Review Article

A review on the pathogenesis, treatment, and prevention of peptic ulcer disease

Abstract

Peptic ulcer disease, defined as the breakdown of the stomach and/or duodenum's epithelial mucosal barrier, is still a leading source of morbidity and mortality. One of the main etiological factors is H. pylori. using nonsteroidal anti-inflammatory medicines while infected with H.Pylori (NSAIDs). Epigastric Patients frequently experience discomfort, heartburn, reflux symptoms, and nausea. Stomach lining inflammation is a symptom of peptic ulcer disease. The majority of the time, the diagnosis is made after endoscopy of the upper gastrointestinal tract. Ulcer is a prevalent condition that affects people all over the world. Allopathic ulcer treatment has negative health consequences due to unpleasant side effects. Numerous herbal plants and secondary metabolites are now used to treat ulcers.The two most frequent causes of peptic ulcers are infection with Helicobacter pylori or taking non-steroidal anti-inflammatory drugs (NSAIDs), such aspirin. NSAIDs are becoming a more common cause of ulceration, notably ulcers worsened by gastrointestinal (GI) bleeding, as H. pylori infection becomes less common in affluent nations. Only around 15% of people infected with H. pylori develop an ulcer in their lifetime, with the risk being dictated by the virulence of the H. pylori strain, host genetics, and environmental factors (particularly smoking). The inhibition of the gastroprotective cyclooxygenase (COX)-1 enzyme is a major cause of NSAID-induced ulcers.

Kewords : H.pylori, Gastroprotective Enzyme, Diagnosis, Prevention, Treatment

INTRODUCTION

Usually occurring in the stomach or proximal duodenum, peptic ulcers are acid-induced lesions of the digestive tract that are characterised by denuded mucosa with the defect extending into the submucosa or muscularis propria. [1]. In the general population, peptic ulcer disease is thought to affect 5–10% of people [2],However, recent epidemiological studies [3,4] have revealed a decline in the incidence, hospital admission rates, and mortality

linked to peptic ulcers. The advent of new treatments and enhanced hygiene practises, which led to a decrease in Helicobacter pylori (H. pylori) infections, are most likely secondary causes of this.

Traditionally, it has been thought that mucosal disruption in people with acid peptic disorder results from a hypersecretory acidic environment combined with dietary factors or stress. H. pylori contamination, alcohol and cigarette usage, use of non-steroidal anti-inflammatory medicines (NSAIDs), and Zollinger-Ellison syndrome are all risk factors for developing peptic ulcers [5]. H. pylori contamination and NSAID use are the key risk factors for both gastric and duodenal ulcers [6]. However, only a small proportion of people who have H. pylori or use NSAIDs develop peptic ulcers.disorder, which means that person susceptibility is vital withinside the starting of mucosal damage. Functional polymorphisms in distinct cytokine genes are related to peptic ulcers. For example, polymorphisms of interleukin 1 beta (IL 1B) have an effect on mucosal interleukin 1 beta production, inflicting H. pylori – related gastroduodenal diseases [7].

Aspirin and NSAID users, on the other hand, had twice the risk and four times the risk, respectively, of stomach ulcer complications [8]. Upper gastrointestinal hemorrhage is more likely when NSAIDs or aspirin are taken in conjunction with anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors [9]. Although H. pylori infections are common in those who take NSAIDs or aspirin, there is debate over the role these medications play in the development of gastric ulcer disease. The use of independently increases the risk of developing stomach ulcer disease, according to a meta-analysis of observational studies [10].

Idiopathic stomach ulcer illnesses, which are categorized as H. pylori-negative, NSAID-negative, and aspirin-negative ulcers, can be identified in roughly one-fifth of cases [11]. The pathogenic mechanism behind the formation of idiopathic gastric ulcer is yet unknown but it is caused by an imbalance between elements that contribute to mucosal integrity and aggressive stroke[5].Danish study has shown that psychological stress can increase the incidence of gastric ulcers [12]. Aside from ischemia, medicines (steroids, chemotherapeutic agents), radiation therapy, viruses, histamine, eosinophil infiltration, gastric bypass surgery, and metabolic problems are further causes [13].

Types of ulcers

1. Peptic ulcer

Any area of the digestive tract exposed to the aggressive action of acid-peptic fluids can develop persistent, most frequently solitary lesions called gastric ulcers. At least 98 percent of gastric ulcers can be found in the stomach or the first section of the duodenum, roughly in a 4:1 ratio[14].The contamination because of the micro-organism H. pylori and acid pepsin secretion are broadly speaking accountable for technology of peptic ulcer even as non-steroidal anti- inflammatory drugs (NSAIDs), shock, intense trauma, septicaemia, intracranial lesions, nearly irritant like alcohol, smoking and spices meals additionally accountable for production of peptic ulcers [15]. Symptoms of peptic ulcers consist of stomach discomfort, pain, weight loss, terrible appetite, bloating, nausea and vomiting normally and blood in stool and vomit rarely [16].

