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Biochemical composition of gastric contents in the discoordination of motor activity of the proximal gastrointestinal tract

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Disorders of neuromuscular coordination at the esophagogastric junction are accompanied by changes in motility and the biochemical composition of gastric contents, which affect the functional state of the mucous membrane. Disturbances in this region, particularly in achalasia of the cardia, allow the nature of these changes to be characterized. The study aimed to analyze biochemical and motor alterations associated with impaired neuromuscular coordination at the esophagogastric junction. To assess biochemical changes, gastric juice samples from 69 patients with impaired relaxation of the lower esophageal sphincter were collected during video gastroscopy. The functional state of the sphincters of the esophagogastroduodenal zone was investigated using balloon manometry under endoscopic guidance. In patients with achalasia of the cardia, a significant increase in the volume of gastric contents (2.9-fold) and in the concentrations of bile acids (by 78.8%), stable NO metabolites (68.2%), neuraminic acids (2.4-fold), and calcium (31.6%) was observed, along with a decrease in the levels of glycoproteins (by 85.7%), fucose (73%), and glycosaminoglycans (35.5%). At the same time, changes in pH and pepsin did not reach statistical significance. Among the manometric parameters, the most pronounced change was a decrease (by 29.2%) in the amplitude of rhythmic contractions of the esophagus. The obtained results indicate a combination of motor disturbances and alterations in the biochemical profile of gastric contents, and may suggest the involvement of mechanisms of duodenogastric reflux along with destabilization of the mucosal barrier in the pathogenesis of these changes.

Key words: stomach; gastric juice; protective factors; aggressive factors; nitric oxide; biomarkers of oxidative stress; calcium; biochemical markers; manometric study; achalasia of the cardia.

INTRODUCTION

The coordinated function of the esophagogastric junction is critically important for maintaining physiological homeostasis in the proximal part of the gastrointestinal tract. Disturbances of neuromuscular regulation in this region may be accompanied by impaired transit of contents, alterations in evacuatory function, and the formation of conditions for remodeling of the local chemical environment, which affects the state of the mucous membrane and the interaction between its protective and aggressive factors. In achalasia as a model of such dysfunction, the most characteristic features are impaired relaxation of the lower esophageal sphincter and the absence or ineffectiveness of esophageal peristalsis, leading to functional obstruction at the level of the esophagogastric junction [1, 2]. Prolonged impairment of esophageal motility may lead to progressive morphological changes. According to multicenter studies, patients with a long course of achalasia often develop esophageal dilatation, sigmoid deformation, and diverticula, reflecting the chronic nature of impaired transit and stasis of food contents [3].

The composition of gastric contents is formed as a result of the interaction of acid-peptic factors, components of the mucosal barrier, mucin glycans, as well as possible admixtures of duodenal refluxate, in particular bile acids.

These components are capable of altering the intraluminal environment of the stomach and modulating the state of the mucous membrane. Accordingly, the relationship between motor disturbances and biochemical alterations should be considered bidirectional: motor dysfunction may contribute to changes in the composition of gastric contents, while aggressive components of the environment may potentially sustain functional disturbances through receptor-mediated and neurohumoral mechanisms of the mucous membrane [4-6].

Most recent studies of achalasia are focused on its pathophysiology, diagnosis, classification, and treatment, whereas studies that simultaneously analyze motor parameters and the biochemical profile of gastric contents within a single clinical model of neuromotor dysfunction remain limited [7]. At the same time, it is known that in achalasia, structural and functional changes in the enteric nervous system, including degeneration of neurons of the myenteric plexus, may be accompanied by alterations in the local microenvironment of the mucous membrane and neurohumoral regulation [8-10].

The parallel assessment of pH, enzymatic activity, markers of the mucosal barrier, and glycoconjugates (including glycoproteins, glycosaminoglycans, fucosylation, and sialylation as indicators of glycan remodeling), as well as markers of neurohumoral and oxidative/nitrosative regulation, may be informative for understanding the mechanisms of mucosal damage and adaptation. Recent reviews emphasize the key role of mucin glycans in maintaining the integrity of the mucosal barrier and in interactions with the microbiota and inflammatory processes [6, 11]. In addition, studies in neurogastroenterology demonstrate that oxidative stress may impair the function of the enteric nervous system and affect the regulation of gastrointestinal motility [12, 13].

