [13,14].

2.1 Gastric Ulcers

Millions of healthcare dollars are frequently spent on treating gastric ulcers, which are a typical clinical presentation in the US. They are a breach larger than 5 mm in diameter in the stomach lining's mucosal barrier that passes through the muscularis mucosa. Realizing that this illness process is curable and preventive is crucial. Depending on the cause of their stomach ulcer, patients may receive different treatments. The mucosa of the stomach is naturally shielded by the body from the gastric lumen's hazardous acidic environment. Changes in these defenses may result in modifications to the stomach mucosa, which may ultimately lead to erosion and ultimately ulceration. Prostaglandins, mucus, growth factors, and sufficient blood supply protect the gastric mucosa. This barrier is known to be harmed by alcohol, alcoholism, smoking, hydrochloric acid, ischemia, NSAIDs, hypoxia, and Helicobacter pylori infection [15].

2.2 Esophageal Ulcer

An esophageal ulcer is a discrete rupture in the mucosal lining of the esophagus. This esophageal mucosal injury is frequently brought on by severe, long-lasting esophagitis from other causes or by gastroesophageal reflux disease. It has been projected that 2% to 7% of people will develop esophageal ulcers as a result of gastroesophageal reflux disease. Gastroesophageal reflux disease is the most common cause of esophageal ulcers, and endoscopic examination often reveals some degree of hiatal hernia in most patients. Normally, the lower esophageal sphincter (LES) prevents the reflux of stomach contents; however, when the LES weakens, this defense mechanism is compromised, exposing the esophageal mucosa to stomach acid and increasing the risk of ulceration. Furthermore, as shown in bulimia nervosa patients, recurrently inducing vomiting exposes the esophageal mucosa to stomach contents, which can either develop an ulcer or exacerbate an already existing ulcer [16].

2.3 Duodenal Ulcers

Peptic ulcer disease is a general term for a group of diseases that includes duodenal ulcers. The term "peptic ulcer disease" describes the illness state and clinical manifestation that arises from a disturbance in the mucosal membrane of the stomach or duodenum, the first segment of the small intestine. Anatomically, pre-epithelial, epithelial, and subepithelial components make up the defensive system on the stomach and duodenal surfaces. Damage to the mucosal surface that penetrates below the surface layer results in ulceration. Although dyspepsia is the most common accompanying symptom of duodenal ulcers, there are other presenting types

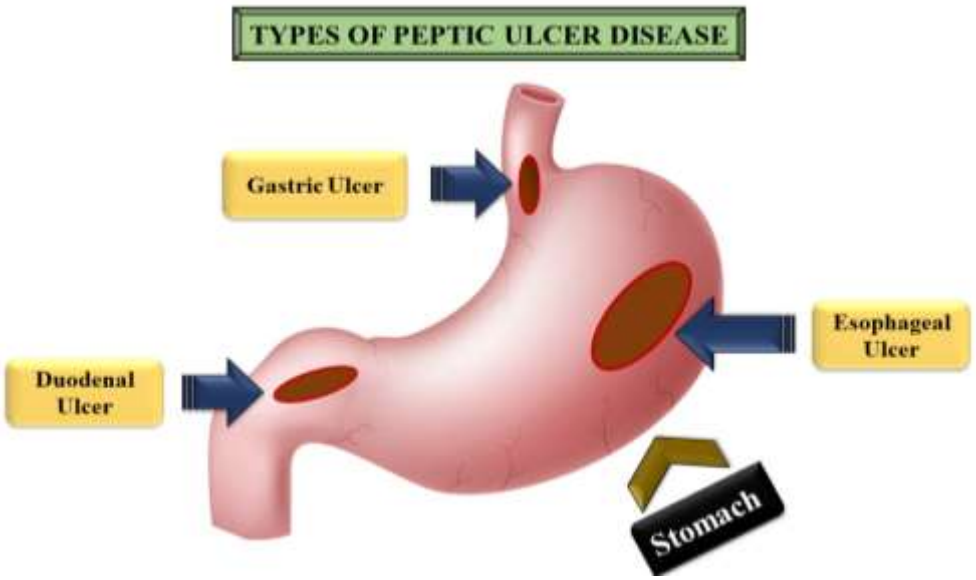

Fig. 1. Peptic ulcer disease systemic types

that might vary in severity, such as gastrointestinal hemorrhage, gastric outlet obstruction, perforation, or the formation of a fistula. As a result, the patient's presentation at the time of diagnosis or as the disease advances greatly influences the care. When a patient reports NSAID usage or a prior Helicobacter pylori diagnosis and exhibits symptoms of dyspepsia or upper abdominal discomfort, it is worth considering whether the patient has a duodenal or gastric ulcer. Since H. pylori is a common cause of peptic ulcer disease, testing for it should be done on every patient with a diagnosis of duodenal ulcers in particular [17].

3. HISTORY

Although heartburn and indigestion have been documented for millennia, the autopsy-based diagnosis of peptic ulcer disease did not occur until the 16th century. Donatus of Mantua conducted research on one of the earliest autopsy in 1586, which revealed pyloric peptic ulcers. In 1679, Bauhin came to the conclusion that a stomach ulcer that eventually burst was caused by inflammation in the stomach. Reports of the first documented stomach bleeding date back to 1704. Matthew Baillie provided the first categorization of stomach illnesses in 1793, clearly defining acute inflammation (arsenic), trichobezoar, ulcer, perforation, pyloric stenosis, scirrhous, and ulcerated cancer. In 1817, Crampton reported cases of perforated gastric ulcers in Dublin, while Travers reported cases of perforated duodenal ulcers in London. Travers also documented bleeding, stenosing, and piercing stomach ulcers. In North India, the first epidemiological investigation on peptic ulcers was carried out in 1963 [18–22]. Roughly 10% of Americans may experience peptic ulcer disease at some point in their lives, with an estimated 500,000 new cases and 4 million recurrences of the condition recorded annually. Up to 20% of individuals experience complications from peptic ulcer disease, such as perforation, bleeding, and blockage; in total, 5% to 12% of patients may experience gastric outlet obstruction. According to Johnson et al., 62% of patients from 1962 to 1975 and 45% of patients from 1975 to 1985 had obstruction due to peptic ulcer illness. found that just 33% of the individuals in their series who had outlet blockage and peptic ulcer disease tested positive for H. pylori [23]. From about 1 case per 1000 people in Japan to 1.5 cases per 1000 people in Norway to 2.7 cases per 1000 people in Scotland, the yearly incidence of stomach ulcers varies. The ratio of gastric to duodenal ulcers often fluctuates with time and location. Although gastric ulcers are more common in some places, such as Japan, Sri Lanka, the Andes, and several islands off the coast of northern Norway, duodenal ulcers are roughly three times more common than gastric ulcers in most other countries [24,25].

