**Pharmacophore**

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

# AN OVERVIEW ON PEPTIC ULCER DISEASE, DIAGNOSIS AND MANAGEMENT APPROACH

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**ARTICLE INFO**

**Received:**
11 Jan 2020
**Received** in revised form:
21 Apr 2020
**Accepted:**
25 Apr 2020
**Available online:**
28 Apr 2020

***Keywords:*** peptic ulcer, diagnosis, management approach

**ABSTRACT.**

**Background**: Peptic ulcer disease is one of the most common complaints in the medical field. NSAID and H.pylori infection are considered the most common causes of this disease. The patient could be completely asymptomatic or could present with epigastric pain and vomiting. Complications could occur like perforation, bleeding, or gastric outlet obstruction. The treatment mainly to treat the underlying cause if it is the H.pylori or NSAID. **Objective:** The objective of this review is to discuss Peptic Ulcer Disease, different presentations, and management plans with the outcome. **Method:** We searched the PubMed database looking for relevant articles to the topic using Mesh terms, "Peptic Ulcer Disease". **Conclusion:** Peptic ulcer disease is a common condition, early diagnosis, and treatment, will not only treat your patient, rather, but it will also prevent serious and life-threatening complications.



**To Cite This Article:** Abdullah Salem Altwejry, Omar Amer Alsaiari, Elbaraa Rafat Saleem, Nawaf Khalid Alshanbri, Abdullah Attiah Alzahrani, Saleh Mofareh Alamri and *et al*., (2020), "An Overview on Peptic Ulcer Disease, Diagnosis and Management Approach", ***Pharmacophore, 11(2),*** *123-126*.

## Introduction

Peptic ulcer was one of the most common diseases which affects the submucosal layer in the stomach and the duodenum; it was mainly associated with H.Pylori infection and excessive use of NSAID (non-steroidal anti-inflammatory drugs) [1]. Nowadays and in the last 20-30 years, the incidence of the disease has shown a sharp decrease, and this phenomenon has been associated with the improvement of drug therapy and the increase of hospital facilities [2]. In this review, we will discuss the pathophysiology of peptic ulcers in addition to the risk factors and epidemiology [3-5]. We will discuss the diagnosing procedure hand to hand with the management plan for peptic ulcers and its complication.

**Epidemiology**:
Prevalence of peptic ulcer disease lifetime was about 5-10%, with the incidence of 0.1-0.3%. In the last 20-30 year, peptic ulcer incidence had been dropped especially in the high-income countries due to increasing of hospital facilities and the introduction of new and effective therapies. [1]

## Discussion

**Pathogenic mechanism and risk factors:**
The main risk factors for peptic ulcer disease, either a gastric ulcer or duodenal ulcer, is H.pyloei infection or use of NSAIDs (non-steroidal anti-inflammatory drugs) and it usually has to be chronic usage of NSAIDs. Also, the use of Aspirin (salicylic acid) could lead to peptic ulcer disease [6]. It has been approved that usage of NSAIDs increases the risk of getting peptic ulcer disease four times more than the normal person and the use of Aspirin increases the risk two times [7]. In the case of H.pylori infection, the major role is the association and balance between the bacterial virulence factors and the immune system of the host, and it has shown that the rate-limiting step in developing the disease is damaging the mucosal layer in the stomach [8]. Knowing that the stomach environment is highly acidic, and to survive in this acidic environment, the bacteria needs to have an alkalic barrier that can protect the bacteria from the harmful effect of stomach acidity, here we are talking

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about the first virulence factor for the H.pylori bacteria which is the urease enzyme this enzyme can use the acidic environment (HCL) to synthesize ammonia and water and the ammonia is alkaline so now the bacteria can cover itself by this barrier [9]. The pathogen also needs adhesive molecules to allow the bacteria adhering to the mucosal layer and starting its harmful effect, so the H.Pylori induce the BabA (blood group antigen adhesin) and OipA (outer inflammatory protein adhesin); those two factors are major ones in playing a role for adhesion properties [10]. Most of the H.Pylori strain has the vacA gene, which is responsible for vacuolating cytotoxin, and its role still not clear enough [10]. Lastly, and one of the most important virulence factors are the inflammatory factors that can be released from the bacteria itself and initiate the harmful effect on the mucosal barrier such as interleukin 1B (IL1B) [11]. Tumor necrosis factors, and lymphotoxin-a; a lot of researches has been conducted and hypothesized that those factors are not only for initiating the inflammatory response in gastric mucosa but also to inhibit the gastric secretion [12].

