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Review Article

Overview of Gastroesophageal Reflux Disease (GERD)

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Abstract

Introduction: Gastroesophageal reflux disease is a common clinical problem that affects millions of people worldwide (GERD). Patients can be identified by both conventional and unusual symptoms. In addition to increasing the risk of esophagitis, esophageal strictures, Barrett esophagus, and esophageal cancer, GERD can affect a patient's quality of life. GERD risk factors include genetic predisposition, tobacco use, and obesity. The typical symptoms of GERD are frequent enough to make the diagnosis, but less typical symptoms and indications, like dysphagia and a persistent cough, can also manifest. A proton pump inhibitor can be used as an experimental treatment for patients with typical GERD symptoms (PPI). Endoscopy, esophageal pH monitoring, and esophageal manometry are advised for individuals who do not react to such treatment or if the diagnosis is not evident. Endoscopy should be performed on patients who have GERD symptoms together with other primary risk factors for esophageal adenocarcinomas, such as older age, male sex, and obesity. These symptoms could include dysphagia, weight loss, bleeding, or older age. The three primary types of treatment for GERD are lifestyle modifications, medications, and surgery. Quitting smoking and losing weight can both be beneficial. The most frequent form of treatment is a medication with a PPI, and after initial full-dosage therapy-typically omeprazole 20 mg once daily-the goal is to utilize the lowest effective dose.

Aim of the Study: The aim of the present review is to understand the various etiology, risk factors, diagnosis, and management of gastroesophageal reflux disease.

Methodology: The review is a comprehensive research of PUBMED from 1988 to 2022.

Conclusion: GERD is linked to severe morbidity and a potential reduction in quality of life. The prevention of GERD consequences depends on the early diagnosis of symptoms. Changes in behavior and technological advancements in acid suppression are still crucial to its therapy. The therapeutic treatment of GERD affects the lives of many individuals and greatly depletes societal and healthcare resources. Lifestyle changes, PPI medication, and surgical fundoplication are all forms of treatment. Endoscopic surgery is developing new, less intrusive techniques. Although proton pump inhibitors use is still the most popular treatment, long-term therapy necessitates monitoring and reevaluation for potential side effects.

Keywords: *GERD; Lifestyle Modifications; Management; PPI*

Introduction

A chronic digestive illness called gastroesophageal reflux disease (GERD) is defined by the regurgitation of stomach contents into the esophagus. With a prevalence 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 the quality of life. 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 esophagus is exposed to acidic gastric contents. Clinically, GERD frequently presents with symptoms of regurgitation and heartburn. Additionally, it can exhibit unusual extra-esophageal symptoms such as chest pain, tooth erosions, a persistent cough, laryngitis, or asthma. GERD is divided into three distinct phenotypes based on endoscopic and histopathologic appearance: non-erosive reflux disease (NERD), erosive esophagitis (EE), and Barrett esophagus (BE). 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 [1].

In North America, the prevalence of gastroesophageal reflux disease (GERD), a highly prevalent digestive illness, is estimated to be 18.1 - 27.8%. At some point, about half of people will report having GERD symptoms. GERD is a condition with bothersome side effects and symptoms brought on by the reflux of stomach contents into the esophagus. After an empiric trial, GERD is often diagnosed based on the presence of the characteristic symptoms and the patient's reaction to acid suppression. Due to lower quality of life and high morbidity, GERD is a health concern. Significant improvements in quality of life, such as reduced physical pain, greater vigor, physical and social function, and mental well-being, have been linked to effective treatment of GERD symptoms. Although GERD drugs are not exceptionally expensive, treating GERD patients has been estimated to be 2-times more expensive than treating similarly situated people who do not have GERD. The higher morbidity among GERD patients and the higher expense of managing the result of GERD that have been not treated properly are probably to blame for this cost disparity [2].

