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Overview of Peptic Ulcer Disease, Etiology, Diagnosis and Treatment

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Abstract: **This review study was aimed to discuss the Peptic ulcer disease (PUD) from different aspects, mostly will try to emphasizes the risk factors associated with PUD, and also pathogenesis, in Addition to aid the diagnostic approaches, and finally the treatment options for PUD. A comprehensive detailed search was conducted to identify literature discussing Peptic ulcer disease (PUD) general population, published up to November 2016. Searching was conducted through; PubMed, EMBASE and the Cochrane library databases, were searched for studies of human subjects only. furthermore, references found in identified articles were manually searched for more relevant studies to be included in this review. Peptic ulcer disease is an issue of the gastrointestinal tract defined by mucosal damage secondary to pepsin and gastric acid secretion. It normally happens in the stomach and proximal duodenum; less frequently, it occurs in the lower esophagus, the distal duodenum, or the jejunum. Testing for and eliminating H. pylori infection in patients is suggested prior to starting NSAID treatment, and for those currently taking NSAIDs, when there is a history of ulcers or ulcer complications. Comprehending the pathophysiology and best treatment strategies for non-NSAID, non-H. pylori-associated peptic ulcers presents a challenge.**

Keywords: **Peptic ulcer disease (PUD), diagnosis and treatment.**

1. INTRODUCTION

Peptic ulcer disease (PUD) consists of both gastric and also duodenal ulcers which positioned a significant danger to the globe's populace over the past two centuries with a high morbidity as well as death. The development of knowledge regarding etiopathogenesis of peptic acid disease from acid-driven disease to an infectious disease has actually opened up this subject for different research studies to find the most effective possible alternatives for management of this disease [(1)]. Annually peptic ulcer disease (PUD) impacts 4 million individuals all over the world [(1,2)]. Complications are experienced in 10%-20% of these patients and 2%-14% of the abscess will certainly bore [(2,3)]. Perforated peptic ulcer (PPU) is a rather rare, but life threatening disease as well as the death varies from 10%-40% [(2,4,5)]. Ladies make up more than half the cases, they are older as well as have a lot more comorbidity compared to their male counterparts [(5)].

PUD develops when the protective devices of the gastrointestinal mucosa, such as produced mucous and also bicarbonate, are overwhelmed by the harmful results of pepsin as well as gastric acid [(6)]. Peptic ulcers, which take place generally in the belly or proximal duodenum, continue to be a relatively typical disease that can impose a considerable socioeconomic problem and also could adversely influence lifestyle. Helicobacter pylori (H. pylori) infection was originally determined as the primary source of PUD. Whereas the occurrence of H. pylori infection has decreased in western countries, gastric abscess is currently connected with using Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and pain killers [(7)]. Tobacco cigarette smoking and also alcohol drinking are recognized risk factors for PUD [(8)].

Management of H. pylori-associated PUD has improved drastically during the past few decades, culminating in the widespread use proton pump prevention (PPI)-based triple therapy for H. pylori obliteration [(9)]. Nevertheless,

prescriptions for medicines linked in the aetiology of PUD, such as aspirin and NSAIDs, have actually additionally raised over this time around period [10] as well as adherence to gastroprotection for prevention of NSAID-induced PUD remains much from optimum [11,12].

This review study was aimed to discuss the Peptic ulcer disease (PUD) from different aspects, mostly will try to emphasizes the risk factors associated with PUD, and also pathogenesis, in Addition to aid the diagnostic approaches, and finally the treatment options for PUD.

2. METHODOLOGY

A comprehensive detailed search was conducted to identify literature discussing Peptic ulcer disease (PUD) general population, published up to November 2016. Searching was conducted through; PubMed, EMBASE and the Cochrane library databases, were searched for studies of human subjects only. furthermore, references found in identified articles were manually searched for more relevant studies to be included in this review.

