

Gastro Esophageal Reflux Disease

Sudhakar Yadavalli¹, Umesh Godugu², Bandhavi Katukojwala³

¹Associate professor, Department of pharmacy practice, Vaagdevi pharmacy college

²Student of M. Pharm, Department of pharmacology, Vaagdevi pharmacy college

³Student of Pharm.D, Department of pharmacy practice, Vaagdevi pharmacy college

ABSTRACT:

Gastroesophageal Reflux Disease (GERD) is a common and chronic condition characterized by the backflow of stomach contents into the esophagus, leading to symptoms such as heartburn, regurgitation, and chest pain. It is a multifactorial disorder, with risk factors including obesity, smoking, and certain lifestyle habits, as well as anatomical and physiological factors such as lower esophageal sphincter dysfunction and hiatal hernia. GERD can significantly impact quality of life and, if left untreated, may lead to serious complications such as esophagitis, strictures, and even esophageal cancer. This review article provides an overview of the pathophysiology, clinical presentation, diagnostic approaches, and management strategies for GERD. A focus is placed on the role of proton pump inhibitors (PPIs) in treatment, alongside alternative therapies and lifestyle modifications. The review also discusses the emerging understanding of the relationship between GERD and extra-esophageal manifestations, including respiratory and dental complications.

Keywords: Gastroesophageal Reflux Disease (GERD), esophagus, heartburn, regurgitation, and chest pain, and proton pump inhibitors (PPIs).

INTRODUCTION:

Gastroesophageal reflux disease (GERD) is a chronic upper gastro intestinal disease characterized by the reflux or backward flow of stomach contents into the esophagus, leading to symptoms and/or complications. It is also called as acid reflux disease. GERD is a common gastrointestinal disorder that affects millions of individuals worldwide. It is characterized by the frequent occurrence of gastroesophageal reflux (GER), where stomach contents, including acid, flow back into the esophagus. This condition is not merely a nuisance; it can lead to significant discomfort and long-term health complications^[1]. The esophagus, a muscular tube connecting the throat to the stomach, relies on the lower esophageal sphincter (LES) to maintain a one-way flow of food and prevent reflux. In GERD, this sphincter does not function properly, allowing gastric acids to irritate the esophageal lining. As a result, patients may experience symptoms ranging from mild heartburn to severe chest pain, often affecting their daily activities and overall quality of life^[2]. It is often underdiagnosed, as many individuals do not seek medical attention for symptoms, they consider typical or manageable. However, chronic GERD can lead to serious complications, including esophagitis, strictures, Barrett's esophagus, and even esophageal cancer. The multifactorial nature of GERD underscores the importance of a comprehensive understanding of its causes, symptoms, diagnostic methods, and treatment options^[3].

EPIDEMIOLOGY:

GERD is one of the most prevalent gastrointestinal disorders worldwide, with varying incidence and prevalence rates reported across different populations^[4]. The prevalence of GERD has been rising globally, attributed to lifestyle factors such as dietary habits, obesity, sedentary lifestyles, and increased stress levels. Estimates suggest that GERD affects approximately 10-20% of the adult population in Western countries, while the prevalence may be lower in Asian countries, typically ranging from 5-10%^[5]. The variation in prevalence can be attributed to dietary habits, lifestyle factors, and genetic predispositions. GERD can occur at any age, but it is more common in adults. The prevalence tends to increase with age, particularly in individuals over 40 years old. Gender differences have also been observed; males generally report higher rates of GERD compared to females. However, after menopause, the prevalence in females may increase due to hormonal changes^[6].

ETIOLOGY:

Gastroesophageal reflux disease (GERD) is primarily caused by the malfunction of the mechanisms that prevent the backflow of gastric contents into the esophagus. The underlying causes can be classified into anatomical, physiological, lifestyle, and other contributing factors.