4. EPIDEMIOLOGY

The proximal duodenum and stomach are the primary sites of occurrence for PUD, which is responsible for an annual incidence of 0.1–0.3%

and a lifetime prevalence of 5–10% in Western countries' general population [26]. In the US, PUD affects over 4.5 million people annually and results in significant healthcare costs of roughly $3.3 billion. The frequency of Helicobacter pylori (H. pylori) infection is correlated with the prevalence of PUD. The seroprevalence of H. pylori infection in the United States varies with age: it is 16.7% in the 20–29 age group and 56.9% in the >70 age group. Additionally, it varies by ethnicity: Mexican Americans make up 61.6%, non-Hispanic Blacks make up 52.7%, and non-Hispanic Whites make up 26.2%. Up to 90% of people can have an illness in underdeveloped nations. According to a systematic evaluation of the literature from developed nations, the incidence and prevalence of PUD diagnosed by physicians worldwide were estimated to be 0.10–0.19% and 0.12–1.50%, respectively. However, the widespread use of acid suppressant medication and the decline in Helicobacter pylori infection prevalence as a result of higher socioeconomic position and the elimination of H. pylori infection after detection have reduced the incidence and prevalence of PUD [27–30].Endoscopy was used to ascertain the prevalence of peptic ulcer disease in the general population of Kashmir, India. The sample group consisted of 2763 persons aged 15 years and above, who were randomly selected and questioned using a questionnaire. 193 (80.7%) of the 239 people who had ulcer symptoms underwent an oesophagus gastroduodenoscopy. 177 people who were chosen at random from the remaining population and did not exhibit any symptoms of ulcers underwent endoscopy. Peptic ulcers had a point frequency of 4.72% and a lifetime prevalence of 11.22%. The ratio of gastric to duodenal ulcers was 17.1:1. In men, duodenal and stomach ulcers were prevalent. Peptic ulcer frequency rose with age, reaching a maximum in the fifth decade of life at 28.8% [31].

5. ETIOLOGY

The presence of a significant loss of substance affecting the stomach and/or duodenum's mucosa, extending into the muscularis mucosa and typically reaching the muscle layer as a result of ambient gastric acid secretion, is known as peptic ulcer disease (PUD). The two most frequent etiological reasons are the use of nonsteroidal anti-inflammatory medicines (NSAIDs), which naturally include acetylsalicylic acid (ASA), and a chronic Helicobacter pylori (Hp) infection. When taken into account collectively, these less frequent reasons account for less than 5% of PU instances. Among these is the neuroendocrine tumor known as gastrinoma or Zollinger-Ellison syndrome, which is hyperactive and secretory of gastrin. It is typically found in the duodenal wall or near the head of the pancreas (32). But it's important to keep in mind that 5–15% of patients who are deemed HP negative, despite extensive and thorough etiological investigations, are unable to determine the exact reason of PU; these people are known as "idiopathic." The O blood group and tobacco addiction are thought to be risk factors for the development of ulcer disease. It is unknown whether hereditary factors play a role, while familial aggregation can happen in certain circumstances. Smoking impedes the healing of ulcers and increases their recurrence, particularly in individuals who are high probability patients or NSAID users [32,33]. H. pylori infection and NSAID use are two factors that contribute to PUD and gastritis. Less frequent risk factors include Crohn's disease, radiation therapy, severe sickness, autoimmune issues, alcoholism, smoking, cocaine, and other drugs [34]. The main causal factor is H. pylori. Up to 50–75% of duodenal ulcers and 60% of gastritis are caused by chronic inflammation brought on by H. pylori colonizing the antral mucosa. Even with the formation of antibodies, the immune system is unable to eradicate the infection. As a result, the bacteria may induce type B gastritis, a chronic, aggressive form of the disease. Gastrin causes parietal cells to produce more stomach acid. The production of ulcers can result from erosion of the mucosa caused by an increase in acid in H. pylori colonization reactions to elevated gastrin. The stomach environment, which is unfavorable to the development of other bacteria, allows H. pylori to live and proliferate. H. pylori can survive in the acidic environment of the stomach thanks to a variety of modifications [34]. Several significant adhesions have been found, despite the fact that the majority of organisms seem to be adherent to the mucosal epithelial cells and build adherence pedestals similar those made by enteropathogenic Escherichia coli. H. pylori lipopolysaccharide has remarkably little proinflammatory activity compared to other bacteria. There is strong evidence linking H. pylori to stomach ulcer illness. It is generally known that H. pylori plays a pathogenic role in chronic active gastritis and that, in 95–99% of cases, there is a connection between H. pylori and duodenal ulcers. In the mammalian stomach, all H. pylori species cause persistent inflammation to varying degrees [34]. Almost all infected persons have arthritis, though most don't

