IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A LITERATURE REVIEW ON PEPTIC ULCER DISEASE

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ABSTRACT

Peptic ulcer disease (PUD) is one of the commonest diseases seen throughout the world. There are various risk factors for the development of peptic ulcer disease, but the most important ones are Helicobacter pylori infection and nonsteroidal anti-inflammatory drugs (NSAIDs). Patients generally present with dyspepsia or peptic ulcer bleeding. Acid suppressant therapy, H. pylori eradication, and avoidance of nonsteroidal anti-inflammatory drugs are the cornerstones of treatment of peptic ulcer disease. Peptic ulcer bleeding could be life-threatening. It is managed by appropriate supportive care, intravenous proton pump inhibitor therapy, and endoscopic hemostasis. Transarterial embolization (TAE) and surgery are rarely required if endoscopic therapy fails.

KEY WORDS: Peptic ulcer disease, Helicobacter pylori, Nonsteroidal anti-inflammatory drugs, Transarterial embolization.

I. INTRODUCTION

Peptic ulcer disease (PUD) is characterized by discontinuation in the inner lining of the gastrointestinal (GI) tract because of gastric acid secretion or pepsin. It extends into the muscularis propria layer of the gastric epithelium. It usually occurs in the stomach and proximal duodenum. It may involve the lower esophagus, distal duodenum, or jejunum. Epigastric pain usually occurs within 15-30 minutes following a meal in patients with a gastric ulcer; on the other hand, the pain with a duodenal ulcer tends to occur 2-3 hours after a meal. Today, testing for Helicobacter pylori is recommended in all patients with peptic ulcer disease. Endoscopy may be required in some patients to confirm the diagnosis, especially in those patients with sinister symptoms. Today, most patients can be managed with a proton pump inhibitor (PPI) based triple-drug therapy. [1]

II. EPIDEMOLOGY

The presence or absence of Helicobacter pylori (H. Pylori) determines the incidence and prevalence of PUD. Countries with greater rates of H. pylori infection have higher rates. About 1 percent of those with H. pylori infection get PUD annually, which is 6–10 times higher than the rate for those without the infection. According to a population-based one-year prevalence of PUD of 0.1 to 1.5 percent based on physician diagnosis and 0.1 to 0.19 percent based on hospitalisation data, a systematic review of seven studies from affluent nations revealed. According to a study conducted in the United States, 2% of asymptomatic persons with H. pylori positivity had endoscopic point prevalence for peptic ulcers[2]. Other studies, in presumably asymptomatic subjects in whom H. Pylori status was unknown, have reported an endoscopic point prevalence ranging from 1 and 6 percent.

The incidence of peptic ulcer disease has changed from being more common in men to being equally common in women. For men, the lifetime prevalence is roughly 11%–14%, and for women, it is 8–11%. When it comes to ulcer occurrence, age trends show that older women have higher rates and younger men have dropping rates, especially for duodenal ulcers[3].

III. ETIOLOGY

A mucous layer covers your digestive tract, which often shields it from acid. However, an ulcer could form if there is a decrease in mucus or an increase in acid[4].

The most common causes of pud are.

- H pylori induced pud
- NSAIDS induced pud
- Stress induced pud
- Other medications

H PYLORI INDUCED PUD

This widespread bacterial illness affects about half of the world's population and is present in the stomach and/or duodenum. It doesn't seem to cause any problems for the majority of people. Children are primarily affected by H. pylori infection. It is more prevalent in underdeveloped nations. About 5% of children under the age of 10 in the United States have H. pylori bacteria. Children who live in crowded regions and unsanitary conditions are more likely to become infected[5]. It can spread from person to person by intimate physical contact, such kissing. H. pylori can also be acquired by eating and drinking[4].

NSAIDS INDUCED PUD

NSAIDs or nonsteroidal anti-inflammatory medicines are the cause of the initial gastric ulcer and encourage its sequelae, including bleeding and perforation. Important risk factors for the formation of ulcers include age over 60, a history of ulcer illness in the past, and concurrent corticosteroid use[6].