Modern standardized criteria for the diagnosis of achalasia are primarily based on high-resolution manometry (HRM), which underlies the Chicago Classification and allows assessment of impaired relaxation of the lower esophageal sphincter and patterns of esophageal contractions [1, 14]. However, such approaches mainly reflect patterns of peristalsis and integrated pressure metrics, whereas other functional aspects of motility may be evaluated using alternative methods. In the present study, modified balloon manometry was used, allowing assessment of pressure parameters during passage through sphincter zones and characteristics of rhythmic contractions. This method does not duplicate standard HRM metrics but complements them, providing an opportunity for integrated analysis of motor characteristics together with the biochemical composition of gastric contents. Experimental data also indicate that changes in the luminal environment may be accompanied by measurable disturbances of gastrointestinal motility, supporting the relevance of integrated physiological analysis [15].

Thus, the physiological and biochemical study of gastric contents in neuromotor dysfunction permits both the description of disturbances and the elucidation of integrated regulatory mechanisms in the proximal gastrointestinal tract.

The aim of this study was to analyze biochemical and motor changes associated with impaired neuromuscular coordination in the esophagogastric junction.

METHODS

Study design. The study included gastric juice samples obtained from 69 patients (median age 48 [34-55] years) with symptoms of impaired relaxation of the lower esophageal sphincter, who underwent video-gastroendoscopic examination for the diagnosis of achalasia of the cardia (ICD-10 K22.0) at the Department of Minimally Invasive Endoscopic Interventions and Instrumental Diagnostics, State Institution "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine".

The control group for biochemical analysis consisted of 26 healthy volunteers with no

clinical or endoscopic signs of gastrointestinal pathology. A separate control group for manometric research was formed, consisting of 20 individuals with preserved motor function of the corresponding zone.

The study was conducted in accordance with the Council of Europe Convention on Human Rights and Biomedicine (April 4, 1997) and the Helsinki Declaration of the World Medical Association on the ethical principles of medical research. The study protocol was approved by the Biomedical Ethics Committee of the State Institution "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine" (Protocol No. 2, dated 07.04.2022).

Biochemical analysis of gastric juice samples. Calcium content was assessed using the reagent kit "Filisit-Diagnostics". The concentration of stable nitric oxide metabolites (NOx) was determined by reducing nitrates to nitrites using vanadium chloride followed by diazotization [16]. The concentrations of pepsin, glycoproteins, fucose, neuraminic acids, hexosamines, and bile acids were measured using standard methods [17].

Assessment of the functional state of the esophagogastroduodenal zone muscles. In addition, patients underwent pneumoballoon manometry. For this purpose, an endoscopic lithoextraction probe (Micro-tech Stone Extraction Balloon SRB-T-9/12/15-20) was used. The manometric study was performed under endoscopic control. Data registration was carried out using an Art-line AS-0013 sensor at a sampling frequency of 1 Hz. Initial data processing was performed using the MNC-01 software-hardware complex, followed by visualization and analysis in Microsoft Excel.

Statistical analysis. The statistical analysis of quantitative characteristics was performed using a software package Real Statistics (USA). Data distribution was tested using the Shapiro–Wilk test and found to be non-normal. Accordingly, data are presented as median (Me) and interquartile range [Q1-Q3]. Differences between groups were assessed using the Mann–Whitney test and were considered statistically significant at $P < 0.05$.

RESULTS AND DISCUSSION

Biochemical characterization of gastric juice in neuromuscular dysfunction of the esophagogastric junction. In patients with achalasia of the cardia, changes in the physicochemical and biochemical composition of gastric contents are complex in nature and may reflect a combination of alterations in secretory processes, the state of the mucosal barrier, and conditions of content evacuation, which in neuromuscular disorders of the esophagogastric junction are interrelated and may potentially influence each other [2].