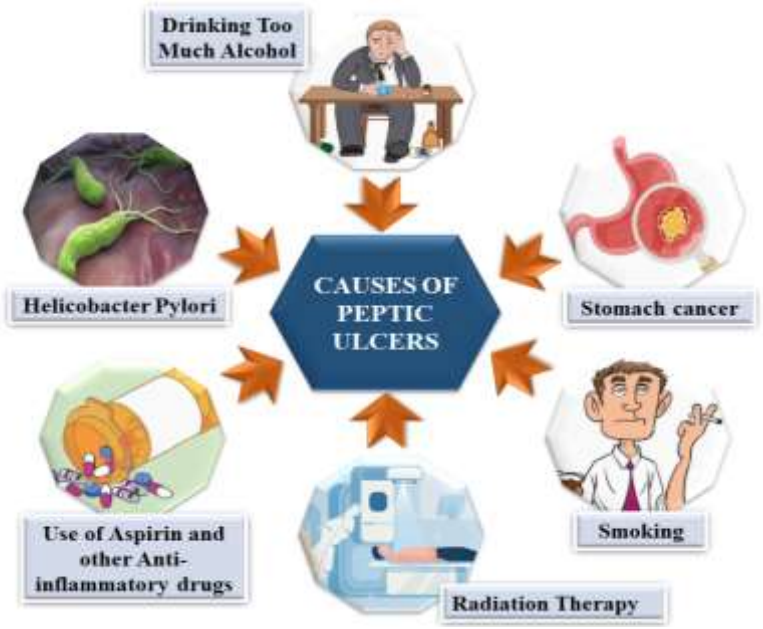

Fig. 2. Few typical causes for peptic ulcers

show any symptoms; just 10% go on to have ulcer disease. People with H. pylori infection are three to twelve times more likely to develop gastric cancer. Numerous hypothesized mechanisms exist for how H. pylori can damage mucosa. For example, urease can produce ammonia, hemostatic factors, and cytotoxins (including lipases, phospholipase A, protease, and vacuolating cytotoxin) can cause damage [34]. Atrophic gastritis, Addison's disease, autoimmune thyroiditis, and hyperparathyroidism are among the digestive and extra-digestive diseases that are most frequently linked to peptic ulcers. These conditions also include the concurrent presence of chronic gastroesophageal reflux disease (GERD), Barrett's esophagus, chronic obstructive pulmonary disease (COPD), liver cirrhosis, and chronic renal failure [35–37].

6. SIGNS AND SYMPTOMS

The first person to link the pathological evidence and clinical symptoms of peptic ulcer disease was Irish surgeon Moynihan. It has been noted that whereas large ulcers might result in significant bleeding, tiny ulcers may not show any symptoms at all. Burning pain is the most typical symptom, especially in the area directly beneath the breast bone [38,39]. Pain from a stomach ulcer is felt noticeably higher in the abdomen and may be less intense than pain from a duodenal ulcer. Rather of reducing pain, eating may actually make participants' suffering worse. Weight loss, vomiting, and nausea are possible additional symptoms. A partial or total obstruction of the stomach outflow may be the cause of vomiting. Patients may experience burning or gnawing sensations in their upper abdomen in addition to being awakened from sleep by duodenal ulcer discomfort. Occasionally, pain in the lower abdomen, back, or chest area might develop when the stomach is empty, which can happen during the night or two hours after a meal. After eating, relief is often experienced. Ulcer disease can also include epigastric discomfort, melena from acute or subacute gastrointestinal bleeding, and total blockage of the gastric outlet [40,41].

7. PATHOPHYSIOLOGY

The inner lining of the gastrointestinal (GI) tract stops working as a result of pepsin or gastric acid release, which is the hallmark of peptic ulcer disease (PUD). The stomach epithelium's muscularis propria layer is where it touches. Usually, it happens in the duodenum and stomach. The jejunum, distal duodenum, or lower esophagus could be affected. Patients with gastric ulcers typically have epigastric pain 15–30 minutes after eating, whereas duodenal ulcer patients typically experience pain 2–3 hours later. These days, it is advised that all patients with peptic ulcer disease undergo testing for Helicobacter pylori [34]. One of the most frequent

causes of peptic ulcer illness is Helicobacter pylori. The organism is acquired in an unhygienic and congested environment throughout childhood. In the antrum, H. Pylori induces more severe epithelial cell degeneration and destruction. Ten to fifteen percent of h. Pylori-infected individuals exhibited increased gastric secretion as a result of hypergastrinemia and decreased antral somatostatin levels, despite the fact that hyposecretion has been linked to the development of gastric ulcers. Histamine secretion rises as a result, and acid or pepsin secretion rises as well [32]. Mucosal atrophy and hypochlorhydria are linked to stomach ulcers. NSAIDS change the phospholipids in mucus, which leads to the uncoupling of mitochondrial oxidative phosphorylation. Mucosal injury is decreased by co-administration of cyclooxygenase-2 (cox-2) and exogenous prostaglandins. NSAIDS are protonated and travel across lipid membranes to enter epithelial cells in response to acidic gastric juice (Ph 7.4), where they ionize and release h+. NSAIDS become hazardous because they are unable to get through the lipid barrier [42].

