REVIEW ARTICLE

CONTENTS

The clinical and pathogenetic manifestations of gastroesophageal reflux disease and obesity and approaches to their diagnosis, treatment, and prevention: current state of the problem (literature review)

Taras I. Griadil, Bohdana V. Bezushko, Oleksandr O. Dutko, Mykhailo M. Lopit
UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

Aim: The purpose of this study is to review the literature to determine the common pathogenetic mechanisms (PM) between gastroesophageal reflux disease (GERD) and obesity, as well as to analyze the impact of one disease on the other, followed by a review of the basic principles of diagnosis and treatment of patients with a combination of these comorbidities.

Materials and Methods: The literature review included an analysis of articles from the Scopus and Web of Science databases, with a focus on pathogenesis, clinical data, diagnosis and treatment of GERD and obesity. The following keywords were used to find relevant materials on the research topic: "GERD", "obesity", "pathogenesis", "treatment", "clinical trials".

Conclusions: A series of studies have shown that there are risk factors that increase the development of GERD: stress, bad habits, excessive body mass index (BMI), advanced age and lifestyle. At the same time, obesity has similar risk factors to GERD, which in turn prompts the search for correction of common PM, new ways of diagnosis and comprehensive personalized treatment.

KEY WORDS: gastroesophageal reflux disease, obesity, pathogenesis, diagnostics, treatment

Wiad Lek. 2025;78(4):937-942. doi: 10.36740/WLek/203909 DOI

INTRODUCTION

According to the World Gastroenterology Organization (WGO), gastroesophageal reflux disease (GERD) is defined as symptoms of reflux, erosive esophagitis, which contribute to a person's quality of life (QOL) (work performance, sleep quality), as well as complications lasting one or more days a week, resulting from retrograde backflow of gastric contents into the esophagus, oropharynx, and/or airways [1].

GERD is a "disease of the XXI century," as it is characterized by the WGO, based on epidemiological data that show that it affects 20 to 50% of the population of different countries [1]. GERD is one of the leading causes of decreased QOL, disability, and the development of a number of complications [2]. The Ukrainian Association of Gastroenterologists began statistical registration of GERD in Ukraine in 2009, and as of 2017, the prevalence was 190 cases per 100,000 people [3].

Obesity is a chronic disease characterized by excessive body fat, which can lead to an increased risk of lipid and carbohydrate metabolism changes and can contribute to the development of type 2 diabetes, cardiovascular disease, and increase the risk of certain cancers and other health problems [4].

According to the World Health Organization, in 2022, one in eight people in the world was obese (about 890 million were obese), while 43% of adults aged 18 years and older were overweight (2.5 billion adults) [4].

Thus, GERD and obesity are one of the most common chronic diseases in the modern world, which can aggravate each other's course through pathogenic links [1, 4].

AIM

The purpose of this study is to review the literature to determine the common pathogenetic mechanisms (PM) between GERD and obesity, as well as to analyze the impact of one disease on the other, and to consider the basic principles of diagnosis and treatment of patients with a combination of this comorbid pathology.

Table 1. Common and distinctive RF for obesity and GERD

RF[1]	Obesity	GERD[2]
I. FRs that cannot be modified		
Age [7]	+	+
Gender [8]	+	+
Genetic predisposition [9]	+	+
II. FRs subject to modification		
Physical inactivity [7]	+	+
Unbalanced diet [11]	+	+
High body mass index [10]	+	+
Abdominal obesity [12]	+	+
Smoking [13]	+	+
Alcohol consumption [14]	+	+
Stress [15, 16]	+	+
Influence of internal abdominal pressure [17]	-	+
Use of non-steroidal anti-inflammatory drugs [18]	-	+
Living conditions (socio-economic and environmental reasons) [7]	+	+

Note: [1] – RF – risk factor, [2] – GERD - gastroesophageal reflux disease.