**Pathophysiology**:
The exact mechanism of how the H.pylori causes peptic or gastric ulcers is not clearly understood, but it is associated with hypochlorhydria and hyperchlorhydria in addition to the location of the infection [13]. In pangastritis H.pylori, this leads to the destruction of parietal cells, which secretes the HCL, and this destruction can be related directly to the H.pylori or to the cytokines that are secreted from, but the outcome in pangastritis is hypochlorhydria, and this will lead to gastric ulcer. In antral gastritis –which is the most common cause 10-15%- the infection is predominantly in the antrum, and this will lead to irritation of G cells which secrete Gastrin, and destruction of D cells which secretes somatostatin [14]. It is well established that the Gastrin hormone is predominantly increased and the led to increasing histaminic receptor activity in the enterochromaffin-like cells, and the outcome is increasing acid secretion. This is also modulated by somatostatin releasing cell destruction, so there is a loss of inhibition and increase in activation in antral H.pylori infection, and this will lead to an increase the level of gastric acidity and increase the level of HCL -hyperchlorhydria- the outcome will be a peptic ulcer [14].
On the Other hand, when we discuss the effect of NSAIDs and Aspirin on the gastric ulcer, it will be linked directly with COX1 –cyclooxygenase1- inhibition that leads to a sharp decrease in the level of prostaglandin, which protects the mucosal layer by increasing the mucus secretion from the mucosal cells, bicarbonate and by also increasing the mucosal layer blood supply [15]. As a result, when NSAIDs stop the prostaglandin pathway and decrease its protective effect on the mucosal layer the stomach acidity will start its harmful effect on the gastric layers. It has also shown that COX1 inhibitor has a negative side effect on oxidative stress and mitochondrial phosphorylation, so selective COX2 inhibitors show a remarkable decrease level in developing peptic ulcer disease [15].

**Clinical Manifestation and Diagnosis:**
It is worth mentioning that two-third of the cases are silent (asymptomatic) [16]. However, if a patient is symptomatic, it will manifest with epigastric abdominal pain, bloating and weight gain or weight loss, in this case, should be considered [17]. In terms of diagnosing peptic ulcer disease, the upper endoscopy has the upper hand on other procedures, and it is considered to be the gold standard in diagnosing steps since it can exclude any other malignant diseases and can confirm peptic or duodenal ulcers in addition to biopsy sometimes [18]. To confirm H.Pylori infection, usually, the physician uses a urea breath test or stool antigen test to confirm or role out H.plori infection. In some cases, a biopsy can also be done, usually, the serological testing of IgG for infection is not recommended to rule out H.pylori infection, but it can be used if the patient is already documented with H.pylori infection because of its high pretest probability [19].