Epidemiology

GERD is a common gastrointestinal condition affecting 20% of adults in western societies. According to El-Serag., *et al*. systematics review, GERD prevalence in the US ranges from 18.1% to 27.8%. Since more people have access to OTC acid-reducing drugs, the actual prevalence of this illness may be higher. Men tend to have GERD at a slightly higher rate than women do. According to a comprehensive meta-analysis study by Eusebi., *et al*. women are somewhat more likely than males to experience GERD symptoms. Women who present with GERD symptoms are more likely than men to develop NERD [3].

Etiology

Currently, there is no understanding of how GERD develops. Numerous risk factors have been discovered and linked to the development of GERD over time. The cause of GERD includes motor abnormalities such as esophageal dysmotility, which impairs esophageal acid

clearance, impairment in lower esophageal sphincter (LES) tone, transitory LES relaxation, and delayed stomach emptying. An increased risk of developing GERD is linked to anatomical variation, such as the development of a hiatal hernia, as found in obesity. Obesity has been linked to an increased chance of developing GERD symptoms, esophageal cancer, and erosive esophagitis, and, according to a meta-analysis by Hampel H., *et al*. [4,5].

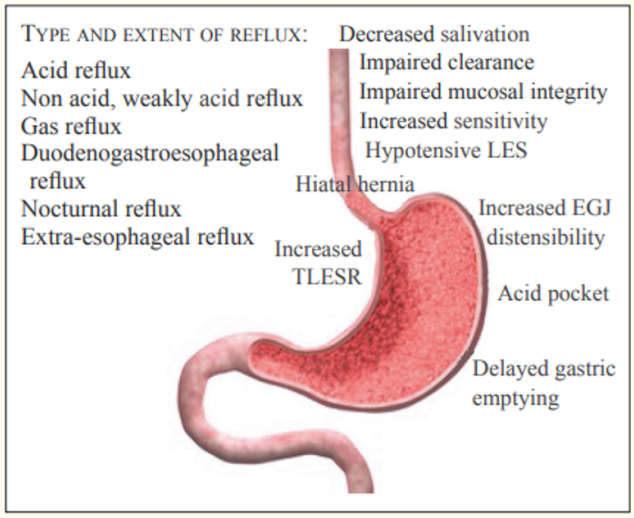

Figure 1: *Etiology for GERD [6].*

Malfertheiner., *et al*. ProGERD's study examined the risk variables for erosive reflux disease in over 6000 GERD patients and found that the odds ratio for the condition rose with body mass index (BMI). Age 50 years, low socioeconomic status, use of tobacco, excessive alcohol consumption, connective tissue disorders, pregnancy, postprandial supination, and various drug classes, such as anticholinergic drugs, benzodiazepines, NSAID, nitroglycerin, albuterol, calcium channel blockers, antidepressants, and glucagon, have also been independently linked to the development of GERD symptoms [5].

Pathophysiology

The pathophysiology of GERD has multiple factors and is best understood by the multiple mechanisms at play, which include the influence of the lower esophageal sphincter's tone, the presence of a hiatal hernia, the esophageal mucosa's protection against refluxate, and motility of esophagus.

Function and transient lower esophageal sphincter relaxations (TLESRs) and impaired lower esophageal sphincter (LES)

At the esophagogastric junction (EGJ), the LES, along with the crural diaphragm, comprise the physiological EGJ barrier, which inhibits the retrograde migration of acidic gastric contents into the esophagus. In normally healthy people, the LES keeps a high-pressure zone above intragastric pressures, temporarily relaxing the LES in response to a meal to facilitate food passage into the stomach. Patients with GERD symptoms may experience frequent transient LES relaxations (TLESRs) that are not brought on by swallowing, which causes the intragastric pressure to be higher than the LES pressures and allows gastric contents to reflux into the esophagus. The unknown is the precise mechanism causing enhanced transient relaxation, yet TLESRs are responsible for 48 - 73% of GERD symptoms. Alcohol consumption, smoking, caffeine use, pregnancy, and some drugs, including nitrates and calcium channel blockers, all have an impact on the LES tone and TLESRs [7].

