REVIEW

Peptic Ulcer Disease: An Overview of Aetiology, Pathophysiology, Clinical Presentation, Diagnosis and Treatment Options

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ABSTRACT

Introduction: Peptic ulcer disease (PUD) is endemic in all parts of the world. It is estimated that as high as 5-10% of the world's population is affected by PUD. Disruption in the gastric protective factors within the gastrointestinal lumen is responsible for the development of PUD. Aggravating factors that promote formation of peptic ulcers include gastric acids, decreased bicarbonate and general decrease in mucosal defences. Non-steroidal anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori (H. pylori)* infection are the two major aetiologic factors contributing to damages to the mucosal defence. The major clinical symptom of PUD is epigastric pain. Others includes bloating, heartburn, nausea or vomiting. Testing for *H. pylori* is important in treatment of PUD. The major complications of *H pylori*-associated and NSAID-induced ulcers include upper gastrointestinal bleeding, perforation, penetration, gastric outlet obstruction and gastric adenocarcinoma.
Purpose: The purpose of this review is to present a general overview of the aetiology, pathophysiology, clinical presentation, diagnosis and treatment options for peptic ulcer disease (PUD).
Conclusion: PUD remains a global health challenge requiring that all patients should be treated. Conventional treatments include gastric acid suppressing agents such as proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists as well as mucosal protective agents. Eradication of H. Pylori is critical in pharmacotherapy of *H. pylori* associate PUD. New approaches to treatments may include the use of antioxidants containing medicinal plants.

Keywords: Peptic Ulcer, *Helicobacter pylori* (*H. pylori*), Non-steroidal anti-inflammatory drugs (NSAIDs), Proton Pump Inhibitors (PPIs), Antioxidants, Herbal Medicine

INTRODUCTION

Peptic Ulcer Disease (PUD) is an acid-induced lesion of the digestive tract usually located in the stomach or proximal duodenum and sometimes on the lining of the esophagus[1,2]. It is characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria[1,2]. PUD causes a major discontinuation in the inner lining of the gastrointestinal (GI) tract resulting in excavations within the gastro-intestinal mucosa[1]. Peptic ulcers are differentiated from common erosions of GIT based on size. Lesions less than 5 mm in diameter are known as erosions, whereas

lesions up to 5 mm in diameter or more are known as ulcers[1-3].

PUD is a global health problem. The lifetime risk of a person developing peptic ulcer ranges from 5% to 10%[1,3]. The incidence of PUD worldwide has been on a decline due to improved hygienic and sanitary conditions combined with effective treatment and judicious use of NSAIDs especially in the advanced countries[4.] Literature shows that untreated PUD especially *H. pylori* related ones could lead to high morbidity and mortality[1-4]. Complications of PUD could be life-threatening. Early diagnosis and treatment could help to reduce the incidence of life-threatening complications as well as improve patient quality of life. *Helicobacter. Pylori (H. pylori) infection*, non-steroidal anti-inflammatory drugs (NSAIDs) use, alcohol and tobacco consumption, and gastrinoma form the core risk factors for the development of peptic ulcers[1,4]. Other risk factors include oxidative stress that results in excessive reactive oxygen species (ROS), genetic factors, hypercalcemia and diet[4,5]. The major aetiologic factors for both gastric and duodenal ulcers remain *H. pylori* infection and chronic NSAIDs use[4,5].

Clinically, Peptic ulcers manifest as gastric and duodenal ulcers[6]. Gastric ulcers usually manifest with epigastric pain within 15-30 minutes after an oral meal. For duodenal ulcers, similar pain is usually felt 2-3 hours following oral meal. Other symptoms of PUD are as follows: abdominal pain, nausea, vomiting, unexplained weight loss, bleeding or perforation with complicated cases[2,6].