Fig. 3. Peptic ulcers disease (PUD) general pathophysiology

8. PEPTIC ULCER DISORDER (PUD) COMPLICATIONS

Fifty percent of occurrences of upper gastrointestinal hemorrhage are related to peptic ulcer disease. In the United States, upper gastrointestinal bleeding is a prevalent clinical issue that causes over 2,50,000 hospitalizations per year. This illness is acknowledged as the most frequent cause of upper gastrointestinal bleeding, accounting for 45-78% of bleeding episodes. Bleeding is the most common and serious complication of peptic ulcers, occurring 50–170 times per 100,000 cases, and is most common in adults over 60. The most deadly side effect of duodenal and stomach ulcers is bleeding, which is nearly always fatal when the condition is surgically treated. Patients in the Forest Class 3 rarely rebleed or require hospitalization when their ulcer displays a clear foundation or flat dot. On the other hand, ulcers that are actively bleeding or that show signs of recent bleeding (forrest class 1 and 2) are more prone to rebleed and may require critical treatment [43–45]. An additional complication of severe duodenal ulcer illness is gastric outlet obstruction, or blockage at the pylorus. A mechanical blockage may result from widespread illness and subsequent scarring in the affected area. The antrum, the stomach's propellant component, loses its ability to empty the stomach as a result of inflammation's long-term damage of the regular emptying process. However, some writers have also come to the conclusion that a high rate of H. pylori infection is linked to gastric outlet obstruction [46]. Ten consecutive individuals with clinically and endoscopically substantial gastric outlet blockage were investigated by Taskin et al. Seven stomach biopsy specimens (from the fundus, corpus, and antrum) were taken during each endoscopy, and they were examined histologically and using the quick urease test to determine whether H. pylori had colonized them. Nine individuals, or ninety percent of the patients, had H. pylori positive antral mucosal biopsy specimens [47,48].

9. DIAGNOSIS

Peptic ulcers were diagnosed mostly on the basis of clinical signs and symptoms until the early 1900s. The direct viewing of ulcer disease was revolutionized in the 1950s by a variety of flexible endoscopies [49]. In order to compile a comprehensive list of all the symptoms and indicators of PUD, a thorough physical examination and a thorough clinical history are required. Additionally, it is crucial to record all past medical history, including the length of alcohol consumption, NSAID and smoking histories, and any potential peptic ulcer events. When diagnosing peptic ulcer disease, there are two main factors to take into account. The first is to evaluate if the symptoms being referred to are unrelated to functional dyspepsia, and the second is to identify the precise cause of the ulcer [37].

9.1 Esophagogastroduodenoscopy

In this unique procedure, gastroenterologists put a tiny tube with a camera via the mouth into the GI tract to view the stomach and small intestine. The physician may biopsy the stomach wall during this examination in order to look for H. pylori [50]. For PUD, upper GI endoscopy is the

most reliable diagnostic procedure. It provides details on the lesion's location and size. Furthermore, mucosal biopsies may be carried out in the event of a bleeding peptic ulcer in order to conduct an endoscopic treatment and make a differential diagnosis. It is also necessary to collect multiple biopsies from the corpus and antrum mucosa in order to identify or rule out concurrent H. Pylori infection. The presence of regular mucosal folds surrounding the ulcer base and the fibrin deposit at the crater base are indicators of a benign etiology. The presence of an ulcerated mass that protrudes into the lumen, uneven or thicker borders, and/or overhanging edges are characteristics that indicate malignancy. It is rare for duodenal ulcers to be malignant. As a result, routine biopsy is not advised. Even though a stomach ulcer appears benign, it is necessary to collect multiple mucosal biopsies from the margins at any gastric ulcer. There will be a follow-up endoscopy till the healing is finished [51]. Every patient with a peptic ulcer should have their H. pylori infection looked into. Numerous changes have been made to the administration after the discovery in 1983. It is well known that there is no gender difference in the infection's prevalence, and it rises with age. A number of tests are performed not only for diagnosis but also for follow-up following the eradication treatment to confirm this one. Direct and indirect tests are utilized to diagnose H. pylori, depending on whether an endoscopy is necessary [52].

9.2 X-ray

In this, the patient is made to consume barium, a white, chalky substance that shows up on an X-ray, and is then made to lie down on an inclined examination table. The barium is dispersed uniformly throughout the upper digestive tract by tilting, and the X-ray can take pictures from various perspectives. This makes it possible for the physician to find the ulcer and assess its kind and severity [49].

9.3 Radiology

Although barium gastroduodenal studies have been almost entirely abandoned in favor of endoscopic explorations in routine diagnostic protocols, they can still be helpful in a small number of patients who refuse to undergo the procedure or in situations where esophageal narrowing prevents endoscopy from being performed. Barium radiography examinations' sensitivity and specificity are dependent on the experience of the radiologist, the method employed, the size of the lesion (less than 0.5 cm in diameter can be hard to find), and the depth of the ulcer. Regular edges and symmetrical mucosal folds, a smooth, translucent band or collar, an ulcer crater surrounding it that suggests edema, and an indentation of the opposing wall are radiologic markers that point to a benign nature. On the other hand, large ulcers, irregular mucosal folds, lack of contrast, or uneven filling are indicators of malignancy [53].

9.4 Computed Tomography

It is a quick method of verifying a suspected peptic ulcer disease-related perforation and penetration diagnosis. In order to analyze the abdominal computed tomography results in patients with peptic ulcer disease and link them with the clinical history, endoscopic and upper GIT series results, and surgery when it is performed, this study is retrospective in nature [54,55].

10. THE PEPTIC ULCER DISEASE (PUD) CURRENT POSSIBLE MEDICINE BASED MANAGEMENT

The majority of H. pylori eradication treatments over the previous 20 years have included antibacterial medicines in combination with antisecretory medications. The current global agreement states that triple therapy, consisting of two PPIs per day, 500 mg of clarithromycin per day, and either 1 g of amoxicillin per day (PPI-CA) or 500 mg of metronidazole per day (PPI-CM) for a duration of 7–14 days, should be the first line of treatment. PPI therapy administered twice a day is more effective than once a day.34 First-line treatments have a 70% to 95% success rate in eradication, and 10- and 14-day regimens are typically 7–9% more effective than the most popular 7-day regimens. The type of antibiotics used depends on treatment failure caused by noncompliance and, depending on the region, bacterial resistance. Since bacteria are more resistant to metronidazole and hardly resistant to amoxicillin, amoxicillin is preferred over metronidazole in first-line therapies [56–59]. The use of PPI-CA as a first-line treatment is also advocated over PPI-CM due to worries that PPI-CM treatment may result in subsequent resistance to the most effective forms of treatment, metronidazole and clarithromycin. As a first-line treatment, quadruple therapy-200 mg of bismuth four times a day, 500 mg of metronidazole three times a day, 500 mg of tetracycline four times a day, and a PPI twice a

