Study The Relatedness of Gastroesophageal Reflux Disease (GERD) and Stress

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Article Info	ABSTRACT			
Article history: Received February, 22, 2025 Revised March, 20, 2025 Accepted April, 12, 2025	A common gastrointestinal condition that many adults suffer from is gastro-oesophageal reflux disease (GERD). This condition arises when the lower esophageal sphincter malfunctions, causing stomach contents to reflux up into the oesophagus. This allows the return of gastric contents to the oral cavity, but not air. A prevalent			
Keywords:	condition that can significantly disrupt a person's quality of life, GERD affects people of all ages. The lower esophageal sphincter			
GERD, Risk Factors, Stress	(LES), a muscular ring that acts as a valve between the oesophagus and stomach, may malfunction, leading to this condition. Pregnancy, obesity, smoking, and several medications represent risk factors for GERD. Treatment for GERD involves medication to lower stomach acid production and lifestyle modifications such avoiding trigger foods. In extreme situations, surgery can be necessary.			
	The objective is to analyze the relationship between gastroesophageal Esophageal Reflux Disease and stress.			
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INTRODUCTION

About 33% of the population suffers Gastroesophageal reflux disease (GERD), worldwide as it can be chronic, progressive, and relapsing condition [1, 2]. It is a quite prevalent gastrointestinal disease [3]. Classically, GERD was divided into two conditions namely, erosive esophagitis (EE) and non-erosive esophageal reflux disease (NERD) [4]. It can develop when the stomach contents reflux and rise up into the esophagus through lower esophageal sphincter dysfunction. As a result, gastric content (excluding the air) returns into the oral cavity [5]. The GERD manifestations contain esophageal syndrome comprising regurgitation, reflux chest pain syndrome and heartburn. Non-cardiac chest discomfort and perhaps extra-esophageal syndrome are among its symptoms. [6]. Peptic stricture, Barrett's oesophagus (BE), ulcers, and/or esophageal adenocarcinoma (EAC) can all be caused by exposing the Oesophagus to gastric acid [7, 8]. The GERD management can be complex due to the high heterogeneous of clinical presentation, while the pathophysiology may involve many mechanism interactions including mechanical, chemical, neurologic and psychologic [9].

PPIs, or proton pump inhibitors, may be the mainstay of treatment for GERD and its aftereffects. Even with regular medication, up to 40% of NERD patients may still experience symptoms. But after eight weeks of treatment, between 10% to 15% of people with EE could not fully recover [10].

GERD treatment can be through:

(1) Changing lifestyle.

(2) Applying drugs including reflux-reducing agents, H2 receptor antagonists, PPIs, and other adjunct medication.

(3) Invasive management including magnetic sphincter augmentation, anti-reflux surgery (ARS), endoscopic therapy and bariatric surgery [2].

Despite the PPIs absolute advantages in drug treatment, many studies showed the long-term usage of PPIs can result in many side-effects including chronic kidney disease, bone fractures, bacterial gastroenteritis, etc. lowering the enthusiasm of patients to take PPIs [9, 11]. In addition, patients suffering refractory GERD have no or a partial clinical respond even after exposing to the maximum PPIs dosage (double the routine dosage) [12].

An increasing the GERD patient numbers can be resorted to physicians and looking for endoscopic assistance. Up to date, four endoscopic therapies, including transoral incisionless fundoplication (TIF), radio-frequency ablation (RFA), anti-reflux mucosectomy (ARMS), and midguts ultrasonic surgical endo-stapler (MUSETM) are in clinical use (Figure 1). Each technique is effective but varied in degrees. Obviously, based on their pathological characteristics and disease scenario, patients suffering GERD require individualized treatment of precision anti-reflux therapy to gain the therapeutic benefit un best safest ways.



Figure 1: Four clinical procedures utilised in modern endoscopic treatments are shown in this schematic figure. The Stretta system uses a flexible catheter to deliver a four-channel radio-frequency transmitter to a location about one centimetre above line Z via titanium electrodes. Line Z (A) can be used to provide radiofrequency energy. Using this equipment, an esophagogastric fundoplication can be performed close to line Z (B). Using an ultrasonic probe, tissue is clamped and sutured in MUSETM (C). ARMS: Using post-operative scar stenosis (D), a three-cm-long crescent-shaped mucosa cut (red) can be made up and down line Z to reconstruct the anti-reflux barrier [13].

Signs and Symptoms:

The most prevalent GERD condition symptom is heartburn. Acid reflux into the oesophagus causes heartburn, a burning feeling in the chest that travels to the mouth. It's interesting to note that one of the most frequent causes of

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non-cardiac chest pain is GERD [14]. Based on etiology, it can be vital to differentiate between varied diagnostic and treatment algorithms and the essential chest pain causal resulting from potentially serious implications related to the cardiac chest pain [15].