The most pronounced difference was an increase in the volume of gastric contents available for sampling during endoscopy. In patients with achalasia, it was 7.65 [5.08-10.08] ml; this is 2.9-fold higher than the corresponding control value of 2.60 [2.10-4.70] ml ($P = 0.001$). This is consistent with the fact that in achalasia, impaired evacuation due to neuromuscular dysfunction is predominant, whereas the causal relationship between stasis and changes in the chemical composition of the contents may be bidirectional [1].

The NOx level increased by 68.2% ($P = 0.017$); this finding is consistent with the role of NO signaling in neuromuscular regulation of motility and possible contribution of nitrosative/oxidative imbalance to smooth muscle dysfunction [10, 13].

Changes in gastric pH (increase from 2.90 to 3.08) did not reach statistical significance ($P = 0.58$), which may indicate relatively preserved or compensated acid production. The pepsin level showed only a tendency to decrease ($P = 0.055$). Therefore, the acid-peptic component should be interpreted cautiously, whereas greater attention may be paid to the barrier component and the altered luminal environment.

Pronounced changes were observed in the components of the mucosal barrier: the concentration of glycoproteins decreased by 85.7%

(P = 0.001), fucose by 73.0% (P = 0.001), and glycosaminoglycans by 35.5% (P = 0.009). These changes are consistent with current data on the importance of fucosylation and the diversity of mucin O-glycans in maintaining the properties of the mucosal barrier and interactions with the microbiota, although direct clinical data specifically for achalasia remain limited [5, 6, 11]. At the same time, a 2.4-fold increase in neuraminic acids (P = 0.007) may reflect remodeling of epithelial surface glycoconjugates and adaptive alterations in the mucosal layer.

An increase in the concentration of bile acids in gastric contents by 78.8% (P = 0.001) supports the presence of duodenogastric reflux, which is regarded as a factor of chemical injury to the mucous membrane and a potential trigger of inflammatory/oxidative mechanisms, especially in combination with weakening of the mucosal barrier [18].

An increase in total calcium by 31.6% (P = 0.045) may also be functionally significant given the role of Ca^{2+} in intracellular signaling and regulation of smooth muscle contractility. Disturbances in calcium-dependent mechanisms are associated with changes in motility and neuromuscular transmission [19, 12], although the clinical interpretation of "increased calcium in contents" requires additional control of potential confounders.

Thus, the obtained data indicate a combination of (a) significant destabilization of the mucosal barrier, (b) signs of duodenogastric reflux, and (c) activation of NO-dependent mechanisms, which together may form an unfavorable biochemical environment of the stomach in achalasia of the cardia. Indicators of the acid-peptic component showed only tendencies; therefore, they should be interpreted as directions of change requiring further clarification in studies with control of potential confounders. Generalized indicators of the biochemical composition of gastric contents are presented in Table 1.

Thus, the obtained results revealed a complex of statistically significant changes and pronounced trends primarily associated with destabilization of the mucosal barrier and signs of duodenogastric reflux, as well as with increased levels of NOx and Ca^{2+} as potentially functionally significant components of neurohumoral regulation. At the same time, the absence of statistically significant differences in pH and only a tendency toward decreased pepsin limit the interpretation of these findings as evidence of a pronounced alteration in the acid-peptic factor.

Disruption of peristaltic activity and sphincter regulation in achalasia of the cardia. In patients with achalasia of the cardia,

Table 1. Biochemical parameters of gastric juice (median [Q1-Q3])

Parameter, unit	Control (n = 26)	Achalasia of the cardia (n=69)	P-value
Volume, ml	2.60 [2.10–4.70]	7.65 [5.08–10.08]	0,001*
pH	2.90 [2.45–3.58]	3.08 [2.18–4.55]	0.58
Pepsin, mg/ml	0.92 [0.70–1.21]	0.50 [0.08–0.80]	0.055
Glycoproteins, mmol/l	0.63 [0.36–0.80]	0.09 [0.06–0.16]	0.001*
Bile acid, μmol/l	118 [113–121]	211 [140–404]	0,001*
Total calcium, μmol/l	0.97 [0.76–1.21]	1.27 [1.08–1.52]	0.045*
Nitric oxide metabolites (NOx), μmol/l	31.03 [24.39–36.63]	52.21 [21.69–119.49]	0.017*
Neuraminic acid, mmol/l	0.08 [0.04–0.08]	0.18 [0.08–0.28]	0.007*
Fucose, mmol/l	1.12 [0.41–1.12]	0.30 [0.18–0.58]	0.001*
Glycosaminoglycans, mmol/l	0.80 [0.55–0.93]	0.52 [0.30–0.73]	0.009*