MATERIALS AND METHODS

The literature review includes the analysis of articles from the scientometric databases Scopus and Web of Science, with a focus on the pathogenesis, diagnosis and treatment of GERD and obesity. The following keywords were used to find relevant materials on the research topic: "GERD", "obesity", "overweight", "pathogenesis", "treatment". All selected sources were carefully analyzed for data on common mechanisms of development of these diseases, as well as methods of their diagnosis and treatment. This study was conducted in compliance with the ethical standards approved by the Ethics Committee of Uzhhorod National University.

REVIEW AND DISCUSSION

According to the literature, GERD and obesity are considered in terms of modifiable and non-modifiable risk factors (RF) [5, 6], pathogenetic features, lifestyle, physiological features, etc.

The most significant gaps in research related to GERD and obesity are not related to the study of the number of RFs and their quality of influence, but to insufficient information about their interaction with each other and their joint impact on the development of certain diseases [6-8, 10, 11].

A number of studies have shown that overweight, in particular abdominal obesity (AO), leads to an increase in intra-abdominal pressure (IAP) [12]. In addition, obese patients are often diagnosed with a hiatal hernia, which further disrupts anti-reflux mechanisms and aggravates GERD [14]. At the same time, an increase in IAP leads to mechanical distortion of the esophageal orifice of the diaphragm and the formation of a partial hernia of the esophageal orifice of the diaphragm, which in turn increases the ingress of acid into the lower esophageal sphincter (LES), contributing to the development of GERD and the risk of esophageal cancer [4, 7, 10, 14].

In addition, an increase in IAP, in turn, leads to a deterioration in the function of the LES and promotes retrograde throwing of gastric contents into the esophagus, increases the frequency of reflex episodes, which contributes to the development of GERD and related complications [14, 15].

Obesity is associated with impaired GERD function, including increased transient GERD relaxation and acid reflux (AR), especially after meals, indicating that impaired GERD function may be an early sign of obesity-related GERD [14, 15].

Obese patients have changes in motility and acid exposure (AE), as well as an increase in the frequency of transient relaxation of the LES, which contributes to a longer exposure to acid in the esophagus [15, 16]. These data are confirmed by increased AE and a significantly higher DeMeester index compared to people with normal body weight [16].

Overweight and obesity, as well as increased waist circumference, correlate with increased IAP and a gastroesophageal pressure gradient that induces reflux [17].

A number of studies have shown that AO is an important factor in the development of GERD due to mechanical pressure on the diaphragm and changes in the function of the LES [18].

Obesity contributes to the displacement and discoordination and imbalance of the structures of the esophageal opening of the diaphragm, which further weakens the anti-reflux barrier [14, 16, 17].

Obesity is clinically and physiologically characterized by excessive accumulation of metabolically active adipose tissue [10, 19]. Adipose tissue secretes a number of pro-inflammatory cytokines, such as interleukin-6, tumor necrosis factor α (TNF-α) and leptin, which contribute to the stimulation of inflammatory processes in the esophagus, worsening the clinical picture of GERD, leading to chronic inflammation in the esophagus, increasing the risk of developing GERD complications such as erosive esophagitis and esophageal adenocarcinoma [10, 20].

However, a study of nearly half a million adults with GERD in Scandinavian countries found that the risk of developing esophageal cancer (EC) in people with non-erosive GERD (about 60-70% of patients with GERD [21, 22]) was not increased compared to the general population. Instead, patients with an existing erosive form of GERD, in which inflammation of the esophageal mucosa occurs, had an approximately 2.4 times higher risk of EC compared to those patients with non-erosive GERD [21, 22].

Obesity is associated with metabolic changes such as an imbalance of hormones, in particular ghrelin and leptin. In the case of reduced ghrelin levels, which are associated with decreased motility of the upper gastrointestinal tract, food stagnation occurs and increases the risk of reflux [5, 10, 11, 19]. On the other hand, elevated leptin levels are associated with the development of leptin resistance, which in turn further worsens the course of GERD [5, 10, 11, 19].

Chronic elevation of IAP in obese individuals is associated with various comorbidities: GERD, hypertension, and other conditions, suggesting that elevated IAP plays a significant role in the pathogenesis of these disorders [23].