3. RESULTS

- **Etiological factors & and pathogenesis of Peptic Ulcer Disease:**

A) H. pylori infection:

H. pylori, a gram-negative, helical, rod-shaped germ, colonizes the gastric mucosa of roughly one-half of the world population [13] and an estimated 30% to 40% of the U.S. population [13,14]. H. pylori is present in 95% of patients with duodenal ulcers and in 70% of those with gastric ulcers [15]. It is generally transferred through the fecal-oral route throughout early youth and persists for decades. The bacterium is a known reason for gastric and duodenal ulcers [16] and is a risk factor for mucosa-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma [17]. (**Table 1**) [18].

B) Non-steroidal anti-inflammatory drugs (NSAIDs):

NSAIDs are the most typical cause of peptic ulcer disease in patients without H. pylori infection [19]. Topical effects of NSAIDs cause submucosal erosions. In addition, by inhibiting cyclooxygenase, NSAIDs hinder the formation of prostaglandins and their protective cyclooxygenase-2- mediated results (i.e., boosting gastric mucosal defense by promoting mucous and bicarbonate secretion and epithelial cell expansion and increasing mucosal blood flow). Existing side-by-side H. pylori infection increases the probability and intensity of NSAID-induced damage (20). The annual risk of a deadly ulcer-related issue is 1 to 4 percent in patients who utilize NSAIDs long-lasting, with older patients at the highest risk [21]. NSAID usage is accountable for around one half of perforated ulcers, which take place most commonly in older patients who are taking aspirin or other NSAIDs for heart disease or arthropathy [22,23]. Other risk factors for NSAID-related ulcers are listed in (**Table 1**) [18]. Proton pump inhibitors and misoprostol (Cytotec) lessen the ulcerogenic capacity of NSAIDs and minimize NSAID-related ulcer recurrence.

Table 1. Causes of Peptic Ulcer disease (PUD)

CAUSE	*COMMENTS*
Common causes	
***Helicobacter pylori* infection**	Gram-negative, motile spiral rod found in 48 percent of patients with peptic ulcer disease[4]
NSAIDs	5 to 20 percent of patients who use NSAIDs over long periods develop peptic ulcer disease
	NSAID-induced ulcers and complications are more common in older patients, patients with a history of ulcer or gastrointestinal bleeding, those who use steroids or anticoagulants, and those with major organ impairment

CAUSE	*COMMENTS*
Other medications	Steroids, bisphosphonates, potassium chloride, chemotherapeutic agents (e.g., intravenous fluorouracil)
Rare causes	
Acid-hypersecretory states (e.g., Zollinger- Ellison syndrome)	Multiple gastroduodenal, jejunal, or esophageal ulcers
Malignancy	Gastric cancer, lymphomas, lung cancers
Stress	After acute illness, multiorgan failure, ventilator support, extensive burns (Curling's ulcer), or head injury (Cushing's ulcer)

NSAID induced ulcers (**Figure 1**) [24] develop a vital subset of abscess that take place as a result of suppression of gastric prostaglandin synthesis. Prostaglandins are important for mucosal stability. Cyclo-oxygenase (COX 1 as well as COX 2) restraint, of COX 2 is meant to trigger gastric abscess. Neutrophil adherence is known to cause damage to mucosa by liberating oxygen cost-free radicals, proteases release as well as decreasing capillary blood flow. The duty of nitric oxide (NO) and hydrogen sulphide (H2S), in keeping honesty of gastric mucosa is popular. NO and also H2S rise blood flow to mucosa, stimulate mucous secretion, as well as inhibit neutrophil adherence. NSAIDs, hinder NO and H2S. We have in our rural arrangement determined NSAID as a vital etiological factor because of indiscriminate use these drugs for dealing with high temperature, joint pains, osteoarthritis of knee joints [24].