Note. P values refer to comparisons between groups. * Statistical significance at $P \leq 0.05$.

changes in the motor activity of the esophagus and adjacent parts of the gastrointestinal tract were observed, which is of clinical significance for understanding disorders of neuromuscular regulation and evacuatory function. The latter is characterized by impaired relaxation of the lower esophageal sphincter associated with degenerative changes in intramural innervation and dysregulation of neurotransmitter mechanisms [1, 9].

According to balloon manometry data, most parameters showed only trends toward differences that did not reach statistical significance ($P > 0.05$; Table 2). This pattern is expected given the heterogeneity of achalasia and interindividual variability of the motor response, as described in recent reviews and classification approaches [2, 7]. Clinical manifestations of achalasia are also closely related to the nature of motor disturbances. Studies indicate that the manometric subtype of the disease may determine the features of symptomatology, including the severity of dysphagia, regurgitation, and chest pain, confirming the clinical significance of motor changes in shaping the disease phenotype [20].

The only manometric parameter showing a statistically significant difference was the amplitude of rhythmic contractions of the esophageal muscles (AMRE), which was reduced by 29.2% compared with the control group ($P = 0.002$). The decrease in contraction amplitude is consistent with the neuromuscular nature of the disease and reflects a reduction in the tone and contractile capacity of esophageal smooth muscles [10, 21].

Peristaltic dysfunction in achalasia is associated not only with the absence or ineffectiveness of peristalsis, but also with changes in the biomechanical properties of the lower esophageal sphincter and esophageal wall. In particular, experimental studies indicate disturbances of adaptive relaxation mechanisms and altered hysteresis of the lower esophageal sphincter, which may limit its ability to respond adequately to distension and contribute to the formation of functional obstruction [22].

The probable morphofunctional basis of these disturbances is damage to the intramural nervous apparatus of the esophagus, with predominant involvement of the intermuscular (myenteric, or Auerbach's) nerve plexus. This structure of the enteric nervous system is located between the circular and longitudinal layers of smooth muscle and plays a key role in the regulation of peristaltic contractions and sphincter relaxation in the digestive tract. Degenerative changes in this plexus are regarded as a central pathogenetic mechanism of achalasia, manifest-

Table 2. Manometric parameters of motor function of the esophagus and gastroduodenal zone in patients with achalasia of the cardia (median [Q1-Q3])

Parameter, unit	Control group (n = 20)	Achalasia of the cardia (n = 69)	P-value
Balloon pressure during pyloric sphincter passage, mmHg	17.58 [15.19-20.11]	23.82 [11.02-43.04]	0.264
Balloon pressure during lower esophageal sphincter passage, mmHg	19.54 [18.25-20.12]	22.80 [9.76-43.69)	0.440
Amplitude of peristaltic wave, mmHg	22.94 [14.52-28.10]	14.99 [14.02-18.58]	0.360
Peristaltic wave period, s	16.98 [14.75-18.31]	19.00 [14.14-22.78]	0.478
Amplitude of rhythmic muscle contractions, mmHg	6.35 [5.39-9.87]	4.50 [2.78-5.28]	0.002*
Period of rhythmic muscle contractions, s	3.21 [2.90- 4.20]	3.82 [3.30-4.49]	0.351

Note. P values refer to comparisons between groups. *Statistical significance at $P \leq 0.05$.

ed by loss or dysfunction of inhibitory neurons that synthesize nitric oxide (NO) and vasoactive intestinal peptide [10, 12]. Selective loss of these neurons leads to an imbalance between excitatory cholinergic and inhibitory nitrergic innervation, resulting in increased tone of the lower esophageal sphincter, impaired relaxation, and loss of coordinated peristalsis in the distal esophagus [1, 9].