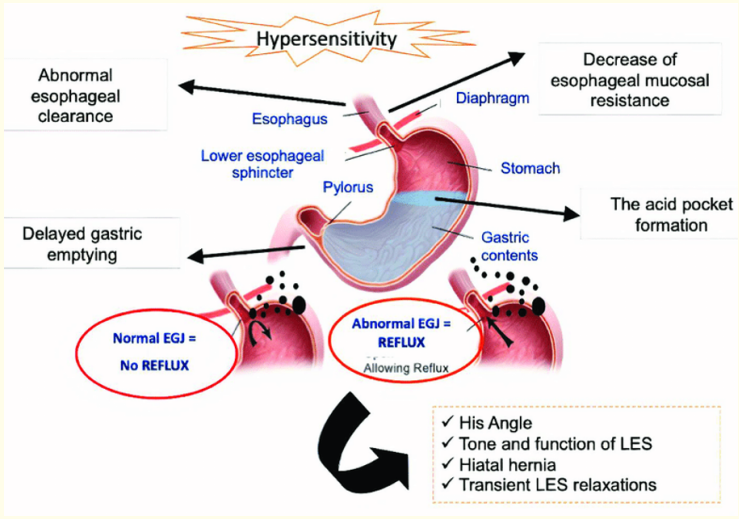

Figure 2: *Pathophysiology of GERD [8].*

Hiatal hernia

A hiatal hernia can exist on its own without presenting any symptoms and is usually linked to GERD. However, because a hiatal hernia impairs LES function, it is important in the pathophysiology of GERD. According to Patti., *et al*. patients with GERD had identical LES function problems and acid clearance, whether they had a minor hiatal hernia or not. The LES was shown to be shorter and weaker in patients with extensive hiatal hernias, which led to more reflux episodes. Additionally, it was noted that patients with significant hiatal hernias had a worsened degree of esophagitis [9].

The esophageal mucosa is made up of a variety of structural and functional components that serve as a defense barrier against the luminal chemicals that GERD sufferers are exposed to. It is unknown whether gastroparesis affects GERD. Due to stomach distention and greater exposure to gastric reflux, it is thought that delayed gastric emptying causes GERD symptoms [10].

Defective esophageal peristalsis

Normal esophageal peristalsis clears the acidic stomach contents that make it there and neutralizes them with salivary bicarbonate. Diener., *et al*. prospective's study found that 21% of GERD patients had impaired esophageal peristalsis, which decreased gastric reflux clearance and resulted in severe reflux symptoms and mucosal damage [10].

Symptoms

Heartburn is the traditional and most typical symptom of GERD. Acid reflux into the esophagus causes heartburn, a burning sensation in the chest that spreads to the mouth. Only a small portion of reflux occurrences, nevertheless, is symptomatic. Another common symptom of heartburn is a regurgitation of gastric acid along with a sour taste in the back of the tongue. Particularly noteworthy, GERD frequently causes non-cardiac chest pain. Due to the possible significant repercussions of cardiac chest pain and the variety of diagnostic and therapy algorithms based on etiology, it is essential to determine the root cause of the discomfort. People with non-cardiac chest discomfort may exhibit GERD symptoms in a thorough clinical history, pointing to GERD as a potential cause [11].

Even though the most common extraesophageal GERD signs are easy to recognize, they are less typically recognized. Hoarseness and throat clearing are extraesophageal symptoms more usually brought on by reflux into the larynx. The globus sensation, often known as a feeling of fullness or a lump in the back of the throat, is a typical complaint among GERD sufferers. Although the exact etiology of the 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. Additionally, some GERD patients may have persistent nauseous and vomiting issues [12].

