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Review

A brief review on the exploration of *peptic ulcers*

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Abstract

Peptic ulcers are lesions that pierce the lining of the stomach or duodenum and cause excruciating pain as well as possible problems. An overabundance of acid production or pepsin activity causes them. Symptoms include epigastric pain, nausea, vomiting, and bloating, which are associated with age, smoking, *H. pylori* infection, and NSAID use. Diagnosis includes clinical suspicion confirmed through Esophagogastroduodenoscopy (EGD), barium swallow, H. pylori tests, and biopsy. Antibiotics are often used to eliminate H. pylori and proton pump inhibitors (PPIs) to minimize acid production. Preventive methods focus on reducing lifestyle risk factors such as nutrition, stress, smoking, and alcohol consumption, as well as employing drugs to protect the stomach lining. Complications of untreated peptic ulcer disease (PUD) include upper gastrointestinal bleeding, gastric outlet obstruction, perforation, and an increased risk of gastric cancer. Despite advances in medical knowledge and treatments, such as targeted antibiotics and PPIs, early diagnosis and intervention remain crucial for effective management and improved outcomes. Ongoing research aims to enhance prevention strategies and develop more effective therapies to reduce the global burden of peptic ulcers. Recent advancements in the treatment and management of peptic ulcers have significantly enhanced patient outcomes and reduced recurrence rates. The development of more effective proton pump inhibitors (PPIs) and the use of targeted antibiotic therapies to eradicate H. pylori have been pivotal. Additionally, innovative diagnostic techniques, such as more accurate and non-invasive H. pylori testing methods, have improved early detection and treatment. Research into the genetic factors influencing ulcer development and the role of the microbiome in gut health is also paving the way for personalized treatment approaches, promising even better management of peptic ulcer disease in the future.

Keywords: Peptic ulcers, *H. pylori,* proton pump inhibitors, Esophagogastroduodenoscopy

INTRODUCTION

Peptic ulcers are open wounds resulting from the rupture or erosion of the mucosal layer as a result of excessive acid production or pepsin, which tears away the stomach lining penetrates through the muscularis mucosa, and extends into the stomach epithelium's muscularis propria layer. Ulcers, on the other hand, may develop in uncommon locations, such as the ileum, proximal esophagus, and jejunum due to Meckel's

diverticulum, inlet patch, and excessive acid secretion (Zollinger-Ellison syndrome) respectively(1). An ulcer is distinguished from erosion by its size; wounds/lesions larger than 5 mm in diameter are referred as ulcers, whereas those smaller than that (<5) are called erosions(2). While analyzing the occurrence and distribution of ulcers, incidence and prevalence are essential epidemiological measurements where an estimated annual 0.1-0.3% incidence of PUD and a lifetime prevalence of 5-10% worldwide have been reported. Numerous studies carried out in the previous 20–30 years have demonstrated a sharp declining tendency in the prevalence of PUD, PUD-related hospital admissions, and PUD-associated mortality due to the application of new anti-PUD therapies, such as the eradication of Helicobacter pylori (H. pylori) and the use of proton-pump inhibitors (PPIs)(3).

Gastric and duodenal ulcers are the two distinct types of peptic ulcers that occur within the digestive system, primarily in the stomach and duodenal lining. Hence, peptic ulcers formed on the stomach's lining are called gastric ulcers and, on the duodenum lining are called duodenal ulcers. These ulcers irritates surrounding nerves and cause a considerable amount of pain. Studies have stated that duodenal ulcers are almost always benign but stomach ulcers may turn malignant. Even though peptic ulcer fatalities are rare, the condition is highly prevalent and can be expensive to treat due to associated discomfort and consequences.

Other than peptic ulcers

Besides peptic ulcers, there are various types of ulcers with distinct characteristics and aetiologies s. Ulcers can also occur due to stress.