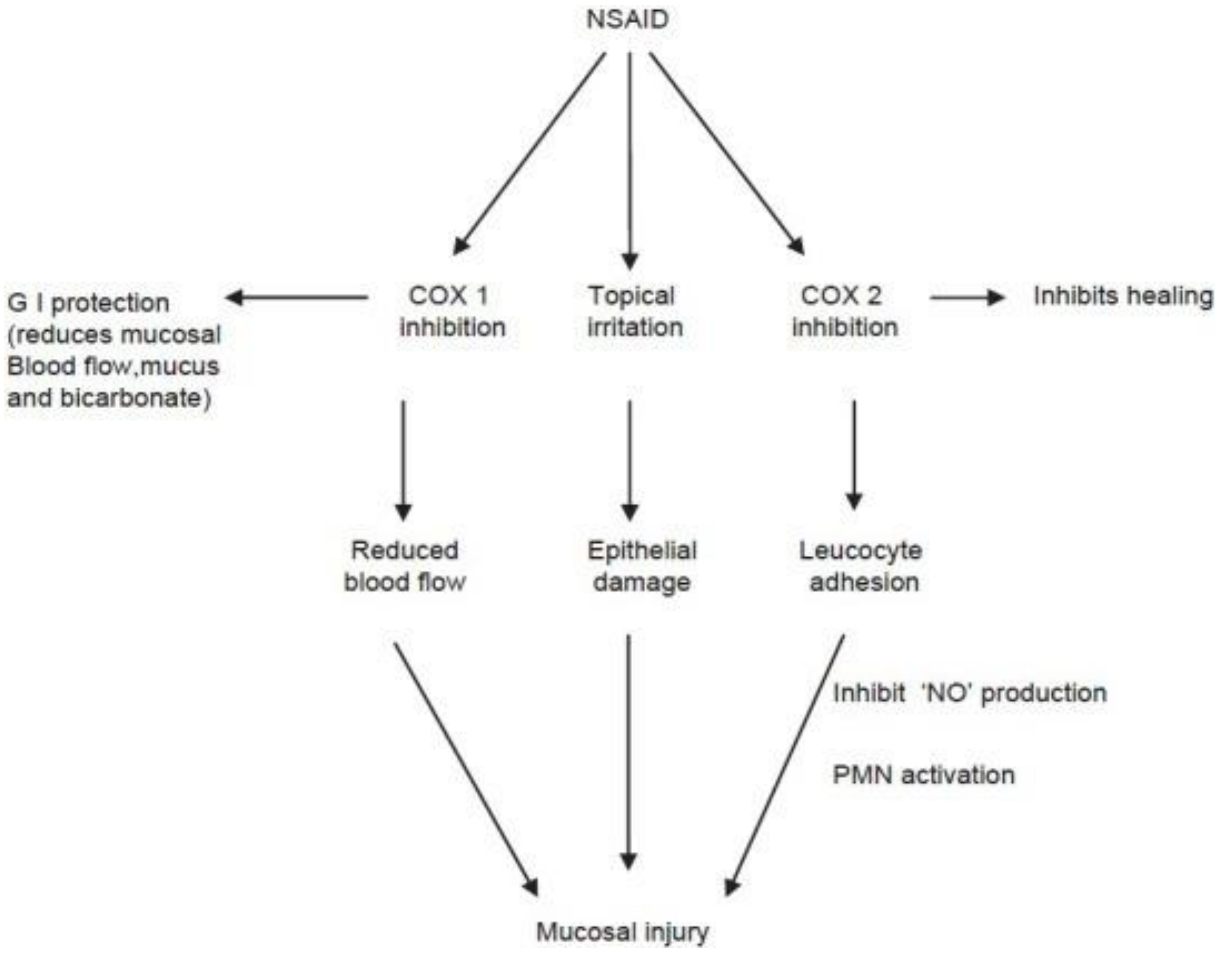

Figure 1: Non-steroidal anti-inflammatory drugs induced PUD

- **Diagnostic methods of PUD:**

A history of night time awakening or episodic epigastric pain eliminated following food consumption are the most particular scientific findings of PUD [25]. Common symptoms of PUD (80% - 90% of patients) consist of episodic gnawing, dull, burning (dyspepsia) epigastric pain. The pain is typically localized and occurs when the stomach is empty, 2-- 5 hours after meals, or in the evening. Pain is alleviated with food, antacids or antisecretory agents [26]. The natural history and scientific discussion of PUD vary in individual populations. Asymptomatic ulcers are common amongst the senior (29.4% - 35%) (27) and in specific parts of the world where two-thirds of patients are reported to be asymptomatic [28]. Dyspeptic signs might be influenced by extrinsic and intrinsic factors such as high body mass index (BMI) due to high plasma levels of endorphins, drinking at least 200 mL of tea day-to-day due to the blocking of adenosine receptors by theophylline, and ulcer size less than 1 cm. Pain awakening the patient from sleep between 12 and 3 a.m. impacts two-thirds of DU patients and one-third of gastric ulcer patients; for that reason, it is a key sign of DUs. Nevertheless, it is likewise seen in one-third of patients with non-ulcer dyspepsia. Considerable vomiting and weight loss recommend gastric outlet obstruction or gastric malignancy. In a meta-analysis, 46% of patients had reflux signs, probably Peptic Ulcer Disease 385 due to concomitant reflux disease including heartburn and acid regurgitation [26]. Less common functions of PUD are indigestion, belching, vomiting connected with gastric or pyloric stenosis, anorexia nervosa, intolerance of fatty foods, anemia triggered by GI blood loss, and a favorable family history. Weight-loss precipitated by fear of food consumption is also characteristic of gastric ulcers [9]. Inflammatory ulcers can produce considerable constitutional symptoms such as weight reduction, cachexia, malnutrition, and chronic abdominal pain. This constellation may deceive the clinician to suspect malignancy as the most likely medical diagnosis. Stomach pain, mainly in the epigastric location, often the left upper quadrant, or radiation into the back, is the most common providing symptom of giant DUs. The pain of these ulcers has actually been referred to as more relentless than classically for small ulcers, and is it not eliminated by food or antacids. Many huge DUs present with hemorrhage that might manifest as melena, hematochezia, hematemesis, or a combination of these. Abdominal pain is more widespread among younger patients than older patients, while the opposite has actually been discovered for bleeding [26].