day for at least seven days-has also gained recognition. A global panel of experts summed up this guiding principle in the Maastricht Consensus Report: since re-treatment with the original regimen is not advised, second-line treatment is carried out using a different selection of antimicrobial medications than those used in first-line treatment. Even with this cautious approach, eradication may not always succeed, necessitating further pharmaceutical intervention. Following this, bacterial culture is used to inform the selection of antibiotic therapy, and the prescription of a third-line treatment is based on the microbial sensitivity to antibiotics [60,61]. The pharmacogenetics of specific PPIs and bacterial resistance have an impact on the rates of H. pylori eradication. The effectiveness of PPIs' antisecretory qualities was assessed by CYP2C19 gene polymorphisms, which also had an impact on H. pylori eradication rates. These findings show that genotyping could be a useful technique for optimizing eradication therapies. CYP2C19 polymorphisms and H. pylori eradication rates with PPI first-line therapies were examined in a recent meta-analysis; however, the results showed that the eradication rates between patients with the heterozygous-extensive-metabolizer genotype and those with the poor-metabolizer genotype were comparable, which reduced the clinical significance of CYP2C19 polymorphisms [62,63]. Triple therapy based on PPIs lead to a significantly lower ulcer recurrence rate of 12–14% when evaluated after two weeks. Similar to complex bleeding ulcers, where the recurrence rate following H. pylori eradication ranged from 1.6% to 2.9%, previous meta-analyses of H. pylori eradication found recurrence rates of 2-3%. According to these research, eliminating H. pylori is a highly successful method for managing and reducing the symptoms of peptic ulcer disease. Research shows that eliminating the infection completely heals peptic ulcers in people with H. pylori infection and dramatically lowers the ulcer recurrence rate, particularly in patients who do not take aspirin or NSAIDs. According to a recent meta-analysis, patients with H. pylori infection did not require continued PPI therapy to repair their ulcers following a course of PPI-based 7-day triple therapy [64–68]. According to certain research, using a PPI for maintenance therapy following eradication can greatly lower the risk of ulcer complications and recurrence. After H. pylori eradication, maintenance therapy with a PPI should be continued for all patients who exhibit ulcer problems [69].

10.1 Medicinal Plants: Potent Treatments that Prevent Ulcers

Medicinal herbs are widely used in traditional Indian medical systems. Phytochemicals from medicinal plants are employed as lead compounds in medication development. Medicinal plants are a source of innovative therapeutics for many medical systems, including traditional medicine, contemporary medication, nutraceuticals, food supplements, folk medicine, pharmaceutical intermediates, bioactive principles, and lead molecules in synthetic drugs. Over 80% of the world's population gets their primary healthcare from plants, according to the WHO. As one of the 12 mega diversity countries in the world, India has a critical stake in the preservation and sustainable use of its biological resources. One of the most promising sources of novel drugs is plant extracts, which have demonstrated efficacy in treating gastrointestinal ulcers. Thus far, anti-ulcer medications have been found in over 240 therapeutic plants and 21 plant-based compounds. The development of an alternative medication with minimal adverse effects on patients is therefore desperately needed. The answer lies in herbal remedies and conventional pharmaceuticals, both of which have minimal potential for adverse effects [70]. Traditional medicine has been used by Homo sapiens for thousands of years. Man started to depend on and learn from nature for his everyday needs. Gradually, a basic understanding- or, to put it another way, a conventional medical system-was established through accidental experiments or unintended findings. A tablet claims that approximately 2600 BC is when people first began using conventional medicine. It lists oils from the following species: myrrh, glycyrrhiza glabra, cupressus sempervirens, cedrus species, and papaver somniferum (poppy juice). It is impossible to completely rule out the chance of side effects or bad consequences changing, no matter how far chemotherapy or allopathic medicine have advanced. Consequently, the development of an alternative medicine for the treatment of disease with minimal adverse effects on the patient is necessary. Using herbal therapies and conventional medications, which have few adverse effects, is the answer. It has been found that a variety of nutrients, plants, and herbs can help prevent or treat stomach and peptic ulcers. Although there aren't many human trials accessible, several in vitro or animal research have produced encouraging findings. Numerous botanical preparations have been found to exhibit

antiulcer activity; nevertheless, the majority of the published literature has concentrated on the pharmacological action of these products in experimental animals. There are few clinical studies supporting the use of herbs as gastro-protective agents, with the exception of a few phytogenic substances (aloe, licorice, and chilly); thus, information on efficacy and safety is scarce. Finally, since most anti-inflammatory drugs used in modern medicine are ulcerogenic, antiulcer substances like flavonoids, aescin, aloe gel, and many more have a great therapeutic benefit. Tannins, terpenoids, and flavonoids are examples of antiulcer substances [71–73].

10.2 Dietary Adjustments

The addition of omega-3 polyunsaturated fatty acids is recommended because they reduce inflammation and guard against stomach ulcers. Eat nothing hot. Avert eating late at night. Eat a well-balanced, low-cholesterol diet [74].

10.3 Lifestyle Adjustments

Refrain from going straight to bed after eating. Raise the bed's head. Stay calm [75].

