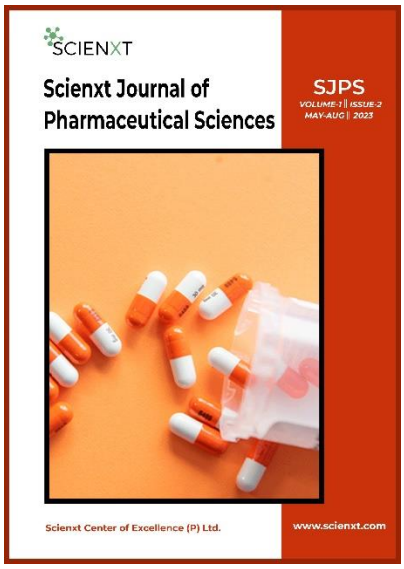

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Overview of peptic ulcer disease: what you need to know

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Abstract:

In 1982 people believed that peptic ulcers were caused due to lifestyle choices. This could have included consuming a diet rich in spicy foods and an inability to properly manage emotional and personal stress. Clinicians thought that these lifestyle factors resulted in an overproduction of gastric acid, leading to the formation of ulcers. Because of this, treatment for peptic ulcers at that time was limited to adopting a bland diet, bed rest, and taking medications that blocked new acid production and neutralized existing acid. In the late 19th century, the Polish clinical researcher Professor W. Jaworski and the Italian medical researcher Giulio Bizzozero both observed spiral-shape micro-organisms in the gastric mucosa of humans and dogs. Again in 1982, two physicians from Perth, Australia, Dr. Robin Warren, and Dr. Barry Marshall observed bacteria associated with ulcerated and inflamed regions of the human gut and began investigating its role in disease. These scientists isolated the bacteria from stomach biopsies and named the organism Helicobacter pylori. Due to their discovery now many Academic and industry scientists are actively pursuing vaccine against Helicobacter Pylori in order to address this world-wide concern.

Peptic ulcer is a common digestive disorder. Peptic ulcer is found to be due to imbalance between aggressive factors such as Hydrochloric acid (HCL), Pepsin, Helicobacter Pylori (H. Pylori), NSAIDs and Defensive factor such as Mucus, Bicarbonate ions, Prostaglandin, mucosal blood flow. The formation of peptic ulcer depends on the presence of gastric juice pH and decrease in mucosal defence. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Helicobacter Pylori (H. Pylori) infection are the two major factors disrupting the mucosal resistance to injury. The idea behind treating ulcer is to digestive disorder lower the amount of acid that our stomach makes, to neutralize the acid that is made and to protect the injured area so it can have time to heal.

Keywords:

Peptic ulcer, digestive disorder, Steroidal Anti-Inflammatory Drugs, gastric acid, Hydrochloric acid

1. Introduction:

An ulcer is a discontinuity or break in the bodily membrane that impedes the organ of which that membrane is the part from continuing its normal functions.

Peptic ulcer is a lesion or sore that occur in the lining of stomach or the duodenum which is caused by gastric acid secretion or pepsin.

Types of peptic ulcers:

2. Peptic ulcer

2.1. Acute peptic ulcer:

Cushing ulcer – gastric, duodenal, or esophageal ulcer arising in patient with intercranial injury or operation.

Curling ulcer – occurring mostly in the proximal duodenum and associated with severe burns and trauma.

2.2. Chronic peptic ulcer:

Duodenal ulcer – have a sore on the upper part of small intestine.

Gastric ulcer – have a sore that is on the inside of the stomach.

Esophageal ulcer – open lesions in the lining of esophageal mostly in the lower end of the esophageal.