At the same time, the submucosal (Meissner's) plexus, which is localized in the submucosal layer and predominantly regulates secretory function, local blood circulation, and trophism of the mucous membrane, is considered to be less involved in the primary mechanisms underlying motor disturbances in achalasia. In most recent studies, the main pathological process is localized specifically in the myenteric plexus, whereas the role of the submucosal plexus has been described to a much lesser extent and remains insufficiently clarified [10].

Recent molecular studies also confirm the complex nature of neuromuscular disturbances in achalasia. Proteomic analyses of lower esophageal sphincter tissue have revealed changes in signaling pathways associated with inflammatory processes, immune response, and neuronal regulation, which may indicate a multifactorial mechanism of neuronal degeneration and impaired motor coordination [23, 24]. Accordingly, further morphological and immunohistochemical studies of intramural nervous structures may be important for clarifying the contribution of different components of the enteric nervous system to the development of neuromuscular disturbances in achalasia.

Taken together, the presented data indicate disturbances of the tonic component of motility and discoordination of motor activity in the esophagogastric junction in achalasia of the cardia. Given that only AMRE demonstrated significant differences, the other manometric parameters should be regarded as descriptive and promising for further stratified analysis taking into account the type of achalasia, disease duration, and treatment effects [7, 25].

Concordance of motor disturbances and biochemical changes in achalasia of the cardia. A comprehensive analysis of biochemical and manometric parameters in patients with achalasia of the cardia indicates a combination of motor dysfunction of the esophagogastric junction with the formation of an altered chemical microenvironment in the proximal gastrointestinal tract. In the literature, achalasia is defined as a primary motor disorder with impaired relaxation of the lower esophageal sphincter and ineffective peristalsis, which is clinically often accompanied by stasis, regurgitation, and aspiration manifestations [1, 2]. In this context, the biochemical shifts obtained in our study should be interpreted not as a consequence of secretion alone but as part of a multicomponent interaction of motility, reflux and stasis, and mucosal barrier and its mediators.

Our data on the decreased amplitude of rhythmic esophageal contractions are consistent with the concept of reduced efficiency of propulsive function in achalasia and with the recognized heterogeneity of manometric phenotypes [20]. The observation that some manometric parameters showed only trends without statistical significance may be explained by individual variability of motor responses, heterogeneity of achalasia phenotypes, and differences in disease stage or compensation. In this context, biochemical markers, especially indicators of barrier function, may be more sensitive to subclinical changes; however, this requires confirmation in study designs with stratification by achalasia type and control of potential confounders. Systematic reviews indicate that different manometric subtypes of the disease are characterized by differences in esophageal contractile activity, sphincter function, and clinical manifestations, underscoring the complexity of the pathophysiology of this disorder [20].

The biochemical profile in our study (increased bile acids and NOx, decreased glycoproteins, fucose, and glycosaminoglycans, and increased neuraminic acids) is consistent with a model in which stasis and duodeno-

gastric reflux enhance the chemical injury of the mucosa, while weakening of the mucosal barrier enhances its vulnerability. The role of bile acids as a damaging factor and a trigger of inflammatory-oxidative cascades in the stomach is widely discussed in reviews on bile reflux, metaplasia, and bile acid-induced mechanisms [5, 11]. Accordingly, the elevated bile acid levels observed in our study, together with decreased components of the mucosal barrier, are consistent with this line of evidence.

Regarding NO-dependent mechanisms, nitric oxide is a key mediator of neuromuscular regulation in the enteric nervous system, and disturbances in its regulation and neuroinflammation are regarded as underlying mechanisms in motor disorders, including achalasia [10, 12]. At the same time, reviews in neurogastroenterology emphasize that oxidative stress may sustain neuronal dysfunction and impair neuromuscular transmission [13]. Therefore, the increase in NOx in our patients should be interpreted as a marker of activation of NO signaling and nitrosative imbalance, which may potentially amplify motor disturbances but does not, by itself, establish the direction of causality.

It is important that the concordance between motility and biochemical changes in our data is most evident for the axis "evacuation/stasis - luminal remodeling - mucosal barrier," whereas the acid-peptic component showed only trends. This is consistent with the view that, under conditions of impaired transit, the biological significance of barrier insufficiency and altered luminal composition may outweigh the role of acid alone.