The stomach lining may become immediately irritated by NSAID use, which facilitates the formation of ulcers. Prostaglandins are a class of substances that have the potential to regulate the stomach's protective lining. NSAIDs may interfere with these chemicals[7].

These medications include ibuprofen (Advil, Motrin IB, others), naproxen sodium (Aleve, Anaprox DS, others), ketoprofen and others[4].

STRESS INDUCED PUD

A stress ulcer result from physiological stress, not psychological, and can lead to the upper gastrointestinal bleeding. It may be a single or multiple mucosal defects and is often associated with shock, sepsis, trauma, or chronic illnesses. These ulcers are a major concern for patients in critical and intensive care settings[8].

OTHER MEDICATIONS

Taking certain other medications along with NSAIDs, such as steroids, anticoagulants, low-dose aspirin, selective serotonin reuptake inhibitors (SSRIs), alendronate (Fosamax) and risedronate (Actonel), can greatly increase the chance of developing ulcers[4].

IV. PATHOPHYSIOLOGY

Role of Helicobacter pylori in causing the duodenal ulcer

- Factors responsible for ulcer formation:
  - Hypergastrenemia which leads to low pH
  - Decreased in Bicarbonate secretion
  - Both of these factors lead to gastric metaplasia induced duodenitis [9]

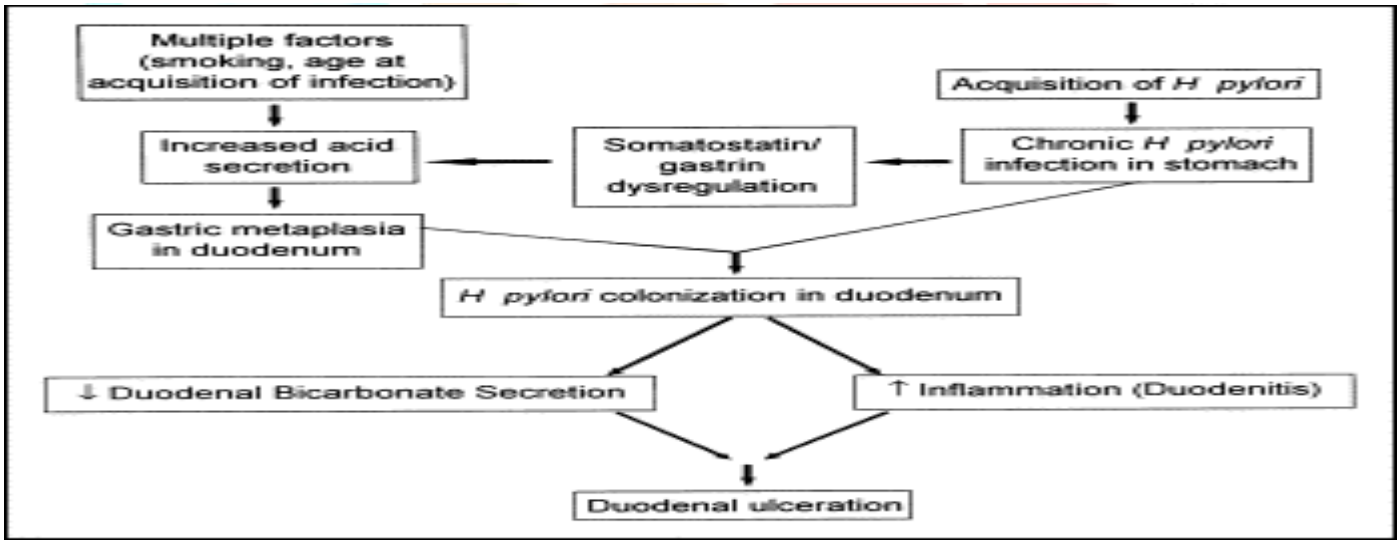

Image -1 Helicobacter pylori induced peptic ulcer disease**.[10]**

Role of NSAIDS

- NSAID's are more commonly responsible for gastric ulcers than duodenal ulcers
- NSAID's cause ulcers by following mechanism:
  - Inhibit systemic prostaglandins production.
    - Decreases blood flow
    - Decreases mucus production
    - Inhibits leucocyte adhesion[9]