METHODS

The following: PubMed, Google Scholar and National Library of Medicine search engines (2005 TO 2021) were used to conduct a literature search of relevant articles on peptic ulcer disease. Citation lists of relevant publications, including studies for randomized controlled trials (RCTs) and review articles were searched. The following subject headings and keywords were used: treatment of peptic ulcer disease, *Helicobacter pylori*, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), proton pump inhibitors (PPIS), alternative management of peptic ulcer, antioxidants and herbal medicine.

RESULTS AND DISCUSSION

A total of 192 relevant articles were found using PubMed, Google Scholar and National Library of Medicine (NLM) search engines. These articles were filtered for relevance to the aim of this review and a total of 50 articles were finally reviewed to arrive at the findings of this article. The findings were quite revealing. While the incidence of PUD is decreasing, it remains a global health concern. Left untreated could lead to high morbidity and mortality especially for H. *Pylori* related cases. Effective eradication of H. *pylori* remains cardinal for treatment while judicious use of NSAIDs is advised.

Epidemiology

Peptic ulcer is a chronic disease affecting up to 10% of the world's population[7]. Approximately 50% of the world populations are also known to be infected with *H. pylori,* especially in the developing countries[7]. Higher rates are found in countries where *H. pylori* infection is higher. *H. pylori* infection is known to be more prevalent among those with lower socioeconomic status and is commonly acquired during childhood. Its prevalence is higher in developing countries including Africa, Central America, Central Asia, and Eastern Europe[7,8]. This bacterium remains one of the most common causes of several gastrointestinal disorders especially peptic ulcer disease[2,3,7].

In Nigeria, the prevalence of *H. pylori* and PUD is not well established in the literature. However, some research show that *H. pylori* infection and peptic ulcer is still endemic in Nigeria. In a 2010 study in Ibadan, a prevalence of 14.0 % PUD in 86 subjects was reported[9]. A related study in 2016 found

a 9.5% prevalence of PUD in 148 subjects in Ilorin[10]. In a similar study in a tertiary hospital in Ile-ife, a 15.8% PUD in 292 subjects was also reported[11]. More recently in the year 2020 a study reported a 7.1% prevalence of peptic ulcer disease in the Nigerian city of Port Harcourt among 434 subjects[7].

Aetiology

There are several etiological factors responsible for peptic ulcers. *Helicobacter pylori* colonization and NSAIDs account for the majority of the cases[1,2,4].

Common causes of PUD are: *H. pylori* infection and NSAIDS use are the two most common causes of PUD[4,6,8]. Chronic use of other medications may contribute to the formation of PUD. Such medications are antiplatelet agents, fluorouracil, corticosteroids, bisphosphonates and potassium chloride[1,2,4]. These medications alone may not fully cause PUD but increase the likelihood in the presence of other factors.

Other uncommon etiologic factors implicated include: Hypersecretory states such as Antral G cell hyperplasia, Zollinger-Ellison syndrome, hyperparathyroidism and cystic fibrosis. Others are Physiological and lifestyle factors including oxidative stress, tobacco smoking and alcoholism[1,2,5]. The following disease states are also known to contribute to PUD: uremic and corrosive gastropathy, celiac disease, bile gastropathy, autoimmune disease, Crohn's disease and viral diseases[1,2,4].

Pathophysiology

A physiologic balance is known to exist between gastric acid secretion and gastroduodenal mucosal defense[5]. Peptic ulceration results from an imbalance between gastric mucosal protective and destructive factors. The destructive factors include *H. pylori*, NSAIDS, gastric hydrochloric acid, bile salts, ethanol, increased pepsin secretion, free radicals and lipid peroxidation. Protective factors are mucin, mucosal bicarbonate layer, prostaglandins, cellular regeneration and mucosal blood flow[12]. Once the protective superficial mucosal layer is damaged, the inner layers are susceptible to acidity as the ability of the mucosal cells to secrete bicarbonate become compromised[1,2,4].

