Review Article

A narrative review of the prevalence of gastroesophageal reflux disease (GERD)

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Abstract: Over the years gastroesophageal reflux disease (GERD) has become a common disease worldwide affecting most countries and their populations. The history of the digestive system dates back to the 1400's and reports on how the stomach had an acidic environment. The acidity and contents of the stomach refluxing up into the esophagus was later found in some cases to cause detrimental effects to one's health. The earliest reports of reflux disease began in 1935 and was described as peptic esophagus. Many GERD patients complain of reflux, which is a back flow of gastric contents from the stomach into the esophagus, throat, lungs and airways. It is knowledge in the present day that GERD has a variety of symptoms such as regurgitation, coughing and heartburn greatly impacting on an individual's quality of life (QOL). An increased awareness of the pathology of GERD has allowed for a number of treatments and medicines to be developed, clinically evaluated and used worldwide. To gain an insight into how prevalent GERD is globally, this review will aim to report on its prevalence in different countries and regions of the world and report on the relevant causes associated with GERD. The influence of age, obesity, pregnancy, stress, smoking and alcohol on GERD will be reviewed along with the role of diet and how certain foods and drinks can trigger reflux events. Future research of the prevalence of GERD will help to educate people on lifestyle choices to manage GERD symptoms which in turn will improve quality of life and prevent GERD and GERD related diseases.

Keywords: Gastroesophageal reflux disease (GERD); epidemiology; global prevalence; history; symptoms

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Introduction

This review takes a historical look into gastroesophageal reflux disease with the first references dating back to the 1400's, where physicians started to understand the function of the digestive system (1). Over the centuries various eminent physicians have reported on gastrointestinal disease, with the twentieth century onwards having a greater awareness and knowledge of the disease (2). This review aims to identify how prevalent gastroesophageal reflux disease (GERD) has become over the centuries by looking at Europe, western countries and eastern countries. It also aims to identify possible reasons why GERD is becoming more common and evaluate possible causes that relate to the disease.

GERD is increasing in its prevalence worldwide (3) and is defined as a disease that develops due to a chronic retrograde flow of gastric contents from the stomach into the esophagus, oral cavity or lungs (4). In many cases GERD causes troublesome symptoms or complications such as acid regurgitation, heartburn and chronic cough (5,6). A clinical evaluation of symptoms is shown in *Figure 1*. Although

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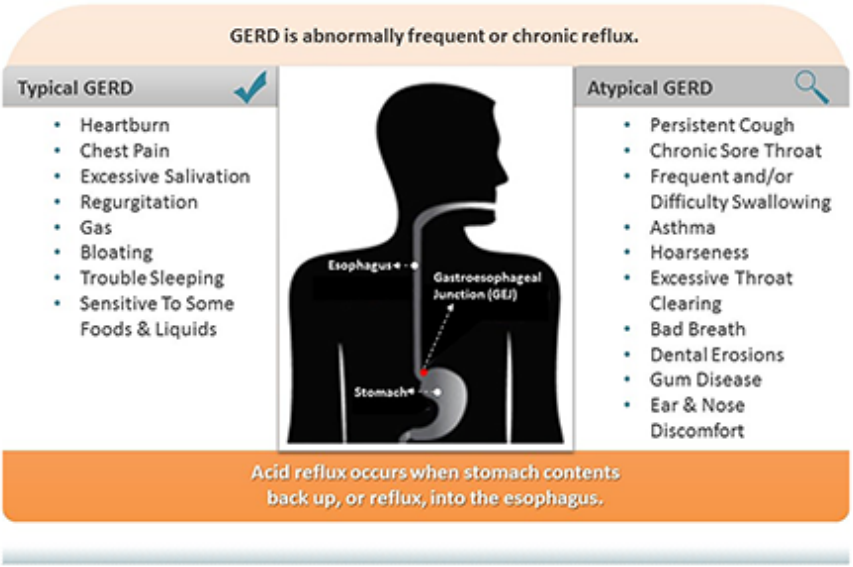

Figure 1 A clinical evaluation of typical and Atypical GERD symptoms adapted from EndoGastricSolutions 2020 (7).