11. CONCLUSION AND FUTURE DIRECTION

Our review articles go into a lot of detail about the signs and symptoms of peptic ulcer disease (PUD), as well as its aetiology, pathophysiology, epidemiology, diagnosis, and current therapies. Pharmaceutical drugs have advantages, but they also frequently have disadvantages, such kidney damage. To learn more about the best course of action for treating peptic ulcer disease (PUD), further randomized controlled trials are required. Our goal is to carry out further study on peptic ulcer disease (PUD). With the assistance of our colleagues, a second study with counseling will be carried out in our country or state to assess patients' mental and physical health and to provide a more comprehensive understanding of peptic ulcer disease (PUD) and its improved treatment.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

Authors would like to thank, Goel Institute of Pharmacy & Sciences (GIPS), Lucknow, Uttar Pradesh, India for extending their facilities.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Goli S. Peptic Ulcer Disease: Maintenance treatment with H2 blockers. Gastroenterol Pancreatol Hepatobilary Disord. 2017;1(1):01–4.
2. Lanas A, Chan FKL. Peptic ulcer disease. Lancet [Internet]. 2017;390(10094):613–24. Available:http://dx.doi.org/10.1016/S0140-6736(16)32404-7
3. Vimala G, Gricilda Shoba F. A review on antiulcer activity of few indian medicinal plants. Int J Microbiol. 2014;2014
4. Lemos LMS, Martins TB, Tanajura GH, Gazoni VF, Bonaldo J, Strada CL, et al. Evaluation of antiulcer activity of chromanone fraction from Calophyllum brasiliesnse Camb. J Ethnopharmacol [Internet]. 2012;141(1):432–9 Available:http://dx.doi.org/10.1016/j.jep.2012.03.006
5. Umre R, Ganeshpurkar A, Ganeshpurkar A, Pandey S, Pandey V, Shrivastava A, et al. In vitro, *in Vivo* and in silico antiulcer activity of ferulic acid. Futur J Pharm Sci [Internet]. 2018;4(2):248–53 Available:https://doi.org/10.1016/j.fjps.2018.08.001
6. Chung KT, Shelat VG. Perforated peptic ulcer - an update. World J Gastrointest Surg. 2017;9(1):1.
7. Yuan Y, Padol IT, Hunt RH. Peptic ulcer disease today. Nat Clin Pract Gastroenterol Hepatol. 2006;3(2):80–9.
8. Singh AK, Singh SK, Singh PP, Srivastava AK, Pandey KD, Kumar A, et al. Biotechnological aspects of plants metabolites in the treatment of ulcer: A new prospective. Biotechnol Reports [Internet]. 2018;18:e00256. Available: https://doi.org/10.1016/j.btre.2018.e00256
9. Viviane A, Alan BN. Estimates of costs of hospital stay for variceal and nonvariceal upper gastrointestinal bleeding in the United States. Value Heal. 2008;11(1):1–3.
10. Yuan Y, Leontiadis GI. Editorial: ulcer-related vs non-ulcer-nonvariceal upper

gastrointestinal bleeding—which has worse outcomes? Aliment Pharmacol Ther. 2019;49(6):818–9.

11. Zhang BB, Li Y, Liu XQ, Wang PJ, Yang B, Bian DL. Association between vacA genotypes and the risk of duodenal ulcer: a meta-analysis. Mol Biol Rep. 2014;41(11):7241–54.
12. Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, et al. Perforated peptic ulcer HHS Public Access. Lancet [Internet]. 2015;386(10000):1288–98. Available:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4618390/pdf/nihms730003.pdf
13. 2014 O. Amandeep, Kaur, et al. "Peptic ulcer: A review on etiology and pathogenesis." Int Res J Pharm 3.6 2012: 34-38. 9–66:37;2012. עלון הנוטע
14. Jaiswal F, Rai AK, Wal P, Wal A, Singh SP. Peptic Ulcer: a Review on Etiology, Pathogenesis and Treatment. Asian J Pharm Educ Res. 2021;10(4):1.
15. Woolf A, Rehman RB, Rose R. Gastric Ulcer. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Available:https://www.ncbi.nlm.nih.gov/books/NBK537128/. 2023;537128
16. Chiejina M, Samant H. Esophageal Ulcer. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Available:https://www.ncbi.nlm.nih.gov/books/NBK470400/. 2023;470400
17. Ocasio Quinones GA, Woolf A. Duodenal Ulcer. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Available:https://www.ncbi.nlm.nih.gov/books/NBK557390/. 2023;557390.
18. Sharma, M. P., and Vineet Ahuja. "Current management of acid peptic disorders." JIACM 4.3 (2003): 228- 33. 2003;7(2):1–16.
19. Jarius S, Wildemann B. The history of neuromyelitis optica. Part 2: "Spinal amaurosis", or how it all began. J Neuroinflammation. 2019;16(1): 1–30.
20. The COF. Rupture of the Stomach, Cavity Of The Abdomen; 1816.
21. Baillie, Matthew. The Morbid Anatomy of some of the most Important Parts of the Human Body. . Longman & Company, 1833. 1833;1833.
22. Redclift M. Baron, J. Hugha, Sonnenberg, Amnonb. Publications on peptic ulcer in Britain, France, Germany and the US. European Journal of Gastroenterology & Hepatology. 2002;52(1):1–5.
23. Chalya PL, Mabula JB, Koy M, Mchembe MD, Jaka HM, Kabangila R, et al. Clinical profile and outcome of surgical treatment of perforated peptic ulcers in Northwestern Tanzania: A tertiary hospital experience. World J Emerg Surg [Internet]. 2011;6(1):31. Available:http://www.wjes.org/content/6/1/31
24. Kurata JH, Honda GD, Frankl H. The incidence of duodenal and gastric ulcers in a large Health Maintenance Organization. Am J Public Health. 1985;75(6):625–9
25. Tarasconi A, Coccolini F, Biffl WL, Tomasoni M, Ansaloni L, Picetti E, et al. Perforated and bleeding peptic ulcer: WSES guidelines. World J Emerg Surg. 2020;15(1):1–24.
26. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: A population-based study. BMC Gastroenterol [Internet]. 2022;22(1):1–13. Available:https://doi.org/10.1186/s12876-022-02130-2
27. Salih B. Helicobacter pylori infection in developing countries: The burden for how long? Saudi J Gastroenterol. 2009;15(3):201–7.
28. Everhart JE, Kruszon-Moran D, Perez-Perez GI, Tralka TS, McQuillan G. Seroprevalence and ethnic differences in Helicobacter pylori infection among adults in the United States. J Infect Dis. 2000;181(4):1359–63.
29. Sandler RS, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, et al. The burden of selected digestive diseases in the United States. Gastroenterology. 2002;122(5):1500–11.
30. Sung JJY, Kuipers EJ, El-Serag HB. Systematic review: The global incidence and prevalence of peptic ulcer disease. Aliment Pharmacol Ther. 2009;29(9):938–46.
31. Khuroo MS, Mahajan R, Zargar SA, Javid G, Munshi S. Prevalence of peptic ulcer in India: An endoscopic and epidemiological study in urban Kashmir. Gut. 1989;30(7):930–4.
32. Mishra V, Srivastava A. Incorporated Approach towards Development of New