Older patients with PUD are less most likely to have signs, and this might place them at higher risk of having a serious complication of PUD such as perforation or GI bleeding. The most typical signs of PUD among aged patients (> 80 years of ages.) are epigastric pain (74%), queasiness (23%), and throwing up (20%) [26]. Amongst elderly patients, perforation might provide with moderate pain or no pain [29]. Among pregnant ladies, ulcer symptoms might remain moderate. Signs my manifest as postprandial or nocturnal vomiting that intensifies during the third trimester [25].

Straightforward PUD can be thought based on the presence of common medical signs such as dyspepsia, epigastric burning pain, nighttime pain, and pain relief with food or antacids. A mindful history and physical examination might help in evaluating the substantial various differential medical diagnosis (**Table 2**). A number of extra tests are helpful in validating the medical diagnosis, confirming or omitting PUD problems, and in narrowing the differential medical diagnosis. Conclusive medical diagnosis is made by direct visualization of the ulcer by means of radiography (upper GI barium swallow, double contrast) or upper GI endoscopy (EGD). Recommendation to EGD need to be considered in all patients 50 years of age or older, with relentless symptoms, anorexia, weight-loss, vomiting, and in the presence of indications of GI bleeding. The existence of H pylori should be verified in all patients presumed of PUD [18]. tests are frequently used: Blood antibody test (enzyme-linked immunosorbent assay [ELISA].

Table 2: Differential diagnosis of peptic ulcer disease

Condition	**Test(s)**	**Findings**
Gastritis	**Upper gastrointestinal endoscopy**	**Gastric inflammation**
Gastroesophageal reflux disease	Symptoms	Dyspepsia worse with eating and upon lying down
Gastroparesis	History	History of diabetes
Cholelithiasis	Examination	Right upper quadrant
	Abdominal ultrasound	tenderness
		Gallstones
Pancreatitis	Amylase/lipase	Elevated
Gastric cancer	Upper gastrointestinal endoscopy	Biopsy
	Abdominal CT scan	
Abdominal aortic	Abdominal ultrasound	Size of aorta
aneurysm	Abdominal CT scan	

Hepatitis	Liver function tests	Elevated
Myocardial ischemia	Cardiac enzymes	Elevated CPK_{MB}
	Electrocardiogram	Elevated troponin
		ST segment changes
		Deep symmetric T wave
		inversion
Mesenteric ischemia	Symptoms	Pain after meals
	Abdominal CT	Mesenteric edema; bowel
		dilatation; bowel wall
		thickening; intramural
		gas; mesenteric stranding

Abbreviation: CPK_{MB}, creatine phosphokinase-MB.