GERD is seen as a non-life-threatening disease, its symptoms can have a detrimental impact on a person's health related quality of life (8). For example the reflux of gastric content into the esophagus leads to mucosal damage (9), therefore increasing the risk of developing esophageal complications including erosive esophagitis (EE), Barrett's esophagus and esophageal adenocarcinoma (10,11).

The incidence of GERD is high in the general population, it is estimated to affect up to 20% of the population worldwide (12,13). Nowadays GERD is found to be the most common diagnosis made in a gastroenterology practice (14). A study in 2014 identified and reported the prevalence of GERD at 10–20% in Europe and the USA, but less than 5% in Asia (15). However, these percentages have increased as our knowledge of GERD and a more specific diagnosis has led to higher reported percentages across the world.

We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx.doi.org/10.21037/aoe-2020-ebmg-03).

Background

History

The recognition of the digestive system dates back to the 1400's, the unpublished notebooks of the Renaissance artist and anatomist Leonardo da Vinci shows a drawing of the stomach and intestines illustrated in *Figure 2*.

In the early sixteenth century a German healer who wanted to reintroduce alchemical theory into medicine, emphasised that the stomach was a chemical laboratory within the body (1). It wasn't until the mid-seventeenth century that Jan Baptiste Van Helmont gave the first chemical account of digestion (1). The awareness of gastric juices and their acidity dates back to the 1800's (17). Here an American army surgeon describes in his notes the exudation of fluids from the gastric cavity and adds reference to how acidic the contents of the stomach were. The stomach acids when refluxed into the oropharynx and/or respiratory tract can have damaging effects (5) and nowadays results in a diagnosis of atypical GERD.

Over the years a dramatic change has developed regarding peoples lifestyle, diet, medication and smoking habits and in turn the prevalence of GERD symptoms, a study recorded around a 50% increase in GERD symptoms up until 1995 and today still continues to be an increasing global burden (18). The prevalence of GERD is illustrated in reviews and articles, with an overall increasing prevalence. *Figure 3* highlights some areas of the world where GERD is prevalent from the Americas in the West ,

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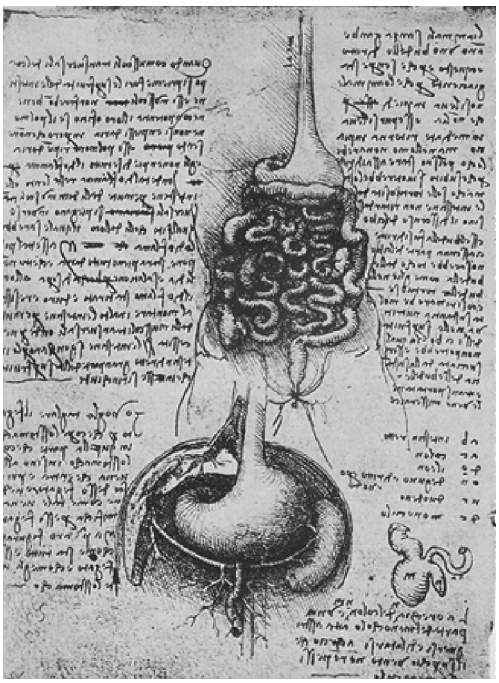

Figure 2 Leonardo da Vinci's interpretation of the stomach and intestines adapted from The Anatomical and Embryological Drawing of Leonardo da Vinci (16).

across Europe and to Asia, China and Japan in the East (20).

Many treatment methods have evolved over the years for gastroesophageal reflux disease. The diagnosis and treatment of GERD are crucial to any patient with regards to how uncomfortable symptoms can get and their consequences (20).

Looking back more than 4,000 years ago, it was reported that Chinese herbalists used extracts of seminal fluid and baby urine to try and relieve symptoms (21). Coral powder was also used in the first century for its calcium properties together with milk as a form of treatment. Around the seventh century kaolin was introduced, while the sixteenth century supported the use of powder of pearls, with some treatments being taken to the extremities of using arsenic, carbolic acid, cannabis and cocaine in the hope of relieving any symptoms. The later part of the nineteenth century saw one treatment route as maintaining a state of rest for the organ by feeding the patient via nutrient enemata and morphine administered by hypodermic syringe for pain relief (21,22).

