

# FEATURES OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH METABOLIC SYNDROME

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## Annotation.

The worldwide incidence of GERD and its complications is increasing along with the exponentially increasing problem of obesity. Of particular concern is the relationship between central adiposity and GERD complications, including oesophageal adenocarcinoma. Pathophysiological disturbances in obesity include esophageal motor disorders, lower esophageal sphincter abnormalities, development of hiatal hernia, increased intragastric pressure and increased gastric capacity.

Purpose – To study the features of GERD and obesity on the background of metabolic syndrome, diabetes mellitus type 2.

Material and methods – We studied 90 subjects who underwent a comprehensive health check-up, which included laboratory test, upper gastrointestinal endoscopy, pH monitoring and complete anthropometric measures. GERD symptoms were evaluated with GerdQ. Endoscopically erosive esophagitis was scored using the Los Angeles classification system.

Results – Compared with patients without metabolic syndrome, patients with erosive esophagitis and metabolic syndrome and diabetes mellitus type 2 had significantly higher BMI, waist circumference, cholesterol and triglyceride levels, HbA1c and HOMA-IR ( $P < 0.05$ ). In the group of patients with the metabolic syndrome, type 2 diabetes was observed more severe erosive reflux esophagitis.

Conclusion – In the group of patients with GERD and MS, type 2 diabetes against the background of obesity and overweight, symptoms of acid regurgitation, heartburn and dysphagia, lipid metabolism disorders are recorded significantly more often than among patients of the 2nd clinical group. The frequency and severity of classic manifestations of GERD (heartburn, acid regurgitation, dysphagia, retrosternal pain) did not differ significantly in the comparison groups by gender.

*Keywords: gastroesophageal reflux disease, obesity, diabetes, metabolic syndrome*

# METABOLIK SINDROMLI BEMORLARDA GASTROEZOFAGIAL REFLYUKS KASALLIGINING XUSUSIYATLARI

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## Annotatsiya.

Butun dunyoda GERK bilan kasallanish va uning asoratlari semirish muammosi bilan birga eksponent ravishda o'sib bormoqda. Markaziy semirish va GERK asoratlari, shu

jumladan qizilo'ngach adenokarsinomasi o'rtasidagi bog'liqlik alohida tashvish tug'diradi. Semirib ketishning patofiziologik buzilishlariga qizilo'ngach harakatining buzilishi, pastki qizilo'ngach sfinkterining ohangining pasayishi, hiatal churra rivojlanish tendentsiyasi, oshqozon ichidagi bosimning oshishi va oshqozon hajmining oshishi kiradi.

Maqsad – Metabolik sindrom, 2-toifa diabet fonida GERK va semirishning xususiyatlarini o'rganish.

Material va usullar – Keng qamrovli tibbiy ko'rikdan o'tgan va laboratoriya tekshiruvlari, yuqori endoskopiya, kunlik pH va antropometrik ko'rsatkichlarni o'z ichiga olgan 90 bemor tekshirildi. GERK belgilari GerdQ so'rovnomasi yordamida baholandi. Endoskopik eroziv ezofagit o'zgartirilgan Los-Anjeles tasnifi bo'yicha baholandi.

Natijalar – Matabolik sindromsiz GERK bilan og'rigan bemorlar bilan solishtirganda, eroziv ezofagit bilan og'rigan bemorlarda tana massasi indeksi, bel atrofi va qondagi xolesterin va triglitseridlar, HbA1c va HOMA-IR ( $p < 0,05$ ) sezilarli darajada yuqori bo'lgan. Metabolik sindromli bemorlar guruhida.

Xulosa – GERK va MS bilan og'rigan bemorlar guruhida, semirish va ortiqcha vazn fonida 2-toifa diabet, kislotali regürjitatsiya, oshqozon yonishi va disfagiya belgilari, lipid metabolizmining buzilishi 2-klinik guruhdagi bemorlarga qaraganda ishonchli tarzda tez-tez qayd etiladi. GERKning klassik ko'rinishlarining chastotasi va zo'ravonligi (oshqozon yonishi, kislotali regürjitatsiya, disfagiya, retrosternal og'riq) gender farqlari bo'yicha taqqoslash guruhlarida sezilarli darajada farq qilmadi.

*Kalit so'zlar: gastroezofagial reflyuks kasalligi, semirish, diabet, metabolik sindrom*

## ОСОБЕННОСТИ ТЕЧЕНИЯ ГЭРБ У ПАЦИЕНТОВ С МЕТАБОЛИЧЕСКИМ СИНДРОМОМ

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### Аннотация.

