

# Gastroesophageal Reflux Disease (Gerd): Review Article

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## Abstract

**Background:** Millions of people across the world suffer from the common clinical illness known as gastroesophageal reflux disease (GERD). Symptoms that are both common and unique can be used to identify patients. Many GERD patients receive therapeutic relief with acid suppression therapy, which also shields them from harmful side effects.

**Objective:** The review's primary goal is to highlight diagnostic and therapeutic approaches for manage and treating gastroesophageal reflux disease.

**Methods:** We looked for data on [Gastroesophageal Reflux Disease, Diagnosis, Complications Treatment] at PubMed, Google Scholar, and Science Direct. However, only the most recent or extensive study was taken into account between August 1999 and Jun 2019. References from related works were also evaluated by the writers. There are not enough resources to translate documents into languages other than English, hence those documents have been ignored. It was generally agreed that documents such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations did not qualify as legitimate scientific study.

**Conclusion:** GERD is a frequent clinical issue that is associated with severe morbidity and a possible decline in quality of life. The prevention of GERD consequences depends on early diagnosis of symptoms. Its management continues to depend on behavioural adjustments and developments in acid suppression.

**Keywords:** Gastroesophageal Reflux Disease, Diagnosis, Complications Treatment.

## INTRODUCTION

A persistent digestive illness called GERD is defined by the regurgitation of the oesophagus with stomach contents. With a frequency of 20%, it is one of the most often diagnosed digestive illnesses in the US, causing a major financial burden in direct and indirect expenditures and negatively affecting quality of life [1, 2].

The esophagogastric junction barrier is disrupted in GERD due to a variety of causes that might be intrinsic, structural, or both. As a result, the oesophagus is exposed to acidic gastric contents. Clinically, GERD frequently presents with symptoms of regurgitation and heartburn. Additionally, it may exhibit unusual extra-esophageal symptoms as chest discomfort, tooth erosions, a persistent cough, laryngitis, or asthma[3–4].

GERD is divided into three distinct phenotypes with reference to endoscopic and histopathologic appearance: non-erosive reflux disease (NERD), erosive esophagitis (EE), and Barrett oesophagus (BE)[5]. In 60–70% of patients, NERD is the most common phenotype, followed by BE and erosive esophagitis in 30% and 6-12% of GERD patients, respectively. [5-6].

Proton pump inhibitors and dietary changes have been the cornerstones of GERD care over time (PPIs). However, medically resistant GERD is growing more prevalent and must be managed with a customised strategy [6].

## HISTORY AND PHYSICAL

Regurgitation and heartburn are the usual clinical signs of GERD. But in addition to these symptoms, GERD can also manifest as dysphagia, odynophagia, belching, epigastric discomfort, and nausea. A retrosternal burning feeling or pain

known as heartburn is described as something that often happens after eating or when lying down. It may also radiate into the neck. Acidic stomach contents might migrate backward into the mouth or hypopharynx during regurgitation. Patients who report with extraesophageal symptoms of GERD, such as chest discomfort, a persistent cough, asthma, laryngitis, dental erosions, hoarseness, dysphonia, and globus feeling, are deemed to have an unusual GERD presentation[3–4].

## ETIOLOGY

At this time, the cause of GERD is unknown. Over time, numerous risk factors have been identified and connected to the emergence of GERD. Esophageal dysmotility, which hinders esophageal acid clearance, impaired lower esophageal sphincter (LES) tone, transitory LES relaxation, and delayed stomach emptying are some of the motor abnormalities that contribute to GERD [7]. An higher risk of GERD is associated with anatomical factors like a hiatal hernia or an increase in intra-abdominal pressure, which is seen in obesity [7].

Additional risk factors that have been independently linked to the emergence of GERD symptoms include age 50 years, low socioeconomic status, tobacco use, excessive alcohol consumption, connective tissue disorders, pregnancy, postprandial supination, and various drug classes such as anticholinergic drugs, benzodiazepines, NSAID or aspirin use, nitroglycerin, albuterol, calcium channel blockers, antidepressants, and glucagon [8-12].

## PATHOPHYSIOLOGY

The major cause of gastroesophageal reflux disease (GERD) is the failure of the lower esophageal sphincter (LES), however other variables may also play a role in the onset of the disorder. Physiological and pathologic variables both have a role in the emergence of GERD. The most frequent cause is transient relaxations of the lower esophageal sphincter (TLESRs). TLESRs are transient episodes of lower esophageal sphincter relaxation [10]. Even though they are common in the postprandial period and are natural, they significantly contribute to acid reflux in GERD patients. Possible causes include hiatal hernias, inadequate esophageal clearance, decreased lower esophageal sphincter (LES) pressure, and postponed stomach emptying [8, 11].