By the twentieth century antacids were used as a suitable therapeutic treatment, which later led to the development of acid inhibitory therapy during the 1970's, known today

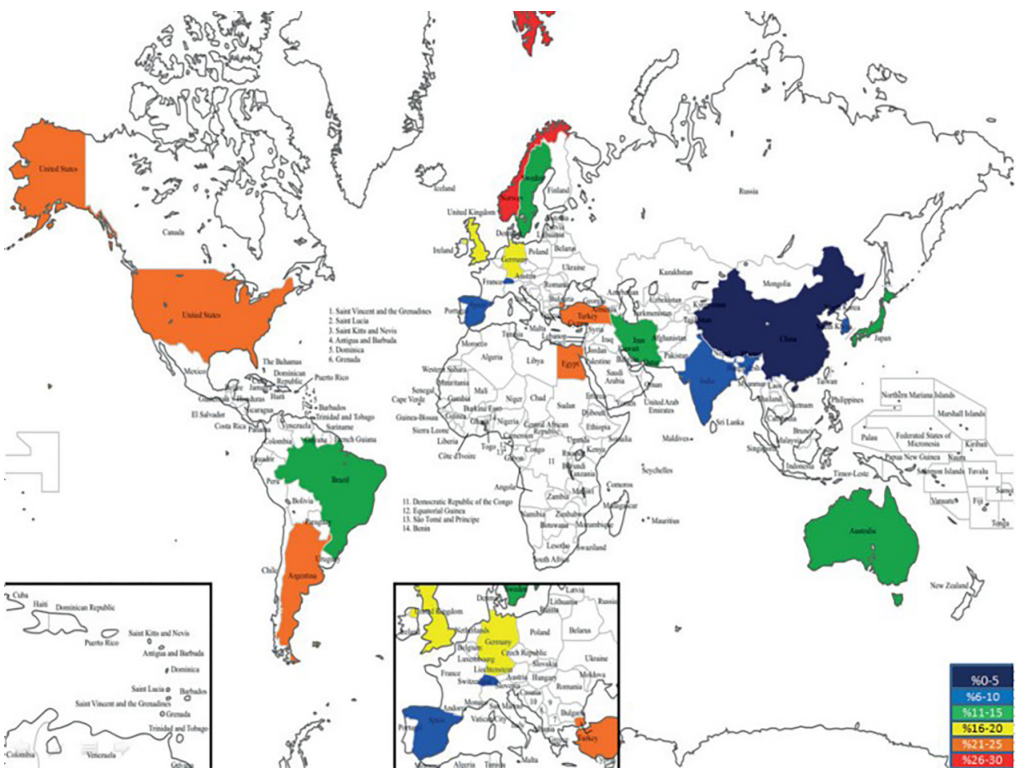

Figure 3 An indication of the prevalence of GERD worldwide adapted from (19) and provided by author.

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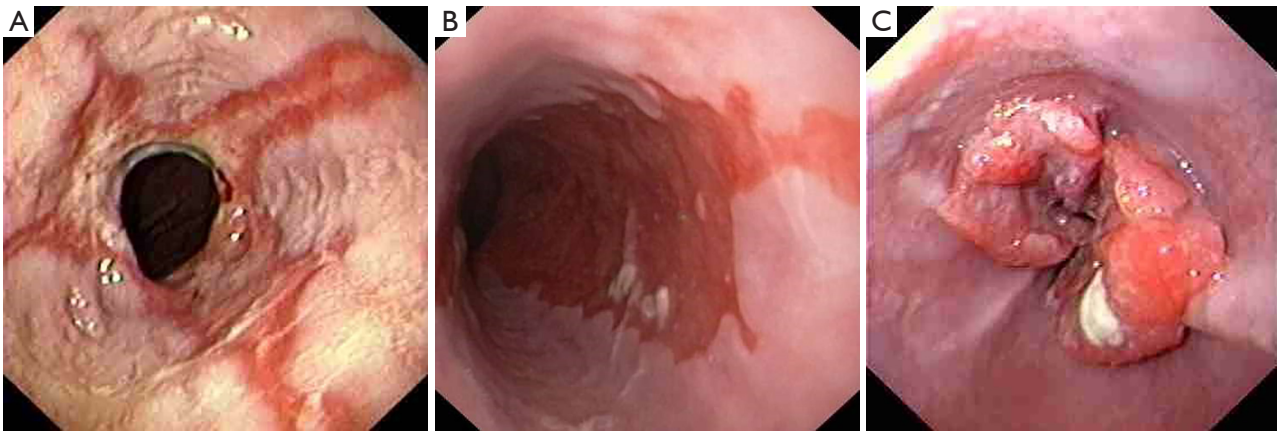