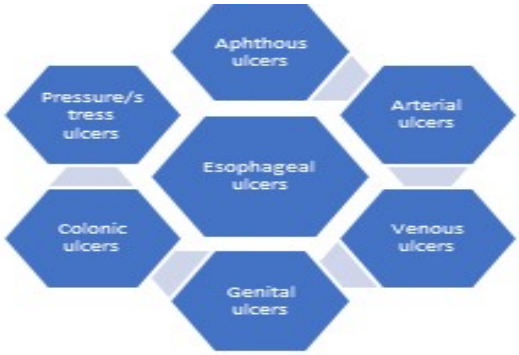

Fig 1: ulcer types

Esophageal ulcers

Esophageal ulcers develop on the lower end of the esophagus, the muscular tube that connects the throat to the stomach. Esophageal ulcers do not constitute a single entity as they might have several underlying causes and the most prevalent cause is gastroesophageal reflux disease (GERD), which has been reported to be the etiology in 65.9% of esophageal ulcer cases according to studies. Although GERD is the most common cause, others include medications such as NSAIDs and antibiotics; infections (herpes esophagitis, candidiasis), Caustic ingestion, and radiation therapy(4).

Aphthous ulcers (Mouth ulcers)

Mouth ulcers also known as Recurrent aphthous stomatitis (RAS) or canker sores are the formation of small, shallow lesions on the non-keratinized oral mucous membrane. Canker sores are the most common type of mouth ulcers. They are generally round and form inside of the lips, cheeks, and underside of the tongue. Along with food preservatives like benzoic acid and benzoates (E210–E219), toothpaste with foaming ingredients, and sodium lauryl sulfate, a number of aetiological variables have been linked to RAS, including haematinic insufficiency, hypersensitivity reactions, and psychological stress(5).

Arterial ulcers

Often called ischemic ulcers, are wounds that are frequently found distally and on the dorsum of the foot or toes, causing excruciating pain. Patho-physiologically, Arterial ulceration can be induced by either Progressive atherosclerosis or arterial embolization which induces cutaneous ischemia and ulceration(6). These arterial ulcers are difficult to heal because of peripheral artery dysfunction or insufficient perfusion pressure to the tissues in the lower limbs. Diabetes, thromboangiitis, pyoderma gangrenosum, thalassemia, and sickle cell disease are some of the causes of arterial ulcers(7).

Venous ulcers

These are chronic wounds associated with long-term venous hypertension, as a consequence of vein valve reflux or in conjunction with venous obstruction occurring in the regions of the leg or foot of lower extremities. Chronic venous ulcer (CVU) lasts longer than 6 weeks, exhibiting symptoms such as pigmentation, edema, and varicose veins, which are indicators of chronic venous insufficiency(8). These ulcers are characterized by delayed healing and high recurrence rate. Different studies have reported a prevalence ranging from 0.7 to 2.4 %, which increases with the aging population(9).

Genital ulcers

Genital ulcer disease (GUD) can be isolated or occur as a symptom of increasingly extensive skin disease and may be located on the penis, vagina, anorectal, or perineal regions which is an important risk factor for the acquisition of HIV. It can be infectious or non-infectious. Herpes simplex virus (HSV) is often listed as the most common cause of genital ulcers, with HSV-2 prevailing over HSV-1 as the primary cause of genital ulcers(10).

Colonic ulcers

Colonic ulcers also referred to as cholorectal ulcers characterized by aberrant inflammation of the rectum and intestine's inner surface, which accounts for the majority of the large intestine's length (11).

Pressure/stress ulcers

A pressure sore, also known as a bed sore or pressure ulcer, is a skin injury that occurs when blood flow to the area is disturbed as a result of sitting or resting in one posture for an extended period. Early detection of early indicators of a pressure sore, such as discomfort and changes in skin colour and temperature, can help you avoid pain and problems (12).

Symptoms

Various PUD symptoms encourage individuals to get help, which raises the possibility of a diagnosis. At the same time, some PUD patients fail to exhibit any symptoms until a potentially fatal side effect like bleeding or perforation appears. Finding risk factors in PUD patients who are asymptomatic could therefore aid in decreasing the frequency of death brought on by unforeseen consequences. Numerous research has shown that the risk factors for asymptomatic PUD include age, smoking habit, obesity, and regular tea consumption.

PUD develops a variety of symptoms, in which epigastric discomfort/pain is the primary symptom. Upper abdominal pain may flare up after lunch or dinner, and some people experience severe stomach pain in addition to vomiting up things, having blood in their stools, or having black or tarry stools. They may also experience retrosternal pain, early satiety, nausea, bloating, burps, or postprandial discomfort. Other symptoms include dyspepsia, nausea, premature satiety, heartburn, and anorexia nervosa(13).