Helicobacter Pylori-Associated PUD

H. pylorus is a gram-negative highly flagellated toxin producing bacillus that is found within the gastric epithelial cells[1,9]. Up to 90% of duodenal ulcers are due to *H. pylori* infection. Similarly, 70% to 90% of gastric ulcers are accounted for by *H. Pylori* colonization[12]. This bacterium has a wide variety of virulence factors making it to adhere to and inflame the gastric mucosal epithelium[12,13].

The major virulence factors of H. *Pylori* include:

1. Urease: The secretion of urease breaks down urea into ammonia which alkalinizes its microenvironment thus enabling the organisms to survive for years in the hostile acidic environment of the stomach, where it causes mucosal inflammation and worsening the severity of peptic ulcer disease[12,14].
2. Toxins: Cytotoxin-associated gene a (CagA) and Vacuolating cytotoxin a (VacA) causes gastric mucosal inflammation and host tissue damage[8,12,14].
3. Flagella: Provides motility and allows movement toward the gastric epithelium[8,12,14].

H. pylori causes an inflammatory response with neutrophils, lymphocytes, plasma cells, and macrophages within the mucosal layer and causes epithelial cell degeneration and injury[12,15]. *H pylori infections is associated with* high levels of gastrin and pepsinogen and reduced levels of somatostatin and bicarbonate secretion. This impaired secretion of bicarbonate promotes the development of acidity and gastric metaplasia[12].

NSAID-associated PUD

NSAIDs are the most prescribed analgesic agents worldwide with up to 30 million people receiving NSAIDs medication

daily[16,17]. These agents remain the most common cause of PUD in persons not infected with *H. pylori*. The use of NSAIDs coupled with coexisting *H. pylori* infection increases the chances and intensity of NSAID-induced mucosal damage. Prostaglandin synthesis normally protects the gastric mucosa. NSAIDs contribute to inducement of peptic ulcers by blocking the synthesis of prostaglandin via inhibition of cyclooxygenase-1 (COX-1) enzyme[4,16,17]. This results in decreased gastric mucus and bicarbonate production and associated decrease in mucosal blood flow. Inhibition of cell proliferation is also observed.

NSAIDs also cause lipid peroxidation. NSAIDs are protonated in the acidic gastric medium to cross lipid membranes and enter alkalinized epithelial cells where they ionize and release hydrogen ions. In ionized forms, NSAIDs are unable to cross the cellular lipid membrane and are, therefore, trapped within epithelial cells. This causes uncoupling of oxidative phosphorylation, decreased mitochondrial energy production, increased cellular permeability and reduced cellular integrity[14,16-18].

Clinical Presentation and Diagnosis

Patients with PUD may be symptomatic or asymptomatic. The most common presenting symptom of patients is dyspepsia/epigastric pain. Signs and symptoms of peptic ulcers usually differ based on the location of the disease and age of the patient[1,2]. Gastric and duodenal ulcers can be differentiated from the timing of their symptoms, in relation to meals. Epigastric pain occurring within 30 minutes of an oral meal is indicative of a gastric ulcer, while duodenal ulcers present with pain occurring 2 to 3 hours after an oral meal or pain on an empty stomach[3,4]. Nocturnal pain also occur with duodenal ulcers. Approximately 50-80% of patients with duodenal ulcers may experience nocturnal pain compared to only 30-40% of patients with gastric ulcers and about 20-40% of patients with non-ulcerative dyspepsia[2,4,5]. Duodenal ulcer is relieved by food intake, antacids, or antisecretory therapy while gastric ulcers may be aggravated by food intake[1,4].

In asymptomatic chronic ulcer patients induced by NSAIDs, upper gastrointestinal bleeding (UGIB) or perforation may be the first clinical manifestation[1,4]. Those with gastric outlet obstruction commonly report a history of abdominal bloating and or fullness. Others may experience abdominal fullness, nausea and vomiting, weight loss/weight gain including hematemesis and melena. Alarm symptoms requiring prompt urgent action include UGIB, early satiety, dysphagia, family history of upper GI malignancy, unintentional weight loss, progressive dysphagia, or new onset upper gastrointestinal symptoms in patients older than 55 years of age, iron deficiency anaemia and recurrent emesis[1,2,4,6].