On the other hand, GERD can cause weight gain due to reduced physical activity (PA) and the use of certain medications. Long-term use of proton pump inhibitors (PPIs) may be associated with weight gain due to the effect on metabolism and possible impaired appetite regulation [8, 24, 25].

The use of anesthesia, in particular in obese patients, decreases the LES pressure and barrier pressure, is more pronounced in obese patients, which increases the risk of regurgitation and aspiration [26].

Patients with GERD can also change their eating habits by eating more food to temporarily relieve symptoms or by choosing high-calorie foods that do not cause esophageal irritation [27].

In addition to eating habits, patients with GERD may often avoid PA due to discomfort or pain during movement, especially when bending over or doing strenuous activities [13].

Modern methods of diagnosing GERD include endoscopic examination, esophageal manometry, and pH metering, and in the case of overweight or obesity, an assessment of BMI and body composition is also added [15, 17, 28, 29].

The prevention of both GERD and obesity is based on lifestyle changes, dietary correction, dosed PA, and, in the presence of bad habits, quitting them. Therefore, only a comprehensive positive impact on the lifestyle of patients can reduce IAP and improve the function of the LES, which is important in preventing the progression of GERD [29-31].

In obese patients, in addition to pharmacotherapy, the treatment plan may also include the use of surgical methods such as bariatric surgery (BS) to achieve weight loss (WL) [32]. Gastric bypass (GB), or sleeve gastrectomy, has been shown to be very effective in reducing the symptoms of GERD [32]. However, some studies show that BS can both improve and worsen patients' condition [32]. There is evidence that patients after sleeve gastrectomy may experience intrathoracic gastric migration due to changes in the anatomy of the esophageal opening of the diaphragm, which causes new episodes of clinical manifestations of GERD, such as heartburn and regurgitation, requiring additional treatment and, accordingly, cost and time with a simultaneous deterioration in QOL [32].

Studies confirm a close and complex multifactorial relationship between obesity, overweight and the development and clinical course of GERD [33-34]. However, despite the progress in understanding the PM, some aspects remain insufficiently investigated, including the prevention and optimal therapy of these conditions [33-34]. Literature data indicate the need for an integrated and personalized approach to patient treatment, combining lifestyle changes, regular dosed physical activity, drug therapy and, in severe cases, surgical methods [33-34].

PPIs are still the main method of medical control of AR, despite the emergence of a new class of drugs, potassium-competitive blockers (PCBs) of hydrochloric acid secretion [34, 35]. In overweight patients, the efficacy of PPIs may be lower due to changes in pharmacokinetics and increased levels of proinflammatory cytokines that affect esophageal sphincter function [33, 34, 35]. In contrast,

PCBs drugs are acid-resistant, lead to reversible inhibition, and can be dosed regardless of meal times [34, 35].

Surgical treatments, such as laparoscopic gastrectomy (LG) or GB, have been shown to be effective in reducing GERD symptoms in obese and overweight patients, although some cases have been reported to persist or worsen after surgery [32, 36].

GB surgery, in particular Roux-en-Y, is often associated with a reduction in GERD symptoms due to the bypass mechanism for stomach acid and a decrease in IAP [37].

A number of studies show that some patients may develop de novo GERD or even Barrett's esophagus after LG [38]. Having a confirmed diagnosis of GERD before BS may be a risk predictor of a higher likelihood of future reoperation [36-38]. Some studies indicate that the effect of surgery may be temporary, for example, in a few years after BS, patients may experience symptoms, especially in the case of LG [39].

Therefore, the question remains as to the long-term effects of preventing possible complications from this type of BS [40].

CONCLUSIONS

In recent decades, the number of obese and overweight people has increased significantly. In turn, GERD affects a large number of people around the world. Therefore, these data are of increased interest in finding and analyzing the close links and development of these diseases.

The literature review confirms that obesity, in particular AO and overweight, negatively affect the functioning of the esophagus, increasing the GERD, which contributes to reflux.

Various risk factors are involved in the mechanisms of GERD induction, each of which plays a role in the pathogenesis of GERD, including muscle abnormalities such as impaired esophageal motility and impaired tone of the LES, while anatomical factors such as hiatal hernia or AO, in particular by increasing the IAP, also significantly affect this condition. This creates a vicious cycle where one disease worsens or induces another.