The increase in total Ca^{2+} in gastric contents may be regarded as potentially functionally relevant, since Ca^{2+}-dependent mechanisms are fundamental to patterns of motility and the interaction of smooth muscles with interstitial cells and neuronal circuits. Recent reviews emphasize the fundamental role of calcium dynamics in the generation of gastrointestinal motor patterns [19]. This makes our observation biologically plausible, although it requires cautious interpretation, as measurement in gastric contents does not directly reflect intracellular processes.

To further strengthen the interpretation, it would be advisable to: (I) perform stratification by achalasia type and disease duration; (II) conduct correlation analysis between AMRE/sphincter pressure and key markers (bile acids, NOx, mucosal glycoconjugates); (III) supplement the data with morphological and immunohistochemical assessment (in particular regarding the state of the intramural nervous apparatus) and/or methods of functional assessment of motility. Such an approach is consistent with contemporary directions of achalasia research that combine functional, molecular, and morphological data [7, 23, 24].

It is important to avoid one-sided causal interpretation: although motor dysfunction logically creates conditions for stasis and reflux, the components of gastric contents themselves (bile acids, pepsin in a non-acidic environment, and alterations in the mucosal barrier) may modulate sensory and neurohumoral reactions of the mucosa and influence motility both through local mechanisms and via enteric nervous system circuits [12, 15]. Accordingly, the associations we obtained should be interpreted as a mutually reinforcing pathological circle rather than as a proven linear sequence of events.

Thus, our results complement the current understanding of achalasia as a neuromuscular disorder in which motor obstruction and impaired propulsion are associated with the formation of an altered chemical environment (in particular bile acid loading) and destabilization of the mucosal barrier [2, 9, 19]. At the same time, NO- and Ca^{2+}-related links remain biologically plausible candidates for explaining the interplay between motility and mediators/stress, but require further verification in study designs with better control of confounders.

CONCLUSIONS

Neuromuscular dysfunction of the esophagogastric junction is associated with combined

motor and biochemical alterations of gastric contents. Reduced esophageal contractility was accompanied by increased gastric volume and higher levels of bile acids, nitric oxide metabolites, and calcium, suggesting a trend toward a more aggressive intraluminal environment. These changes were paralleled by alterations in mucosal barrier markers.

Integrated assessment of motility and gastric biochemistry may provide additional insight into functional disturbances in achalasia and suggests the involvement of motor, barrier, and oxidative–nitrosative mechanisms in its pathogenesis.

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БІОХІМІЧНИЙ СКЛАД ШЛУНКОВОГО ВМІСТУ ПРИ ДИСКООРДИНАЦІЇ МОТОРНОЇ АКТИВНОСТІ ПРОКСИМАЛЬНОГО ВІДДІЛУ ТРАВНОГО ТРАКТУ

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Порушення нейром'язової координації у стравохідно-шлунковому переході супроводжуються змінами моторики та біохімічного складу шлункового вмісту, що впливає на функціональний стан слизової оболонки. Зміни в цій зоні, зокрема при ахалазії кардії, дає змогу простежити характер зазначених змін. Метою нашого дослідження було проаналізувати біохімічні та моторні зміни при порушенні нейром'язової координації в ділянці стравохідно-шлункового переходу. Для оцінки біохімічних змін були використані проби шлункового соку 69 пацієнтів із порушенням розслаблення нижнього стравохідного сфінктера, зібрані під час відеогастроендоскопії. Функціональний стан сфінктерів езофагогастродуоденальної зони досліджували методом балонної манометрії під ендоскопічним контролем. У пацієнтів з ахалазією кардії встановлено достовірне підвищення об'єму шлункового вмісту (у 2,9 раза), концентрацій жовчних кислот (на 78,8%), стабільних метаболітів NO (68,2%), нейрамінових кислот (у 2,4 раза) і кальцію (31,6%), а також зниження вмісту глікопротеїнів (на 85,7%), фукози (73%) та глікозаміногліканів (35,5%). При цьому зміни pH і пепсину не сягали статистичної значущості. Серед манометричних показників найбільш вираженим було зниження (на 29,2%) амплітуди ритмічних скорочень стравоходу. Отримані результати свідчать про поєднання моторних порушень із змінами біохімічного профілю шлункового вмісту та можуть вказувати на участь механізмів дуоденогастрального рефлюксу й дестабілізації слизового бар'єра в патогенезі цих змін.