- **Lower Esophageal Sphincter Dysfunction:** The lower esophageal sphincter (LES) is a critical structure that normally maintains a high-pressure zone to prevent reflux. Dysfunction may occur due to structural abnormalities or a reduction in muscle tone, leading to impaired closure of the LES. The LES may also experience transient relaxations that are not associated with swallowing, allowing gastric contents to escape into the esophagus. These relaxations are a significant contributor to reflux episodes^[7].
- **Esophageal Motility Disorders:** The esophagus relies on coordinated muscular contractions to push food toward the stomach. Disorders that disrupt this motility, such as achalasia or scleroderma, can lead to ineffective clearance of refluxed material, increasing the risk of GERD. A slower esophageal clearance rate means that refluxed contents linger longer in the esophagus, potentially causing more damage^[8].
- **Gastric Factors:** Conditions such as obesity and pregnancy can raise intra-abdominal pressure, contributing to reflux by pushing stomach contents up into the esophagus. If the stomach takes longer to empty its contents, it can lead to an increased volume and pressure within the stomach, further promoting reflux^[9].
- **Hiatal Hernia:** A hiatal hernia occurs when a portion of the stomach protrudes through the diaphragm into the thoracic cavity. This anatomical change can disrupt the normal function of the LES, increasing the likelihood of reflux^[10].
- **Lifestyle and Dietary Factors:** Certain foods and beverages—such as fatty foods, chocolate, caffeine, citrus, and spicy dishes—can relax the LES or increase gastric acidity, exacerbating GERD symptoms. Smoking and excessive alcohol consumption can contribute to GERD by relaxing the LES and affecting esophageal motility. Additionally, obesity is a significant risk factor, as excess weight can increase abdominal pressure^[11].
- **Hormonal Influences:** Hormonal changes, particularly during pregnancy, can relax the LES due to the influence of progesterone. This can result in increased reflux symptoms among pregnant individuals^[12].

- **Neurological Factors:** Conditions affecting the nervous system may alter the normal function of the esophagus, including its motility and sensory perception. Neurological disorders can lead to dysphagia (difficulty swallowing) and may predispose individuals to GERD^[13].
- **Genetic and Environmental Factors:** Genetic predisposition plays a role in determining an individual's susceptibility to GERD. GERD risk has been closely linked to a number of single-nucleotide polymorphisms in several genes, including DNA repair, anti-inflammatory cytokine, MHC, CCND1, and FOXF1. Family history may contribute to the likelihood of developing the condition. Environmental factors, such as stress, may exacerbate symptoms or influence dietary habits^[14].

CLINICAL PRESENTATION:

Gastroesophageal Reflux Disease (GERD) is characterized by the retrograde flow of gastric contents into the esophagus, leading to a spectrum of symptoms and potential complications. The clinical presentation of GERD can be broadly categorized into typical and atypical symptoms^[15].

TYPICAL SYMPTOMS:

- **Heartburn:** The most common symptom, often described as a burning sensation behind the sternum, usually occurring after meals or at night. It commonly occurs after meals, when bending over, or while lying down, particularly at night. Patients often report that certain foods, such as spicy or fatty items, exacerbate the sensation. This symptom results from irritation of the esophageal mucosa due to acid exposure, often related to lower esophageal sphincter (LES) dysfunction^[16].
- **Regurgitation:** A sour or bitter taste in the mouth due to the backflow of stomach contents. May be accompanied by a feeling of food "sticking" in the throat. Regurgitation may occur due to increased intra-abdominal pressure or a weak LES, allowing gastric contents to flow back into the esophagus^[17].
- **Dysphagia:** Dysphagia refers to difficulty swallowing, which can manifest as a sensation of food getting stuck in the throat or chest. Difficulty swallowing, which may result from inflammation or strictures in the esophagus due to chronic acid exposure^[18].
- **Chest Pain:** Some individuals may experience chest pain that mimics cardiac pain. This discomfort can be acute and severe, leading to significant anxiety. It's crucial to differentiate this from cardiac-related pain through appropriate evaluation, as misdiagnosis can have serious implications^[19].

ATYPICAL SYMPTOMS:

- **Chronic Cough:** A persistent cough can develop, often worse at night. It may be dry or productive, and patients might notice it is triggered by lying down. This may be due to aspiration of refluxed material into the airway or a reflex mechanism linked to esophageal irritation^[20].
- **Laryngitis:** Inflammation of the larynx, leading to hoarseness or voice changes. GERD can cause laryngeal irritation, leading to hoarseness, throat clearing, or a sensation of a lump in the throat (globus sensation).
- **Asthma Exacerbations:** GERD can worsen asthma symptoms or trigger new episodes, potentially due to aspiration or vagal reflexes. Individuals with asthma may find that their symptoms worsen with GERD, potentially due to refluxed acid irritating the airways or triggering bronchospasms. Addressing both GERD and asthma is important for effective treatment and symptom control. GERD can worsen asthma symptoms or trigger new episodes, potentially due to aspiration or vagal reflexes^[21].

- **Dental Erosion:** The acidic nature of regurgitated gastric contents can lead to dental erosion over time, impacting oral health. Erosion of dental enamel may occur due to exposure to acidic gastric contents. Dentists may notice wear on tooth enamel, particularly on the surfaces that are commonly exposed to acidic content.
- **Nausea and Vomiting:** Although less common, some patients report nausea and occasional vomiting, particularly after meals or when lying down. This may stem from the irritation of the gastric lining or delayed gastric emptying.