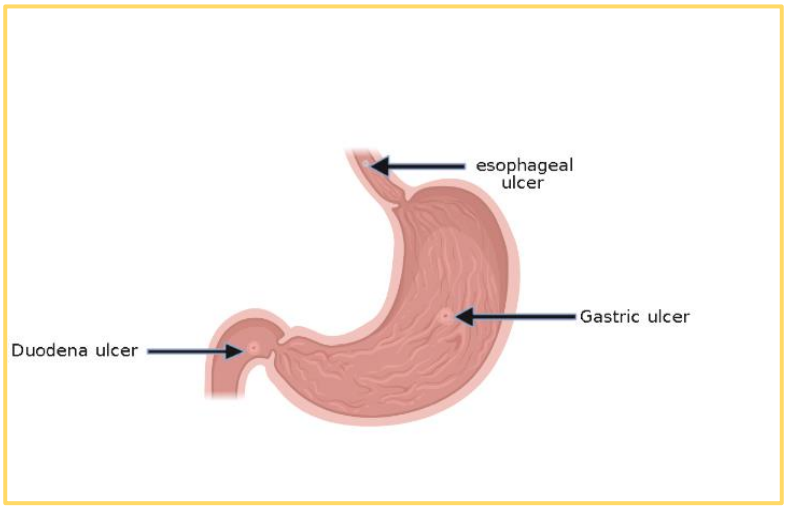


Figure.1: different ulcers found in stomach

Epigastric pain usually occurs within 15 to 30 minutes following a meal in patient with gastric ulcer whereas the pain with a duodenal ulcer patient tends to occur for 2 to 3 hours after a meal.

The most common symptom is burning pain in stomach which usually last for few minutes to a few hours. For some people the pain may come when the stomach is empty at night and for some, eating may make the pain worse.

Other common symptoms include:

- ✓ Pain or discomfort in the upper part of abdomen.
- ✓ Feeling full too soon while eating meal.
- ✓ Difficulty drinking as much liquid as usual.
- ✓ Nausea and vomiting
- ✓ Bloating

In some cases, ulcer can cause severe signs and symptoms and bleeding like:

- ✓ Vomiting blood
- ✓ Black and tar stools with dark red blood

Peptic ulcer occurs due to several potential causes, but two most common are:

1. Helicobacter pylori (H. Pylori]
2. Excessive use of NASID (non-steroidal anti-inflammatory drugs]

H. Pylori infection is a common cause of peptic ulcer. It is present in almost all patient with duodenal ulcers and 70% cases with gastric ulcer. The bacteria may spread from person to person through contact with an infected person, it can also be spread through food and water. They live in the mucus that coats the lining of the stomach and duodenum and produces urease an enzyme that neutralizes stomach acid by making it less acidic. The bacteria cause ulcer by weakening the defence system of the stomach which leads to inflammation. About 10% of people with H. Pylori will develop ulcer. Inflammation of the stomach lining causes irritation and swelling (gastritis).

NSAIDs such as aspirin, ibuprofen and naproxen are another common cause of peptic ulcer. They are normally used to relive pain, inflammation and bring down high temperature but they can also make the stomach lining more prone to damage and ulcers.

We have high chances to develop peptic ulcer if we take NSAIDs:

- For long time
- Types of NSAIDs which is more likely to cause an ulcer
- Higher dose of NSAIDs

Other causes of peptic ulcers include smoking cigarettes and drinking alcohol, infection by certain viruses, fungi, and bacteria other than H. Pylori.

Cause ulcer. Stress and eating spicy food can make ulcer worse and make it hard to treat.

2. Epidemiology:

Peptic ulcer is common and it has been estimated that up to 10% of the population has an ulcer and annual incidence of symptomatic peptic ulcer about 0.3% also 0.03-0.17% when based on hospitalization data.

Incidence of peptic ulcer increases with age, gastric ulcer peak in the fifth to seventh decades and duodenal ulcer 10 to 20 years earlier. Both sexes are similarly affected. The epidemiology of peptic ulcer disease largely reflects the epidemiology of the two major's aetiology factors, H.pylori and NSAIDs.

In the developed world, H.pylori incidence has been slowly declining over the past 50 years and NSAIDs use has increased. This has resulted in a decline in duodenal ulcer and an increase in gastric ulcer.

According to the WHO data published in 2020 peptic ulcer disease deaths in India reached 68,108 or 0.80% of total death. The age adjusted death rate is 6.24 per 100,000 of population and ranks India 42 in the world.