## SYMPTOMS

The traditional and most prevalent symptom of GERD is heartburn. Heartburn is a burning sensation in the chest that can also travel to the mouth and is brought on by acid reflux into the oesophagus. However, only a very small percentage of reflux events are symptomatic. A sour taste in the back of the mouth is another typical heartburn symptom, along with regurgitation of the refluxate. Notably, GERD frequently results in non-cardiac chest pain [12–13]. Due to the potentially significant consequences of cardiac chest pain and the variety of diagnostic and therapeutic algorithms based on aetiology, it is crucial to identify the underlying cause of the chest pain. In individuals with non-cardiac chest discomfort, a thorough clinical history may reveal GERD symptoms, pointing to GERD as a probable explanation [13].

Extraesophageal manifestations of GERD are widespread but less frequently diagnosed, despite the fact that basic GERD symptoms are simple to identify. Extraesophageal symptoms like hoarseness and throat clearing are more frequently caused by reflux into the larynx. The globus sensation, often known as a sense of fullness or a lump at the back of the throat, is a typical complaint among GERD patients[14]. Although the exact aetiology of globus is unknown, it is believed that exposure to acid in the hypopharynx increases the tonicity of the upper esophageal sphincter (UES). Acid reflux may also cause bronchospasm, which can aggravate underlying asthma and cause coughing, dyspnea, and wheezing. Chronic nausea and vomiting have been reported in certain GERD patients [14–15].

In order to prompt an endoscopic evaluation, patients should be examined for GERD warning symptoms. Alarming symptoms could be a sign of malignancy. An upper endoscopy is not required when GERD symptoms are present. Endoscopy is nevertheless advised for screening and when alarm symptoms exist those who are at high risk for issues (such as those with Barrett's oesophagus, particularly those who have frequent and/or chronic symptoms, are older than 50, are Caucasian, and have central obesity). The frightening symptoms of dysphagia (difficulty swallowing) and odynophagia (painful swallowing) may point to conditions including strictures, ulceration, and/or malignancy. Other red flags and symptoms include anaemia, bleeding, and weight loss[16].

Distinguishing dyspepsia from GERD symptoms is important. Epigastric pain lasting more than a month without heartburn or acid regurgitation is a symptom of dyspepsia. Possible adverse effects include bloating, epigastric fullness, belching, nausea, and vomiting. The treatment for dyspepsia may differ from that for GERD and may include an endoscopic evaluation and H. pylori tests [17].

## HISTOPATHOLOGY

The oesophagus squamous epithelium acts as a preventive defensive barrier to stop refluxate from migrating backward. In GERD and NERD, disruption of this epithelial defence is a frequent occurrence [18]. Due to varied sensitivity and specificity in the diagnosis and low biopsy criteria for diagnosis, the histological characteristics of GERD are not specific to this condition[19]. In actuality, a number of microscopic findings, including signs of inflammation, basal cell hyperplasia, papilla elongation, and intercellular space dilatation, are used to make the histopathologic diagnosis of GERD[20].

## COMPLICATIONS

### A. Erosive Esophagitis (EE)

Esophageal mucosa erosions or ulcers are symptoms of EE[21]. Patients may appear with no symptoms or increasing GERD symptoms. The Los Angeles esophagitis classification system employs the A, B, C, and D grading system based on factors such the length, location, and circumferential severity of mucosal breaches in the oesophagus for endoscopic evaluation of the degree of esophagitis [22].

### B. Esophageal Strictures

A peptic stricture can develop as a result of chronic acid irritation of the distal oesophagus, which can cause scarring. Patients may exhibit signs of food impaction or esophageal dysphagia. To avoid the need for further esophageal dilations, the ACG recommendations advise esophageal dilatation and continued PPI medication [23].

### C. Barrett Esophagus

Chronic exposure to pathogenic acid damages the distal esophageal mucosa, resulting in this condition. In the normal state, the stratified squamous epithelium lines the distal esophageal mucosa, undergoes a histological alteration and becomes metaplastic columnar epithelium. Barrett's oesophagus increases the risk of esophageal cancer development and is more frequently found in Caucasian males over 50, obese, and smokers[24]. Patients with a diagnosis of Barrett's oesophagus are advised to undergo routine surveillance endoscopy on a regular basis[25].

