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## Gastroesophageal Reflux Disease: Epidemiology, Pathogenesis and Therapeutic Approaches

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**ABSTRACT:**Gastroesophageal reflux disease (GERD) is a disorder that is characterized by upward flux of gastric chyme into the oesophagus. It may happen with no erosion as retrograde flow disorder or can cause erosive esophagitis. It has impact on quality of life of patients causing health and social problems and is correlated with a high risk of malignant esophageal tumor, columnar-lined esophagus, esophageal narrowing and stenosis, and inflammation of esophagus. Genetic predisposition, cigarette smoking, and obesity, bad lifestyle are considered as risk factors for causing GERD. Classical GERD symptoms are usually clear to reach the accurate diagnosis, but less frequent symptoms and signs, such as chronic coughing and dysphagia, may also happen. Lifestyle management, antacid therapy, and surgical procedures are the major treatment strategies for GERD.

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### 1. INTRODUCTION

GERD stands for Gastroesophageal Reflux Disease, an irritation and burning sensation in the chest caused by acid regurgitation or specific symptoms. The condition affects millions worldwide who are identified through both classic and atypical signs. For many individuals with GERD, acid suppressive therapy is helpful in managing symptoms and preventing complications that can arise from the disease. We have made significant strides in diagnostic and therapeutic modalities that help us better detect disease processes while managing its complications since GERD is defined as a condition resulting from troublesome symptoms and various organ pathologies due to gastric fluid reflux up into esophagus according to Montreal definition (Clarrett & Hachem, 2018 ; Maret-Ouda et al., 2020).

Gastroesophageal reflux disease (GERD) is a highly concerned health issue, linked with a lower quality of life and considerable morbidity. Successfully treating symptoms of GERD has shown to significantly enhance the quality of life in many ways, including lowering physical pain-related complaints and boosting energy levels and daily functionality — this typically results from decreased social restrictions plus emotional well-being enhancement. Even though medications for GERD are not very costly, the cost for managing patients with GERD has been considered twice as much as the amount spent on similar individuals with no GERD (Bloom et al., 2001).

The management of GERD is a health care topic that touches many lives and siphons plenty of resources from society. The treatments for this include anti-reflux surgery such as lifestyle modification, Proton pump inhibitors (PPI), and laparoscopic fundoplication. We're seeing more advanced forms of these procedures emerging— though PPI still takes the lead as the primary treatment, its long-term use should be monitored for any adverse effects due to therapy (Maret-Ouda et al., 2020).

### EPIDEMIOLOGY

GERD impacts around 20% of adults in wealthy nations. It is highly prevalent globally as a common digestive malady: estimates peg its occurrence between 18.1% and 27.8% in North America alone. About half the adult population will have complaints of reflux at some point (Clarrett & Hachem, 2018 ; Maret-Ouda et al., 2020).

A systematic review performed by El-Serag et al. established the prevalence of GERD in the USA to range between 18.1% and 27.8%. Nevertheless, this disease's actual prevalence might be even greater as more people have easy access to over-the-counter acid suppression medications. The incidence of GERD is slightly more common in men than women: according to an extended meta-analysis done by Eusebi et al., the combined ratio of male to female with GERD symptoms was higher for women at 54% compared with men at 46%. For female patients presenting GERD symptoms, NERD is predominant among them while erosive esophagitis predominates among men with similar presentations (El-Serag, et al., 2014; Eusebi et al., 2018; Kim et al., 2019).

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## RISK FACTORS

Factors that increase risk of GERD include: Anxiety or depression, smoking, high body mass index (BMI), old age and sedentary work. Acidic food in large portions late at night is bad for sleep and makes GERD worse— thus paying attention not only to the quality but also to timing of meals can help prevent this condition. Recreational physical activity seems protective except when done after eating; that's actually bad for GERD (Zheng et al., 2007; Emerenziani et al., 2005).

Obesity increases the risk of GERD, but interestingly most bariatric surgeries worsen reflux. In addition, it's important to note that all individuals suffering from GERD should steer clear of NSAIDs due to their negative impact on physiological mucosal protection mechanisms (Clarrett & Hachem, 2018).

The origin of GERD, unfortunately, remains a mystery as no known cause explains its development. Nevertheless, through the years various risk factors have been discovered that play a role in the pathogenesis of GERD which include muscle abnormalities such as esophageal dysmotility and impairment of the LES tone, among others. Anatomical factors like hiatal hernia or obesity (due to increased intra-abdominal pressure) also contribute significantly to this condition (Argyrou et al., 2018).