2.1. Peptic ulcer disease (WHO data published in 2020):

Table. 1: Death Rate per 100,000

SI.No	Country	Death rate
1.	Niger	10.80
2.	India	6.24
3.	Afghanistan	10.64
4.	Zimbabwe	8.45

5.	Yemen	7.19
6.	Pakistan	4.53
7.	China	2.05
8.	Nepal	1.16
9.	Japan	0.61
10	Sri Lanka	0.15

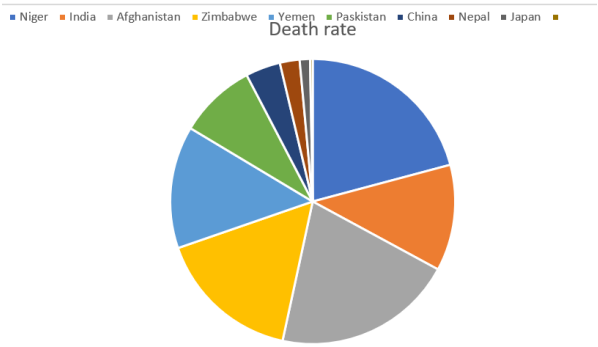


Figure. 2: Death Rate per 100,000

3. Pathophysiology:

Secretion of acid and pepsin in the stomach is stimulated by gastrin and is inhibited by prostaglandin mainly PGE2 and PGI2. Other defensive factors include mucosal blood flow, nitric oxide, bicarbonate ions, and mucus gel barrier.

Mucus is an insoluble gel layer rich in bicarbonate and remains adherent to gastroduodenal mucosa and protects it from gastric acidity and pepsin.

Bicarbonate ions are secreted by the surface epithelial cell which neutralises acid.

Breakdown of the protective mucus gel barrier is the main cause of peptic ulcer disease. Which is caused due to imbalance between the aggressive factors and protective factors.

H. pylori produces urea which breaks down ammonium ion to ammonia which is toxic to mucosa. It inhibits the D-cell (Delta) which are responsible for releasing somatostatin to

decrease the production of gastric acid. Due to inhibition of D-cell (Delta) inflammation occurs leading to wounding of stomach lining (Ulcer).

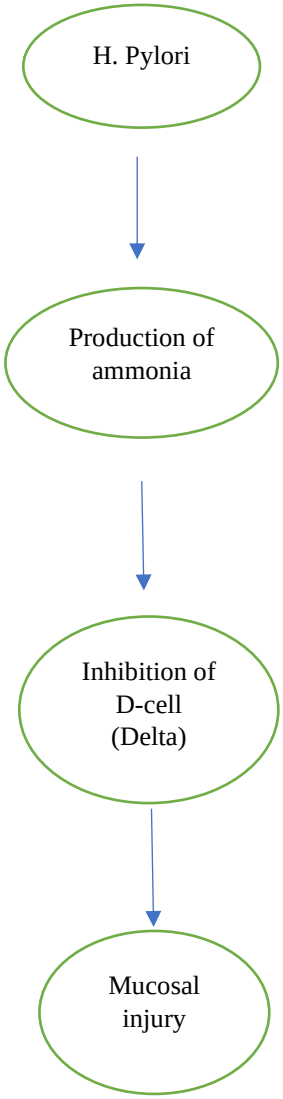
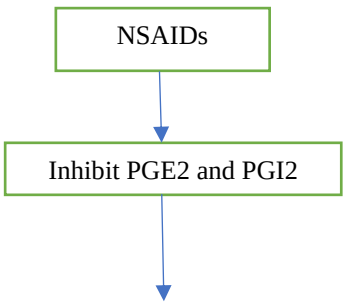


Figure.3(a): The process which leads to ulcer

NSAIDs inhibits the synthesis of prostaglandin (PGE2 and PGI2) by the mucosal cells which stimulate the synthesis of mucus and bicarbonate (neutralize the acid) leads to decrease blood flow, decrease mucus production, and inhibit leucocyte adhesion.



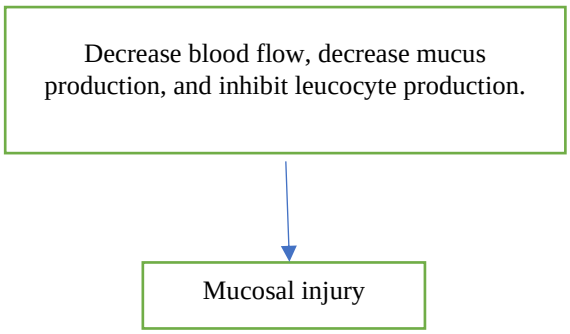


Figure.3(b): The process which leads to ulcer

Severe stress causes increase in the production of gastric acid and increases the risk of ulcer formation.

