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# Introductory Chapter: Do We Really Know GERD?

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## 1. Introduction

Gastroesophageal reflux disease (GERD), commonly known as heartburn, has been one of the most prevalent digestive disorders for the past few decades. Despite various definitions in different parts of the world, GERD generally refers to the effortless movement of stomach contents into the esophagus causing troublesome symptoms, typically a burning sensation in the chest, which may radiate toward the neck, throat, and the back, inducing pain. Chronic GERD can lead to several complications, including erosive esophagitis, esophageal strictures, and esophageal epithelial transformation into Barrett's Esophagus (squamous epithelium turning into columnar epithelium), a precancerous condition to adenocarcinoma. Therefore, early diagnosis and proper treatment are critical for the prevention of these potential complications and malignancy. Due to its popularity, GERD has not only deteriorated the quality of life for many people all over the world, but it has also brought up tremendous economic pressure on many countries and regions. European Digestive Health Summit 2018 reported a 26% reduction in productivity across Europe because of GERD, costing employers ~\$4.4 billion [1]. In the United States, the expenses on GERD were estimated to be at least \$24 billion/year [2].

## 2. How many people are affected by GERD? we do not know

There has never been a unifying definition for GERD; consequently, GERD diagnosis has never had a gold standard. Mostly, it is made based on questionnaires in combination with a few additional examinations and tests, including responsiveness to acid-suppressive drugs, esophagogastroduodenoscopy (EGD), and ambulatory reflux monitoring. Weekly heartburn or acid regurgitation is the first indicator of GERD. Heartburn refers to a retrosternal burning sensation that typically occurs after a meal or when in a reclined position, and regurgitation is the backflow of stomach contents into the mouth or throat. However, some GERD patients are asymptomatic. As reported in Europe, 44–46% of the patients with Barrett's Esophagus never showed any sign of heartburn or acid regurgitation [3]. Among those presenting these symptoms, on the other hand, a significant proportion is caused by other pathological conditions rather than GERD. As evidenced in the United Kingdom, only 66% of the patients with heartburn or regurgitation were confirmed to be GERD by endoscopic examination and 24-hr pH monitoring [4]. Likewise, among the real GERD patients, only 49% ever experienced heartburn or

acid regurgitation. Therefore, having GERD symptoms does not necessarily mean having GERD.

In addition to heartburn and acid regurgitation, other less common discomforts can also be connected to GERD, including burping, hiccups, water brash, dysphagia, odynophagia, chronic cough, chronic laryngitis, asthma, nausea, and vomiting. However, these symptoms are often seen in other disorders as well, such as eosinophilic esophagitis [5], functional dyspepsia [6], gastroparesis [7], and coronary artery disease [8].

Nowadays, many acid-suppressive drugs are accessible without prescription. Taking these medications, especially Proton Pump Inhibitors (PPI), can conceal GERD-induced esophageal abnormalities. In such cases, even EGD cannot always identify GERD, but ambulatory esophageal pH monitoring can help to correlate the symptoms with pathological acid exposure. Barium radiographs can also be helpful in the detection of esophagitis, esophageal strictures, hiatal hernia, and esophageal tumors.

All of these factors often make GERD diagnosis difficult. As a result, the exact number of people affected by GERD remains to be a mystery. We can only guess how many GERD people are out there, based on the published data. A recent meta-analysis using the data from January 1, 1947, to June 30, 2018, might be able to give us a general idea. According to this study, the global GERD population is likely to be around 1.03 billion (920,661,200–1,148,796,172), representing 13.98% of the current human population on this planet. To make matters worse, the number is still growing year after year.

### **3. What causes GERD? we do not know**

Since the backflow of gastric contents into the esophagus is harmful, to prevent this to happen, the esophagus is anatomically separated from the stomach by the gastroesophageal barrier that consists of two tough muscular components, the lower esophageal sphincter (LES) and the diaphragm. The LES is the 3–4 cm (in adults) distal portion of the esophagus penetrating the diaphragm through the hiatus and entering the abdominal cavity where it connects to the stomach. The diaphragm keeps the esophagus and the stomach in the thoracic cavity and the abdominal cavity separately. The LES and the diaphragm are anchored to each other by the phrenoesophageal ligament so that these two components contract coordinately to prevent the backflow of the stomach contents into the esophagus. For this reason, anything disturbing the function of the gastroesophageal barrier is a potential cause of GERD.