## DIAGNOSIS

When the typical symptoms of GERD are present, the diagnosis is often made[26–27]. People who have reflux may not exhibit any symptoms, and reflux of stomach contents must also be present for the diagnosis to be made [28].

Esophagogastroduodenoscopy is one possible further inquiry (EGD). Diagnostic purposes should not be served by barium swallow X-rays [27]. Esophageal manometry is only advised before surgery; it is not advised for use in the diagnosis. Ambulatory esophageal pH monitoring is not required in patients with Barrett's oesophagus but may be helpful in those who do not improve following PPIs. Most of the time, testing for *H. pylori* is not necessary [27].

Esophageal pH monitoring is the current gold standard for the diagnosis of GERD. It provides for tracking of GERD patients' responses to medication or surgical therapy and is the most accurate test to detect reflux disease. Proton-pump inhibitors are one method for diagnosing GERD, with improvement in symptoms indicating a successful diagnosis. In individuals with symptoms indicative of GERD, short-term therapy with proton-pump inhibitors may help anticipate aberrant 24-hour pH monitoring findings [28].

## TREATMENT / MANAGEMENT

The objectives of GERD management are to deal with symptom relief and avoid complications including esophagitis, BE, and esophageal cancer. Changes in lifestyle, medical care with antacids and antisecretory drugs, surgical treatments, and endoluminal therapies are all possible forms of treatment.

### Lifestyle Modifications

The core component of any GERD treatment is thought to be lifestyle changes. The relevance of weight loss should be discussed with patients given that studies have linked weight gain in persons with a normal BMI with the onset of GERD symptoms and that underlying obesity is a substantial risk factor for the development of GERD [29]. Because it has been demonstrated that minimum sleep interruptions are associated with the suppression of TLESRs, resulting in fewer reflux episodes, people should also be counselled about avoiding meals at least three hours before bedtime and practising great sleep hygiene[30-33].

### Medical Therapy

Patients who do not react to lifestyle changes may consider medical treatment. Antacids, antisecretory drugs such as histamine (H<sub>2</sub>) receptor antagonists (H<sub>2</sub>RAs) or PPI therapy, and prokinetic drugs make up medical treatment. There are now two over-the-counter H<sub>2</sub>RAs that have been authorised by the US Food and Drug Administration (FDA): famotidine and cimetidine. Due to an unanticipated impurity in the active component, the other frequently used H<sub>2</sub>RA known as ranitidine has been recalled as a possible health risk or safety issue. Due to similar worries, the less well-known, prescription-only H<sub>2</sub>RA nizatidine has also been withdrawn. There are now six PPIs on the market in the United States, three of which are OTC (omeprazole, lansoprazole, and esomeprazole) and three of which are Rx-only (pantoprazole, dexlansoprazole, and rabeprazole). Based on several large-scale trials, PPI medication is thought to be the most effective treatment option for both erosive and non-erosive GERD. In addition, these trials have demonstrated superior symptom management, esophagitis healing, and lower recurrence rates when compared to H<sub>2</sub>RAs [34-35].

### **Surgical therapy and endoscopic Therapy**

Surgical intervention may be an option for patients who have GERD that is medically intractable, who are uncooperative or experiencing negative effects from medication, who have an underlying big hiatal hernia, or who want to stop receiving long-term medical care[36]. Laparoscopic Nissen fundoplication, Laparoscopic Anterior 180° Fundoplication (180° LAF), and bariatric surgery in obese individuals are the surgical treatments available for GERD[22]. As far as surgical care of GERD patients is concerned, laparoscopic Nissen fundoplication has been the gold standard. However, gastric bypass surgery is quickly replacing other surgical options for GERD due to the tremendous rise in obesity in the United States[22].

There are many different kinds of endoscopic treatments that have been created for the therapy of GERD in the era of minimally invasive surgical procedures. Due to their inability to show long-term efficacy, the most of them were abandoned. Magnetic sphincter augmentation (MSA) and transoral incision-free fundoplication utilising the EsophyX are two of the current endoluminal treatments that are accessible ([22]).