Smoking leads to mucosal damage or alters the healing of ulcer. Also decreases the production of prostaglandin.

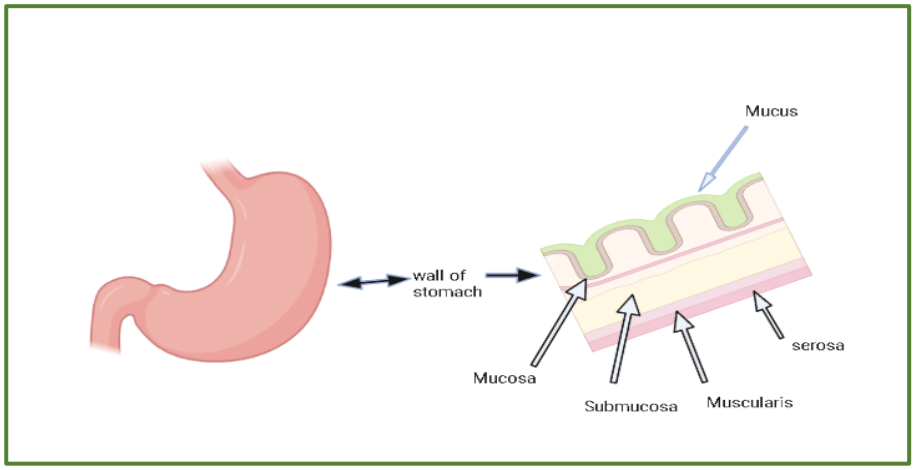


Figure.3(c): The process which leads to ulcer

4. Novel drug target:

- **Glutamine**

  Only one animal study has evaluated the use of L-glutamine in aspirin-induced peptic ulcer model. They found out the L-glutamine was effective in protecting against aspirin-induced gastric lesions in rats. L-Glutamine, commonly used in sports medicine for muscle recovery, has gained medical importance because of its antioxidant properties. The antioxidant properties of L-glutamine have been claimed to be useful in the treatment of peptic ulcer disease in animal studies as well as in very few human studies. Only a few animal studies have been done so far to investigate the role of L-glutamine

in the treatment of H. pylori infections, and it was found to be positive, yet human trials have not been done in large.

- **Coenzyme Q10**

  Recent evidence also says coenzyme Q10 is used in treatment of peptic ulcer. Few animal studies have tried the use of coenzyme Q10; in one study, indomethacin-induced ulcer in Wistar rats was treated using coenzyme Q10, and favourable results were obtained. CoQ10 mediated gastroprotective effect involves preservation of microvascular permeability, elevation of prostaglandin E2, improvement of redox status as well as boosting of nitric oxide.

- **Mucosal coating agent**

  Sucralfate is a basic sulphated disaccharide with aluminium sulphate complex. It helps in forming an adherent coating at the mucosal sites which are ulcerated. It acts by reducing pepsin activity, adsorbs bile salts and acts as barrier to hydrogen ion diffusion. It also binds to both epidermal growth factor (EGF) and fibroblast growth factor (FGF) and helps in enhancing ulcer healing. It is found effective in H. pylori infection.

- **H2 receptor antagonist**

  These drugs act by blocking the H2 receptor and thereby reduce the release of gastric acid. It is very helpful in reducing 90% of the basal, food-stimulated and nocturnal secretion of gastric acid as well. Literature evidence says it also helps in prevention of stress-induced gastric ulcers. They are used in combination with antacids in the treatment of stress-induced ulcers. These drugs include mainly ranitidine, cimetidine, famotidine and nizatidine. One of the major drawbacks is long duration of administration for ulcer therapy, and recurrence of ulcer after healing is a frequent complication

- **Orally disintegrating tablets for peptic ulcer treatment**

  Officials with FDA have approved glycopyrrolate orally disintegrating tablets (Dartisla OTD) to reduce the symptoms of peptic ulcer and as an adjunct to treatment of peptic ulcer. According to the press release the 1.7mg release orally disintegrating tablet are the first and the only ODT form of glycopyrrolate. The product was launched in early 2022.