Over the years, many factors have been evaluated for a possible connection with the disease but no one is singled out. Based on the statistical significance, the top five reasons for GERD occurrence are listed as follows.

- 1. Overweight/obesity.** Body weight has been commonly recognized as a major contributor to GERD development. The excessive body fat, especially around the abdominal region, puts constant pressure on the stomach, squeezing the gastric fluid to break the gastroesophageal barrier entering the esophageal lumen frequently, damaging the esophageal lining. According to a meta-analysis [9], GERD was detected in 6.64% of the people with a body mass index (BMI) below 18.5, but in 22.63% of the individuals with a BMI above 30, which is the baseline defined for obesity.

2. **Hiatal hernia.** The hiatus is the small opening in the center of the diaphragm, which allows the esophagus to pass through from the thoracic cavity into the abdominal cavity where it connects to the stomach. In the condition of hiatal hernia, an upper portion of the stomach along with the LES bulges through the hiatus into the thoracic cavity, making the stomach contents easily get into the esophagus. A German study found hiatal hernia in 95% of GERD patients [10].
3. **Frequent transient LES relaxation.** Normally, the LES is conically contracted at rest to produce a concentric occlusion, keeping the stomach contents from backing up. When we are swallowing, the LES relaxes for a few seconds to allow the ingested object to enter the stomach. However, several activities can potentially increase the frequency and duration (> 20 seconds) of the transient LES relaxation, for example, smoking, drinking, and taking certain medications. Many medications are known to cause more frequent or extended transient LES relaxation, such as nitrates, calcium channel blockers, anticholinergic drugs, benzodiazepines, nitroglycerin, albuterol, antidepressants, glucagon, and non-steroidal anti-inflammatory drugs (NSAIDs) [11, 12]. Based on a meta-analysis [9], 24.47% of the NSAID users were found to have GERD, compared with 17.34% of the non-users. Interestingly, however, the study also showed that drinking coffee, tea, or carbonated beverages all increase the odds of GERD, but drinking alcoholic beverages does not seem to be a significant factor [9]. Overall, frequent transient LES relaxation is connected to 48–73% of GERD symptoms [13].
4. **Impairment of esophageal motility.** A healthy esophagus is capable to handle occasional gastric refluxes through frequent peristalsis and the neutralization of salivary bicarbonate. However, due to various pathologic reasons, the esophageal motility becomes weak and consequently, the acidic refluxate cannot be cleared from the esophageal lumen instantly, resulting in mucosal damage and GERD symptoms. According to multiple studies, up to 63.95% of GERD patients were noted to have impaired esophageal peristalsis [14–16].
5. **Non-biological factors.** Several social economic factors have been repeatedly found in connection to GERD occurrence. For instance, people with an advanced degree of education are less likely to develop GERD [9]. The ratio is about 2:1 between the people who did not go to college (16.78%) and the ones who went beyond college education (8.98%). Marital status is also a factor. Singles (12.85%) are less likely to develop GERD than married, divorced, or widowed individuals (22.95%). More interestingly, GERD is found more prevalent in developed countries than in developing or poor countries, but more common in people with low income (blue collars) than those in a better economic condition (white collars) [17]. The mechanisms behind all these observations are unclear.

Other controversial factors are noted in GERD development, including delayed gastric emptying, gastric acid over-secretion, age, gender, and race. Take gastric emptying as an example. For a normal person, the entire process from ingestion to defecation takes about 2–5 days to finish. After a meal, the stomach first relaxes to accommodate the ingested food and then breaks it down by rhythmic churning and grinding motions accompanied by the secretion of acid and digestive enzymes, which takes about 2–4 hours before releasing the food remnants into the small intestine for full digestion and absorption. Several factors can slow down the process, such as overeating,

high-fat meals, low hormone secretion, low physical activity, and gastroparesis. In such cases, the accumulating food in the stomach builds up the intra-gastric pressure to push the gastroesophageal barrier to open, allowing the stomach contents to run into the esophagus instead of going down into the intestine [18, 19]. However, several studies did not find a strong correlation between delayed gastric emptying and GERD occurrence [20–22]. For this reason, using prokinetics to improve gastric motility is not recommended by American College of Gastroenterology (ACG) for GERD relief. Similarly, there are conflicting data about age. Biologically speaking, the gastroesophageal barrier should be like any other part of the body, growing stronger before 40 and getting weaker as the age approaches seniors. However, according to the meta-analysis [9], GERD is found in 8.70% of the people at the age of 18–34 and 14.53% in the age group of 35–59 but comes down after the age of 60.