Во всем мире заболеваемость ГЭРБ и ее осложнений растет экспоненциально вместе с проблемой ожирения. Особую озабоченность вызывает связь между центральным ожирением и осложнениями ГЭРБ, в том числе аденокарциномы пищевода. Патологические нарушения при ожирении включают нарушения моторики пищевода, ослабление тонуса нижнего пищеводного сфинктера, тенденцию к развитию грыжи пищеводного отверстия диафрагмы, повышение внутрижелудочного давления и увеличение объема желудка.

Цель исследования – Изучить особенности течения ГЭРБ и ожирения на фоне метаболического синдрома, сахарного диабета 2-го типа.

Материал и методы – Было исследовано 90 пациентов, которым проводилось комплексное медицинское обследование и включало лабораторные исследования, верхнюю эндоскопию, суточную рН-метрию и антропометрические показатели. Симптомы ГЭРБ были оценены с помощью опросника GerdQ. Эндоскопически эрозивный эзофагит оценивали по модифицированной Лос-Анджелесской классификации.

Результаты – По сравнению с пациентами с ГЭРБ без метаболического синдрома, у пациентов с эрозивным эзофагитом был зарегистрирован значительно

более высокий индекс массы тела, окружности талии и уровень холестерина и триглицеридов в крови, HbA1c и HOMA-IR ( $P < 0,05$ ). В группе пациентов с метаболическим синдромом.

Заключение – В группе пациентов с ГЭРБ и МС, СД 2 типа на фоне ожирения и избыточной массы тела симптомы регургитации кислым, изжоги и дисфагии, нарушения липидного обмена регистрируется достоверно чаще, чем среди пациентов 2-ой клинической группы. Частота и выраженность классических проявлений ГЭРБ (изжога, регургитации кислым, дисфагия, ретростерральная боль) значительно не различались в группах сравнения по гендерным отличиям.

*Ключевые слова: гастроэзофагеальная рефлюксная болезнь, ожирение, сахарный диабет, метаболический синдром*

### Introduction/The relevance of research.

In the last decade, there has been an increase in the incidence of gastroesophageal reflux disease (GERD) among the adult population, a decrease in the quality of life and the development of complicated forms of the disease, such as Barrett's esophagus (PB) and esophageal adenocarcinoma (AP). GERD occupies a leading position in the United States in terms of treatment costs among other gastroenterological diseases. According to international statistics, the prevalence of GERD in the USA is 21-27% of the population, in Japan about 16%, in Asian countries 2-10% [1,3].

Two large multicenter epidemiological studies of the prevalence of GERD were conducted in Russia: MAGRE (Multicenter study "Epidemiology of gastroesophageal reflux disease in Russia") and ARIADNA (Analysis of the prevalence of heartburn: a national epidemiological study of the adult urban population), according to which the prevalence of GERD was about 24% [2, 4].

Obesity is a disease that globally covers the whole world. According to WHO, more than 1.9 billion adults aged 18 and over are overweight, of which over 600 million are obese. Epidemiological data show that, in general, obesity (usually measured as BMI – kg/m<sup>2</sup>) is a risk factor for both GERD and AP. Obesity is an even more widespread health problem worldwide. A statistically significant increase in the risk of developing symptoms of GERD, PB and AP in

obese patients was shown by the results of a meta-analysis [6]. According to the data obtained within the framework of the National Health and Nutrition Examination Program of the US population, in 2011-2014 the prevalence of obesity among the adult population was 36.5% [13, 14]. Cross-sectional epidemiological studies have demonstrated a higher prevalence of GERD among obese patients compared to healthy volunteers. Small studies also confirm the link between obesity and GERD. In a study conducted by El-Serag et al., 453 clinic staff were interviewed, and weekly symptoms of heartburn and/or regurgitation were detected in 26% of respondents. [7, 8]. Upper endoscopy was performed in 196 patients who agreed to the study, as a result, the proportion of patients with GERD symptoms was 23.3%, 26.7% and 50% for their respective groups with BMI <25 kg/m<sup>2</sup>, BMI – 25-30 kg/m<sup>2</sup> and BMI>30 kg/m<sup>2</sup>, respectively. The prevalence rates of erosive esophagitis for these groups were 12.5%, 29.8% and 26.9%, respectively.

In a cohort study conducted in Japan, with the inclusion of 42862 adults, among 18792 patients who underwent endoscopy of the upper digestive tract, 4355 (23.1%) were diagnosed with reflux esophagitis, 4731 (25.1%) – hernia of the esophageal orifice of the diaphragm, 1492 (7.9%) – Barrett's esophagus [9]. Multivariate analysis of the study results showed that male gender (OR 2.02; 95% CI 1.832.23; p=0.0001), young age (OR 0.99; 95% CI 0.980.99; p=0.0001), hypertriglyceridemia (OR 1.001; 95% CI 1.0011.002, p=0.0001), obesity (OR 1.51; 95% CI 1,401.64, p=0.0001), hypertension (OR 1.11; 95% CI 1,011.21, p=0.02) and alcohol consumption (OR 1.30; 95% CI 1,171.44; p=0.0001) were independent risk factors for reflux esophagitis [5, 9, 11].