Ключові слова: шлунок; шлунковий сік; захисні фактори; агресивні фактори; оксид азоту; біомаркери оксидативного стресу; кальцій; біохімічні маркери; манометричне дослідження; ахалазія кардії.

REFERENCES

1. Savarino E, Bhatia S, Roman S, Sifrim D, Tack J, Thompson SK, Gyawali CP. Achalasia. Nat Rev Dis Primers. 2022 May 5;8(1):28. doi: 10.1038/s41572-022-00356-8.
2. Pesce M, Pagliaro M, Sarnelli G, Sweis R. Modern achalasia: diagnosis, classification, and treatment. J Neurogastroenterol Motil. 2023 Oct 30;29(4):419-27. doi: 10.5056/jnm23125.
3. Sato H, Fujiyoshi Y, Abe H, Shiwaku H, Shiota J, Sato C, Sakae H, Ominami M, Hata Y, Fukuda H, Ogawa R, Nakamura J, Tatsuta T, Ikebuchi Y, Yokomichi H, Terai S, Inoue H. Development of dilated esophagus, sigmoid esophagus, and esophageal diverticulum in patients with achalasia: Japan achalasia multicenter study. J Neurogastroenterol Motil. 2022;28(2):222-30. doi: 10.5056/jnm21188.
4. Arai J, Hayakawa Y, Tateno H, Fujiwara H, Kasuga M, Fujishiro M. The role of gastric mucins and mucin-related glycans in gastric cancers. Cancer Sci. 2024;115:2853-61. doi: 10.1111/cas.16282.
5. Brockhausen I, Falconer D, Sara S. Relationships between bacteria and the mucus layer. Carbohydr Res. 2024 Dec;546:109309. doi: 10.1016/j.carres.2024.109309.
6. Fekete E, Buret AG. The role of mucin O-glycans in microbiota dysbiosis, intestinal homeostasis, and host-pathogen interactions. Am J Physiol Gastrointest Liver Physiol. 2023 Jun 1;324(6):G452-G65. doi: 10.1152/ajpgi.00261.2022.
7. Ali AH, Ichkhanian Y, Sloan JA, et al. Updates in the work-up and management of achalasia: a contemporary review. Curr Treat Options Gastroenterol. 2025;23:20.