Diagnosis

With the aid of the typical symptoms and reaction to acid suppression, GERD is typically diagnosed clinically. Typically, heartburn alone-with or without regurgitation-is enough to raise the possibility of GERD, especially if these symptoms worsen after eating or when lying down. A diagnosis is made when symptoms stop after starting treatment with proton pump inhibitors (PPIs) or histamine type 2 (H2) receptor blockers [13].

Upper gastrointestinal endoscopy, also known as esophagogastroduodenoscopy, is the most common diagnostic procedure for the assessment of GERD and its potential consequences (EGD). The direct observation of the esophagus mucosa is the main advantage of endoscopy. This aids in the diagnosis of GERD problems such as Barrett's esophagus, strictures, and esophagitis. The Los Angeles classification, which rates the severity of GERD from A to D, with D being the most severe, is one endoscopic grading method. The gold standard for identifying acid reflux is ambulatory pH monitoring. Ambulatory pH monitoring enables the link between symptoms and the objective detection of acid reflux occurrences. This is especially beneficial for those who have symptoms and normal endoscopic findings [13].

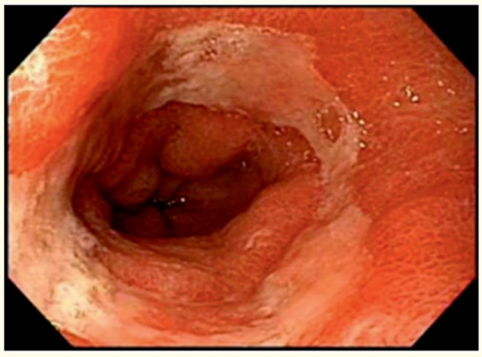

Figure 3: *Endoscopy in GERD [6].*

Ambulatory pH testing has strong repeatability (84 - 93%), sensitivity (96%), and specificity (96%) when done correctly. pH probes (catheter or wireless capsule) are inserted into the esophagus for 24 to 48 hours to complete the test. The main factor utilized in the diagnosis of GERD is the percentage of time when the esophageal pH is less than 4. It has the advantage of detecting dynamic pH changes while standing and lying flat. pH probes also keep track of how frequently reflux occurs, how much reflux occurs nearby, and how long each incident lasts. Additionally, a link between reflux and symptoms has been observed. You can take PPI therapy while taking this test or not [14].

Impedance testing can be added to ambulatory esophageal pH testing in order to increase the diagnostic yield in GERD suspect patients. The same process for inserting probes into the esophagus is used for this test, which instead assesses the electrical characteristics of the contents. Reflux of liquids, for instance, exhibits low impedance and high conductance, but that of gases, as observed in belching,

exhibits high impedance and low conductance. Some patients have reflux symptoms both under normal and too-acidic esophageal exposure, and combined monitoring makes it possible to identify nonacid reflux events that would otherwise go undetected with pH monitoring alone [15].

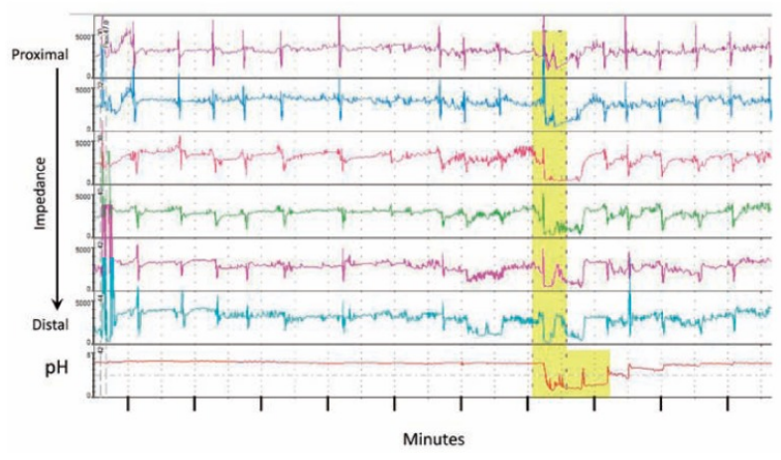

Figure 4: *[6].*

Treatment

Patients with GERD should be examined for alarm features because they should demand an immediate endoscopic examination. The first care of GERD should focus on lifestyle adjustment if no alarm signs are present. The majority of studies on dietary and lifestyle changes in GERD have not been properly powered, which is crucial to highlight. However, lifestyle modifications continue to be the first line of GERD care with the main objectives of symptom reduction and quality of life enhancement [16].