According to where they develop, gastric ulcers are separated into gastric ulcers and duodenal ulcers, and they happen in the stomach and duodenum, respectively. On the basis of severity, it can also be separated into acute and chronic ulcers. Acute gastric ulcers appear in the form of single or multiple lesions with submucosal tissue in all parts of the stomach and depths up to the first centimeter of the duodenum.Chronic gastric ulcers develop by themselves in the pyloric antrum of the stomach and duodenum and can penetrate the epithelial and muscular layers of the stomach or duodenum to spread to the nearby pancreas or liver [17]. They can cause complications such as obstruction, bleeding, perforation and malignant transformation [15].

2. Esophageal ulcer

A lesion that develops in the esophagus is called an esophageal ulcer (the food pipe). These are most frequently developed at the esophageal margin and can cause pain directly below the sternum, where heartburn symptoms are also felt. Esophageal ulcers are associated with gastroesophageal reflux disease or long- term use of drugs such GERD, NSAIDs, and smoking. [18].

3. Aphthous ulcer

Aphthous ulcers are typically recurrent round or oval sores or ulcers inside the mouth on areas where the skin is not tightly bound to the underlying bone, such as on the inside of the lips and cheeks or underneath the tongue. These sores or ulcers have a yellow greyish pseudo membrane surrounded by raised margins and an erythematous hole. They are sometimes referred to as canker sores, mouth ulcers, aphthosis, and aphthous stomatitis [19, 20]. Mouth ulcers occur in families (up to 40%) and are usually traumatic (due to improper placement of

teeth, damage to teeth and fillings), anemia, ulcers, viral infections, oral candidiasis, chronic infections, and laryngeal cancer, mouth cancer and vitamin B deficiency. According to estimates, 50–66% of people in North America and 15-20% of the world's population experience mouth ulcers [16]. They are herpetiform ulcers (less than 5 mm in size, 10-14 percent duration, and 5-10 percent prevalence), big ulcers (above 10 mm in size, more than 2-week duration), and moderate ulcers (size 510 mm, duration 10-14 days, prevalence 75–80%) [20].

Prevalence

Modern times have seen a decline in the prevalence of peptic ulcer disease (PUD), in part due to the widespread use of proton pump inhibitors (PPIs) and in part due to the early detection and treatment of H. pylori infections. An infection of the stomach epithelium by the gram-negative spiral bacillus H. pylori leads to the development of gastric ulcers. Infection with Helicobacter pylori continues to be the most frequent cause of PUD, accounting for 95% of duodenal ulcers and 70% of stomach ulcers [21]. Increaseduse on NSAIDs further increases the prevalence of PUD, which accounts for the majority of the remaining 30% of stomach ulcer disease (21). A higher risk of hemorrhagic PUD complications is also linked to the use of NSAIDs [22, 23]. Predisposition to gastric ulcer disease includes the use of corticosteroids, physiological stress, inflammatory bowel disease, and Zollinger-Ellison syndrome [24]. In addition, smoking and drinking lead to the development of more severe PUD and delayed healing of the treated disease. [25]

Pathogens

Lesions, defenses, and repairs of the gastric mucosa that are continuously exposed to the harmed environment play a role in the development of gastric ulcers. [26]These harmful environments disagree between harmful factors (e.g., Pepsin, acid, H. pylori infection) and protective factors (e.g., Prostaglandins, mucins, nitrogen monoxide, bicarbonate, and growth factors). It is due to. The main risk factors for stomach ulcer are frequent use of NSAIDs, heavy alcohol consumption, a poor diet, smoking habits, and psychological stress. [27]. In an etiology of peptic ulcer, NSAID overdose and H. pylori play the most significant roles (Fig. 1).

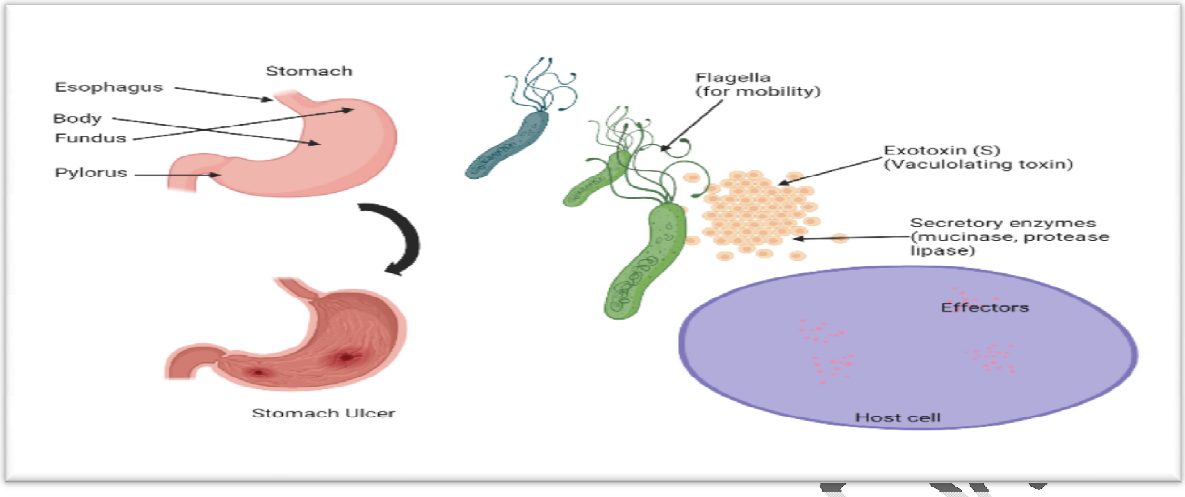

Fig.1 Pathogenesis of peptic ulcer disease. The secretion during the pathogenesis is shows. The normal stomach and the formation of peptic ulcer are also displayed.