For people with severe symptoms who don't respond to existing therapies, the U.S. Food and Drug Administration (FDA) authorised the LINX in 2012. It comprises of a series of metal beads with magnetic cores that are surgically positioned around the lower esophageal sphincter. Although there is little information on long-term consequences, the Nissen fundoplication improves GERD symptoms in a manner comparable to that of that procedure. The surgery has demonstrated a decrease in frequent complications including gas bloat syndrome when compared to Nissen fundoplication surgeries [37]. Chest discomfort, nausea, vomiting, and trouble swallowing are examples of negative reactions. The use of the device is not recommended for those who are or may become allergic to titanium, stainless steel, nickel, or ferrous iron components. A caution states that patients who might undergo or be subjected to magnetic resonance imaging (MRI) should not use the equipment because doing so could cause serious harm to the patient and damage to the device [38].

## **CONCLUSION**

GERD is a frequent clinical issue that is associated with severe morbidity and a possible decline in quality of life. The prevention of GERD consequences depends on early diagnosis of symptoms. Changes in behaviour and technological advancements in acid suppression are still crucial to its therapy.

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## **REFERENCES**

1. Fass R, Frazier R. The role of dexlansoprazole modified-release in the management of gastroesophageal reflux disease. *Therap Adv Gastroenterol.* 2017 Feb;10(2):243-251.
2. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut.* 2014 Jun;63(6):871-80.
3. Hom C, Vaezi MF. Extraesophageal manifestations of gastroesophageal reflux disease. *Gastroenterol Clin North Am.* 2013 Mar;42(1):71-91.
4. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R., Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol.* 2006 Aug;101(8):1900-20; quiz 1943.
5. Fass R, Ofman JJ. Gastroesophageal reflux disease--should we adopt a new conceptual framework? *Am J Gastroenterol.* 2002 Aug;97(8):1901-9.
6. Fass R. Erosive esophagitis and nonerosive reflux disease (NERD): comparison of epidemiologic, physiologic, and therapeutic characteristics. *J Clin Gastroenterol.* 2007 Feb;41(2):131-7.