Figure 4 The endoscopic images of (left-right) Erosive Oesophagitis, Barrett's Oesophagus and Adenocarcinoma provided by author.

as H_2 receptor antagonists (H2RA) (2), which decrease the acidity of gastric fluid and esophageal refluxate. More development and research was undertaken and in the 1980's proton pump inhibitors (PPI) were introduced and used in most countries in order to decrease gastric acid production by inhibiting H^+/K^+ adenosine triphosphatase in parietal cells (23,24). Prior to PPI's, alginates were developed as an alternative therapeutic approach, which could be alone or in combination with PPI's. An alginate based pharmaceutical formulation such as Gaviscon is ideal for forming a raft within the stomach to suppress gastric reflux and is product used widely today. Alginates occur naturally as structural polysaccharides in brown algae (seaweed), the stem of the *Laminaria hyperborea* seaweed is harvested for its properties of creating raft formation (19).

Pathology

A major role in the pathogenesis of GERD is the abnormal incidence of reflux, which contains bile, pepsin, acid and duodenal contents coming into contact with esophageal mucosa resulting in troublesome symptoms (25). The duration of acid and its exposure to the esophagus increases the risk of complications. This complication can manifest into Barrett's esophagus (26), which is considered as a pre-cancerous metaplasia and can also cause mucosal damage, leading to the development of esophageal adenocarcinoma, see *Figure 4*. Biliary acids or pancreatic enzymes within the refluxed material also add to the pathogenesis of GERD (27).

As far back as 1841 reflux (pyrosis) was described as a health issue (24), but early reports of the start of reflux disease began in 1935 and was described as peptic esophagus. Later discoveries of peptic ulcers, hiatal hernia and the bacteria *Helicobacter pylori* (*H. pylori*) gave belief that GERD was not just the result of one mechanism, but regarded more as a multifactorial disease (24). Today it is understood that the major motor component involves the stomach, gastroesophageal junction, nervous structures, the esophagus and its sphincters (28). Within GERD patients the transient relaxation of the lower sphincter causes a reflux episode to occur. Therefore health issues such as a hiatal hernia that cause a delay in gastric emptying and decrease pressure in the lower sphincter, give rise to a GERD diagnosis (28). Knowledge of the evolution of GERD helps healthcare providers give correct and essential therapeutic options for their patients (10).

Over time epidemiological data has associated GERD with obesity, this is an important finding as the obesity rates worldwide have tripled since 1975 affecting both adults and children (29). Other potential risk factors for GERD include increasing age, genetics, pregnancy and dietary/lifestyle choices, alcohol consumption and cigarette smoking (29). The progression of GERD has increased since 1995 (18), this is due to the dietary patterns of the younger generations and a worldwide increase of overweight or morbid obesity in both the adolescent and paediatric population (30). A health issue such as asthma can be enhanced by developing GERD and studies have reported that between 34% and 89% of asthmatic patients have GERD (31-33).

Methods

Sources of information

The information used to write this narrative review was collected from books, online websites and published papers

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retrieved from the PubMed database.

Examples of databases

- Books were sourced to search for early illustrations of the stomach anatomy and any early reports of surgery.
- Searches online. KEY WORDS: GERD symptoms; GERD; GERD images.
- PubMed Search 1962 to March 2020. KEY WORDS: Prevalence review of GERD; GERD and Obesity; GERD prevalence with age; Causes of GERD; Global prevalence of GERD; GERD in western countries; GERD in developing countries; GERD Meta-analysis.
- Searches of the references of retrieved literature.
- Discussion with an expert in Gastroenterology.