When we talk about obesity as a risk factor for GERD, we mean pathophysiological disorders of esophageal motility, a weakening of the tone of the lower esophageal sphincter, a tendency to develop a hernia of the esophageal orifice of the diaphragm, increased intragastric pressure and an increase in stomach volume [6, 11, 12]. In addition, changes in the secretion of

proinflammatory cytokines, adiponectin and leptin, by adipocytes of visceral adipose tissue lead to the development of systemic inflammation and insulin resistance, as well as an increase in the incidence of erosive forms of GERD. The participation of leptin in the formation of erosive forms of GERD and Barrett's esophagus is demonstrated by data from numerous studies [16, 17,18].

According to some studies, obesity and overweight contribute to the occurrence of more pathological reflux. Asymptomatic obese patients have an increased number of acid reflux compared to patients with normal body weight. In the groups of obese patients with and without heartburn symptoms, there was no significant difference in the number of acid reflux [15].

There are conflicting data in literature reviews regarding the severity of clinical manifestations, daily pH measurement data, and endoscopic signs in patients with GERD and obesity, which requires further research.

### **Research materials and methods.**

The study included 90 patients with GERD and metabolic syndrome, type 2 diabetes mellitus. The research sample was formed in accordance with the inclusion/exclusion criteria among those who applied for an appointment for GERD symptoms. The patients were divided into 2 groups:

Group 1 – patients with GERD and metabolic syndrome (MS), type 2 diabetes mellitus (type 2 diabetes);

Group 2 – patients with GERD.

Group 1 consisted of 45 patients with a BMI of  $\geq 25$  kg/m<sup>2</sup>, of which 22 were men (48.8%) and 23 were women (52.2%) aged 43 to 60 years inclusive. Patients with type 2 diabetes were treated with oral hypoglycemic drugs (SSPs). In all patients, DM was in the compensation stage.

The 2nd group consisted of 45 patients with a BMI of  $\geq 25$  kg/m<sup>2</sup>, of which 21 were men (46.6%) and 24 were women (53.4%), aged 47 to 60 years

inclusive. The study groups did not have significant differences in gender ( $p>0.05$ ) and age ( $p>0.05$ ) (Table 1).

The clinical study included a survey of patients (identification of complaints and anamnesis), a comprehensive clinical examination, including physical examination (body weight, height, waist circumference, shoulder volume), the results of laboratory and instrumental studies, including EGDS and daily (24-hour) pH-metry. Data on taking medications at the time of treatment, observation by an endocrinologist, and consultations with specialized specialists, if necessary, were taken into account. The patient was also given a GerdQ questionnaire to fill out. The duration of gastroesophageal reflux and the features of reflux were evaluated based on the results of daily pH-metry. The degree of lesion of the mucous membrane of the esophagus, during EGDS, was assessed according to the modified Los Angeles classification, according to indications, chromendoscopy and endoscopy with magnification were performed.

Table №1.

## Demographic indicators of the studied groups

Group number	Total patients	Age			Sex	
		Average	up to 50 years old	over 50 years old	Men	women
Group 1	45	51,75±8,19, $p < 0,05$	21	24	22	23
Group 2	45	53,85±5,88 $p < 0,05$	20	25	21	24

Table №2.

## BMI indicators in the surveyed groups

Indicator	Group 1	Group 2	P
BMI (average), kg/m <sup>2</sup>	36,1±7,9	31,1±5,1	< 0,01
Men, kg/m <sup>2</sup>	37,81±7,63	33,53±7,45	< 0,05
Women, kg/m <sup>2</sup>	35,55±11,90	30,86±8,82	< 0,05

**The results and their discussion.**

When comparing the frequency and severity of clinical symptoms in patients of group 1 with GERD and metabolic syndrome and type 2 diabetes, the most common complaints were heartburn and regurgitation with acidic stomach contents. In patients of the 2nd clinical group, heartburn and dysphagia were significantly less common compared with the 1st group. When assessing the frequency of esophageal complaints, patients of the 1st clinical group were more often concerned about heartburn (51.9% vs. 98.5% in the second group, at  $p < 0.05$ ), regurgitation (40.7% vs. 68.2% in the second group, at  $p < 0.05$ ), 33.9% of patients had no complaints. When analyzing the data of the physical examination of patients of the 1st group with MS and type 2 diabetes, a statistically significant change in the BMI index of  $36.1 \pm 7.9$  kg/m<sup>2</sup> was obtained, which significantly differed from the results of the 2nd group of patients of  $31.1 \pm 5.1$  kg/m<sup>2</sup> ( $p < 0.01$ ). As can be seen from Table 2, the BMI values of men and women in group 1 were statistically higher than the BMI values in similar subgroups ( $p < 0.05$ ). Statistically significant changes were also detected when measuring waist circumference in patients of group 1,  $95.53 \pm 7.00$  cm versus  $86.51 \pm 5.18$  cm of group 2 ( $p < 0.05$ ), and in the subgroup of men with metabolic syndrome, type 2 diabetes, indicators were significantly higher ( $102.11 \pm 9.74$  vs.  $94.34 \pm 7.22$ , at  $p < 0.01$ ).