Helicobacter pylori and its role to induce ulcer

The primary contributing factor to duodenal and stomach ulcers has been identified as H. pylori (Fig. 1). The majority of pathogens populating the human gastric antral mucosa are H. pylori [28], which is also responsible for around 95% of gastric and 70% of duodenal ulcerations in humans [29].The epithelium is harmed as a result of an inflammatory reaction inside the mucosa brought on by the local irritation brought on by H. pylori infection. The most hazardous virulence genes linked to peptic ulcer illness are vacuolating cytotoxin (VacA) and cytotoxin associated gene A (CagA) in H. Pylori, which contains a variety of genes [30].The CagA gene is in charge of translocating a carcinogenic material into the host gastric cells. The type IV secretion system (T4SS), encoded by the cag pathogenicity island (cag-PAI), is used for the translocation [31]. A group of 31 genes known as the pathogenicity island have been identified in specific bacterial strains [32]. According to earlier publications, some of the cag-PAI genes contained T4ss [33], which formed a syringe-like pilus structure that extended from the bacterial surface into host cells for the delivery of the virulence factors, primarily CagA [34]. After injection, CagA is tyrosine- phosphorylated, causing changes in the intracellular signaling system, which virtually leads to infection. T4SS is a solid indicator of severe gastric ulcer infection. Therefore, advanced research to investigate the role of T4SS in CagA transmission is very important. In addition, Cagl is also involved in CagA secretion and is capable of binding to integrin membrane β1 as an additional T4SS component [26]. It is believed that the host's genetic makeup has a significant role in determining how duodenal or gastric ulcers develop in terms of their pattern of gastric

inflammatory development. [32] The only means to ensure their survival is by the creation of the urease enzyme by H. pylori, which converts urea to ammonia and carbon dioxide. As the urease enzyme is produced, stomach acid is subsequently buffered, allowing bacteria to defend themselves against the acidic gastric environment. [35] It is known that the environment's alkalinity release prevents the stimulating release of somatostatin from antral D cells. The less stimulation of somatostatin inhibits the control of gastrin secretion by antral G cells [36]. Results to hypergastrinemia, excessive gastric acid secretion and parietal cell hyperplasia [37] due to the uncontrolled production of gastrin. H. pylori infection is also interfered the neural pathways of the brain in term of regulation the secretion of gastric acid and impede the inhibitory reflex that down regulates the release of acid. Moreover, an impaired signal from the neural pathway results in hypersecretion of stomach acid thus diminishes the pH inside the duodenum. The duodenal bulb contains this. The optimal environment for H. pylori colonization, which ultimately leads to ulceration, is metaplasia.

Diagnosis of peptic ulcer

The most typical method of diagnosing ulcers is by symptoms, which also consider the patient's age and the location of the ulcer. A stomach ulcer is a painful condition that typically starts on an empty stomach, is treated with antacids and food, but is also brought on by alcohol and caffeine. However, stomach ulcer disease is more likely to cause weight loss and gastrointestinal bleeding. Duodenal ulcers typically cause more persistent pain in the morning, which is only reduced by eating and sleeping for a short while at night. Signs of bleeding, repeated vomiting, or abdominal pain are important in diagnosing duodenal ulcer [38].

Peptic ulcer can be diagnosed specifically by direct visualization by endoscopy or radiology and by detection of H. pylori by various endoscopic and non-endoscopic tests. Endoscopic tests involve Histology, Culture of Biopsy, Rapid urease detection with ammonia, while non-endoscopic tests consist of detection of antibodies to H. pylori in serum, Urea breathe test (H. pylori urease breaks down ingested labelled C urea, patient exhales labelled CO2) and stool antigen test (presence of antigen against H. pylori in stool changes its colour which can be detected visually or by spectrophotometer). [39] fig.2 below