ALARM SYMPTOMS:

Patients should be evaluated urgently if they present with alarm symptoms, which may indicate complications or alternative diagnoses. These include:

- **Unexplained weight loss:** This could signal an underlying malignancy or severe dysphagia.
- **Dysphagia or odynophagia (painful swallowing):** Severe swallowing difficulties or pain warrant further investigation.
- **Gastrointestinal bleeding:** This may present as vomiting blood or melena (black, tarry stools), indicating significant mucosal damage.
- **Anemia:** Can result from chronic blood loss due to esophageal erosion or ulcers^[22].

DIAGNOSIS:

Gastroesophageal reflux disease (GERD) is characterized by the chronic backflow of stomach contents into the esophagus, leading to symptoms like heartburn and regurgitation, as well as potential complications such as esophagitis, strictures, and Barrett's esophagus. Accurate diagnosis is essential for effective management^[23].

- **Endoscopy:** Esophagogastroduodenoscopy (EGD) is performed to visualize the esophagus and stomach. It helps identify complications like esophagitis, Barrett's esophagus, or strictures. Endoscopy is particularly important in patients with alarm symptoms (e.g., dysphagia, odynophagia, weight loss, or gastrointestinal bleeding). The patient is set for 12 hours of fasting after which the test is performed. It is a procedure to examine the upper part of the digestive tract with a narrow, flexible tube with a light and a small video camera attached to the tube^[24].
- **Esophageal pH Monitoring:** 24-hour pH monitoring is the gold standard for confirming acid reflux. A catheter is placed in the esophagus to measure pH levels over a 24-hour period. A positive result typically shows pH levels dropping below 4 for a significant portion of the monitoring period. This test helps differentiate GERD from other conditions, especially in patients with atypical symptoms^[25].
- **Esophageal Manometry:** This test measures esophageal motility and sphincter function. It can help assess whether a motility disorder is contributing to symptoms. Decreased lower esophageal sphincter (LES) pressure can be indicative of GERD^[26].
- **Imaging Studies:** While not routinely used for GERD diagnosis, studies like ultra sound of abdomen, CECT- scan of abdomen can help identify structural abnormalities such as hiatal hernias and metastasis of cancer.

Differential Diagnosis:

It's crucial to differentiate GERD from other conditions that may present similarly, such as:

- Functional dyspepsia

- Esophageal motility disorders (e.g., achalasia, nutcracker esophagus)
- Cardiac conditions
- Peptic ulcer disease^[27].

TREATMENT:

Treatment for GERD is multifaceted, encompassing lifestyle modifications, pharmacological therapies, and surgical interventions. The choice of treatment is influenced by the severity of symptoms, the presence of esophageal damage, and individual patient factors. While lifestyle changes and over-the-counter medications can alleviate symptoms in many cases, more severe manifestations may require prescription medications or surgical options to provide lasting relief.

LIFESTYLE MODIFICATIONS:

- Avoid trigger foods such as fatty foods, chocolate, caffeine, spicy foods, citrus fruits, and carbonated beverages.
- Encouraging smaller, more frequent meals can also help reduce symptoms.
- Losing weight can significantly decrease the frequency and severity of reflux symptoms, particularly in overweight individuals.
- Raising the head of the bed by 6-8 inches can help prevent nighttime reflux.
- Avoid smoking and alcohol. Both smoking and alcohol can relax the lower esophageal sphincter (LES), exacerbating symptoms.
- Avoid eating 2-3 hours before bedtime can reduce night time reflux.
- In pregnancy (>7 months and postpartum) increase the frequency of meal to decrease the pressure on stomach.
- Avoid drugs like calcium channel blockers, NSAID's, opioids, anti – depressants which causes increase in gastric acid secretions^[28].

PHARMACOLOGICAL TREATMENTS

Antacids: Over-the-counter medications like aluminium hydroxide, magnesium hydroxide, and calcium carbonate provide quick relief by neutralizing stomach acid. However, they do not heal the esophagus or prevent reflux. They act by neutralizing the acid in the stomach and by inhibiting pepsin, which is a proteolytic enzyme and decreases the heart burn^[29].

H₂-Receptor Antagonists: Medications such as ranitidine, cimetidine, famotidine and nizatidine (Dose: 20 to 120mg in tablet and IV form) reduce acid production and are effective for mild to moderate GERD. They can be used as needed or on a regular basis. It will prevent the gastric acid secretion by binding to H₂ receptors in gastric parietal cells in stomach^[30].