When assessing biochemical parameters, attention is drawn to higher levels of HbA1c ( $6.20 \pm 1.31$  vs.  $4.08 \pm 0.31$ ,  $p < 0.05$ ) and HOMA-IR ( $6.83 \pm 3.92$  vs.  $2.90 \pm 0.88$ ,  $p < 0.05$ ) in the 1st clinical group. Statistically significant differences in lipid spectrum parameters were observed in the group of patients with GERD and MS, type 2 diabetes due to total cholesterol ( $3.80 \pm 0.09$  vs.  $2.86 \pm 0.18$ ;  $p < 0.05$ ), and LDL fractions ( $2.73 \pm 0.64$ ;  $p < 0.05$ ) and VLDL ( $1.27 \pm 0.36$ ;  $p < 0.05$ ), which were statistically significantly higher compared to the data of the 2nd group, and the HDL fraction ( $1.16 \pm 0.54$ ,  $p < 0.05$ ) were significantly higher in the group of patients with GERD. There were no statistically significant differences in the assessment of lipid fractions in the subgroups divided by gender.

When evaluating the endoscopic picture, which was performed according to the Los Angeles Classification of reflux esophagitis (Montreal Revision), the following changes were revealed in clinical groups of patients: non-erosive form of GERD (catarrhal esophagitis, stage 0, and cases of absence of macroscopically visible changes) and degree A was registered in 14 (31.11%,  $p = 0.05$ ) and 7 ( $5.3 \pm 1.9\%$ ,  $p = 0.05$ ) patients, respectively, in the 2nd group of patients with GERD, which was significantly higher compared to the 1st group. The reliability of the difference between the two groups according to the Student's criterion is  $p = 0.05$ , i.e. the severity of reflux esophagitis in degrees B - 12 (26.66%), C - 10 (22.22%), D - 7 (15.55%) in patients of the first group was significantly higher than in patients of the second group. It was also found that 9 patients of the 1st clinical group have endoscopic signs of hernia of the esophageal orifice of the diaphragm.

A daily (24-hour) pH measurement was performed to analyze the frequency and duration of gastroesophageal reflux. Reflux with lower pH values ( $\text{pH} < 4.0$ ) was significantly longer in time in patients of the 1st clinical group and amounted to  $2.43 \pm 0.71$  ( $p < 0.05$ ) compared with those of the 2nd clinical group  $-1.91 \pm 0.78$  ( $p < 0.05$ ). In the group of patients with GERD and



MS, type 2 diabetes, the number of pathological reflux with pH <4 was  $44.01 \pm 8.17$  ( $p < 0.05$ ), the number of reflux lasting more than 5 minutes was  $3.26 \pm 1.40$  ( $p < 0.05$ ), compared with the group of patients with GERD, in which similar indicators were  $35.18 \pm 5.66$  ( $p < 0.05$ ) and  $2.14 \pm 0.7$  ( $p < 0.05$ ), respectively. The longest reflux was recorded in the group of patients with GERD and MS, type 2 diabetes and amounted to  $10.13 \pm 10.47$  minutes ( $p < 0.05$ ).

### Conclusion.

- In the group of patients with GERD and MS, type 2 diabetes on the background of obesity and overweight, symptoms of acid regurgitation, heartburn and dysphagia, lipid metabolism disorders are recorded significantly more often than among patients of the 2nd clinical group. The frequency and severity of classical manifestations of GERD (heartburn, acid regurgitation, dysphagia, retrosternal pain) did not significantly differ in the comparison groups by gender differences.

- Analysis of the results of endoscopy of the upper digestive tract revealed that for patients of the 2nd group suffering from GERD, the non-erosive form of the disease is the most characteristic, and among patients with GERD and MS, type 2 diabetes, a more severe course of erosive reflux esophagitis (stage B, C, D) was observed.

- Time, number and the duration of pathological reflux during the day was statistically significantly higher among patients of the 1st clinical group, which indicates a more severe course of GERD in obese and overweight individuals.

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