doi: 10.1007/s11938-025-00485-5.
8. Geng ZH, Zhu Y, Chen WF, Fu PY, Xu JQ, Wang TY, et al. The role of type II esophageal microbiota in achalasia: activation of macrophages and degeneration of myenteric neurons. Microbiol Res. 2023 Nov;276:127470. doi: 10.1016/j.micres.2023.127470.
9. Jia X, Chen S, Zhuang Q, Tan N, Zhang M, Cui Y, Wang J, Xing X, Xiao Y. Achalasia: the current clinical dilemma and possible pathogenesis. J Neurogastroenterol Motil. 2023 Apr 30;29(2):145-55. doi: 10.5056/jnm22176.
10. Niesler B, Kuerten S, Demir IE, Schäfer KH. Disorders of the enteric nervous system: a holistic view. Nat Rev Gastroenterol Hepatol. 2021 Jun;18(6):393-410. doi: 10.1038/s41575-020-00385-2.
11. Chahal G, Padra M, Erhardsson M, Jin C, Quintana-Hayashi M, Venkatakrishnan V, Padra JT, Stenbäck H, Thorell A, Karlsson NG, Lindén SK. A complex connection between the diversity of human gastric mucin O-glycans, *Helicobacter pylori* binding, Helicobacter infection and fucosylation. Mol Cell Proteomic. 2022;21(11):100421. doi: 10.1016/j.mcpro.2022.100421.
12. Sharkey KA, Mawe GM. The enteric nervous system. Physiol Rev. 2023 Apr 1;103(2):1487-564. doi: 10.1152/physrev.00018.2022.
13. Stavely R, Ott LC, Sahakian L, Rashidi N, Sakkal S, Nurgali K. Oxidative stress and neural dysfunction in gastrointestinal diseases: can stem cells offer a solution? Stem Cells Transl Med. 2023 Dec 18;12(12):801-10. doi: 10.1093/stcltm/szad063.
14. Fox MR, Sweis R, Yadlapati R, Pandolfino J, Hani A, Defilippi C, Jan T, Rommel N. Chicago classification version 4.0 technical review: update on standard high-resolution manometry protocol for the assessment of esophageal motility. Neurogastroenterol Motil. 2021 Apr;33(4):e14120. doi: 10.1111/nmo.14120.
15. Korinchak LM. Prebiotic prevents the development of gastrointestinal motility disorders caused by omeprazole. Fiziol Zh. 2023 Sep 10;69(5):83-8. doi: 10.15407/fz69.05.083.
16. Kaur S, Gupta KB, Kumar S, Upadhyay S, Mantha AK, Dhiman M. Methods to detect nitric oxide and reactive nitrogen species in biological sample. Method Mol Biol. 2022;2413:69-76. doi: 10.1007/978-1-0716-1896-7_9.
17. Rudenko AI, Maykova TV, Mosiychuk LM, Ponomarenko OA, Tolstykova TM, Syrotenko AS. Clinical and laboratory assessment of the functional state of the secretory glands of the stomach: methodological recommendations of the MHU. Kyiv; 2004. [Ukrainian].
18. McCabe ME 4th, Dilly CK. New causes for the old problem of bile reflux gastritis. Clin Gastroenterol Hepatol. 2018 Sep;16(9):1389-92. doi: 10.1016/j.cgh.2018.02.034.
19. Sanders KM, Drumm BT, Cobine CA, Baker SA. Ca^{2+} dynamics in interstitial cells: foundational mechanisms for the motor patterns in the gastrointestinal tract. Physiol Rev. 2024 Jan 1;104(1):329-98. doi: 10.1152/physrev.00036.2022.
20. Katsumata R, Manabe N, Sakae H, Hamada K, Ayaki M, Murao T, Fujita M, Kamada T, Kawamoto H, Haruma K. Clinical characteristics and manometric findings of esophageal achalasia: a systematic review regarding differences among three subtypes. J Smooth Muscle Res. 2023;59:14-27. doi: 10.1540/jsmr.59.14.
21. Zhuang Q, Tan N, Hou X, Chen S, Jia X, Zhang M, Chen F, Zhang Z, Xing X, Xiao Y. Differential neurogenesis status among achalasia subtypes. Neurogastroenterol Motil. 2025 Jul;37(7):e70021. doi: 10.1111/nmo.70021.
22. Jain AS, Breaux W, Robertson JK, Kim SE, McAdoo B, Keilin S, Fernandez F, Srinivasan S, Mittal RK. Hysteresis of the lower esophageal sphincter: relevance to the pathogenesis of esophageal achalasia and its phenotypes. Am J Physiol Gastrointest Liver Physiol. 2025;329(3):G500-G9. doi: 10.1152/ajpgi.00089.2025.
23. Chen S, Xing X, Hou X, Zhuang Q, Tan N, Cui Y, Wang J, Zhang M, Hu S, Xiao Y. The molecular pathogenesis of achalasia: a paired lower esophageal sphincter muscle and serum proteomic study. Gastroenterol Rep. 2023;11:goad031. doi: 10.1093/gastro/goad031.
24. Patel CK, Kahrilas PJ, Hodge NB, Tsikretsis LE, Carlson DA, Pandolfino JE, Tétreault MP. RNA sequencing reveals molecular and regional differences in the esophageal mucosa of achalasia patients. Sci Rep. 2022 Nov 30;12(1):20616. doi: 10.1038/s41598-022-25103-7.
25. Riccio F, Costantini M, Salvador R. Esophageal achalasia: diagnostic evaluation. World J Surg. 2022;46:1516-21. doi: 10.1007/s00268-022-06483-3.

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