5. Treatment:

Treatment for peptic ulcer depends on the cause, usually the treatment involves in killing H. Pylori bacterium if present or reducing the use of NSAIDs.

Medication includes:

- ✓ Antacids neutralize gastric acid – Antacid neutralize existing stomach acid and can provide rapid pain relief. Antacid can provide symptom relief but generally are not used to heal ulcer. The disadvantage is that it must be taken in relatively large dose for them to effective.

  Magnesium carbonate – is an antacid used for symptomatic relief of heartburn, indigestion and upset stomach.

  Mechanism of action – Magnesium carbonate react with hydrochloric acid in the stomach to form carbon dioxide and magnesium chloride thus neutralizing excess acid in the stomach.

  Side effect – Nausea, Constipation, Diarrhoea, Headache

  Calcium carbonate – is an ionic compound used as a calcium supplement or antacid for the symptomatic relief of heartburn, acid indigestion and sour stomach.

  Mechanism of action – is a basic inorganic salt that acts by neutralizing hydrochloric acid in gastric secretion. It also inhibits the action of pepsin by increasing the pH and by absorption. Neutralization of HCL acid result in the formation of calcium chloride, carbon dioxide and water

  Side effect – Constipation, Nausea, vomiting, Gas, Loss of appetite
- ✓ Histamine (H_2) blocker reduces gastric acid by blocking the H_2 receptor. It reduces the amount of gastric acid released into the digestive tract, which relive ulcer pain and encourages healing. They are available by prescription or over the counter like famotidine, cimetidine and nizatidine.

  Famotidine – is used to treat ulcers of the stomach and intestine and to prevent intestinal ulcer from coming back after they have healed.

  Mechanism of action – Histamine act as a local hormone that stimulate the acid output parietal cell by a paracrine mechanism. Gastrin cell releases gastrin which works on CCK2 (Chloecsytokinin-2) Receptor on ECL (Enterochromaffin-like) cells. Upon release histamine react on H_2 receptor leading to increased intracellular cAMP level and activated proton pumps on parietal cell. Proton pump releases more proton in the stomach, thereby increasing the secretion of acid. Famotidine works on H_2 receptor and blocks the action of histamine.

Side effect – Hallucination, Confusion, seizure, weakness, agitation, dullness, disorientation.

Cimetidine – is an H_2 receptor antagonist used to manage GERD, peptic ulcer disease and indigestion.

Mechanism of action – Cimetidine binds to the H_2 receptor located on the basolateral membrane of the gastric parietal cell, blocking histamine effect. This competitive inhibition result in the reduced gastric acid secretion and reduction in gastric volume and acidity.

Side effect – Headache, Dizziness, Drowsiness, Diarrhoea.

Nizatidine – is an H_2 receptor antagonist and used to treat GERD and various ulcer.

Mechanism of action – Nizatidine competes with the histamine for binding at the H_2 receptor. Competitive inhibition result in the reduction of basal and nocturnal gastric acid secretion. The drug also decreases gastric acid response to stimuli such as food, caffeine, insulin, betazole or pentagastrin.

Side effect – headache, dizziness, drowsiness, constipation, stomach pain.

- ✓ Proton pump inhibitor (PPIs) are the drugs that block the three major pathway for acid production. PPIs suppress acid production much more effectively than H_2 blocker. PPIs are the gold standard in medication therapy of peptic ulcer disease.

  Omeprazole – can be used alone or with other medication to treat GERD and to promote healing of tissue damage and ulcers caused by gastric acid and H. Pylori infection.

  Mechanism of action – Omeprazole binds covalently to cysteine residue by disulfide bridge on the alpha subunit of H (+)/K (+)-ATPase pump inhibiting gastric acid secretion for up to 36 hour.

  Side effect – Back, leg or stomach pain, bloody or cloudy urine, difficult, burning, or painful urination, Headache.

  Lansoprazole – is a proton pump inhibitor used to help gastrointestinal ulcer, to treat GERD, to eradicate H. Pylori and to treat Zollinger Ellison Syndrome.