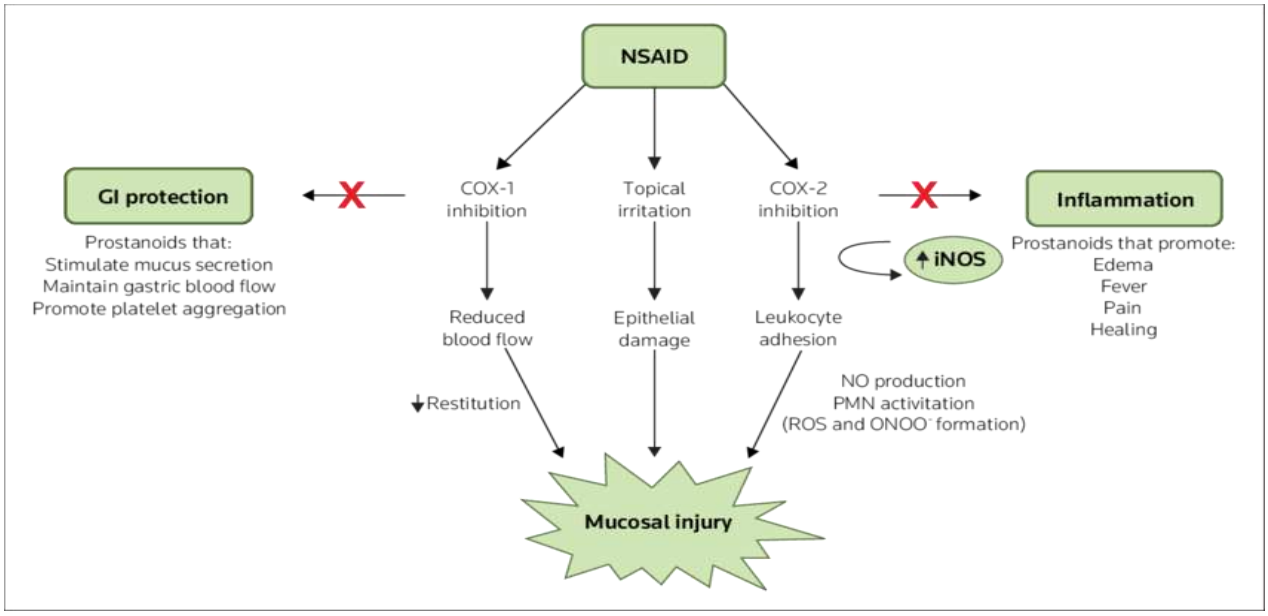

Image -2 NSAID induced peptic ulcer disease[11]

V. CLINICAL FEATURES

Stomach discomfort that burns is the most typical symptom of a peptic ulcer. An empty stomach and stomach acid exacerbate the agony. Eating specific foods that buffer stomach acid or taking an acid-reducing medicine can typically reduce the pain, although the pain may return later. The pain could be more severe at night and in between meals.

- Burning stomach pain
- Feeling of fullness, bloating or belching
- Intolerance to fatty foods
- Heartburn
- Nausea

Many people with peptic ulcers don't even have symptoms.
Less often, ulcers may cause severe signs or symptoms such as:

- Vomiting or vomiting blood — which may appear red or black
- Dark blood in stools or stools that are black or tarry
- Trouble breathing
- Feeling faint
- Nausea or vomiting
- Unexplained weight loss
- Appetite changes[4]

VI. RISK FACTORS

- Age 70 or over
- Female
- Taking more than two types of NSAIDs
- Taking NSAIDs regularly for a long time
- Previous peptic ulcer
- Two or more medical conditions
- Taking corticosteroids or medicines to increase your bone mass

- Drinking alcohol or smoking

Zollinger-Ellison Syndrome

Zollinger-Ellison syndrome is a rare condition that can cause peptic ulcers. Those who have it have one or more tumors in the pancreas and duodenum that produce a large amount of gastrin hormone. This leads to large amounts of acid in the duodenum and upper intestine.