#### **4. How to cure GERD? we do not know**

Because we cannot nail the ultimate cause of GERD, our treatment strategy for this disease is not targeted specifically. It involves changing eating habits, modifying lifestyle, suppressing gastric acid, and surgical intervention.

##### **1. Changing eating habits**

As discussed above, many common foods and drinks have been found to trigger GERD occurrence, including coffee, tea, soda, juice, wine, liquor, chocolate, tomatoes, spicy food, high-fat food, etc. The question is can we really stop all of these?

##### **2. Modifying lifestyle**

Compared to changing eating habits, modifying a lifestyle may be more doable. We can cut back on tobacco smoking or replace it with nicotine-free cigarettes. We can cut back on night snacks or avoid eating anything 3 hours before bed. We can sit straight during and after meals or stay up an hour or two after a meal. We can cut back the size of each meal to control the body weight. We can raise the head end of the bed or put one more pillow under the head before sleep. We can try to sleep on the left side more often. For some of us, this might be still a little hard to put into action, but we can always make effort for the sake of health.

##### **3. Suppressing stomach acid**

It is commonly thought that acid is the main trigger for GERD symptoms. For this reason, tremendous effort has been put into developing anti-acid drugs. From anti-acids to H<sub>2</sub> blockers (famotidine and cimetidine) to PPIs (omeprazole, lansoprazole, esomeprazole, pantoprazole, dexlansoprazole, and rabeprazole), it has been a multibillion industry that keeps growing year after year. Based on numerous studies, it is true that taking these drugs improves GERD symptoms effectively [23–25]. However, improving is not curing. The reduction of acid secretion is simply not enough to stop GERD completely. Increasing evidence suggests that acid reflux may contribute to esophageal erosion but does not lead to malignancy; it is the bile reflux that induces the development of Barrett's esophagus and adenocarcinoma [26–31].



#### 4. Surgical intervention

Surgical intervention is the last option if other therapeutic management fails to achieve satisfaction. Among several GERD surgeries, laparoscopic Nissen fundoplication has been the gold standard, because it intends to restore the function of the gastroesophageal barrier [32]. However, patients undergoing fundoplication are at risk for developing postoperative adverse events, such as bloating, dysphagia, and belching. One study showed that 62% of the GERD patients who had fundoplication surgery came back on PPI medication later [33]. Magnetic sphincter augmentation (MSA) can be an alternative procedure to replace fundoplication. MSA uses a necklace of titanium beads with magnetic cores that encircle the distal esophagus and thereby strengthen the LES function. Compared with fundoplication, MSA is less invasive, and has a shorter operation time, less gas bloat, and better ability to belch and vomit [34]. For obesity-related GERD patients, Roux-en-Y gastric bypass (RYGB) is recommended by the ACG to be the best option [35–37]. However, a Swedish cohort study reported that among 2454 participants who had undergone RYGB, 48.8% (95% CI, 46.8–51.0) had GERD recurrence within 2 years of the operation [38].

#### 5. Closing remarks

Despite the long history of GERD study and the tremendous effort that has been put in to find a cure, we still do not have the exact knowledge of how many people are affected, what causes the disease, and how to prevent the disease. Current treatment strategies simply cannot cure the disease. Maybe it is time to reexamine the evidence, come up with a different explanation, and explore the matter in a new direction.