Diagnosis of PUD requires history taking, physical examination, and invasive/non-invasive medical tests. Any patient presenting with alarm symptoms should be referred for further investigation of complications of PUD. When symptoms are suggestive of possible peptic ulcer disease and with no alarm symptoms noted, empiric treatment with anti-secretory agents may be initiated. In older patients and those with alarm symptoms, endoscopy is recommended to establish definitive diagnosis[1,2,4,6].

Some diagnostic tests for PUD are as follows:

1. Esophagogastroduodenoscopy (EGD): This is the ultimate gold standard and the most accurate diagnostic procedure with sensitivity and specificity as high as 90% in the diagnosis of gastric and duodenal ulcers[1,2,4]. Patients with alarm symptoms should undergo EGD irrespective of age. Also, patients ≥ 50 years without alarm symptoms but had new onset dyspeptic symptoms should also undergo EGD. This procedure also helps to rule out malignancy[1,2,4-6].
2. Barium swallow: Useful when EGD is contraindicated.
3. When Zollinger Ellison syndrome is suspected, Serum gastrin is tested.

4. *Helicobacter pylori* testing: This could be done using invasive and non-invasive tests. Bacterial culture, Rapid urease test, PCR assay, and histology are the invasive methods applied to diagnose *H. pylori* infection in different biologic sources while urea breath test, Serologic testing, stool antigen test and urine-based tests are non-invasive procedures[1,2,4-6].

Complications

The major complications of *H pylori*-associated and NSAID-induced ulcers include upper gastrointestinal bleeding, perforation, penetration, gastric outlet obstruction and gastric carcinomas. Patients who use NSAIDs have a four-fold increased risk of ulcer complications when compared to non-NSAID users[1,4,6]. Patients at higher risk for ulcer complications are those with a previous history of ulcers or ulcer complications, advanced age, comorbidities, *H pylori* infection, use of high-dose NSAIDs, and concomitant use of corticosteroids, aspirin or anticoagulants[1,6].

Upper gastrointestinal Bleeding (UGIB): Peptic ulcer disease (PUD) is the most common cause of UGIB and remains a serious condition carrying a substantial risk for morbidity and mortality. Approximately 28% to 59% of all cases of UGIB is attributable to PUD[19,20]. UGIB is the most common and severe complication of PUD. The mortality rate from peptic ulcer-induced UGIB is between 5% to 10% worldwide[21]. Available evidence suggests that bleeding is more common as age increases[19-20]. UGIB occurs in about 15-20% of ulcer patients. UGIB remains a medical emergency. Although there has been a significant improvement in non-surgical therapies for UGIB such as the use proton pump inhibitors and therapeutic endoscopy, surgical procedures for peptic ulcer bleeding remains the absolute treatment option for most patients[20,21].

Perforation is the next most common complication of PUD. It occurs in 2-10% of peptic ulcer cases[22]. Perforation occurs when an ulcer eats through the wall of the stomach or intestine creating a hole in the within the affected portion of the gastrointestinal tract[23,24]. When peptic ulcer perforates, gastric juices, partially digested food, bacteria, and enzymes spill into the gastric peritoneal cavity resulting in peritonitis[22-25]. A study involving 84 patients with perforated peptic ulcer disease reported that the commonest presenting symptoms included sudden onset of severe epigastric pain (97.6%), abdominal distention (76.2%) and vomiting (36.9%)[23]. Perforation is a less frequent complication of peptic ulcer when compared to bleeding. Perforation is a common problem in people who have unsuspected or untreated peptic ulcers[22-24].

Penetration: This is a rare but possible complication of PUD. This occurs when ulcer crater erodes through the gastric wall or intestinal wall into the surrounding organs but without free leakage of luminal contents into the peritoneal cavity[26]. Penetrating ulcers usually presents with a sudden change in symptoms. These changes could appear as a loss of association of the pain with meals, and loss of relief of pain with food intake and medical therapy. Penetrating ulcers could erode into the following surrounding organs; pancreas, liver, bile duct, or colon.