Proton Pump Inhibitors (PPIs): Drugs like pantoprazole, omeprazole, esomeprazole, and lansoprazole (Dose: 20mg, 40mg, 80mg in tablet and IV form) are more effective for healing esophagitis and controlling symptoms. They inhibit acid production and are the first-line treatment for moderate to severe GERD. Long-term use requires monitoring due to potential side effects such as vitamin B12 deficiency and increased risk of fractures. PPI's binds to H⁺/K⁺ exchanging ATPase (proton pump) in gastric parietal cells, resulting in blockage of acid secretion^[31].

SURGICAL INTERVENTIONS

Fundoplication: The most common surgical treatment, where the top of the stomach is wrapped around the lower esophagus to reinforce the LES. This procedure can be performed laparoscopically, resulting in shorter recovery times. Fundoplication is a surgical procedure designed to treat gastroesophageal reflux disease (GERD) by reinforcing the lower esophageal sphincter (LES). This technique involves wrapping the top portion of the stomach (the fundus) around the lower esophagus, thereby enhancing the barrier against acid reflux. It is typically considered for patients with severe GERD who do not respond to conservative measures or pharmacological treatment^[32].

Transoral Incisionless Fundoplication (TIF): Transoral Incisionless Fundoplication (TIF) is a minimally invasive surgical procedure designed to treat gastroesophageal reflux disease (GERD). Unlike traditional fundoplication techniques, which often require abdominal incisions, TIF is performed through the mouth, offering a less invasive alternative with potentially quicker recovery times and fewer complications. TIF is indicated for:

- Adults with chronic GERD symptoms not adequately controlled by medical therapy, especially PPIs.
- Patients with esophagitis or Barrett's esophagus seeking surgical intervention.
- Individuals who prefer a minimally invasive option and wish to avoid traditional fundoplication^[33].

CONCLUSION:

Gastroesophageal reflux disease (GERD) is a prevalent condition characterized by the chronic regurgitation of stomach contents into the esophagus, leading to a range of symptoms and potential complications. Its multifactorial etiology includes factors such as diet, lifestyle, and anatomical abnormalities. Effective management strategies encompass lifestyle modifications, pharmacotherapy, and, in some cases, surgical interventions. Continued research into the pathophysiology of GERD is essential for the development of novel therapeutic approaches. Overall, a comprehensive understanding of GERD is crucial for improving patient outcomes and enhancing quality of life. Future directions should focus on personalized treatment plans and the exploration of emerging therapies to address this widespread health issue.

REFERENCES:

1. Kahrilas PJ. GERD pathogenesis, pathophysiology, and clinical manifestations. *Cleveland Clinic journal of medicine*. 2003 Nov 5;70(5):S4.
2. Oezcelik A, DeMeester SR. General anatomy of the esophagus. *Thoracic surgery clinics*. 2011 May 1;21(2):289-97.
3. Falk GW. Barrett's esophagus. *Gastroenterology*. 2002 May 1;122(6):1569-91.
4. Wong BC, Kinoshita Y. Systematic review on epidemiology of gastroesophageal reflux disease in Asia. *Clinical gastroenterology and hepatology*. 2006 Apr 1;4(4):398-407.
5. Boulton KH, Dettmar PW. A narrative review of the prevalence of gastroesophageal reflux disease (GERD). *Annals of Esophagus*. 2022 Mar 25;5.
6. Richter JE, Rubenstein JH. Presentation and Epidemiology of Gastroesophageal Reflux Disease. *Gastroenterology*. 2018 Jan;154(2):267-276. doi: 10.1053/j.gastro.2017.07.045. Epub 2017 Aug 3. PMID: 28780072; PMCID: PMC5797499.