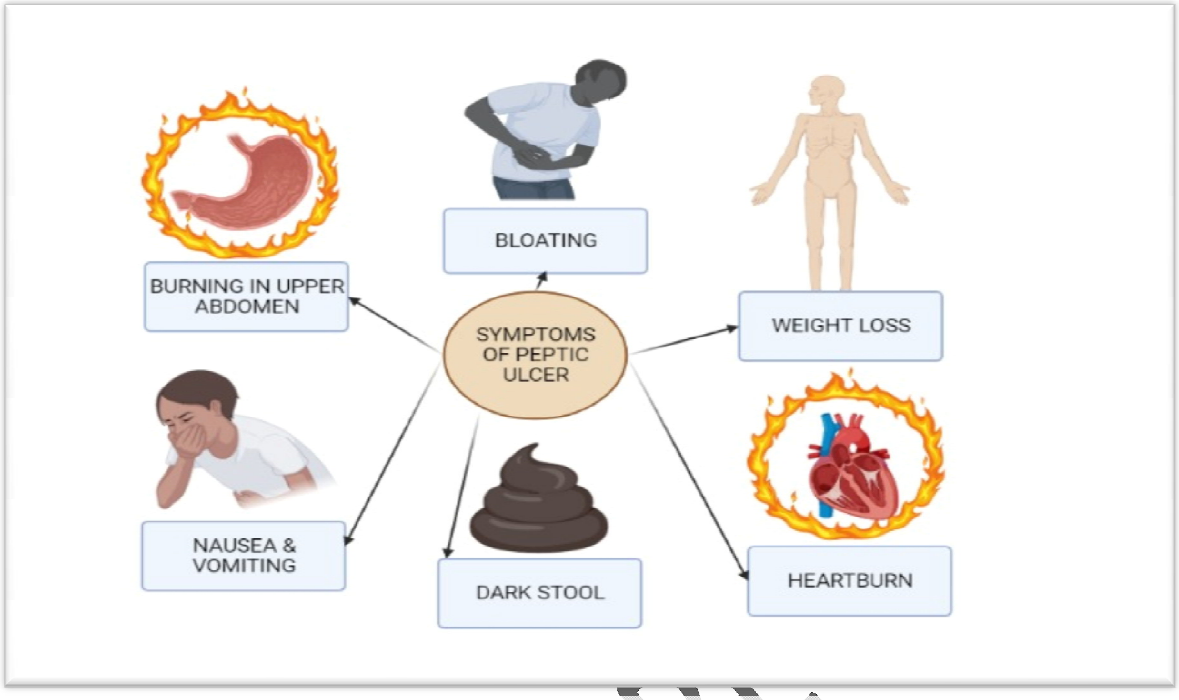

Fig 2: Symptoms of peptic ulcer

Anatomy and location of peptic ulcer disease

Both the duodenum and the stomach can develop peptic ulcers. The gastric cardia, fundus, body, antrum, and pylorus are the different parts of the stomach. Visceral peritoneum lines every side of the stomach. The incisura angularis is an acute angle indentation along the lesser curvature of the stomach wall and marks the division of the stomach body and the antrum [Fig. 1] Gastric ulcers typically occur at the gastric antrum, with the lesser curvature being the most common location [40]. With the use of NSAIDs, peptic ulcers can also develop along the larger curvature of the stomach [41].

There is no mesentery in the duodenum, and the peritoneum only partially encloses the organ. [42] There are four sections in the duodenum. The duodenal bulb, which rises from the pylorus, is the first portion of the duodenum.Only the bulb of the duodenum has visceral peritoneum covering its whole surface. The duodenum's remaining sections are retroperitoneal. The pancreatic duct and common bile duct are located in the second section of the duodenum, which descends. At the level of the second lumbar vertebral body, the third (horizontal) portion crosses the retroperitoneal median. From the aorta to the Treitz ligaments is the fourth segment of the duodenum. [42] See below, fig.