Herbal Drugs for Peptic Ulcer Disease. Biomed Sci Herb Med; 2018.
33. Kusters JG, Van Vliet AHM, Kuipers EJ. Pathogenesis of Helicobacter pylori infection. Clin Microbiol Rev. 2006;19(3): 449–90.
34. M. Asali A, Alghamdi MA, Fallatah SA, Alholaily WA, Aldandan RG, Alnosair AH, et al. Risk factors leading to peptic ulcer disease: systematic review in literature. Int J Community Med Public Heal. 2018; 5(10):4617.
35. Kulnigg-Dabsch S. Autoimmungastritis. Wiener Medizinische Wochenschrift. 2016;166(13–14):424–30.
36. Rodriguez-Castro KI, Franceschi M, Miraglia C, Russo M, Nouvenne A, Leandro G, et al. Autoimmune diseases in autoimmune atrophic gastritis. Acta Biomed. 2018;89:100–3.
37. Graham DY, Khalaf N. Peptic Ulcer Disease. Geriatr Gastroenterol Second Ed. 2021;(March):1565–95.
38. Duodenal ON, Notes W. MR. B. G. MOYNIHAN ON DUODENAL ULCER. :340–6.
39. Gibiøki K. A review of seasonal periodicity in peptic ulcer disease. Chronobiol Int. 1987;4(1):91–9.
40. Helal OK, Yousef MM, Elnaa M. Possible protective effect of gum arabic on experimentally induced gastric ulcer in adult male albino rats. Egypt J Histol. 2011;34(3):546–53.
41. Malik TF, Gnanapandithan K, Singh K. Peptic Ulcer Disease. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available: https://www.ncbi.nlm.nih.gov/books/NBK534792/. 2023;534792
42. Kawade D, Shahu N, Bahadurkar P, Hiradewe P, Dhote N. Peptic Ulcer: A Review on Its Etiology, Pathogenesis and Pharmacotherapy. Kawade al World J Pharm Res 558 World J Pharm Res SJIF Impact Factor [Internet]. 2020;9(5):84. Available : www.wjpr.net
43. Yen HH, Wu PY, Wu TL, Huang SP, Chen YY, Chen MF, et al. Forrest Classification for Bleeding Peptic Ulcer: A New Look at the Old Endoscopic Classification. Diagnostics. 2022;12(5).
44. Pahwa R, Kumar V, Kohli K. Clinical Manifestations , Causes and Management Strategies of Peptic Ulcer Disease. Int J Pharm Sci Drug Res. 2010;2(2):99–106.
45. Kim DS, Jung Y, Rhee HS, Lee SJ, Jo YG, Kim JH, et al. Usefulness of the forrest classification to predict artificial ulcer rebleeding during second-look endoscopy after endoscopic submucosal dissection. Clin Endosc. 2016;49(3):273–81.
46. Kaur J, Stoukides G, Amaturo M. Closed-Loop gastric outlet obstruction secondary to duodenal ulcer in a patient with esophageal stricture. Cureus. 2023;15(3):1–9.
47. Misra SP 1, Dwivedi M VM. Malignancy is the most common cause of gastric outlet obstruction even in a developing country. 2013;29–32.
48. Kalpande S, Pandya JS, Tiwari A, Adhikari D. Gastric outlet obstruction: An unusual case of primary duodenal tuberculosis. BMJ Case Rep. 2017;2017:1–3.
49. Nawaz M, Jehanzaib M, Khan K, Zari M. Role of barium meal examination in diagnosis of peptic ulcer. J Ayub Med Coll Abbottabad. 2008;20(4):59–61.
50. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. What happens during a gastroscopy? 2015 Jun 30 [Updated 2015 Jun 30]. Available:https://www.ncbi.nlm.nih.gov/books/NBK310264/. 3(1):1–10. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:EM+Demystified:+An+Expectation-Maximization+Tutorial#0%0Ahttps://www2.ee.washington.edu/techsite/papers/documents/UWEETR-2010-0002.pdf%0Ahttp://dx.doi.org/10.1038/srep22311%0Ahttp://www.life.um
51. Banerjee S, Cash BD, Dominitz JA, Baron TH, Anderson MA, Ben-Menachem T, et al. The role of endoscopy in the management of patients with peptic ulcer disease. Gastrointest Endosc. 2010;71(4):663–8.
52. Garza-González E, Perez-Perez GI, Maldonado-Garza HJ, Bosques-Padilla FJ. A review of helicobacter pylori diagnosis, treatment, and methods to detect eradication. World J Gastroenterol. 2014;20(6):1438–49.
53. Ahlawat R, Hoilat GJ, Ross AB. Esophagogastroduodenoscopy. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available:https://www.ncbi.nlm.nih.gov/books/NBK532268/. 2023;532268