7. 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 J Clin Cases*. 2018 Aug 16;6(8):176-182.
8. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med*. 2005 Apr 02;143(3):199-211.
9. Malfertheiner P, Nocon M, Vieth M, Stolte M, Jaspersen D, Koelz HR, Labenz J, Leodolter A, Lind T, Richter K, Willich SN. Evolution of gastro-oesophageal reflux disease over 5 years under routine medical care--the ProGERD study. *Aliment Pharmacol Ther*. 2012 Jan;35(1):154-64.
10. El-Serag HB, Hashmi A, Garcia J, Richardson P, Alsarraj A, Fitzgerald S, Vela M, Shaib Y, Abraham NS, Velez M, Cole R, Rodriguez MB, Anand B, Graham DY, Kramer JR. Visceral abdominal obesity measured by CT scan is associated with an increased risk of Barrett's oesophagus: a case-control study. *Gut*. 2014 Feb;63(2):220-9.
11. Mohammed I, Nightingale P, Trudgill NJ. Risk factors for gastro-oesophageal reflux disease symptoms: a community study. *Aliment Pharmacol Ther*. 2005 Apr 01;21(7):821-7.
12. Eusebi LH, Ratnakumaran R, Yuan Y, Solaymani-Dodaran M, Bazzoli F, Ford AC. Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. *Gut*. 2018 Mar;67(3):430-440.
13. Patti MG. An Evidence-Based Approach to the Treatment of Gastroesophageal Reflux Disease. *JAMA Surg*. 2016 Jan;151(1):73-8.
14. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Prevalence of gastro-oesophageal reflux symptoms and the influence of age and sex. *Scand J Gastroenterol*. 2004 Nov;39(11):1040-5.
15. Kim SY, Jung HK, Lim J, Kim TO, Choe AR, Tae CH, Shim KN, Moon CM, Kim SE, Jung SA. Gender Specific Differences in Prevalence and Risk Factors for Gastro-Esophageal Reflux Disease. *J Korean Med Sci*. 2019 Jun 02;34(21):e158.
16. Lin M, Gerson LB, Lascar R, Davila M, Triadafilopoulos G. Features of gastroesophageal reflux disease in women. *Am J Gastroenterol*. 2004 Aug;99(8):1442-7.
17. Savarino E, Bredenoord AJ, Fox M, Pandolfino JE, Roman S, Gyawali CP., International Working Group for Disorders of Gastrointestinal Motility and Function. Expert consensus document: Advances in the physiological assessment and diagnosis of GERD. *Nat Rev Gastroenterol Hepatol*. 2017 Nov;14(11):665-676.
18. Kandulski A, Weigt J, Caro C, Jechorek D, Wex T, Malfertheiner P. Esophageal intraluminal baseline impedance differentiates gastroesophageal reflux disease from functional heartburn. *Clin Gastroenterol Hepatol*. 2015 Jun;13(6):1075-81.
19. Allende DS, Yerian LM. Diagnosing gastroesophageal reflux disease: the pathologist's perspective. *Adv Anat Pathol*. 2009 May;16(3):161-5.
20. Sandhu DS, Fass R. Current Trends in the Management of Gastroesophageal Reflux Disease. *Gut Liver*. 2018 Jan 15;12(1):7-16.
21. Kellerman R, Kintanar T. Gastroesophageal Reflux Disease. *Prim Care*. 2017 Dec;44(4):561-573.
22. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol*. 2013 Mar;108(3):308-28; quiz 329.
23. Numans ME, Lau J, de Wit NJ, Bonis PA. Short-term treatment with proton-pump inhibitors as a test for gastroesophageal reflux disease: a meta-analysis of diagnostic test characteristics. *Ann Intern Med*. 2004 Apr 06;140(7):518-27.
24. Hirano I, Richter JE., Practice Parameters Committee of the American College of Gastroenterology. ACG practice guidelines: esophageal reflux testing. *Am J Gastroenterol*. 2007 Mar;102(3):668-85.
25. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA. Body-mass index and symptoms of gastroesophageal reflux in women. *N Engl J Med*. 2006 Jun 01;354(22):2340-8.
26. Kahrilas PJ, Shaheen NJ, Vaezi MF, et al.. American Gastroenterological Association Medical Position Statement on the management of gastroesophageal reflux disease. *Gastroenterology*. 2008 Oct 135 (4): 1383–91.
27. Numans ME, Lau J, de Wit NJ, Bonis PA. Short-term treatment with proton-pump inhibitors as a test for gastroesophageal reflux disease: a meta-analysis of diagnostic test characteristics. *Annals of Internal Medicine*. 2004 Apr 140 (7): 518–27.
28. Fujiwara Y, Arakawa T, Fass R. Gastroesophageal reflux disease and sleep disturbances. *J Gastroenterol*. 2012 Jul;47(7):760-9.
29. Zhang JX, Ji MY, Song J, Lei HB, Qiu S, Wang J, Ai MH, Wang J, Lv XG, Yang ZR, Dong WG. Proton pump inhibitor for non-erosive reflux disease: a meta-analysis. *World J Gastroenterol*. 2013 Dec 07;19(45):8408-19.
30. Khan M, Santana J, Donnellan C, Preston C, Moayyedi P. Medical treatments in the short term management of reflux oesophagitis. *Cochrane Database Syst Rev*. 2007 Apr 18;(2):CD003244.
31. Chang P, Friedenber F. Obesity and GERD. *Gastroenterol Clin North Am*. 2014 Mar;43(1):161-73.
32. Garg SK, Gurusamy KS. Laparoscopic fundoplication surgery versus medical management for gastro-oesophageal reflux disease (GORD) in adults. *Cochrane Database Syst Rev*. 2015 Nov 05;2015(11):CD003243.
33. Gerson L, Stouch B, Lobonțiu A. Transoral Incisionless Fundoplication (TIF 2.0): A Meta-Analysis of Three Randomized, Controlled Clinical Trials. *Chirurgia (Bucur)*. 2018 Mar-Apr;113(2):173-184.

34. Skubleny D, Switzer NJ, Dang J, Gill RS, Shi X, de Gara C, Birch DW, Wong C, Hutter MM, Karmali S. LINX® magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease: a systematic review and meta-analysis. *Surg Endosc.* 2017 Aug;31(8):3078-3084.
35. Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, Johnson F, Hongo M, Richter JE, Spechler SJ, Tytgat GN, Wallin L. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut.* 1999 Aug;45(2):172-80.
36. Wang KK, Sampliner RE., Practice Parameters Committee of the American College of Gastroenterology. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. *Am J Gastroenterol.* 2008 Mar;103(3):788-97.
37. Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. *World Journal of Gastrointestinal Pharmacology and Therapeutics.* 2014 5(3): 105–12.
38. Medical Device Approvals: LINX Reflux Management System - P100049 Archived 10 November 2013 at the Wayback Machine, U.S. Food and Drug Administration, U.S. Department of Health and Human Services, Update of 17 January 2014