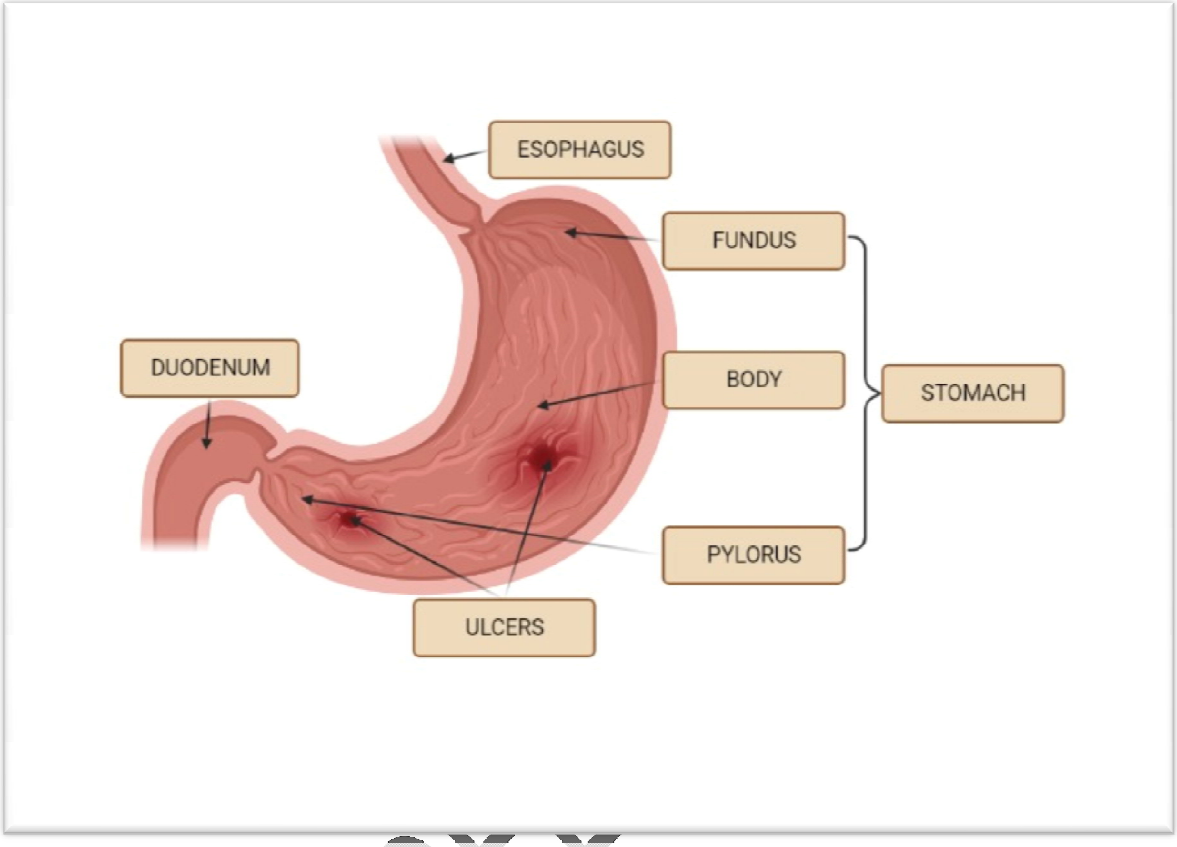

Fig 3: Cross sectional view of duodenum

95 percent of duodenal ulcers occur in the duodenal bulb, making it the most frequent place [40,43,44]. Ulcers distal to the duodenal bulb, known as post-bulbar ulcers, are uncommon, occurring in only 3-5 percent of patients. Rare etiologies like Zollinger-Ellison Syndrome or Crohn's disease should be taken into consideration when post-bulbar ulcers are observed. [40,43, 44] Additionally, compared to bulbar ulcers, post-bulbar ulcers are more likely to bleed because of their closeness to the gastroduodenal artery. [44]

The majority of posterior duodenal ulcers develop on the duodenum's anterior wall, close to the ampulla. Due to edema, reactive tissue, and spasm at the ulcer disease site, duodenal ulcers might show an inward bowing of the opposite all that can conceal an outpouching characteristic of an ulcer crater. As a result, this inflammatory process may make it difficult to spot ulcer craters, which are a particular feature that can be seen on fluoroscopic imaging (44).

Epidemiology and etiologic factors

Gastric ulcers are the cause of significant morbidity and mortality worldwide. Results can range from abdominal pain and gastrointestinal bleeding to obstruction or perforation of the gastric outlet.

According to estimates, 8.4 percent of Americans have a stomach ulcer. [45] It has been established that the high prevalence of stomach ulcer disease is related to male gender, smoking, and chronic illnesses.[45,46] Stomach Ulcer disease is also known to be associated with aging.[47] Over time, a significant reduction in the diagnosis of gastric ulcer and the number of associated complications has been observed both in the United States and elsewhere in the world. [48, 49] fig.4 below

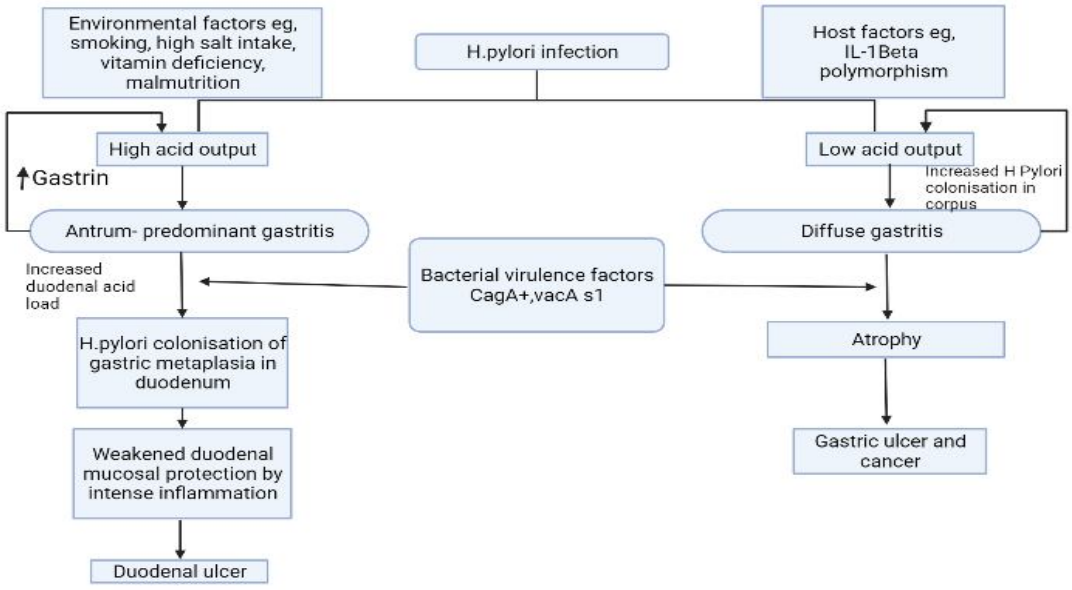

Fig 4: Diagnosis of gastric ulcer and the number of associated complications

The majority of peptic ulcer sickness instances at the moment are recognized to be related to. pylori contamination and/or the usage of NSAIDs.[50] A gram-poor bacteria called Helicobacter pylori colonises the gastrointestinal mucosa and may cause gastritis, peptic ulcer disease, and even gastric cancer.[51;52] H. pylori impacts a massive section of the populations, but simplest a small subset will increase scientific sickness.[52] NSAID use, which includes aspirin, is not unusual place and results in an improved chance of

gastrointestinal negative activities which includes peptic ulcer sickness. The relative chance of growing a symptomatic ulcer is 4.0 for non-aspirin NSAID users and 2.9 for patients taking aspirin. [53] fig. 5 below