54. Jacobs JM, Hill MC, Steinberg WM. Peptic ulcer disease: CT evaluation. Radiology. 1991;178(3):745–8.
55. Møller MH, Adamsen S, Wøjdemann M, Møller AM. Perforated peptic ulcer: How to improve outcome? Scand J Gastroenterol. 2009;44(1):15–22.
56. Lahaie RG, Gaudreau C. Helicobacter pylori antibiotic resistance: Trends over time. Can J Gastroenterol. 2000;14(10):895–9.
57. Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, et al. Management of Helicobacter pylori infection - The Maastricht IV/ Florence consensus report. Gut. 2012;61(5):646–64.
58. Vallve M, Vergara M, Gisbert JP, Calvet X. Single vs. double dose of a proton pump inhibitor in triple therapy for Helicobacter pylori eradication: A meta-analysis. Aliment Pharmacol Ther. 2002;16(6):1149–56.
59. Calvet X, García N, López T, Gisbert JP, Gené E, Roque M. A meta-analysis of short versus long therapy with a proton pump inhibitor, clarithromycin and either metronidazole or amoxycillin for treating Helicobacter pylori infection. Aliment Pharmacol Ther. 2000;14(5):603–9.
60. Laine L. Is it time for quadruple therapy to be first line? Can J Gastroenterol. 2003;17 Suppl B(June):33–6.
61. Gisbert JP, Pajares JM. Review article: Helicobacter pylori "rescue" regimen when proton pump inhibitor-based triple therapies fail. Aliment Pharmacol Ther. 2002;16(6):1047–57.
62. Furuta T, Shirai N, Ohashi K, Ishizaki T. Therapeutic impact of CYP2C19 pharmacogenetics on proton pump inhibitor-based eradication therapy for Helicobacter pylori. Methods Find Exp Clin Pharmacol [Internet]. 2003;25(2):131—143.
Available: https://doi.org/10.1358/mf.2003.25.2.723687
63. Padol, S., et al. "The effect of CYP2C19 polymorphisms on H-pylori eradication rates with PPI dual and triple first line therapies-a meta-analysis." Gastroenterology. Vol. 128. No. 4. Independence Square West Curtis Center, Ste 300, Philadelphia, PA 19106. 2005;1(1):1–8.
Available:http://dx.doi.org/10.1016/j.cirp.2016.06.001%0Ahttp://dx.doi.org/10.1016/j.powtec.2016.12.055%0Ahttps://doi.org/10.1016/j.ijfatigue.2019.02.006%0Ahttps://doi.org/10.1016/j.matlet.2019.04.024%0Ahttps://doi.org/10.1016/j.matlet.2019.127252%0Ahttp://dx.doi.o
64. Ford A et al. Eradication therapy for peptic ulcer disease in Helicobacter pylori positive patients. The Cochrane Database of Systematic Reviews. Issue 4, Art. No. CD003840.pub2. 2004;(4):3840.
65. Gisbert JP, Pajares JM. Systematic review and meta-analysis: Is 1-week proton pump inhibitor-based triple therapy sufficient to heal peptic ulcer? Aliment Pharmacol Ther. 2005;21(7):795–804.
66. Arkkila, Perttu ETa; Seppälä, Karia; Kosunen, Timo Ub; Sipponen, Penttic; Mäkinen, Juditd; Rautelin, Hilpib; Färkkilä, Marttia. Helicobacter pylori eradication as the sole treatment for gastric and duodenal ulcers. European Journal of Gastroenterology & H. 2005;1(1):1–8.
Available:http://dx.doi.org/10.1016/j.cirp.2016.06.001%0Ahttp://dx.doi.org/10.1016/j.powtec.2016.12.055%0Ahttps://doi.org/10.1016/j.ijfatigue.2019.02.006%0Ahttps://doi.org/10.1016/j.matlet.2019.04.024%0Ahttps://doi.org/10.1016/j.matlet.2019.127252%0Ahttp://dx.doi.o
67. Gisbert JP et al. H. pylori eradication therapy vs. antisecretory non-eradication therapy (with or without long-term maintenance antisecretory therapy) for the prevention of recurrent bleeding from peptic ulcer. The Cochrane Database of Systematic Reviews, Issue 2, Art. No. CD004062.pub2. 2004;(2):4062.
68. Leodolter A, Kulig M, Brasch H, Meyer-Sabellek W, Willich SN, Malfertheiner P. A meta-analysis comparing eradication, healing and relapse rates in patients with Helicobacter pylori-associated gastric or duodenal ulcer. Aliment Pharmacol Ther. 2001;15(12):1949–58.
69. Ohara, Tadashi, et al. "Usefulness of proton pump inhibitor (PPI) maintenance therapy for patients with H. pylori-negative recurrent peptic ulcer after eradication therapy for H. pylori: pathophysiological characteristics of H. pylori-negative recurrent u. 2004;2004:9.
Available:http://biblioteca.usac.edu.gt/tesis/08/08_2469_C.pdf
70. Singh A, Vl AB, Azamthulla M. Herbal Remedies Used for the Treatment of Peptic Ulcer. 2022;8(02):346–55.
71. Al Mofleh IA. Spices, herbal xenobiotics and the stomach: Friends or foes?

World J Gastroenterol. 2010;16(22): 2710–9.
72. D. Mehta, “Ulcer-review on types, anti-ulcer drugs, anti-ulcer medicinal plants, antiulcer drug market, diagnostics and current global clinical trials status”. Invent Rapid Pharm Pract, 2, 2016. pp.1-8. 2016;2016.
73. Kuna L, Jakab J, Smolic R, Raguz-Lucic N, Vcev A, Smolic M. Peptic ulcer disease: A brief review of conventional therapy and herbal treatment options. J Clin Med. 2019;8(2).
74. Wierenga KA, Pestka JJ. Omega-3 Fatty Acids and Inflammation—You Are What You Eat! Front Young Minds. 2021;9:1–7.
75. Rani Ds. Peptic ulcer: mini review with respect to case abstract. Int Res J Hum Resour Soc Sci. 2019;224(11): 122–30.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/109508