Gastric Outlet Obstruction (GOO): This occurs when an inflamed or scarred stomach ulcer obstructs the normal passage of food through the digestive system[27-29]. PUD accounts about 90% of all cases of GOO[27,28]. GOO secondary to peptic ulcer disease remains prevalent and represents approximately 5% to 8% of ulcer related complications[27]. This complication can present with early satiety, bloating, weight loss, indigestion, nausea and vomiting[1,4]. Pyloric channel stenosis could lead to stasis and consequent rise in gastric pH due to increased gastrin and gastric acid production[28]. This is compounded by significant gastric distention that further increases gastrin release. Endoscopy can be used to confirm obstruction.

Gastric Cancer: Gastric cancer is the sixth most common cancer and the third most

common cause of cancer-related death in the world[30]. Patients with persistent non healing gastric ulcers are also at an increased risk of developing gastric malignancy. *H. pylori* is the first formally recognized human bacterial carcinogen[12]. *H. pylori* is associated with atrophic gastritis, which, in turn, predisposes to mucosa-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma[30,31]. The risk is approximately 2% in the initial three years of PUD development[30]. Infection with *H. pylori* is the strongest recognized risk factor for gastric adenocarcinoma[30].

Approaches to Therapeutics of Peptic Ulcer Disease

The aims of ulcer treatment include to improve healing process, to reduce pain, to prevent complications and recurrences, minimize side effects of medical treatment, and reduce costs of treatment. Patients should be advised to avoid NSAID intake, quit smoking, and only consume alcohol in moderation. For *H. pylori* positive patients, eradication of the infection should be pursued, and eradication of infection confirmed four weeks or more after completion of therapy[13]. Several categories of drugs are deployed for the management of PUD.

They include:

1. **Antisecretory Agents**
   a. Muscarinic receptor (M1) antagonists
   These agents act by suppressing the secretion of gastric acid, reduce gastrointestinal motility and relieve stomach cramps[32]. Common examples include: telenzepine, propantheline, scopolamine and pirenzepine. They also confer cytoprotective effect within the gastrointestinal lumen. They help to protect against gastric mucosal lesions induced by alcohol, sodium hydroxide (NaOH) and other aggressive agents[32].
   b. H2 receptor antagonists
   They act primarily by blocking the H2 receptors thereby reducing the release of gastric hydrochloric acid. They are very helpful in reducing up to 90% of the basal, food-stimulated and nocturnal secretion of gastric acid[32,33]. They also help in the prevention of stress-induced gastric ulceration. They are used in combination with antacids in the management of stress-mediated ulcers. Examples are ranitidine, cimetidine, famotidine and nizatidine[34].
   c. H+/K+ ATPase inhibitors/Proton pump inhibitors (PPI)
   They act by directly blocking the gastric proton pump rather than blocking histamine and cholinergic receptors. They block the final step of gastric acid secretion. They have better control over basal as well as nocturnal acid secretion[32,35,36]. Examples are omeprazole, lansoprazole, rabeprazole and pantoprazole. They are also known to inhibit the growth of *Helicobacter pylor*i. They are now used as first-line agents in the treatment of peptic ulcer. They have largely replaced H2 antagonists due to their superior healing ability and efficacy[35,36,37]. Treatment may be incorporated with calcium supplements as long-term use of the PPIs can increase the risk of fractures.
2. **Cytoprotective Agents**
   a. Prostaglandins Analogues
   Misoprostol and other prostaglandin analogues help to protect the gastrointestinal mucosa against gastric acids. They act by inhibiting gastric acid secretion and help in protection against ulcers caused by NSAIDs, certain food, alcoholic beverages, tobacco smoking and stress[38]. Prostaglandin analogues such as misoprostol, acts by increasing the secretion of mucus as well as bicarbonate, thereby protecting against chronic ulcers[39]. Misoprostol is used concomitantly to reduce the risk of NSAID-induced gastric ulcers but not duodenal ulcers in high risk

patients[32]. Nevertheless, prostaglandin analogues are inferior to H2-receptor antagonists as regards their effects on ulcer healing, pain relief, and relapse prevention and less effective than expected from their acid inhibitory action[39]. They are contraindicated in pregnancy due to its abortifacient property. Arbaprostil, enprostil, rioprostil and trimoprostil are other known compounds[38,39].