Genetics

About 20% of people with peptic ulcer disease have a family history of duodenal ulcers. Researchers have found some genetic basis for susceptibility to H. pylori infection. This genetic research is still very early, but in the future, it might show those at greater risk.

Lifestyle Risk Factors

Research indicates that smoking cigarettes can raise your risk of developing an ulcer, particularly if you have an H. pylori infection. Additionally, smoking promotes the recurrence of ulcers and hinders the healing of pre-existing ulcers.

Although there is no evidence linking alcohol intake to peptic ulcers, individuals with cirrhosis of the liver—a condition frequently associated with excessive alcohol consumption—are more likely to develop ulcers. When you have an ulcer, drinking alcohol might make it more uncomfortable.

A bland diet is no longer advised for those who suffer from peptic ulcers, even if spicy foods, coffee, and acidic drinks do not cause ulcers. While your ulcer is being treated and healed, you may discover that certain items make your symptoms worse, in which case you might decide to avoid them.

Although emotional stress is no longer considered to be the cause of ulcers, those who are experiencing it frequently report their ulcers hurting worse[12].

VII. LABORATORY INVESTIGATIONS

- If there is the history of peptic ulcer disease then following laboratory test are done
  - Complete blood count
  - Liver function tests
  - Serum lipase and amylase
  - Iron studies
  - Some patients with peptic ulcer disease may have reduced serum ferritin, which is usually suggestive of bleeding which requires further endoscopy to rule out bleeding
  - **Patient with a family history of peptic ulcer or there is history of refractory ulcer to treatment**:

- A fasting serum gastrin level can be done to screen for Zollinger- Ellison syndrome
- If the diagnosis of Zollinger-Ellison syndrome cannot be made on the basis of the serum gastrin level, then next step is to measure secretin stimulation test

Following test can be done to document the residual infection after eradication therapy:

- Urea Breath Test (carbon 13) tests: This is used to document eradication therapy and should be performed four to six weeks after completion of eradication therapy
  - Urea Breath Test require the ingestion of urea labeled with the nonradioactive isotope carbon 13 or carbon 14
  - Proton Pump Inhibitor's (PPIs) should be stopped for two weeks before the test
- Stool monoclonal antigen tests-This detect active infection and can be used as a test of cure
  - PPIs should be stopped for two weeks before testing
  - This can be done by following methods:

- Enzyme Immunoassay
- Immunochromatography
- Antibody tests[13]

VIII. TREATMENT

TREATMENT FOR H PYLORI ASSOCIATED PUD

Eradication of H. pylori is recommended in all patients with PUD. First-line therapy should have an eradication rate of more than 80%.Because pretreatment susceptibility is rarely known to the primary care physician, therapy must be chosen empirically based on regional bacterial resistance patterns, local recommendations and drug availability. Table 1 includes treatment options; standard triple therapy is a reasonable initial therapy where clarithromycin resistance is low[14].