## PATHOPHYSIOLOGY

GERD's pathophysiology is a many-pieced puzzle, with players including those transient lower esophageal sphincter relaxations and abnormalities in pressure mechanics along the lower esophagus. This mishmash begets a reflux not only of acid but also bile, pepsin, and pancreatic enzymes— culprits all in their own right— that collectively conspire to curtail esophageal mucosa quality time. There are other cast members contributing to this physiological drama; hiatal hernia waltzes onto stage alongside impaired esophageal clearance, delayed gastric emptying and even impaired defensive factors at the mucosal level! Hiatal hernia plays its role well by fostering dysfunction down at our sphincter site; meanwhile, another actor (impaired oesophageal clearance) ensures that our leading lady (mucosa) is left basking in an extended acid exposure (De Giorgi et al., 2006).

Delayed emptying of the stomach, which leads to distension, has the ability to significantly increase the rate of transient lower esophageal sphincter relaxations post meal— a major contributing factor to GERD. The defensive mucosal factors play their part in preventing GERD by neutralizing hydrogen ions from diffusing back into the esophageal tissue; however, while we now have a good understanding of how esophageal symptoms manifest themselves pathogenically, the mechanisms underlying airway manifestations still remain elusive. There have been two main hypotheses proposed: one suggests that gastric acid comes into direct contact with the upper airway leading to bronchospasm while another talks about a vago-vagal reflex elicited by acidification at certain points in the oesophagus. GERD does not arise due to any single cause but rather should be seen as resulting from numerous interacting factors (all facilitating varying extents of damage on different parts of esophageal lining through exposure to acidic gastric contents); these include but are not limited to those discussed above. (Buckles et al., 2004).

The predominant and classic indication of GERD is heartburn. A burning feeling felt in the thoracic area which moves upwards to the mouth due to the flow of acid back into the esophagus. Nevertheless, symptomatic reflux events only make up a small fraction. Moreover, heartburn commonly comes with a sour taste at the rear part of the mouth — sometimes even without regurgitation of the refluxate (Clarrett & Hachem, 2018).

GERD stands out as a significant source of non-cardiac chest pain. Given that the presence of cardiac chest pain carries grave implications but the distinction with non-cardiac chest pain can help guide different diagnostic and treatment pathways based on etiology, it is worthwhile to make the differentiation between these two types of chest pain. A keen clinical history should be able to identify GERD symptoms in patients presenting with non-cardiac chest pain which may point towards GERD as an underlying cause (De Giorgi et al., 2006).

The signs extruded in the larynx (through reflux) generate hoarseness and frequent throat clearing— symptoms of extraesophageal reflux rather than the common typical GERD presentations. Another unusual complaint among patients with GERD is globus sensation; they feel a lump or fullness in the back of their throat. The cause of this symptom isn't well established, but it is presumed that exposure of acid to hypopharynx leads to a high tonicity at UES: thus, triggering more reflux into bronchiolar tree during aspiration which can cause bronchospasm worsening underlying asthma leading to dyspnea and wheezing, on top of cough. Vomiting and chronic nausea are other atypical presentations (Mittal & McCallum, 1988).

Symptoms of GERD need to be distinguished from dyspepsia. Dyspepsia is described as pain or discomfort located in the upper abdomen which can be with or without related symptoms such as heartburn and acid regurgitation that lasts more than one month; it may be associated with vomiting or nausea, belching and bloating. Dyspepsia is a condition in itself, warranting different management strategies from GERD and sometimes requiring endoscopic evaluation along with testing for *H. pylori* (Dent et al., 2004).

## TREATMENT

The primary step in managing GERD, when no alarm symptoms are detected, is to focus on lifestyle modification. Nonetheless, it should be kept in mind that a large proportion of researches on lifestyle and dietary alterations in GERD lack statistical power. Despite this, lifestyle adjustments still take precedence as the first approach to GERD management— aimed at

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symptom alleviation and enhancement of quality of life. The sole evidenced-based lifestyle change for GERD management is elevating the head of the bed (HOB). This has shown to decrease esophageal acid exposure and time taken for clearance by decreasing symptoms among patients with supine GERD. It is also recommended that factors contributing to TLESRs should be minimized or avoided since these lead to additional incidence of acid reflux symptoms. Some of these are smoking, drinking large amounts of alcohol, consuming heavy evening meals plus snacks at night, and high fat diet. In patients with GERD, diet modification by removing spicy foods, caffeine and chocolate— citrus and carbonated beverages is also a controversial issue. On the other hand, these suggestions are not standard practice (Meining & Classen, 2000).