  Mechanism of action – Lansoprazole is a prodrug and require protonation by acidic environment to activate. Once protonate they are to react with cysteine (Cys813 and Cys321) on the parietal H (+)/K (+)-ATPase resulting in stable disulfide.

  Side effect – Headache, Skin rashes, Constipation, dizzy or tired.

- ✓ Antibiotic medication to kill H. Pylori: the first line treatment is a triple drug therapy of clarithromycin, PPIs, and amoxicillin for 14 days. Metronidazole can be used instead

if the patient has penicillin allergy. Bismuth quadruple therapy is also recommended in areas where resistant to clarithromycin is seen. Bismuth quadruple therapy includes PPIs, bismuth, tetracycline and nitroimidazole for 10 to 14 days.

- ✓ Medication that protects the lining of the stomach and small intestine: cytoprotective agents like sucralfate and misoprostol helps protect the tissues that line the stomach and small intestine.

  Sucralfate – is a gastro duodenal protective agent used in the treatment of gastric and duodenal ulcer

  Mechanism of action – it increases the tissue level of fibroblast growth factor and epidermal growth factor leading to increase in prostaglandin at the gastro intestinal lining which promotes healing of gastrointestinal ulcer. Sucralfate has also been shown to absorb bile salt in the laboratory which further contribute to its beneficial in ulcer healing.

  Side effect – bloated, constipation, diarrhoea, black ache, gas in the stomach, headache.

  Misoprostol – is a Prostaglandin E1 analogue used to reduce the risk of NSAIDs induced gastric ulcer.

  Mechanism of action – stimulate the prostaglandin E1 receptor in the parietal cell in the stomach to reduce gastric acid secretion. Mucus and bicarbonate secretion are also increased along with the thickening of the mucosal bilayer.

  Side effect – Diarrhoea, headache, constipation, gas, vomiting, Indigestion.

- ✓ Surgical: The rate of surgical procedure for the peptic ulcer disease has been declining but highly selective or parietal cell vagotomy is still used is rare. Duodenal ulcer is more likely to be operated on. Surgery includes removing ulcer, tying off bleeding blood vessels, sewing tissue from another site onto the ulcer and cutting the nerve that controls stomach acid production.
- ✓ Remedies for ulcer:

- Probiotic: Which include yogurt, fermented food and all have living organism that help restore balance to the bacteria in the digestive tract which help with treating ulcer. When taken alongside with other treatment help eradicate harmful bacteria.
- Ginger: Studies have suggested that ginger can help with gastric ulcer caused by H. Pylori bacteria. Eating ginger may also prevent ulcer caused by NSAIDs.
- Colourful fruits: They contain flavonoid which help with stomach ulcer. They protect the stomach lining from developing ulcer by increasing stomach mucus. Flavonoid also have antioxidant properties.

- Honey: Manuka honey has antimicrobial effect against H. Pylori. Therefore, can be useful for treating stomach ulcer.
- Turmeric: It is a popular spice used all over India. They contain curcumin which has anti-inflammatory and antioxidant activities which help to prevent stomach ulcer.
- Licorice: Popular spice that is native to the Mediterranean region and Asia. Some people believe that eating dried licorice root can help and cure peptic ulcer. Study have found that taking licorice supplement can help fight H. Pylori infection by preventing the bacteria from growing.

6. Conclusion:

As we know that peptic ulcer is a common digestive disease where a sore or a lesion is formed on the lining of the stomach caused due to gastric acid and decrease in the mucosal defence. And the common reason for the formation of peptic ulcer is because of NSAIDs as they inhibit prostaglandin which is responsible to stimulate mucus and bicarbonate ion, and H. Pylori which break down ammonium ion to ammonia and inhibit D-cell which are responsible to decrease gastric acid. Treatment is also there to relive a person from pain and cure a person like Antacid such as Magnesium carbonate, Sodium bicarbonate and some treatment which we can do from home like regularly taking Yogurt (Probiotic), taking colourful fruits, Turmeric, etc. but if we consume alcohol, smoke, or take spicy food it can make ulcer worse or slow down the healing process. If a person is showing serious symptoms like blood in the stool the person needs to visit a physician.

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