Despite the easily recognized of GERD classic symptoms, the GERD Extraesophageal manifestations may be not uncommon but unrecognizable at all times. Extraesophageal symptoms are most likely to occur due to reflux into the larynx, which may end up with the clearing of throat and hoarseness. It cannot be exceptional to patients who suffering GERD to express fullness or a lump in the back symptoms of their throat feelings, termed Globus sensation [16]. To date, the globus cause has not been fully understood but it is presumed if hypopharynx expose to an acidic medium, it may result in an increase in the tonicity of upper esophageal sphincter (UES). Moreover, bronchospasm may be triggered by acid reflux, enabling exacerbating underlying asthma, thereby inflicting cough, dyspnea, and wheezing [17]. Sometimes, GERD patients can also suffer vomiting and chronic nausea.

Conceivably, it can be essential to consider dyspepsia as distinct from GERD symptoms. Dyspepsia can be defined as an epigastric discomfort, without an acid regurgitation or heartburn, which may exceed more than a month. This condition can be coupled with belching, bloating/epigastric fullness, vomiting, and nausea. Whereas, the term Dyspepsia can be defined as an entity that can be handled in a different way from GERD and may be assessed through early endoscopy and H. pylori testing, as well [18].

Risk factors of GERD:

There are some risk factors that associated with GERD including:

1- Obesity: can be the major risk factor for GERD through increasing the pressure on the stomach and esophagus, leading to acid reflux. Previous works suggested the individuals who were suffering a higher body mass index (BMI), the most likely to develop GERD symptoms [19].

2- Smoking: this factor a known risk for GERD as it weakens the lower esophageal sphincter (LES), which is responsible for preventing acid reflux. Smoking also increases the production of stomach acid and reduces saliva production, which neutralizes acid [20].

3- Alcohol consumption: Heavy alcohol consumption can increase the GERD risk through causing the lower esophageal sphincter (LES) to relax and allowing acid to reflux into the esophagus [21].

4- Certain medications: Certain medications such as non-steroidal anti-inflammatory drugs (NSAIDs), calcium channel blockers, and nitrates enable maximizing the GERD risk through relaxing the lower esophageal sphincter (LES) or irritating the esophagus [22].

GERD and Stress:

Stress and reflux esophagitis:

Despite the fact that the aforementioned research show no connection between exposure circumstances or stress and esophageal acid reflux, the aforementioned is thought to increase the permeability of the esophageal mucosa, which can lead to reflux oesophagitis. Acute stress may cause an increase in submucosal mast cells in an experimental rat model, whereas acid pepsin may cause mucosal permeability [23]. An electron microscopy assessment revealed stressed rats suffered when the dilated intercellular spaces in the esophageal mucosa increased. Furthermore, a mass group experiment involved around 6834 Korean patients revealed a significant correlation between stress and reflux esophagitis was noticed (the value of odds ratio 1.94, 95% CI 1.25-3.02). Fascinatingly, reflux esophagitis severity was shown to be linked to the stress degree. However, two major limitations were observed in that study, the 1st, the responder bias as data collection was based on self-report system and 2nd, selection bias as this survey was restricted to those patients who undertook the medical checkups [24].

Category	1	2	3	4	5
Stress Type	Acute psychological stress induced by IQ test	Auditory	Psychological	Psychological (Stroop test) and physical (cold pressor test)	Stress tasks
Subjects	No. of normal volunteers=15 No. of GERD patients=10	No. of normal volunteers=10 No. of heartburn patients=46	No. of heartburn patients acid/regurgitation (21 received stressor) =42	No. of patients=60	No. of GERD patients=17
Outcomes	Lack of any increase in esophageal acid perception between subjects	Patients reported suffering GERD can enhanced perceptual response to intraesophageally acid exposure compared to healthy subjects	Lack of any increase in reflux was reported	Lack of any changes in esophageal motility in response to stressor	Lack of any increase in total acid exposure, number of reflux episodes, duration of longest reflux episode
Reference	(Hem <mark>mink <i>et</i> al, 2009)</mark>	(Fass et al, 2005)	(Wright et al, 2005)	(Johnston et al, 2006)	(Bradley et al, 1993)

Treatment of GERD:

Current treatments for GERD include medications and lifestyle changes:

Medications: There are several medications available to treat GERD, including proton pump inhibitors (PPIs), H2 receptor antagonists (H2RAs), and antacids. PPIs are the most effective and widely prescribed treatments for GERD. They work by lowering the amount of acid produced in the stomach. H2RAs and antacids are less potent but can provide relief of mild to moderate symptoms [25].