In many cases, patients suffering from heartburn take antacids without a doctor's prescription. Acid suppressive medications are divided into two main groups: H<sub>2</sub> blockers and proton pump inhibitors. H<sub>2</sub> blockers work by reducing the production of gastric acid — they do this by stopping histamine from stimulating parietal cells. On the other hand, proton pump inhibitors reduce the amount of acid secreted by parietal cells into the stomach cavity. Although H<sub>2</sub> blockers have exhibited some advantages in symptomatic individuals, PPIs are preferred in those for whom they are not contraindicated as they are more effective therapy. There is no established role for prokinetic agents like metoclopramide in treating GERD, as per contraindication (Katz et al., 2013).

Antacids, antisecretory agents such as histamine (H<sub>2</sub>) receptor antagonists (H<sub>2</sub>RAs) or PPI therapy, and prokinetic agents constitute medication therapy. There are currently two FDA-approved H<sub>2</sub>RAs (famotidine and cimetidine) in the US that can be obtained over-the-counter. The frequently used H<sub>2</sub>RA ranitidine has been recalled due to safety concerns stemming from an impurity found in its composition. Similarly, nizatidine— another obscure prescription has also been mentioned for similar reasons. In the US, there are six available PPIs: three (esomeprazole, lansoprazole, and omeprazole) are over-the-counter while the other three (rabeprazole, pantoprazole, dexlansoprazole) require a prescription upon purchase. When it comes to medical choices, proton pump inhibitor (PPI) therapy is identified as the top choice for both erosive and non-erosive gastroesophageal reflux disease (GERD) according to numerous large-scale studies. The primary outcomes in these trials were improvement in symptom control due to hyperacidity, healing of underlying esophagitis, and relapse rate after treatment (Zhang et al., 2013).

The most common medication is a PPI-based treatment, typically omeprazole 20 mg once daily after the full-dose therapy. The aim post initial therapy is to find the lowest effective dose. While several adverse effects have been hinted by observational studies post long-term PPI, these findings are yet to be confirmed and should not guide clinical practice. Laparoscopic fundoplication is an invasive alternative but may be considered in some select patients after a comprehensive and unbiased assessment— especially if they are young and fit. Emerging endoscopic as well as less invasive surgical techniques are on the horizon that might cut down on the use of long-term PPIs and funduplications but their safety and efficacy over the long haul still need more concrete scientific establishment (Maret-Ouda et al., 2020).

Patients presenting either with GERD that is refractory to medication, noncompliant, or experiencing adverse effects with medical therapy; those with large hiatal hernia as an underlying condition; or individuals opting to avoid long-duration drug therapy can opt for surgery. There are two available surgical options for GERD patients, laparoscopic Nissen fundoplication and Laparoscopic anterior 180° fundoplication (180° LAF); bariatric surgery is also an option in obese cases. In treating GERD surgically, Laparoscopic Nissen fundoplication has traditionally been considered the gold standard. However, given obesity's rapid rise in prevalence within the United States, gastric bypass surgery is emerging as the most frequent alternative option for GERD's surgical management (Katz et al., 2013).

The study conducted by Jancelewicz et al., (2017) was a systematic review aiming to derive recommendations from medical literature on surgical treatment in pediatric patients with GERD. They concluded that there was insufficient evidence to make recommendations on all aspects. Fundoplication does not impact the rate of hospitalization for aspiration pneumonia, apnea or reflux symptoms; findings are inconclusive regarding its effectiveness. Laparoscopic fundoplication may be as effective as open fundoplication in certain cases while partial and complete funduplications show similar efficacy levels except for some specific conditions like neurologic impairment or esophageal atresia (Jancelewicz et al., 2017).

## CONCLUSIONS

The evolution of diagnostic and therapeutic approaches have enriched our capacity in disease complication recognition and its control. This includes a detailed description on the pathophysiology and complications of GERD. Clinical approach to GERD should start with lifestyle modifications as a primary goal that reduces symptoms and improves quality of life. The most common medication used in treating GERD is PPI; after the initial full-dose therapy (commonly omeprazole 20 mg once daily), the dose is tapered to the lowest effective dose with an aim to maintain efficacy.

## REFERENCES

- 1) Argyrou, A., Legaki, E., Koutserimpas, C., Gazouli, M., Papaconstantinou, I., Gkiokas, G., & Karamanolis, G. (2018). Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. *World journal of clinical cases*, 6(8), 176–182. <https://doi.org/10.12998/wjcc.v6.i8.176>