Aetiology

It is widely acknowledged that one of the main ulcerogenic factors that contribute to the development of gastric ulcer disease is gastric acid. About half of patients with stomach ulcers are considered to have pepsin and acid hyper-secretors. Nonetheless, gastric acid has a specific role in the stomach's defense system. It is the mucosa's first line of defense against bacteria, limiting their access into the mucosal layer and preventing colonization. Acid secretion is suggested to be stimulated by three principle secretion is suggested to be stimulated by three principle secretagogues histamine, acetylcholine and gastrin. H2 receptors that react to histamine released from specialized mast cells and receptors sensitive to muscarinic gastrin are among the receptors on the surface of parietal cells. Gastrin increases the production of acid by either directly stimulating the parietal cells or by causing the ECL cells to release histamine (14).

A vast number of aetiologies have been linked to PUD, with the most common risk factors being H. pylori infection, NSAID use, gastric bypass surgery(15), smoking(16), use of selective serotonin reuptake inhibitors, stress, lifestyle choices, and genetic makeup. Research indicates that H. pylori infection is linked to 90% of duodenal ulcers and 70% of stomach ulcers (17). Nevertheless, this declining tendency has plateaued in recent years, which may be connected to the fact that non-steroidal anti-inflammatory drug (NSAID) use has replaced H. pylori infection as the primary cause of ulcers in many countries. Medications such as aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) cause approximately 10% of peptic ulcers and have a stronger association with gastric ulcers than duodenal ulcers.

Some of the cases of non-H. Pylori and non-NSAID peptic ulcers are

- Gastric adeno carcinoma
- Gastric lymphoma
- Anastomotic ulceration after previous gastric surgery
- Zollinger Ellison syndrome (gastrinoma)
- Hyperparathyroidism

- Systemic mastocytosis
- Duodenal Crohn's disease
- Idiopathic eosinophilic and lymphocytic gastritis
- Coeliac axis stenosis

Prevention

Peptic ulcer is the predominant bleeding source, accounting for around 40% of upper gastrointestinal bleeds. Several instances involve older adults who take multiple drugs and have comorbidities. This, together with frequent presentations of shock, explains why, even with advancements in treatment and management, ulcer bleeding is still linked to a 5–10% rate of mortality. In this case, better bleeding control, rebleed prevention, ulcer formation and bleeding prevention are necessary(18).

The emerging field of research indicates that, with advancements in dietetics and therapy, stomach ulcers may be avoided. This could be accomplished by fortifying the stomach mucosa's defense systems while simultaneously reducing the aggressiveness of the risk variables that lead to gastric ulcers. These defenses can endure insults from food, gastric enzymes, and acid secretion.

PPIs for the prevention of peptic ulcers

Prior to the discovery of *H. pylori*, ulcers were known to recur, and for many years the standard practice was to maintain patients on acid-suppressive drugs. Proton-pump inhibitors (PPIs), along with histamine-2 receptor antagonists, and prostaglandin analogues have all been investigated for their effect on gastroprotection. Despite several studies and treatment regimens, quantifying the effects of gastroprotection remains challenging. A comprehensive review evaluated on the impact of PPIs on subsequent bleeding and its repercussions and PPI medication dramatically reduces the risk of bleeding and the need for blood transfusions, endoscopic interventions, and surgery. Gastroprotection, particularly with PPIs, reduces ulcer incidence and bleeding by approximately five times compared to no protection, and improves ulcer healing by five times (18). It has long been hypothesized that the usage of proton pump inhibitors (PPIs) can lower the risk of major gastrointestinal problems when using NSAIDs and more evidence for this theory was provided by revealing that PPI use was linked to a statistically significant decrease in the risk of ulcers in both acute and long-term NSAID users. Preventing peptic ulcers involves addressing several other key factors, primarily centered around

A. Lifestyle risk factors
a. Diet
B. Psychological factors:
a. Stress
b. Smoking
c. Excess alcohol intake

Diagnosis

Diagnosis begins with clinical suspicion when patients present with symptoms such as epigastric abdominal pain, burning, post-prandial fullness, or early satiety.

Interventions

To help diagnose peptic ulcers, various interventions need to be conducted:

Esophagogastroduodenoscopy (EGD)

With sensitivity and specificity of up to 90%, the gold standard and most precise diagnostic test can identify gastric and duodenal ulcers. The American Society of Gastrointestinal Endoscopy has issued guidelines about the role of endoscopy in patients who come with upper abdomen discomfort or dyspeptic symptoms suggestive of PUD.During an EGD, a thin, flexible tube known as an endoscope is introduced via the mouth and guided into the esophagus, stomach, and duodenum. This procedure provides for direct visibility of the upper gastrointestinal tract, which includes the esophagus, stomach, and the first section of the small intestine (duodenum)(2).