Lifestyle changes: Modifications in lifestyle can also help reduce the symptoms of GERD. Weight loss, avoiding trigger foods, raising the head of the bed, and not lying down after meals are a few examples. Reducing alcohol intake and quitting smoking can also help reduce the symptoms of GERD [26].

CONCLUSION

This study suggests the Gastro Esophageal Reflux Disease (GERD) may emerge and be widely spread due to stresses of life. This disease can be managed or cured through medical treatments or procedures. However, GERD can be controlled by changing lifestyle and food habits. Genetics of people suffering this disease may contribute to have GERD. Thus, gene therapy may provide a solution to manage this issue. Gene editing through CRISPER-CAS can be a powerful tool and the best solution to cure GERD for life term. Gene mapping of the patients suffering

GERD can provide useful information regarding causes and curing this disorder. Genetic data base through chasing family history of patients are required to study whether GERD is related to a genetic disorder, as well.

REFERENCES

- El-Serag, H. B., Sweet, S., Winchester, C. C., & Dent, J. (2014). Update on the epidemiology of gastrooesophageal reflux disease: A systematic review. Gut, 63, 871–880. <u>https://doi.org/10.1136/gutjnl-2012-304269</u>
- [2] Gyawali, C. P., & Fass, R. (2018). Management of gastroesophageal reflux disease. Gastroenterology, 154, 302–318.
- [3] Abdulwahhab, S. H., Al Hashimi, B. A., & Alkhalidi, N. M. (2022). Prevalence and associated factors of gastro-esophageal reflux disease among a sample of undergraduate medical students in Baghdad. Journal of the Faculty of Medicine Baghdad, 63(4), 163–170. Retrieved from https://iqimc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/1865
- [4] Locke, G. R., III, Talley, N. J., Fett, S. L., Zinsmeister, A. R., & Melton, L. J., III. (1997). Prevalence and clinical spectrum of gastroesophageal reflux: A population-based study in Olmsted County, Minnesota. Gastroenterology, 112, 1448–1456.
- [5] Marwa, K., Alkhaldi, E., Alhenaki, G., Alqahtani, L., Hussamuldin, A., & Alquraish, D. (2022). The association of depression and anxiety with hypertension among adults in Riyadh, Saudi Arabia 2022. Medical Science, 26.
- [6] Maneerattanaporn, M., Pittayanon, R., Patcharatrakul, T., Bunchorntavakul, C., Sirinthornpanya, S., & Pitisuttithum, P., et al. (2022). Thailand guideline 2020 for medical management of gastroesophageal reflux disease. Journal of Gastroenterology and Hepatology, 37, 632–643. <u>https://doi.org/10.1111/jgh.15758</u>
- [7] Ronkainen, J., Talley, N. J., Storskrubb, T., Johansson, S. E., Lind, T., & Vieth, M., et al. (2011). Erosive esophagitis is a risk factor for Barrett's esophagus: A community-based endoscopic follow-up study. American Journal of Gastroenterology, 106, 1946–1952.
- [8] Hunt, R., Armstrong, D., Katelaris, P., Afihene, M., Bane, A., & Bhatia, S., et al. (2017). World Gastroenterology Organisation global guidelines: GERD global perspective on gastroesophageal reflux disease. Journal of Clinical Gastroenterology, 51, 467–478.
- [9] Vaezi, M. F., Yang, Y. X., & Howden, C. W. (2017). Complications of proton pump inhibitor therapy. Gastroenterology, 153, 35–48.
- [10] Fass, R., Shapiro, M., Dekel, R., & Sewell, J. (2005). Systematic review: Proton-pump inhibitor failure in gastro-oesophageal reflux disease—Where next? Alimentary Pharmacology & Therapeutics, 22, 79–94. https://doi.org/10.1111/j.1365-2036.2005.02531.x
- [11] Kia, L., & Kahrilas, P. J. (2016). Therapy: Risks associated with chronic PPI use—Signal or noise? Nature Reviews Gastroenterology & Hepatology, 13, 253–254.
- [12] Triadafilopoulos, G. (2016). Endoscopic options for gastroesophageal reflux: Where are we now and what does the future hold? Current Gastroenterology Reports, 18, 47.
- [13] Chen, S., Du, F., Zhong, C., Liu, C., Wang, X., Chen, Y., Wang, G., Gao, X., Zhang, L., Li, L., & Wu, W. (2021). Gastroesophageal reflux disease: Recent innovations in endoscopic assessment and treatment. Gastroenterology Reports (Oxford), 9(5), 383–391. <u>https://doi.org/10.1093/gastro/goab029</u>
- [14] Bredenoord, A. J., Weusten, B. L., Curvers, W. L., Timmer, R., & Smout, A. J. (2006). Determinants of perception of heartburn and regurgitation. Gut, 55, 313–318.