**Treatment:**
In the case of H.pylori infection, the main concerns of pharmacological therapy are H.pylori eradication. There are two common therapies a triple and quadruple therapies. The triple therapy consists of PPI (Proton Pump Inhibitor): Omeprazole and two antibiotics like clarithromycin and metronidazole or amoxicillin [20]. This triple therapy should be taken for 10-14 days to reach its maximum therapeutic effect, but nowadays, a lot of cases of H.pylori clarithromycin resistance have been shown 15% and this resistance had a remarkable negative effect on the triple therapy. The most common causes of bacterial resistance are non-compliance with the treatment regimen or the suboptimal dose that is given for the patient [21]. In the quadruple therapy, the physician adds bismuth sulfate with a single PPI and two antibiotics, and usually, the clarithromycin is not one of them, so the quadruple therapy will be as Bismuth sulfate, Omeprazole, Tetracyclin, and Amoxicillin the course should be taken for 14 days, and this quadruple therapy has shown an eradication up to 93% of H.Pylori. Currently, it is one of the most common therapies used in treating H.Pylori infection [22].
The second line of therapy that can be used to treat H.pylori infection is Levofloxacin quadruple therapy, which is combined with amoxicillin and PPi it shows an eradication of 74-81%, and the course of treatment is two weeks (14 days), but it is usually kept to the last after the 1st line therapies [23].
In the case of NSAIDs (non-steroidal anti-inflammatory drugs) or Aspirin-induced peptic ulcer disease, the most common therapy that is used in this case is combining of therapy with PPI or H2 receptor antagonist, which both tend to decrease the acidity of the stomach and thus the harmful effect can also be decreased [24]. The mechanism of PPI is direct inhibition of the proton pump (Hydrogen/potassium) pump in the parietal cells in the stomach, which decreases the acid secretion as well as using of COX2 selective inhibitor also shows positive results in protection of peptic ulcer [25]. So PPI is one of the most effective prophylactic treatment that can be used a hand to hand with NSAIDS, but chronic usage of PPI has shown a very

undesirable side effects like the osteoporosis because the decreasing of stomach acidity also affect the absorption of Calcium ions and this can lead to osteoporosis and repetitive bone fractures so in some cases the stopping of taking NSAIDS is much better than giving the combined therapy for the long term period [26]. In alternative ways to protect the GI system from the H.Pylori infection, there is a lot of non-pharmacological suggestions can be used as a prophylactic therapy such as Korean Red Ginseng, Allium Sativum, Cistus Laurifolius, Camellia Sinensis (green tea), and Curcuma Longa, all these plants have shown an alternative protecting or decreasing the risk of developing peptic ulcer some are with known mechanism and some with an unknown mechanism [27].

**Management of complication of peptic ulcer:**

The most common complications of peptic ulcer disease are bleeding, perforation, and gastric outlet obstruction, respectively [28]. Bleeding of peptic ulcer is the most common complication with a mortality rate of 10% and a lot of comorbidities; the endoscopy is the gold standard in diagnosing and treating bleeding ulcers, acute upper gastrointestinal bleeding is the most common presentation of bleeding ulcer patients can also be associated with hypotensive shock and metabolic acidosis, so hemostasis endoscopy is required to treat the condition in addition to blood transfusion, and high doses of PPI intravenously should be used for at least three days [29]. A perforated peptic ulcer is less common than bleeding, but it has the highest mortality rate upon the complications with 30%; it is a medical emergency condition that requires a direct surgical intervention with no delaying because it has been approved that the delay increases the mortality probability [30]. The clinical manifestation of perforating patient is diffuse, acute, and sudden severe abdominal pain with rebound tenderness in case of peritonitis, fever, and leukocytosis are indicated with the perforation triad which is: tachycardia, abdominal pain, and rigidity [30]. The abdominal CT scan is the most sensitive diagnostic procedure, in this case, so it is usually used in suspicion of perforation, surgical intervention is highly required as fast as possible with nil per oral status and nasogastric suction in addition to broad-spectrum antibiotic administration and PPI [30]. Gastric outlet obstruction is the least common complication of peptic ulcer the diagnosis is made by upper endoscopy, and it mainly tends to rule out the malignancies since nowadays it is more common than the peptic ulcer complication [31]. The treatment of benign gastric outlet obstruction can be achieved by intensive anti-secretory therapy with intravenous PPI if the medical therapy was not effective it could be treated by endoscopic therapy such as balloon dilatation [31].

**Conclusion:**

Peptic ulcer disease was very common in the past; nowadays, it is less common in high-income countries. It is usually associated with H.pylori infection or chronic use of NSAIDs. In the case of H.pylori infection, we usually use triple or quadruple therapy: PPI, two antibiotics with or without bismuth sulfate. In NSAIDs cases, PPI can be combined with NSAIDs or discontinue the NSAIDs. The complication of peptic ulcer disease is very dangerous and common, and it needs a fast intervention either by surgical or medical intervention to save the patient's life.

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