The combination of GERD and obesity is a complex medical problem that requires a multidisciplinary and comprehensive approach to the treatment and prevention of comorbidities. WL is a key component of therapy and an important step in the prevention of GERD and obesity complications. The main principles of GERD treatment aimed at reducing the IAP and are crucial for reducing the risk of GERD episodes and include WL, diet and food control, PA and the use of antisecretory drugs, BS.

REFERENCES

1. WGO Practice Guideline. Gastroesophageal reflux disease (GERD). World Gastroenterology Organisation. https://www.worldgastroenterology.org/guidelines/gastroesophageal-reflux-disease. [Accessed 1 March 2025]
2. Nakaz Ministerstva okhorony zdorov'ia Ukrainy vid 31 zhovtnia 2013 roku № 943. Unifikovanyi klinichnyi protokol pervynnoi, vtorynnoi (spetsializovanoi) medychnoi dopomohy. Hastroezofagealna refliuksna khvoroba 2013. [Order of the Ministry of Health of Ukraine dated October 31, 2013 No. 943. Unified clinical protocol of primary, secondary (specialized) medical care. Gastroesophageal reflux disease 2013.]. https://www.dec.gov.ua/wp-content/uploads/2019/11/2013_943_ykpmd_gerx.pdf [Accessed 1 March 2025] (Ukrainian)
3. Derzhavnyi ekspertyi tsentr Ministerstva okhorony zdorov'ia Ukrainy. Ukrainska asotsiatsiia hastroenterolohiv. Hastroezofagealna refliuksna khvoroba. Klinichna nastanova 2017. [State Expert Center of the Ministry of Health of Ukraine. Ukrainian Association of Gastroenterologists. Gastroesophageal Reflux Disease. Clinical Guidelines 2017.]. https://www.dec.gov.ua/wp-content/uploads/2019/11/2017_akn_gerh.pdf [Accessed 1 March 2025] (Ukrainian)
4. Obesity and overweight. World Health Organization. 1 March 2024. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. [Accessed 1.11. 2024]
5. Taraszewska A. Risk factors for gastroesophageal reflux disease symptoms related to lifestyle and diet. Rocz Panstw Zakl Hig. 2021;72(1):21-28. doi: 10.32394/rpzh.2021.0145. DOI
6. Sadafi SS, Azizi A, Pasdar Y et al. Risk factors for gastroesophageal reflux disease: a population-based study. BMC Gastroenterol. 2024;24(1):64. doi: 10.1186/s12876-024-03143-9. DOI
7. Sreekala KN, Das CC, Michael J et al. Smoking, diabetes mellitus, and obesity as risk factors of gastroesophageal reflux disease and extraesophageal symptoms of gastroesophageal reflux disease: a case-control study. Natl J Physiol Pharm Pharmacol. 2022;12(2):107–107. doi: 10.5455/njppp.2022.12.08277202106082021. DOI
8. Erridge S, Moussa OM, Ziprin P et al. Risk of GERD-related disorders in obese patients on PPI therapy: a population analysis. Obes Surg. 2018;28:2796–2803. doi: 10.1007/s11695-018-3246-4. DOI
9. Sohail R, Mathew M, Patel KK et al. Effects of non-steroidal anti-inflammatory drugs (NSAIDs) and gastroprotective NSAIDs on the gastrointestinal tract: a narrative review. Cureus. 2023;15(4):e37080. doi: 10.7759/cureus.37080. DOI
10. Patti M, Schlottmann F, Farrell T. Pathophysiology of gastroesophageal reflux disease in obese patients. The Perfect Sleeve Gastrectomy:

A Clinical Guide to Evaluation, Treatment, and Techniques. 2020. doi:10.1007/978-3-030-28936-2_14. DOI
11. Argyrou A, Legaki E, Koutserimpas C et al. Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. World J Clin Cases. 2018;6(8):176-182. doi: 10.12998/wjcc.v6.i8.176. DOI
12. Siboni S, Bonavina L, Rogers BD et al. Effect of increased intra-abdominal pressure on the esophagogastric junction: a systematic review. J Clin Gastroenterol. 2022;56(10):821–830. doi: 10.1097/MCG.0000000000001756. DOI
13. Shephard RJ. Physical activity and gastro-oesophageal reflux. Health Fit J Can. 2015;8(4):25–51. doi: 10.14288/hfjc.v8i4.197. DOI
14. Yen HH, Tseng PH, Shih MC et al. Derangement of esophageal anatomy and motility in morbidly obese patients: a prospective study based on high-resolution impedance manometry. Surg Obes Relat Dis. 2020;16(12):2006-2015. doi: 10.1016/j.soard.2020.07.023. DOI
15. Kahrilas P, Mittal R, Bor S et al. Chicago Classification update (v4.0): Technical review of high-resolution manometry metrics for EGJ barrier function. Neurogastroenterol Motil. 2021;33(10):e14113. doi: 10.1111/nmo.14113. DOI
16. Yang Y, Lin J, Li Y et al. Effect of body weight and obesity on esophageal function. Physiological Research. 2023;72(4):525–537. doi:10.33549/physiolres.935067. DOI
17. de Mello Del Grande L, Herbella FAM, Katayama RC et al. Transdiaphragmatic pressure gradient (TPG) has a central role in the pathophysiology of gastroesophageal reflux disease (GERD) in the obese and correlates with abdominal circumference but not with body mass index (BMI). Obes Surg. 2020;30(4):1424-1428. doi: 10.1007/s11695-019-04345-x. DOI
18. Chandar A, Iyer P. Role of Obesity in the Pathogenesis and Progression of Barrett's Esophagus. Gastroenterol Clin North Am. 2015;44(2):249-64. doi: 10.1016/j.gtc.2015.03.001. DOI
19. Heyn GS, Corrêa LH, Magalhães KG. The impact of adipose tissue–derived miRNAs in metabolic syndrome, obesity, and cancer. Front Endocrinol. 2020;11:563816. doi: 10.3389/fendo.2020.563816. DOI
20. Paris S, Ekeanyanwu R, Jiang Y et al. Obesity and its effects on the esophageal mucosal barrier. Am J Physiol Gastrointest Liver Physiol. 2021;321(3):G335-G343. doi: 10.1152/ajpgi.00199.2021. DOI
21. Zhou J, Ho V. Non-erosive reflux disease and oesophageal carcinoma: risk assessment is complicated by the dynamic nature of reflux disease. BMJ. 2023:382:1979. doi: 10.1136/bmj.p1979. DOI
22. Harris E. Most People With GERD Don't Have Increased Esophageal Cancer Risk. JAMA. 2023;330(15):1422. doi: 10.1001/jama.2023.18744. DOI
23. Mohan S, Lim ZY, Chan K, Shelat V. Impact of obesity on clinical outcomes of patients with intra-abdominal hypertension and abdominal compartment syndrome. Life (Basel). 2023;13(2):330. doi: 10.3390/life13020330. DOI
24. Barceló M, Sánchez AA, Sánchez RG et al. Weight gain and somatization are associated with the onset of gastroesophageal reflux disease: results of two 5-year follow-up studies. J Clin Gastroenterol. 2016;50(3):202-7. doi: 10.1097/MCG.0000000000000364. DOI
25. Danalioglu A, Kayar Y, Baysal B et al. Upper gastrointestinal system endoscopic findings in obese patients. Gastroenterology. 2015;148(4):S-674. doi:10.1016/S0016-5085(15)32276-9. DOI
26. Boonsombat T, Akavipat P, Suchartwatnachai P et al. Incidence of complications in obese patients undergoing elective spine surgery under general anesthesia: a retrospective study. J Neuroanaesthesiol Crit Care. 2024;11(1):046–051. doi:10.1055/s-0044-1782507. DOI
27. Lee H. Weight management as a treatment option for gastroesophageal reflux disease: a mechanical or metabolic rescuer? Gut Liver. 2018;12(6):607-608. doi: 10.5009/gnl18451. DOI
28. Kuribayashi S, Hosaka H, Nakamura F et al. The role of endoscopy in the management of gastroesophageal reflux disease. DEN Open. 2021. doi:10.1002/deo2.86. DOI
29. Malamood M, Shahsavari D, Parkman H. Modern evaluation of esophageal function in the gastrointestinal motility laboratory: a narrative review. Ann Esophagus. 2021. doi:10.21037/aoe-21-36. DOI
30. Barnhart C. Obesity prevention and management across the lifespan. Open Access Libr J. 2020;7(10):1–28. doi: 10.4236/oalib.1106733. DOI
31. Aboubakr A, Ghosh G, Yeung M et al. A gastroenterology-based multi-disciplinary weight management program reduces acid suppression therapy in patients with GERD: a prospective cohort study. Am J Gastroenterol. 2021;116:S152. doi:10.14309/01.ajg.0000773876.78026.ca. DOI
32. Masood M, Low D, Deal S et al. Gastroesophageal reflux disease in obesity: Bariatric surgery as both the cause and the cure in the morbidly obese population. J Clin Med. 2023;12(17):5543. doi: 10.3390/jcm12175543. DOI
33. Khan A, Kim A, Sanossian C, François F. Impact of obesity treatment on gastroesophageal reflux disease. World J Gastroenterol. 2016;22(4):1627-38. doi:10.3748/wjg.v22.i4.1627. DOI
34. Han S, Choi HY, Kim YH et al. Effect of food on the pharmacokinetics and pharmacodynamics of a single oral dose of tegoprazan. Clin Ther. 2021;43(8):1371–1380. doi: 10.1016/j.clinthera.2021.06.007. DOI
35. Mulford DJ, Leifke E, Hibberd M, Howden CW. The effect of food on the pharmacokinetics of the potassium competitive acid blocker Vonoprazan. Clin Pharmacol Drug Dev. 2022;11(2):278–284. doi: 10.1002/cpdd.1009. DOI