The American College of Gastroenterology (ACG) suggests screening for H. pylori infection in patients with active PUD or history of PUD, dyspepsia symptoms, or gastric MALT lymphoma [14]. The reasoning for testing patients with a history of PUD who are currently asymptomatic is that discovering and treating H. pylori infection can reduce the risk of reoccurrence. The test-and-treat method for spotting H. pylori is appropriate in patients with dyspepsia and low risk of gastric cancer (age below 55 years and no alarm symptoms such as unusual weight loss, progressive dysphagia, odynophagia, reoccurring throwing up, family history of gastrointestinal cancer, obvious gastrointestinal bleeding, abdominal mass, iron shortage anemia, or jaundice) [15]. Endoscopy is advised for patients who are 55 years or older, or who have alarm signs.

- **Treatment approaches of PUD:**

Treatment of PUD consists of recovering the ulcer and avoidance of issues. All plans ought to include suitable management of PUD risk factors. Patients must be advised to discontinue cigarette smoking; furthermore, they must be provided stress management programs and counseled to prevent NSAIDs, aspirin, and alcohol abuse. Management of patients with PUD needs detection and elimination of H pylori infection and the administration of antisecretory therapy, ideally PPIs, for a minimum of 4 weeks (**Table 3**) [30,31] (summed up an additional drugs used for PUD). If patients recover after the very first course of treatment, they need to be observed. If signs continue, antisecretory therapy with PPIs or histamine receptor (H2) blockers should be continued for an additional 4 to 8 weeks, and repeat EGD ought to be thought about. Patients likewise ought to be re-evaluated for H pylori infection. Economic modeling recommends that Cox-1 NSAIDs plus H2 blockers or Cox-1 NSAIDs plus PPIs are the most cost-effective methods for preventing endoscopic ulcers in patients requiring long-lasting NSAID therapy [30]. PPIs are more efficient than H2-blockers at basic doses in lowering the risk of duodenal and gastric ulcer, and transcend to miso-prostol in avoiding not gastric but duodenal lesions [31].

Table 3: medications used for treatment of peptic ulcer disease

Class	Medication	Typical Dose	Precautions
Histamine -2 Receptor blocker	Cimetidine	400 mg BID	High incidence of side
			effects and potential for
			drug interactions due to
			inhibition of CYP450
	Ranitidine	150 mg BID	—
	Nizatidine	150 mg BID	—
	Famotidine	20 mg BID	—
Proton pump inhibitors	Omeprazole	20 - 40 mg daily	Altered metabolism of
	Lansoprazole	15-30 mg daily	medications through
	Pantoprazole	40 mg BID	CYP450
	Rabeprazole	20 - 60 mg daily	Inhibits absorption of
	Esomeprazole	20 - 40 mg daily	vitamin B12
Prostaglandins	Misoprostol	200 mg QID	Dose-dependent diarrhea
			and abdominal pain
			Avoid in fertile women and

			during pregnancy
Other medications	Sucralfate	1 g QID	Contains aluminum, should
			be avoided in patients
			with renal failure
			Can prevent absorption of
			other medications

4. CONCLUSION

Peptic ulcer disease is an issue of the gastrointestinal tract defined by mucosal damage secondary to pepsin and gastric acid secretion. It normally happens in the stomach and proximal duodenum; less frequently, it occurs in the lower esophagus, the distal duodenum, or the jejunum. Testing for and eliminating H. pylori infection in patients is suggested prior to starting NSAID treatment, and for those currently taking NSAIDs, when there is a history of ulcers or ulcer complications. Comprehending the pathophysiology and best treatment strategies for non-NSAID, non-H. pylori-associated peptic ulcers presents a challenge.

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