Medicine	Mechanism of action	Adverse Effects	References

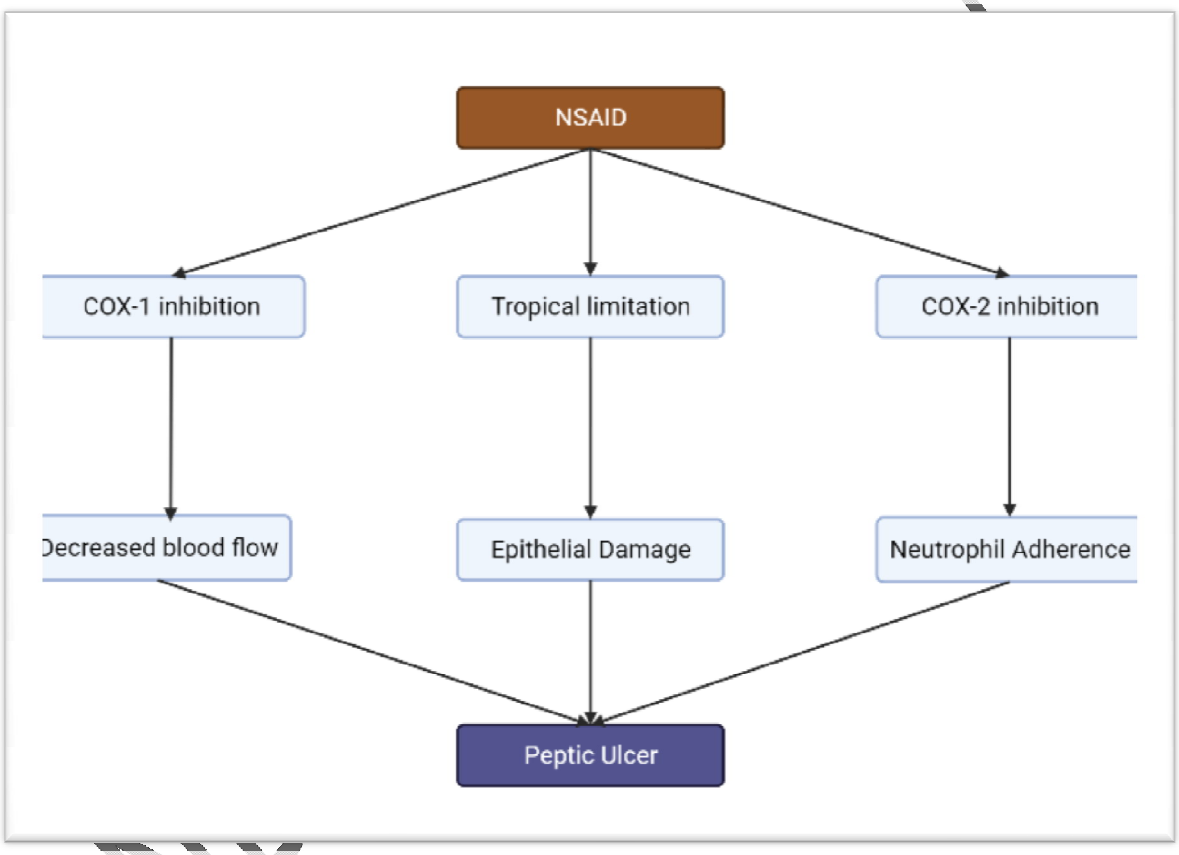

Fig 5: Non-aspirin NSAID

The use of H. pylori and NSAIDs are the major causes of gastric ulcer disease, but other less common causes have been identified, including gastrinoma(such as Zollinger-Ellison syndrome), other drugs, and other etiologies, as detailed in table 1. [54,55]

Treatment

Overview of conventional antiulcer treatment options is summarized in table 1 and table 2.[91]

H2 Receptor Blockers Cimetidine Famotidine Nizatidine Ranitidine	Blocking the activity of histamine on parietal cells' histamine H2 receptors.	Headache, Dizziness, Depression, Anxiety, Cardiovascular, Events, Thrombocytopenia.	56
Proton pump inhibitors(PPIs) Omeprazole Pantoprazole Lansoprazole Rabeprazole Esomeprazole	Inhibition of the gastric H/K-ATPase (proton pump) enzyme system	Headache Abdominal pain Nausea Vomiting Constipation Vitamin B12 Deficiency Osteoporosis Flatulence	57,58
Antacids Aluminium Hydroxide Magnesium Hydroxide	Increases gastric pH to greater than four, and inhibits the proteolytic activity of pepsin Causes osmotic retention of fluid	Frequency not defined: Nausea Vomiting Hypophosphatemia Chalky taste Constipation Abdominal Cramping Diarrhoea Electrolyte imbalance	59
Potassium-competitive acid blocker Vonoprazan	Inhibits H+, K+-ATPase in gastric parietal cells at the final stage of the acid secretory pathway	Contusion Nasopharyngitis Fall Upper respiratory Tract inflammation Eczema Diarrhoea Constipation	60,61,62,63,64

Table 1: Mechanisms of action and adverse effects of the most commonly used antiulcer treatment options.