36. Nguyen AD. Effects of obesity surgery on GERD and esophageal motility. Foregut. 2021;1(4):380–385. doi: 10.1177/26345161211069178. DOI
37. Ashrafi D, Osland E, Memon MA. Bariatric surgery and gastroesophageal reflux disease. Ann Transl Med. 2020;8(1):S11. doi: 10.21037/atm.2019.09.15. DOI
38. Bolckmans R, Roriz-Silva R, Mazzini G. Long-term implications of GERD after sleeve gastrectomy. Curr Surg Rep. 2021;9:1–13. doi:10.1007/s40137-021-00284-8. DOI
39. Elzouki A, Waheed MA, Suwileh S et al. Evolution of GERD symptoms after bariatric surgery: A dose-response meta-analysis. CC BY 4.0. 2021. doi:10.21203/RS.3.RS-408294/V1. DOI
40. Misra S, Nandhini BD, Christinajoice S et al. Is laparoscopic Roux-en-Y gastric bypass still the gold standard procedure for Indians? Mid-to long-term outcomes from a tertiary care center. Obes Surg. 2020;30:4482–4493. doi: 10.1007/s11695-020-04849-x. DOI

The work was carried out in accordance with the plan of the research program of the Department of Therapy and Family Medicine of the Faculty of Postgraduate Education and Pre-University Training of Uzhhorod National University "Optimization of prevention and treatment of obesity and diabetes mellitus and Helicobacter», where the authors are co-authors.

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Taras I. Griadil
Uzhhorod National University
148 Sobranetska St., 88017 Uzhhorod, Ukraine
e-mail: taras.griadil@uzhnu.edu.ua

ORCID AND CONTRIBUTIONSHIP

Taras I. Griadil: 0000-0002-1048-0656 A B D E F
Bohdana V. Bezushko: 0000-0002-0953-8478 A B D E
Oleksandr O. Dutko: 0000-0002-4063-8194 A B D E
Mykhailo M. Lopit: 0000-0002-6425-2990 A B D E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 09.11.2024
ACCEPTED: 30.03.2025