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## References

- [1] European Digestive Health Summit. Combatting the burden of digestive diseases through tighter controls on the alcohol and food industry. *United European Gastroenterology Journal*. 2018;**6**:159
- [2] Brook RA, Wahlqvist P, Kleinman NL, Wallander MA, Campbell SM, Smeeding JE. Cost of gastro-oesophageal reflux disease to the employer: A perspective from the United States. *Alimentary Pharmacology & Therapeutics*. 2007;**26**(6):889-898. DOI: 10.1111/j.1365-2036.2007.03428.x
- [3] Zagari RM, Fuccio L, Wallander MA, Johansson S, Fiocca R, Casanova S, et al. Gastro-oesophageal reflux symptoms, oesophagitis and Barrett's oesophagus in the general population: The Loiano-Monghidoro study. *Gut*. 2008;**57**(10):1354-1359. DOI: 10.1136/gut.2007.145177
- [4] Dent J, Vakil N, Jones R, Bytzer P, Schöning U, Halling K, et al. Accuracy of the diagnosis of GORD by questionnaire, physicians and a trial of proton pump inhibitor treatment: The diamond study. *Gut*. 2010;**59**(6):714-721. DOI: 10.1136/gut.2009.200063
- [5] Spechler SJ, Genta RM, Souza RF. Thoughts on the complex relationship between gastroesophageal reflux disease and eosinophilic esophagitis. *The American Journal of Gastroenterology*. 2007;**102**:1301-1306
- [6] Tack J, Caenepeel P, Arts J, Lee KJ, Sifrim D, Janssens J. Prevalence of acid reflux in functional dyspepsia and its association with symptom profile. *Gut*. 2005;**54**(10):1370-1376. DOI: 10.1136/gut.2004.053355
- [7] Gourcerol G, Benanni Y, Boueyre E, Leroi AM, Ducrotte P. Influence of gastric emptying on gastro-oesophageal reflux: A combined pH-impedance study. *Neurogastroenterology and Motility*. 2013;**25**(10):800-e634. DOI: 10.1111/nmo.12181
- [8] 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. *The American Journal of Gastroenterology*. 2006;**101**(8):1900-1920. DOI: 10.1111/j.1572-0241.2006.00630.x
- [9] Nirwan JS, Hasan SS, Babar Z, Conway BR, Ghorri MU. Global prevalence and risk factors of gastro-oesophageal reflux disease (GORD): Systematic review with meta-analysis. *Scientific Reports*. 2020;**10**:5814. DOI: 10.1038/s41598-020-62795-1
- [10] Fuchs KH, Lee AM, Breithaupt W, Varga G, Babic B, Horgan S. Pathophysiology of gastroesophageal reflux disease – Which factors are important? *Translational Gastroenterology and Hepatology*. 2021;**6**:53. DOI: 10.21037/tgh.2020.02.12
- [11] 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;**67**(3):430-440
- [12] De Giorgi F, Palmiero M, Esposito I, Mosca F, Cuomo R. Pathophysiology of gastro-oesophageal reflux disease. *Acta Otorhinolaryngologica Italica*. 2006;**26**(5):241-246

- [13] Mittal RK, McCallum RW. Characteristics and frequency of transient relaxations of the lower esophageal sphincter in patients with reflux esophagitis. *Gastroenterology*. 1988;**95**(3):593-599
- [14] Diener U, Patti MG, Molena D, Fisichella PM, Way LW. Esophageal dysmotility and gastroesophageal reflux disease. *Journal of Gastrointestinal Surgery*. 2001;**5**(3):260-265
- [15] Shetler KP, Bikhtii S, Triadafilopoulos G. Ineffective esophageal motility: Clinical, manometric, and outcome characteristics in patients with and without abnormal esophageal acid exposure. *Diseases of the Esophagus*. 2017;**30**:1-8
- [16] Jiang LQ, Ye BX, Wang MF, Lin L. Acid exposure in patients with gastroesophageal reflux disease is associated with esophageal dysmotility. *Journal of Digestive Diseases*. 2019;**20**:73-77
- [17] Zheng Z, Shang Y, Wang N, Liu X, Xin C, Yan X, et al. Current advancement on the dynamic mechanism of gastroesophageal reflux disease. *International Journal of Biological Sciences*. 2021;**17**:4154-4164. DOI: 10.7150/ijbs.65066
- [18] Penagini R, Bravi I. The role of delayed gastric emptying and impaired oesophageal body motility. *Best Practice & Research. Clinical Gastroenterology*. 2010;**24**:831-845
- [19] Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. *Gastroenterology*. 2018;**154**:267-276
- [20] Camlleri M, Parkman HP, Shafi MA, Abell TL, Gerson L. Clinical guideline: Management of gastroparesis. *The American Journal of Gastroenterology*. 2013;**108**:18-37
- [21] Gourcel G, Benanni Y, Boueyre E, Leroi AM, Ducrotte P. Influence of gastric emptying on gastroesophageal reflux: A combined pH-impedance study. *Neurogastroenterology and Motility*. 2013;**25**:800-807
- [22] Stacher G, Lenglinger J, Bergmann H, Schneider C, Hoffmann M, Wolfl G, et al. Gastric emptying: A contributory factor in gastro-oesophageal reflux activity? *Gut*. 2000;**47**:661-666
- [23] Zhang JX, Ji MY, Song J, Lei HB, Qiu S, Wang J, et al. Proton pump inhibitor for non-erosive reflux disease: A meta-analysis. *World Journal of Gastroenterology*. 2013;**19**(45):8408-8419
- [24] Robinson M, Sahba B, Avner D, Jhala N, Greski-Rose PA, Jennings DE. A comparison of lansoprazole and ranitidine in the treatment of erosive oesophagitis. Multicentre Investigational Group. *Alimentary Pharmacology and Therapeutics*. 1995;**9**(1):25-31. DOI: 10.1111/j.1365-2036.1995.tb00347.x
- [25] Kirchheiner J, Glatt S, Fuhr U, Klotz U, Meineke I, Seufferlein T, et al. Relative potency of proton-pump inhibitors-comparison of effects on intragastric pH. *European Journal of Clinical Pharmacology*. 2009;**65**(1):19-31. DOI: 10.1007/s00228-008-0576-5
- [26] Souza RF. The role of acid and bile reflux in esophagitis and Barrett's metaplasia. *Biochemical Society Transactions*. 2010;**38**:348-352
- [27] Debruyne PR, Witek M, Gong L, Birbe R, Chervoneva I, Jin T, et al. Bile acids induce ectopic expression of intestinal guanylyl cyclase through