Table 2: Types and efficiency of Helicobacter(H-pylori) eradication options.[91]

Type	Duration	Efficiency	References
First line PPI+two antibiotics (clarithromycin + metronidazole or amoxicillin)	7-14 days	70-85%	[65]
Second line ***Bismuth-containing quadruple therapy:*** PPI + bismuth salt + tetracycline + metronidazole	14 days	77-93%	[66,67]
Non- bismuth based concomitant therapy: PPI + clarithromycin + amoxicillin + metronidazole	14 days	75-90%	
Levofloxacin triple therapy: PPI+ amoxicillin + levofloxacin	14 days	74-90%	
Salvage regimens ***Rifabutin- based triple therapy:*** PPI + rifabutin + amoxicillin	10 days	66-70%	[68]

Complication

Constant symptoms, bleeding, perforation, penetration, restriction of the stomach outlet, and gastric cancer were all PUD consequences (adenocarcinoma and MALT lymphoma). The most frequent consequence, bleeding, affects 15 to 20% of patients. Most acute upper gastrointestinal bleeding (between 40 and 60 percent) is caused by PUD [69]. Upper gastrointestinal bleeding is an emergency that has to be evaluated and treated right away. Early warning to a GI consultant when examining a bleeding patient can help coordinate the care of critically ill patients. Glasgow-Blatchford and Rockall scores were used for risk stratification [70]. Proper resuscitation with IV fluid and blood products to maintain the target hemoglobin greater than 7 is essential for treatment [71].

In order to decrease the chance of IV PPI to identify High risk- Stigma during endoscopy and discard risk, all patients receiving intravenous PPI therapy must begin with the top GI bladder on the presentation [72]. They promote platelet aggregation and increase the in-stomach pH that provides clot stability. It may also be assumed that occupants like erythromycin or metoclopramide enhance endoscopic visibility and

diagnostic yield [73]. Initial endoscopy, which should be done as soon as possible (preferably within 24 hours), offers both predictive and therapeutic outcomes. It is advised to begin or continue the PPI after endoscopy if High Risk Stigmata are discovered by bleeding.Studies have shown that giving PPI intravenously twice daily is just as effective as giving it continuously, and it also saves a lot of money [74,75]. Repeated endoscopy, angiographic embolization using interventional radiology, or surgical intervention may be necessary to treat recurrent bleeding, which is linked to a high death rate.

Antidotes such vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrate (PCC), or recombinant factor VIIa should be taken into consideration as part of care if the patient has coagulation problems brought on by warfarin. However, because they may have unfavorable consequences, these substances must be used with caution. For instance, when therapeutic anticoagulant therapy needs to be resumed (e.g., when changing a prosthetic heart valve) after bleeding has stopped, large dosages of vitamin K prolong the time it takes for warfarin to reach therapeutic levels. There is likely to be. FFP carries the risk of volume overload, and recombinant factor VIIa increase the risk of thrombosis and is costly. Utilized more frequently, new oral anticoagulants (ZOACs) are irreversible with vitamin K. The NOACs rivaroxaban and dabigtran enhance the risk of gastrointestinal bleeding when compared to warfarin, whereas apixaban does not seem to do so[76]. To treat a NOAC overdose, activated charcoal can be administered within four hours of consumption. Life-threatening bleeding brought on by dabigatran can be treated with hemodialysis and idarucizumab [77]. If hemostasis has been reached, anticoagulants and antiplatelet medicines can be resumed. The timing is based on how quickly anticoagulation needs to be restored. After having a drug-eluting stent implanted, patients undergoing dual antiplatelet therapy are more susceptible to developing an acute thrombosis, thus they should avoid stopping both medications. Patients who start taking aspirin right away (within 1-3 or 7 days) after achieving hemostasis [73]. Patients with mechanical mitral valves or other thrombotic conditions are advised to cross-link with low molecular weight heparin since their warfarin levels are below therapeutic limits.

Perforation is the second most common complication of PUD, which occurs in 2-10% of gastric ulcers and can manifest as sudden severe abdominal pain with hemodynamic instability or shock [78]. Hyperactive bowel movements may at first be detected during a physical examination, but these sounds may eventually quiet down and be replaced with a stiff, bouncing abdomen that may indicate peritonitis. Endoscopy should be avoided in this circumstance because the presence of free air on the image supports this diagnosis. Perforated gastric ulcers are typically best treated surgically.[79]. Medical management with nasal gastric (NG) aspiration, infusion, antibiotics, and acid suppression is available in patients who are unsuitable for surgery and whose perforations have been contained for more than 24 hours (based on studies with water-

soluble contrast media). It will be an option. Penetrating ulcers can also erode nearby organs such as the pancreas, liver, bile ducts and colon.