Head of bed (HOB) elevation is the only GERD management strategy with a track record of success. In individuals with supine GERD, raising the head of the bed has been proven to reduce esophageal acid exposure and esophageal clearance time, which in turn reduces symptoms. It is also suggested that circumstances that increase the likelihood of TLESRs be reduced or avoided. These include smoking, binge drinking, eating a lot at dinner, snacking late at night, and eating a lot of fat in your diet. Patients with GERD who are overweight are highly encouraged to lose weight, but there is little evidence of a benefit for those who are normal weight. The majority of bariatric procedures worsen reflux, despite the fact that obesity is a risk factor for GERD [16].

Non-steroidal anti-inflammatory medicines (NSAIDs), which alter the physiological systems that protect the mucosa, should also be avoided by all GERD patients. The goal of GERD medication therapy is to lessen symptoms and prevent mucosal damage from acid reflux. With the exception of Zollinger-Ellison syndrome, there does not seem to be a clear correlation between the severity of GERD and high gastric acid levels, even if acid suppression is effective in the treatment of GERD [17].

Before seeking medical care, many patients with heartburn attempt over-the-counter antacids, H2 blockers, and proton pump inhibitors are the two main drugs used to reduce acid production. H2 blockers reduce stomach acid production by preventing the activation of the parietal cell by histamine. The acid released into the stomach lumen from parietal cells is lessened by proton pump inhibitors. H2 blockers have been demonstrated to provide some clinical benefit over a placebo, although PPIs are the most successful treatment for pa-

tients who have no contraindications. Prokinetic medications like metoclopramide have no well-defined use in the management of GERD. The most effective group of antacid drugs is called proton pump inhibitors [18].

They are dosed once or twice a day, and taking them 30 to 60 minutes before meals maximize their effectiveness. After stopping PPI, many individuals will experience a return of their symptoms, necessitating the need for lifetime therapy. Concerns about PPIs causing bone fractures, electrolyte deficits, infections (such as Clostridium difficile and pneumonia), and renal insufficiency have grown recently. The smallest dose needed for maintenance should be employed, and periodic attempts of weaning should be tried, given the theoretical possibility of side effects from PPI medication. There is some evidence that suggests adding a nightly H2 blocker may be helpful for GERD patients who are resistant to twice-daily PPI treatment [19].

Other conditions, such as eosinophilic esophagitis, pill esophagitis, delayed stomach emptying, duodenogastric/bile reflux, irritable bowel syndrome, psychiatric disorders, achalasia, and Zollinger-Ellison syndrome, should be taken into account in refractory cases. It has been debatable whether anti-reflux surgery (fundoplication) should be used. Studies demonstrate that surgery has very modest long-term clinical benefits over PPI medication, along with a higher incidence of dysphagia and dyspepsia. Patients who respond well to surgery are often those who respond favorably to PPIs, making them candidates for medicinal management. Patients who are PPI-refractory, on the other hand, are not likely to benefit from surgery. A surgical revision is eventually necessary for about half of all patients [20].

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 the early diagnosis of symptoms. Changes in behavior and technological advancements in acid suppression are still crucial to its therapy. Numerous people's lives are impacted by the therapeutic management of GERD, which also significantly depletes society and healthcare resources. Lifestyle changes, PPI medication, and surgical fundoplication are all forms of treatment. Endoscopic surgery is developing new, less intrusive techniques. Although PPI use is still the most popular treatment, long-term therapy necessitates monitoring and re-evaluation for potential side effects.

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