Barium swallow

A barium meal can help diagnose stomach ulcers. This is not uncomfortable and poses no risk. The patient swallows Barium, a white chalky material observable on x-rays, and then lies down on a tilted examining bench. Tilting uniformly distributes barium throughout the upper digestive tract and allows for X-ray images to be captured from various angles. This enables the doctor to find the ulcer and assess its severity(19)

Helicobacter pylori testing

Serologic testing

Serological testing for signs of H. pylori infection might be utilized as part of the initial assessment of patients thought to have one of the following conditions:

a. Active peptic ulcer disease
b. A past history of documented peptic ulcer disease
c. Atrophic gastritis/chronic gastritis
d. Gastric MALT lymphoma
e. Gastric adenocarcinoma
f. Undiagnosed dyspepsia (with no warning symptoms and a duration of less than 45–55 yrs) before long-term usage of non-steroidal anti-inflammatory medications.

Stool antigen test (SAT)

There are two forms of SATs for diagnosing H. pylori infection: enzyme immunoassay (EIA) and immunochromatography (ICA). Although both types of testing have excellent specificity and sensitivity, a recent study found that presently accessible ICA-based assays are less reliable than EIA-based tests. However, ICA-based tests are uncomplicated to carry out and beneficial for in-office quick diagnoses of H. pylori infection(20).

Urea breath test

The urea breath test (UBT) is a non-invasive diagnostic method used to detect Helicobacter pylori (H. pylori) infection, where Patients are ingested urea solution containing a labeled carbon isotope, and if H. pylori bacteria are present in the stomach, they produce an enzyme called urease, which breaks down the urea into ammonia and carbon dioxide containing the labeled isotope(21). After a waiting period, the patient exhales into a collection device, and the exhaled breath, including any labeled carbon dioxide, is analyzed. Elevated levels of labeled carbon dioxide indicate the presence of H. pylori. The UBT's accuracy, simplicity, and non-invasiveness make it a preferred method for diagnosing H. pylori infection and monitoring treatment effectiveness in patients with peptic ulcers.

Endoscopic biopsy

Due to its cost, duration, and intrusive nature, culture is often discouraged. It is recommended if the eradication treatment is unsuccessful or if antibiotic resistance is suspected. To improve sensitivity, biopsies must be taken from at least 4-6 locations. The smaller curvature between the fundus and antrum is where gastric ulcers are most frequently found. The duodenum's first section is where most duodenal ulcers are found(2). Serum gastric is ordered if Zollinger-Ellison syndrome is suspected.

Treatment

***H. Pylori* Treatment**

The standard first-line therapy consists of a triple therapy that includes two antibiotics (such as metronidazole or amoxicillin plus clarithromycin) and a proton pump inhibitor (PPI) administered for seven to fourteen days (22). However, over the past ten to fifteen years, there has been a noticeable drop in the effectiveness of triple therapy due to the rising frequency of antibiotic resistance, particularly for clarithromycin.

To eradicate H. pylori, antibiotic susceptibility examinations must be employed as susceptibility testing is not always accessible in clinical practice, first-line therapies should prioritize the local prevalence of antibiotic resistance. Clarithromycin-based regimens should be avoided in areas with more than 15% resistance.

The recommended first-line therapy is a 14-day bismuth-containing quadruple therapy (PPI, bismuth salt, tetracycline, and metronidazole) or a 14-day concomitant therapy (PPI, clarithromycin, amoxicillin, and metronidazole) for patients who are intolerant of bismuth. Both regimens yield eradication rates of more than 90% (23).

In the ea of PPI therapy, there is only a limited role for H2Ras (H2 Receptor antagonist) in treating peptic ulcer disease. In comparison to H2RAs, PPIs have been shown to improve peptic ulcer healing rates. Using PPIs can result in false negative test results when patients with ulcers attributable to H. pylori undergo testing after receiving antibiotics to confirm the eradication of H. pylori. It is therefore advised that for the two weeks leading up to H. pylori eradication tests, patients switch from using PPIs to H2RAs.