b. Mucosal coating agents
Sucralfate is composed of sucrose octa-sulfate and aluminum hydroxide, which dissociate in the acid environment of the stomach helping to form adherent coating at the mucosal sites which are ulcerated[40]. It protects the ulcer against hydrogen ion back-diffusion, pepsin and bile and therefore promotes ulcer healing. It also binds to both epidermal growth factor (EGF) and fibroblast growth factor (FGF) and helps in enhancing ulcer healing. Sucralfate also inactivates pepsin, adsorbs bile acids and is believed to be cytoprotective by stimulating prostaglandin synthesis[40].

c. Antacids
They are weak bases that neutralize gastric acid, thereby relieving or eliminating the irritation and erosion to the stomach wall and the ulcer sites[41]. They also inhibit the formation of pepsin because pepsinogen is converted to pepsin in acidic medium. Antacids can be systemic or non-systemic. An example of systemic antacid is sodium bicarbonate. Non-systemic antacids include magnesium trisilicate, magnesium Hydroxide and aluminium hydroxide[41]. They are available in the form of chewable pills and liquids.

3. Antibiotics
Antibacterial agents may be deployed for the eradication of *H. Pylori.* They are usually used in combination with other class of anti PUD drugs[42]. A major problem in the pharmacotherapy of peptic ulcers is the rising incidence resistance of *H. pylori* to antibiotics. This is more on in Nigeria where there is poor antimicrobial stewardship. PPIs are synergistic with antibiotics in the eradication *H. pylori*[1,2]. Following increased resistance to antibiotics, the efficacy of most triple therapy has fallen below 70% in many countries[1,2,4]. Antimicrobial sensitivity should be confirmed before initiating treatment with antibiotics. Some of the antibiotics in synergistic use with PPI in clinical practice are penicillin (Amoxicillin), tetracyclines, metronidazole, clarithromycin and levofloxacin[42-44].

4. Herbal Remedies and Antioxidants
Following the understanding of the role of ROS in the pathogenesis of peptic ulcer disease, many antioxidants are proposed to be useful in the management of PUD[45]. There are many herbs, nutrients, and plant products that have been found to play a role in protecting or helping to heal PUD[45,46]. Herbal medicines are considered as better alternatives for the treatment of peptic ulcer[46]. Most of such herbal products have antioxidants properties. Few human trials are available, but many have shown good potential in animal or *in vitro* studies. Plant extracts and their crude are the most significant sources of new drugs including those for PUD management[46]. Some medicinal plants with known anti-inflammatory and antioxidant activity against *H. pylori* and PUD are presented in the Table 1 below.

Table 1: Medicinal plants with activities against *H. pylori* and PUD

S/NO	HERBAL PRODUCT	CONSTITUENTS	USEFUL PHARMACOLOGIC EFFECT
1	Korean red ginseng[32]	ginsenosides, phenolics, saponins	Increase eradication rates of *H. pylori*; reduction of gastric inflammation and oxidative DNA damage
2	*Allium sativum*[45]	Organo-sulphuric compounds	Antioxidant; suppresses effect of *H. pylori*-induced gastric inflammation *in vivo* and *in vitro*
3	*Zingiber officinalis*[32]	Phenolic compounds such as gingerol and gingerone	Anti-inflammatory and antioxidant effects
4	*Camellia sinensis*[32]	polyphenols and epigallocatechin gallate	Antioxidant and inhibition of urease activities of *H. pylori*.
5	*Carica papaya*[45]	Papain, chymopapain, pectin, carposide, carpaine, pseudocarpaine,	Antioxidant and anti-inflammatory effects
6	*Aloe vera*[32]	Anthraquinone, Cardiac glycosides, flavonoids, terpenoids and lectins	Antioxidant and anti-inflammatory effects
7	Ubiquinone[46]	Vitamin Q10/ CoQ-10	Antioxidant and anti-inflammatory effects