7. Holloway RH, Dent J. Pathophysiology of gastroesophageal reflux: lower esophageal sphincter dysfunction in gastroesophageal reflux disease. *Gastroenterology clinics of North America*. 1990 Sep 1;19(3):517-35.
8. Kahrilas PJ, Bredenoord AJ, Carlson DA, Pandolfino JE. Advances in management of esophageal motility disorders. *Clinical Gastroenterology and Hepatology*. 2018 Nov 1;16(11):1692-700.
9. Argyrou A, Legaki E, Koutserimpas C, Gazouli M, Papaconstantinou I, Gkiokas G, Karamanolis G. Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. *World journal of clinical cases*. 2018 Aug 8;6(8):176.
10. Kahrilas PJ. The role of hiatus hernia in GERD. *The Yale journal of biology and medicine*. 1999 Mar;72(2-3):101.
11. Newberry C, Lynch K. The role of diet in the development and management of gastroesophageal reflux disease: why we feel the burn. *Journal of thoracic disease*. 2019 Aug;11(Suppl 12):S1594.
12. Argyrou A, Legaki E, Koutserimpas C, Gazouli M, Papaconstantinou I, Gkiokas G, Karamanolis G. Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. *World journal of clinical cases*. 2018 Aug 8;6(8):176.
13. Vandenplas Y, Hassall E. Mechanisms of gastroesophageal reflux and gastroesophageal reflux disease. *Journal of pediatric gastroenterology and nutrition*. 2002 Aug 1;35(2):119-36.
14. Argyrou A, Legaki E, Koutserimpas C, Gazouli M, Papaconstantinou I, Gkiokas G, Karamanolis G. Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. *World journal of clinical cases*. 2018 Aug 8;6(8):176.
15. Richter JE. Typical and atypical presentations of gastroesophageal reflux disease: the role of esophageal testing in diagnosis and management. *Gastroenterology Clinics*. 1996 Mar 1;25(1):75-102.
16. Ang D, Sifrim D, Tack J. Mechanisms of heartburn. *Nature clinical practice Gastroenterology & hepatology*. 2008 Jul;5(7):383-92.
17. Orenstein S. Regurgitation & GERD. *Journal of pediatric gastroenterology and nutrition*. 2001 Apr 1;32:S16-8.
18. Wilkinson JM, Codipilly DC, Wilfahrt RP. Dysphagia: evaluation and collaborative management. *American Family Physician*. 2021 Jan 15;103(2):97-106.
19. Hershcovici T, Achem SR, Jha LK, Fass R. Systematic review: the treatment of noncardiac chest pain. *Alimentary pharmacology & therapeutics*. 2012 Jan;35(1):5-14.
20. Wu J, Ma Y, Chen Y. GERD-related chronic cough: Possible mechanism, diagnosis and treatment. *Frontiers in Physiology*. 2022 Oct 20;13:1005404.
21. McCallister JW, Parsons JP, Mastronarde JG. The relationship between gastroesophageal reflux and asthma: an update. *Therapeutic advances in respiratory disease*. 2011 Apr;5(2):143-50.
22. Wo JM. Alarm symptoms of GERD. *Current GERD Reports*. 2007 Dec;1(4):215-9.
23. Gyawali CP, Kahrilas PJ, Savarino E, Zerbib F, Mion F, Smout AJ, Vaezi M, Sifrim D, Fox MR, Vela MF, Tutuian R. Modern diagnosis of GERD: the Lyon Consensus. *Gut*. 2018 Jul 1;67(7):1351-62.
24. Muthusamy VR, Lightdale JR, Acosta RD, Chandrasekhara V, Chathadi KV, Eloubeidi MA, Fanelli RD, Fonkalsrud L, Faulx AL, Khashab MA, Saltzman JR. The role of endoscopy in the management of GERD. *Gastrointestinal endoscopy*. 2015 Jun 1;81(6):1305-10.
25. Sifrim D, Fornari F. Esophageal impedance-pH monitoring. *Digestive and Liver Disease*. 2008 Mar 1;40(3):161-6.

26. Mello M, Gyawali CP. Esophageal manometry in gastroesophageal reflux disease. *Gastroenterology Clinics*. 2014 Mar 1;43(1):69-87.
27. Manabe N, Tanaka S, Sasaki A, Hata J, Haruma K, Chayama K. Differential diagnosis of GERD. *Nihon rinsho. Japanese Journal of Clinical Medicine*. 2004 Aug 1;62(8):1492-7.
28. Festi D, Scaiola E, Baldi F, Vestito A, Pasqui F, Di Biase AR, Colecchia A. Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. *World journal of gastroenterology: WJG*. 2009 Apr 4;15(14):1690.
29. Ching CK, Lam SK. Antacids: indications and limitations. *Drugs*. 1994 Feb;47:305-17.
30. Keithley JK. Histamine H₂-receptor antagonists. *Nursing Clinics of North America*. 1991 Jun 1;26(2):361-73.
31. Dekel R, Morse C, Fass R. The role of proton pump inhibitors in gastro-oesophageal reflux disease. *Drugs*. 2004 Feb;64:277-95.
32. Frazzoni M, Piccoli M, Conigliaro R, Frazzoni L, Melotti G. Laparoscopic fundoplication for gastroesophageal reflux disease. *World journal of gastroenterology: WJG*. 2014 Oct 10;20(39):14272.
33. Chang KJ, Bell R. Transoral incisionless fundoplication. *Gastrointestinal Endoscopy Clinics*. 2020 Apr 1;30(2):267-89.