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- 2) Bloom, B. S., Jayadevappa, R., Wahl, P., & Cacciamanni, J. (2001). Time trends in cost of caring for people with gastroesophageal reflux disease. *The American journal of gastroenterology*, 96(8 Suppl), S64–S69. [https://doi.org/10.1016/s0002-9270\(01\)02587-4](https://doi.org/10.1016/s0002-9270(01)02587-4)
- 3) Buckles, D. C., Sarosiek, I., McMillin, C., & McCallum, R. W. (2004). Delayed gastric emptying in gastroesophageal reflux disease: reassessment with new methods and symptomatic correlations. *The American journal of the medical sciences*, 327(1), 1–4. <https://doi.org/10.1097/00000441-200401000-00001>
- 4) Clarrett, D. M., & Hachem, C. (2018). Gastroesophageal Reflux Disease (GERD). *Missouri medicine*, 115(3), 214–218.
- 5) De Giorgi, F., Palmiero, M., Esposito, I., Mosca, F., & Cuomo, R. (2006). Pathophysiology of gastro-oesophageal reflux disease. *Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale*, 26(5), 241–246.
- 6) Dent, J., Armstrong, D., Delaney, B., Moayyedi, P., Talley, N. J., & Vakil, N. (2004). Symptom evaluation in reflux disease: workshop background, processes, terminology, recommendations, and discussion outputs. *Gut*, 53 Suppl 4(Suppl 4), iv1–iv24. <https://doi.org/10.1136/gut.2003.034272>
- 7) El-Serag, H. B., Sweet, S., Winchester, C. C., & Dent, J. (2014). Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*, 63(6), 871–880. <https://doi.org/10.1136/gutjnl-2012-304269>
- 8) Emerenziani, S., Zhang, X., Blondeau, K., Silny, J., Tack, J., Janssens, J., & Sifrim, D. (2005). Gastric fullness, physical activity, and proximal extent of gastroesophageal reflux. *The American journal of gastroenterology*, 100(6), 1251–1256. <https://doi.org/10.1111/j.1572-0241.2005.41695.x>
- 9) Eusebi, L. H., Ratnakumaran, R., Yuan, Y., Solaymani-Dodaran, M., Bazzoli, F., & Ford, A. C. (2018). Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. *Gut*, 67(3), 430–440. <https://doi.org/10.1136/gutjnl-2016-313589>
- 10) Jancelewicz, T., Lopez, M. E., Downard, C. D., Islam, S., Baird, R., Rangel, S. J., Williams, R. F., Arnold, M. A., Lal, D., Renaud, E., Grabowski, J., Dasgupta, R., Austin, M., Shelton, J., Cameron, D., & Goldin, A. B. (2017). Surgical management of gastroesophageal reflux disease (GERD) in children: A systematic review. *Journal of pediatric surgery*, 52(8), 1228–1238. <https://doi.org/10.1016/j.jpedsurg.2016.09.072>
- 11) Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. *The American journal of gastroenterology*, 108(3), 308–329. <https://doi.org/10.1038/ajg.2012.444>
- 12) Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. *The American journal of gastroenterology*, 108(3), 308–329. <https://doi.org/10.1038/ajg.2012.444>
- 13) Kim, S. Y., Jung, H. K., Lim, J., Kim, T. O., Choe, A. R., Tae, C. H., Shim, K. N., Moon, C. M., Kim, S. E., & Jung, S. A. (2019). Gender Specific Differences in Prevalence and Risk Factors for Gastro-Esophageal Reflux Disease. *Journal of Korean medical science*, 34(21), e158. <https://doi.org/10.3346/jkms.2019.34.e158>
- 14) Maret-Ouda, J., Markar, S. R., & Lagergren, J. (2020). Gastroesophageal Reflux Disease: A Review. *JAMA*, 324(24), 2536–2547. <https://doi.org/10.1001/jama.2020.21360>
- 15) Meining, A., & Classen, M. (2000). The role of diet and lifestyle measures in the pathogenesis and treatment of gastroesophageal reflux disease. *The American journal of gastroenterology*, 95(10), 2692–2697. <https://doi.org/10.1111/j.1572-0241.2000.03175.x>
- 16) Mittal, R. K., & McCallum, R. W. (1988). Characteristics and frequency of transient relaxations of the lower esophageal sphincter in patients with reflux esophagitis. *Gastroenterology*, 95(3), 593–599. [https://doi.org/10.1016/s0016-5085\(88\)80003-9](https://doi.org/10.1016/s0016-5085(88)80003-9)
- 17) Zhang, J. X., Ji, M. Y., Song, J., Lei, H. B., Qiu, S., Wang, J., Ai, M. H., Wang, J., Lv, X. G., Yang, Z. R., & Dong, W. G. (2013). Proton pump inhibitor for non-erosive reflux disease: a meta-analysis. *World journal of gastroenterology*, 19(45), 8408–8419. <https://doi.org/10.3748/wjg.v19.i45.8408>
- 18) Zheng, Z., Nordenstedt, H., Pedersen, N. L., Lagergren, J., & Ye, W. (2007). Lifestyle factors and risk for symptomatic gastroesophageal reflux in monozygotic twins. *Gastroenterology*, 132(1), 87–95. <https://doi.org/10.1053/j.gastro.2006.11.019>