Most Effective Regimens for the Eradication of *Helicobacter pylori*

Therapy	Dose	Duration of Course	Eradication Rate, %
	Dual Therapy		
Ranitidine bismuth citrate[26]	Ranitidine bismuth citrate, 400 mg twice daily; and clarithromycin, 500 mg 3 times daily	Ranitidine bismuth citrate, 4 wk; and clarithromycin, 2 wk	82
Omeprazole and clarithromycin[38-40]	Omeprazole, 40 mg daily; and clarithromycin, 500 mg 3 times daily	Omeprazole, 4 wk; and clarithromycin, 2 wk	64-83
Lansoprazole and clarithromycin[45]	Lansoprazole, 30 mg twice daily; and clarithromycin, 400 mg twice daily	14 d	72.4
	Bismuth-Based Triple Therapy		
Bismuth, metronidazole, and tetracycline (BMT)[50]	Colloidal bismuth subcitrate, 120 mg 4 times daily; metronidazole, 250 mg 4 times daily; and tetracycline, 250 mg 4 times daily	14 d	96.3
Bismuth, metronidazole, and tetracycline (BMT)[52]	Colloidal bismuth subcitrate, 120 mg 4 times daily; metronidazole, 250 mg 4 times daily; and tetracycline, 500 mg 4 times daily	7 d	83.7
Bismuth, metronidazole, and amoxicillin (BMA)[2]	Bismuth subsalicylate, 302 mg 4 times daily*; metronidazole, 500 mg 3 times daily; and amoxicillin, 500 mg 3 times daily	14 d	84
Bismuth, clarithromycin, and tetracycline (BCT)[53]	Bismuth subsalicylate, 302 mg 4 times daily*; clarithromycin, 500 mg 3 times daily; and tetracycline, 500 mg 4 times daily	14 d	93
	Proton Pump Inhibitor–Based Triple Therapy		
Metronidazole, omeprazole, and clarithromycin (MOC)[41,61,77]	Metronidazole, 500 mg twice daily; omeprazole, 20 mg twice daily; and clarithromycin, 500 mg twice daily	7-10 d	88-95
Metronidazole, omeprazole, and amoxicillin (MOA)[58]	Metronidazole, 250 mg 4 times daily; omeprazole, 20 mg twice daily; and amoxicillin, 1 g 3 times daily	14 d	90
Omeprazole, amoxicillin, and clarithromycin (OAC)[62]	Omeprazole, 20 mg twice daily; amoxicillin, 1 g twice daily; and clarithromycin, 500 mg twice daily	7 d	96
Lansoprazole, clarithromycin, and metronidazole (LCM)[64]	Lansoprazole, 30 mg twice daily; clarithromycin, 250 mg twice daily; and metronidazole, 400 mg twice daily	7 d	90.4
Lansoprazole, amoxicillin, and clarithromycin (LAC)[64]	Lansoprazole, 30 mg twice daily; amoxicillin, 1 g twice daily; and clarithromycin, 250 mg twice daily	7 d	89.7
	Quadruple Therapy		
Bismuth, tetracycline, metronidazole, and omeprazole[71]	Colloidal bismuth subcitrate, 120 mg 4 times daily*; tetracycline, 500 mg 4 times daily; metronidazole, 500 mg 3 times daily; and omeprazole, 20 mg twice daily	7 d	98
Bismuth, tetracycline, metronidazole, and omeprazole[72]	Colloidal bismuth subcitrate, 108 mg 4 times daily*; tetracycline, 250 mg 4 times daily; metronidazole, 200 mg 4 times daily; and omeprazole, 20 mg twice daily	12 d	97.6

**Bismuth-subsalicylate available in 151-mg tablets as Pepto Bismol. Dose is 2 tablets. Colloidal bismuth subcitrate is available as De-Nol outside the United States. The dose is as chewable tablets.*

Table -1 Helicobacter pylori induced PUD treatment regimen[15].

Eradication heals most duodenal ulcers and greatly diminishes the risk of recurrent bleeding.[3] A systematic review found that treatment of H. pylori infection is more effective than antisecretory noneradicating therapy (with or without long-term maintenance antisecretory therapy) in preventing recurrent bleeding from peptic ulcer.[17] Current data suggest that increasing the duration of therapy to 14 days significantly increases the eradication rate[14].

NSAIDS ASSOCIATED PUD

If the offending medication is stopped, 6–8 weeks of PPI therapy can heal ulcers more than 85% of the time in PUD cases related with NSAIDs or aspirins. Continued use of NSAIDs can still result in ulcer healing, although it will take longer. Patients on aspirin may begin anti-secretory medication to prevent PUD. PPIs are significantly more successful than other medications in treating NSAID-associated PUD, even though they can also be used in conjunction with misoprostol, sucralfate and H2 blockers[16].