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- [15] Gastal, O. L., Castell, J. A., & Castell, D. O. (1994). Frequency and site of gastroesophageal reflux in patients with chest symptoms: Studies using proximal and distal pH monitoring. Chest, 106, 1793–1796.
- [16] Tokashiki, R., Funato, N., & Suzuki, M. (2010). Globus sensation and increased upper esophageal sphincter pressure with distal esophageal acid perfusion. European Archives of Otorhinolaryngology, 267, 737–741.
- [17] Irwin, R. S., French, C. L., Curley, F. J., Zawacki, J. K., & Bennett, F. M. (1993). Chronic cough due to gastroesophageal reflux: Clinical, diagnostic, and pathogenetic aspects. Chest, 104, 1511–1517.
- [18] 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), iv1–iv24.
- [19] El-Serag, H. B., Graham, D. Y., Satia, J. A., & Rabeneck, L. (2005). Obesity is an independent risk factor for GERD symptoms and erosive esophagitis. American Journal of Gastroenterology, 100(6), 1243–1250. https://doi.org/10.1111/j.1572-0241.2005.41512.x
- [20] Jacobson, B. C., Somers, S. C., Fuchs, C. S., Kelly, C. P., & Camargo, C. A. Jr. (2006). Body-mass index and symptoms of gastroesophageal reflux in women. New England Journal of Medicine, 354(22), 2340– 2348. <u>https://doi.org/10.1056/NEJMoa054391</u>
- [21] Kaltenbach, T., Crockett, S., & Gerson, L. B. (2006). Are lifestyle measures effective in patients with gastroesophageal reflux disease? An evidence-based approach. Archives of Internal Medicine, 166(9), 965–971. <u>https://doi.org/10.1001/archinte.166.9.965</u>
- [22] Festi, D., Scaioli, E., Baldi, F., Vestito, A., Pasqui, F., Di Biase, A. R., & Colecchia, A. (2009). Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. World Journal of Gastroenterology, 15(14), 1690.
- [23] Peterson, W. L. (1995). The role of acid in upper gastrointestinal hemorrhage due to ulcer and stress-related mucosal damage. Alimentary Pharmacology & Therapeutics, 9(Suppl 1), 43–46.
- [24] Song, E. M., Jung, H. K., & Jung, J. M. (2013). The association between reflux esophagitis and psychosocial stress. Digestive Diseases and Sciences, 58(2), 471–477.
- [25] Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. American Journal of Gastroenterology, 108(3), 308–328. https://doi.org/10.1038/ajg.2012.444
- [26] Fass, R., & Sifrim, D. (2009). Management of heartburn not responding to proton pump inhibitors. Gut, 58(2), 295–309. <u>https://doi.org/10.1136/gut.2008.167510</u>

دراسة العلاقة بين مرض الارتجاع المعدي المريئي (GERD) والتوتر أو الإجهاد

الخلاصة

يُشار إلى الاضطراب المعدي المريئي عادةً باسم مرض الارتجاع المعدي المريئي (GERD) وهو مرض شائع للغاية بين البالغين، حيث أن هذا الاضطراب المعدي المريئي منتشر إلى حد كبير. يحدث هذا الاضطراب عند ارتداد محتويات المعدة إلى المريء نتيجة لخلل في العضلة العاصرة المريئية السفلية. ونتيجة لذلك، يمكن أن يعود محتوى المعدة (ولكن ليس الهواء) إلى تجويف الفم. يعد الارتجاع المعدي المريئي اضطراباً شائعاً يصيب الأشخاص في أي عمر وقد يكون له تأثير كبير على جودة حياتهم. يمكن أن يحدث هذا الاضطراب بسبب خلل في العضلة العاصرة المريئية السفلية من العضلات تعمل كصمام بين المريء والمعدة.

تشمل عوامل الخطر الناتجة عن الارتجاع المعدي المريئي التدخين والحمل والسمنة وبعض الأدوية. يتضمن علاج الارتجاع المعدي المريئي التدخين والحمل والسمنة وبعض الأدوية. يتضمن علاج الارتجاع المعدي المريئي تعديلات على نمط الحياة، مثل تجنب الأطعمة المحفزة، والأدوية لتقليل كمية الحمض المنتجة في المعدة. ومع ذلك، قد تكون الجراحة ضرورية في الحالات الشديدة.

إستهدفت هذه الدراسة تقييم العلاقة بين مرض الارتجاع المعدي ا<mark>لمريئي والتوتر أو الإج</mark>هاد.