nuclear factor- $\kappa$ B and CDX2 in human esophageal cells. *Gastroenterology*. 2006;**130**:1191-1206

[28] Chai J. Esophagus and esophageal cancer. In: Chai J, editor. *Esophageal Cancer and beyond*. London: IntechOpen; 2018. pp. 1-10. DOI: 10.5772/intechopen.77995

[29] Dang T, Meng X, Modak C, Wu J, Chang Z, Che N, et al. Overexpression of CCN1 in Het1A cells attenuates bile-induced esophageal metaplasia through suppressing non-canonical NF $\kappa$ B activation. *Cytokine*. 2019;**116**:61-69. DOI: 10.1016/j.cyto.2018.12.020

[30] Dang T, Chai J. Molecular dynamics in Esophageal adenocarcinoma: Who's in control? *Current Cancer Drug Targets*. 2020;**20**:789-801. DOI: 10.2174/1568009620666200720011341

[31] Chang Z, Dang T, Meng X, Chai J. The role of CCN1 in Esophageal adenocarcinoma: What we have learned from the lab. *Cancer Control*. 2022;**29**(1-9):10732748221074734. DOI: 10.1177/10732748221074734

[32] Spechler SJ, Lee E, Ahnen D, Goyal RK, Hirano I, Ramirez F, et al. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: Follow-up of a randomized controlled trial. *Journal of the American Medical Association*. 2001;**285**(18):2331-2338. DOI: 10.1001/jama.285.18.2331

[33] Maret-Ouda J, Wahlin K, El-Serag HB, Lagergren J. Association between laparoscopic antireflux surgery and recurrence of gastroesophageal reflux. *Journal of the American Medical Association*. 2017;**318**(10):939-946. DOI: 10.1001/jama.2017.10981

[34] Aiolfi A, Asti E, Bernardi D, Bonitta G, Rausa E, Siboni S, et al.

Early results of magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: Systematic review and meta-analysis. *International Journal of Surgery*. 2018;**52**:82-88. DOI: 10.1016/j.ijso.2018.02.041

[35] Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Jon SS. ACG Clinical Guideline for the diagnosis and management of gastroesophageal reflux disease. *The American Journal of Gastroenterology*. 2022;**117**:27-56. DOI: 10.14309/ajg.0000000000001538

[36] Sandhu DS, Fass R. Current trends in the Management of Gastroesophageal Reflux Disease. *Gut Liver*. 2018;**12**(1):7-16

[37] Chang P, Friedenber F. Obesity and GERD. *Gastroenterology Clinics of North America*. 2014;**43**(1):161-173

[38] Holmberg D, Santoni G, Xie S, Lagergren J. Gastric bypass surgery in the treatment of gastro-oesophageal reflux symptoms. *Alimentary Pharmacology & Therapeutics*. 2019;**50**(2):159-166. DOI: 10.1111/apt.15274