An ulcer history, prolonged high-dose NSAID use, aspirin, anticoagulants, or corticosteroids are risk factors for NSAID-induced gastrointestinal toxicity. Aside from typical NSAIDs, therapies targeted at preserving the mucosa include PPIs, the prostaglandin analogue misoprostol (Cytotec), histamine H2 receptor antagonists, and a cyclooxygenase-2 (COX-2) inhibitor. For the best gastrointestinal safety, high-risk patients should take a COX-2 inhibitor along with a PPI, according to a Cochrane analysis on the efficacy of these treatments when compared to placebo[14].

Treatment Option	Drug Class	Dosing Regimen	Brand
Discontinuation of NSAID	PPI	Dexlansoprazole 30-60 mg po daily *or*	Dexilant
		Esomeprazole 20-40 mg po daily *or*	Nexium
		Lansoprazole 15-30 mg po daily *or*	Prevacid
		Omeprazole 20-40 mg po daily *or*	Prilosec
		Pantoprazole 40 mg po daily *or*	Protonix
		Rabeprazole 20 mg po daily	Aciphex
	H_2RA	Cimetidine 300 mg po qid (400 mg bid or 800 mg qhs) *or*	Tagamet
		Famotidine 20 mg po bid (40 mg qhs) *or*	Pepcid
		Nizatidine 150 mg po bid (300 mg qhs) *or*	Axid
		Ranitidine 150 mg po bid (300 mg qhs)	Zantac
	Mucosal protective agent	Sucralfate 1 g po qid (2 g po bid)	Carafate
Continuation of NSAID	PPI	Same as PPI above	Same as PPI above
H pylori positive	Multiple	Triple or quadruple therapy regimen (see Table 4)	Multiple

bid: twice daily; H: Helicobacter; H_2RA: histamine-2 receptor antagonist; po: oral route; NSAID: nonsteriodal anti-inflammatory drug; PPI: proton pump inhibitor; qhs: bedtime; qid: four times daily; tid: three times daily. Source: References 3, 12, 13.

Table – 2 NSAID induced PUD treatment regimen[17]

PROGNOSIS

Most peptic ulcers heal within a few weeks. Most people will only need medication for about two months. Medications are very effective in treating peptic ulcers. People with chronic conditions, like Zollinger-Ellison syndrome, may need to take them for life.

Rarely, some people have persistent stomach ulcers that don't respond to treatment or that keep coming back after treatment. They can cause chronic pain, excessive scarring and other complications. These cases might require surgery to:

Remove the scar tissue or open up the outlet (Pyloroplasty)

Seve the nerve that triggers the stomach acid (vagotomy)[5]

Unfortunately, recurrence is common with rates exceeding 60% in most series. NSAID-induced gastric perforation occurs at a rate of 0.3% per patient per year. However, unlike in the past, mortality rates for peptic ulcer disease have decreased significantly[18].

IX. COMPLICATIONS

PUD can cause bleeding, perforation, penetration, obstruction of the stomach outlet, persistent symptoms, and gastric cancer (adenocarcinoma and MALT lymphoma). The most frequent consequence, bleeding, affects 15-20% of individuals. A significant amount (about 40–60%) of acute upper GI bleeding is caused by PUD[16]. Prolonged ulcerative inflammation and scarring can restrict the duodenum, potentially obstructing the gastric exit.Moreover, it triggers an overactive immunological response and chronic inflammation, both of which lead to carcinogenesis. Less than 2% of people worldwide ever have stomach cancer, despite the fact that 50% of people have H. pylori infection[14].

X. CONCLUSION

In high-income nations today, peptic ulcer disease is less common than it was a century ago. NSAID use for an extended period of time or H. pylori infection are typically linked to it. Triple or quadruple therapy is typically used when treating H. pylori infection. This includes PPI, two antibiotics, and bismuth sulfate. When using NSAIDs, PPI can be taken in addition to them or substituted for them altogether. Peptic ulcer disease complications are extremely common and deadly; prompt medical or surgical intervention is required to preserve the patient's life[19].

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