Table 1: Medication and their effects

Type of medication	Drug	Mechanism of action
Antibiotics to kill *H. Pylori*	Amoxicillin	Interferes with bacterial cell wall synthesis by inhibiting the transpeptidase enzyme, ultimately weakening the bacterial cell wall and leading to cell lysis.
	Clarithromycin	Inhibits protein synthesis by binding to the bacterial ribosome, thus preventing the synthesis of essential proteins needed for bacterial survival.
	Metronidazole	Disrupting the bacterial DNA structure and inhibiting nucleic acid synthesis.
	Tinidazole	Disrupting the DNA structure of bacteria, including H. pylori, through the formation of cytotoxic nitro radicals. This action leads to DNA damage and inhibition of nucleic acid synthesis, ultimately resulting in bacterial cell death.
	Levofloxacin	Disrupts bacterial DNA synthesis and leads to the accumulation of DNA breaks, ultimately causing bacterial cell death
	Tetracycline	Inhibits bacterial protein synthesis by binding to the bacterial ribosome and blocking the attachment of aminoacyl-tRNA molecules. This action prevents the elongation of the polypeptide chain during protein synthesis, thereby halting bacterial growth
Blocking acid production (Proton pump inhibitors)	omeprazole	Act inhibiting the proton pump enzyme (H+/K+ ATPase), in the gastric parietal cells which is responsible for pumping hydrogen ions into the stomach lumen, resulting in reducing the production of gastric acid, leading to a decrease in the acidity level within the stomach.
	lansoprazole	
	rabeprazole	
	esomeprazole	
	pantoprazole	
Reduce acid production (histamine (H-2) blockers)	Famotidine	They inhibit the histamine H2 receptors on the basolateral membrane of parietal cells in the stomach. Thus, reducing the secretion of gastric acid, which is crucial in the pathogenesis of peptic ulcers
	Cimetidine	
	Nizatidine	
Antacids that neutralize stomach acid	Aluminium hydroxide	These alkaline compounds chemically neutralize the acid, forming water and salt, thereby reducing the overall acidity of the gastric contents. This neutralization reaction helps to raise the pH of the stomach, which in turn reduces the irritation and damage to the gastric mucosa caused by excess acid, providing relief from symptoms associated with peptic ulcers, such as pain and discomfort.
	Magnesium hydroxide	
	Calcium carbonate, or Sodium bicarbonate	
Protect the lining of your stomach and small intestine.	Sucralfate	They stimulate the secretion of mucus and bicarbonate, which form a protective layer over the mucosal lining, shielding it from the corrosive effects of gastric acid. Additionally, prostaglandin analogues help maintain mucosal blood flow, promoting tissue repair and regeneration.
	Misoprostol	Sucralfate binds to the exposed proteins in the ulcer crater and forms a viscous gel-like substance that adheres to the ulcer surface, acting as a physical barrier against gastric acid, bile salts, and other injurious agents. This protective barrier promotes ulcer healing by providing a conducive environment for tissue repair and regeneration(24).

Complications

Peptic ulcer disease (PUD) if not diagnosed and treated promptly can lead to serious complications such as

- Upper gastrointestinal bleeding
- Gastric outlet obstruction
- Perforation
- Penetration
- Gastric cancer

CONCLUSION

Peptic ulcers are still a significant threat to health, although better management and preventive techniques have been made possible by advances in medical knowledge and available treatments. Early diagnosis and care of peptic ulcer disease, as well as prevention for high-risk patients, are imperative. Early diagnosis of H. pylori and adequate therapy are crucial, as is judicious use of NSAIDs. Peptic ulcer prevalence can differ by geographic area and population demographics. It may also fluctuate over time as a result of modifications to a person's diet, lifestyle, medical procedures, and medical therapy approaches. The development of more potent antibiotics to eradicate H. pylori and the introduction of proton pump inhibitors (PPIs) to control acid production are two examples of how advances in medical knowledge and treatment options might affect the occurrence and treatment of peptic ulcers. The frequency of ulcers brought on by the H. pylori bacteria may decline in certain groups as a result of the increasing efficacy of efforts to remove the illness by targeted antibiotic therapy. Furthermore, peptic ulcer disease therapy has been completely transformed by the widespread use and availability of proton pump inhibitors (PPIs), which effectively suppress gastric acid output.

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