Another PUD consequence is gastric outlet obstruction (GOO), which can cause premature satiety, bloating, weight loss, dyspepsia, nausea, and vomiting.On physical examination, you may hear squirting due to the air and water trapped in your stomach. Ulcers that appear in GOO are often found in the pyloric canal or duodenal bulbs. Drug therapy usually includes NG aspiration and antisecretory therapy. To treat chronic obstruction, endoscopic balloon dilation or pylorus surgery are options [78].

Prevention of Peptic Ulcer Disease

NSAIDs increase the risk of rebleeding in patients with a history of gastric ulcer. The 2012 ACG Guidelines for the Management of Hemorrhagic Ulcer Patients Carefully Note the Need for Continued Use of NSAIDs in Patients with a History of Gastric Ulcer Disease and, if Possible, permanent Discontinuation of NSAIDs. Recommended to evaluate [80]. It is advised to use PPIs with NSAIDs that are selective for cyclooxygenase (COX) 2 at the lowest effective dose. Combining proton pump inhibitors with COX2 selective NSAIDs lowers the risk of rebleeding. This is believed to be caused by COX1's diminished impact on the gastrointestinal mucosa. [81,82]

In addition, when taking NSAIDs and having H. pylori infection, the risk of bleeding is higher than when taking NSAIDs by themselves. [83] Eradication lowers the likelihood of rebleeding in people with H. pylori infection who are unable to quit taking NSAIDs. Long-term PPI medication paired with H. pylori infection.For patients with gastric ulcer due to 57H. H. pylori alone. These patients do not require long-term PPI therapy because the H. pylori infection can be treated effectively. [80]

Aspirin is also significantly associated with gastric ulcer and bleeding. In one study, the relative risk of bleeding from low-dose aspirin was 1.80 (95% confidence interval 1.59 to 2.03) compared to placebo.[84]However, the mortality rate of those who restarted aspirin immediately after discharge is much lower in patients taking aspirin for secondary prevention of cardiovascular and cerebrovascular illness. In one study, patients with comorbid cardiovascular disease who discontinued aspirin after admission due to gastric ulcer bleeding died and had cardiovascular events within the first 6 months compared to patients who resumed aspirin at discharge. We found that the risk of bleeding was significantly increased (31% vs. 8%). [85]In a controlled experiment conducted in 2011, patients taking low doses of aspirin and receiving endoscopic hemostatic therapy for gastric ulcer bleeding were treated with continuous aspirin therapy for gastric ulcer bleeding. We have found that the risk of recurrence is increased, but the mortality rate may be reduced. For this reason, ACG guidelines may recommend it to patients. It will be restarted as soon as

feasible to take aspirin for secondary prophylaxis. In these patients, aspirin administration should ideally be resumed within 1-3 days and within 7 days. [86,87] PPI should be administered in addition to aspirin therapy. Aspirin should generally not be used again for primary prophylaxis unless specifically recommended, and each individual case should be evaluated on its own merits. [80]

It is less known how to treat idiopathic ulcers (H. pylori negative, not caused by NSAIDs or aspirin, for example). Compared to controls who had pylori-positive ulcers, H. pylori patients with idiopathic ulcers had a greater relative risk of rebleeding and mortality. [88] The ACG Guideline conditionally recommend daily PPI therapy for these patients, but the data are very limited.[80]

Evaluation techniques for anti-ulcer activity

Physiological, pharmacological, or surgical interventions that are pathogenically relevant to the production of gastric ulcers are typically used to cause gastric ulcers in rodents. The following are some models used experimentally to the test and evaluate the efficacy of anti-ulcer drugs. [89,90]

- Ethanol induced mucosal damage in rats (cytoprotective activity)
- Sub-acute gastric ulcer in rats
- Stress ulcer through immobilization stress
- Gastric ischemia-reperfusion injury in rats
- Water-immersion stress or cold-water-restraint
- NSAIDs- (indomethacin, aspirin, and ibuprofen) induced gastric ulcers
- Acetic acid induced gastric ulcers
- Reserpine induced gastric ulcers
- Histamine induced gastric ulcers
- Serotonin induced gastric ulcers
- Pylorus-ligated-induced peptic ulcers
- Methylene blue-induced ulcers
- Diethyl-dithio-carbamate (DDC)-induced peptic ulcers
- Ischemia-reperfusion induced gastric ulcers
- Cysteamine induced duodenal ulcers
- Indomethacin-histamine-induced duodenal ulcers
- Acetic acid-*H-pylori*-induced ulcers
- Ferrous iron-ascorbic acid-induced gastric ulcers

CONCLUSION

The clinical burden of PUD is decreasing as a result of a decline in H. pylori infections, improved accessibility to anti-secretory drugs, and more cautious NSAID use. However, because of its high lifetime frequency and diverse clinical presentation, early detection and treatment are essential.PUD care is essential for avoiding and minimizing serious consequences.The review could be valuable in supplementing knowledge on identifying symptoms, diagnosing them, treating them, determining their prevalence, managing them, and using allopathic medications to treat ulcers. This article encourages scientists and helps to identify ulcer illness.

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