Discussion

Many countries have reported on GERD and its symptoms and interestingly some parts of the world are affected more than others and ultimately results in high healthcare costs worldwide. Investigating the factors such as lifestyle choices within different countries helps to evaluate the prevalence of GERD around the world.

GERD prevalence in the West

The prevalence of GERD is reported to be higher in western countries compared to eastern countries. It was first evident in western societies with the trend then extending worldwide (24). In 1989 a reported prevalence of reflux esophagitis in western countries was at 2% and reflux at 5%, this percentage has risen up to almost 50% since 1995 (34). The improvement in socioeconomic status has impacted the prevalence of GERD. A reported prevalence from 2017 in adults within western populations was at 30%, yet below 10% in East Asia (35). Western countries are reported to have heartburn as the most predominant symptom and more complications such as Barrett's esophagus, erosive esophagus and associated esophageal adenocarcinoma (36).

An estimated 60–70 million Americans are affected by gastrointestinal diseases annually (37). It is also estimated that 40% of the USA population experience GERD symptoms with 10–20% of people being affected on a weekly basis (38,39). A study by Dent *et al.* (2005) reported a finding of 36 studies analysing the prevalence of gastroesophageal reflux disease in Minnesota. Between 1997 and 1999 an estimated 20% of residents from Olmsted County had weekly heartburn and/or acid regurgitation, with the latter being less common. Evidence reported from previous years showed a percentage of 17.8%, resulting in an increase of up to 3% in a relatively short period of time (40,41). A 2020 population-based study was performed by Delshad *et al.* showed that in a total of 71,812 participants, it was reported that two out of five participants had experienced GERD symptoms in the past and one out of three participants had GERD symptoms occurring within the past week, acknowledging an ongoing rise in North America. It was reported in a study from 2015 that GERD was 50% higher in the USA, with North America having a prevalence of 18–27% and 23% in south America (42).

The prevalence of GERD in Europe was estimated at around 25.9% in 2005 (43), this prevalence proved difficult to pin point an exact figure due to the potential for patients to treat symptoms themselves, the variations used in diagnostic practices and the definitions used for GERD (43). Several reviews across Europe have looked at GERD symptoms in the UK, Finland and Italy, all reporting over 10% prevalence of GERD in the study population (40,44-46).

GERD prevalence in the East

In 1997 Taiwan was reported to have almost 6% of patients attending a GI clinic complaining of heartburnand now known to be suffering from gastroesophageal reflux, this was comparable to the 7% recorded in Nabel (USA) in 1976. Factors affecting Taiwan's GERD diagnosis are that a more westernised diet is being adopted and an elderly population (47). Similarly, Turkey reported 22.8% of the population had heartburn and 12.7% experienced regurgitation. Interestingly Turkey is a country of low income and alcohol consumption, although smoking is very common (48).

In Asia there is an increase in smoking. For example, studies in Japan reported cigarette smoking as one of the main causes of GERD (49). Terms used for describing GERD can vary between countries, the most commonly used terms to describe GERD symptoms are heartburn, reflux, indigestion and burning stomach (50).

A study from 1998 reviewed reflux esophagitis around the world and noted the condition was much lower in Asia and Africa (51,52). Medical literature on the first reports of GERD in Asians was in 1993 (53). In 2010 it was reported that GERD was increasing in Asian countries (54). Many factors are the cause of this rise, including environmental and genetic factors along with dietary and health habits (55). A recent study has estimated 7.8% of the population in

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East Asia are diagnosed with GERD (56). Interestingly tea consumption is reported to be linked with GERD, more so in the Asian population (56), however studies are conflicting and more investigative studies are needed to confirm if tea is a risk factor or not. China has around 5.2% of its population experiencing heartburn and/or regurgitation on a weekly basis (55,57), this low percentage could be based on patients having limited understanding of the definition of heartburn and acid regurgitation and limited experience of their diagnosis.

GERD prevalence with age

Age is becoming an increasing factor in GERD prevalence, many populations across the world are living longer, in turn this is causing an increase in health issues including GERD. GERD has been linked with older age and appears to be more prevalent in males. A recent study in Pakistan investigated a local population of GERD patients and reported on the higher age range of patients having a more impaired quality of life (58). The main reason is that the older generation have a weaker esophageal acid clearance and in turn acquire decreased defense mechanisms on the esophageal mucosa, in the event of reflux (55).