Options for *H. pylori* Eradiation

In *H. pylori*- associated PUD, eradication alone will lead to ulcer healing and prevent further mucosal injury[1,9,11]. The recommended therapeutic regimen is summarized in Table 2 below:

Table 2: Combination regimen for *H-pylori* eradication

S/NO	TYPE	DURATION	EFFICIENCY
1	**First line Option** **Standard triple therapy[47]:** PPI + two antibiotics (clarithromycin + metronidazole or amoxicillin) **Second Line Options**	7–14 days	70–85%
2	**Bismuth-containing quadruple therapy[44]:** PPI + bismuth salt + tetracycline + metronidazole	14 days	77–93%
3	**Non-bismuth based concomitant Therapy[48]**: PPI + clarithromycin + amoxicillin + metronidazole	14 days	75-90%
4	**Levofloxacin triple therapy[47]:** PPI + amoxicillin + levofloxacin	1 4 days	74-81%
5	**Salvage regimens[49]:** Rifabutin-based triple therapy: PPI + rifabutin + amoxicillin	10 days	66-70%

Specific Considerations for NSAIDS/Medications Induced PUD

There is possible synergistic interaction between *H. pylori* and NSAIDs use in the aetiology of gastroduodenal ulcers. This was shown by a meta-analysis of endoscopic studies in NSAID users in which uncomplicated PUD was twice as common in *H. pylori* positive subjects compared to those negative for *H. pylori*[50].

Patients suffering from NSAID-induced PUD should be switched to safer analgesic alternatives or should use lowest effective dose where necessary. Other medications such as oral steroids, bisphosphonates, and antiplatelets agents should also be discontinued, if possible. NSAID-induced peptic ulcers may be prevented by concomitant administration with a PPI or a prostaglandin analogue. Withdrawal of an offending agent and administration of a PPI for 6-8 weeks usually results in 100% healing in as high as 85% of cases[1,4]. Continuous use of NSAIDS may delay ulcer healing even with appropriate PPI therapy. It advisable to institute anti-secretory preventive therapy for patients who are at risk of ulcer but require aspirin or other anti-thrombotic medications.

CONCLUSION

Peptic ulcer disease remains a global health challenge. It is noteworthy that the clinical incidence is decreasing due to the decline in *H. pylori* infections, as well as increased access to treatment. However, *H. pylori* and NSAID-related peptic ulcer disease can have a high reoccurrence rate and varied clinical presentation and complications. It is, therefore, imperative to understand the clinical course of this disease to ensure effective and appropriate management and minimize significant complications.

Testing for *H. pylori* is vital in PUD management. Endoscopy is required for definitive diagnosis of peptic ulceration. The principle of test and treat for all *H. pylori* positive patients should be vigorously pursued, where appropriate, to minimize other risks associated with this medical condition.

Patients should be advised on the need to minimize NSAID-use to reduce mucosal injury. Where NSAIDs-use is necessary, concurrent PPI prophylaxis or choosing COX-2 selective NSAIDS should be advised. Proton pump inhibitor (PPI) based triple-drug therapy forms the mainstay of current therapy of PUD.

Oxidative stress leading to release of reactive oxygen species also known as free radicals have been shown to be a major contributing factor towards PUD. This makes herbal medicines with antioxidants properties qualify as potential agents for PUD management. These herbal medications may be used synergistically with standards anti-ulcer medications. However, more research is needed, in this regard, to provide further evidence for practice.

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