GERD prevalence with obesity

Obesity is defined as a body mass index (BMI) of >30 (59) and obesity has increased in many countries for example in the United States, Europe and Asia, mainly due to populations increasing their food intake (40). Many papers have reported a trend in GERD symptoms in obese individuals indicating a link between obesity and GERD (60). A study reviewing the association between obesity and GERD by El-Serag *et al.* found several studies conducted in North America and Western Europe, with high association between body mass and GERD (59). It was found that having a BMI greater than 35 increased the risk of developing new reflux symptoms (59). Individuals who are obese may experience extrinsic gastric pressure by the surrounding excess adipose tissue, causing increased intragastric pressures and relaxation of the lower esophageal sphincter, allowing a reflux episode to take place (24). The risk of GERD symptoms is lowered by avoiding weight gain. Treating obese patients regarding GERD also has its complications, a study by Perez *et al.* (2001) investigated the outcome of antireflux operations on obese patients. It was hypothesized that obesity had a negative impact on the success of laparoscopic antireflux surgery. It was demonstrated that obese patients had a higher rate of surgical failure than non-obese patients (61).

An increased pressure around the abdomen also makes pregnant women at risk of GERD symptoms, due to the effects pregnancy can have on the lower esophageal sphincter (18), with women reporting noticeable GERD symptoms after 5 months of gestation (18). A study based in Turkey by Bor *et al.* observed a higher number of pregnant women experiencing heartburn and regurgitation than a previous study had seen. It was reported that women experiencing heartburn during pregnancy had a higher risk of continued GERD symptoms for up to 10 weeks post birth (62).

GERD prevalence other causes

Certain foods and drinks are associated with the incidence of reflux and studies have shown that consuming large amounts of fatty foods and chocolate cause episodes of reflux (18). Drinks involving caffeine and alcohol are also strongly associated with causing reflux (18). Alcohol and cigarette smoking exacerbate reflux by weakening lower esophageal sphincter pressure (63,64). Studies have also reported that chronic stress might have a role in GERD disease (65). A study in 2013 defined stress as being a measure of adverse psychosocial influences in adult life and reported findings where participants who had been exposed to more life stresses were more complainant of GERD symptoms (66-68). Stress can heighten the feeling of intra-esophageal acid exposure and can have an influence on health related behaviours for instance smoking, alcohol consumption, diet or physical activity, therefore influencing the risk of reflux (69,70). Studies have shown a correlation between reflux and advanced levels of physical activity, with symptoms noted as heartburn, regurgitation and belching (71-75). A study by Mendes-Filho *et al.* observed an overall hypothesis that patients with GERD experienced induced reflux incidences more frequently when exercising, compared to those that occurred during their usual activities (71).

Many categories of drugs are associated with increasing GERD symptoms, by causing mucosal damage lowering sphincter pressure or by affecting esophagogastric motility (76). A study by Mungan and Pinarbasi Simsek 2017 concluded that estrogen replacement therapy, calcium channel blockers (CCB), nitrates and tricyclic antidepressant drugs are amongst some of the drugs known to either cause or increase GERD symptoms. Interestingly, even non-steroidal

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anti-inflammatory drugs inhibit cyclooxygenase enzymes, therefore increasing the secretions of gastric contents (77).

Summary

GERD is one of the most prevalent health issues worldwide, the incidence and our knowledge of the disease has greatly increased over the last 50 years. Interaction between environmental factors and genetic predisposition, changes in diet and physical activity have added to its prevalence. A higher prevalence of GERD could have some reflection on the fact that life expectancy has now increased worldwide. Although a far firmer understanding is known today on GERD's pathology and symptoms, there is still more research that can be done for the development of non-invasive diagnostic tests and novel treatments. A clearer understanding of reflux across all countries would improve how accurate the prevalence of GERD really is. The more known about gastroesophageal disease and who is at the greatest risk will help to educate people on their lifestyle choices and how to manage their GERD symptoms, improving their quality of life and in turn preventing GERD and GERD related diseases.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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