THE REPUBLIC OF AZERBAIJAN

on the rights of manuscript

ABSTRACT
of the dissertation for the degree of Doctor of Philosophy

ASSESSMENT OF RISK FACTORS, COMPREHENSIVE DIAGNOSIS AND CLINICAL FORMS OF GASTROESOPHAGEAL REFLUX DISEASE

Speciality: 3205.01 – Internal diseases

Field of science: Medicine

Applicant: **Govhar Agha Asgar Imanli**

BAKU – 2025

The work was performed at the Educational-Therapeutic Clinic of Azerbaijan Medical University, Central Neftchilar Hospital and Leyla Medical Center.

Scientific supervizor: Doctor of Philosophy in Medicine, associate professor **Inara Chingiz Alikhanova**

Official opponents: Doctor of Medical Sciences, professor **Azer Alicabbar Karimov**

Doctor of Medical Sciences, associate professor **Samir Khasay Mehdiyev**

Doctor of Philosophy in Medicine **Murad Rahim Ibrahimov**

Dissertation Council ED 2.27 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the Azerbaijan Medical University

Chairman of the Dissertation council: Doctor of Medical Sciences, professor **Vasadat Ali Azizov**

Scientific secretary of the Dissertation council: Doctor of Philosophy in Medicine, associate professor **Tora Akif Sadigova**

Chairman of the scientific seminar: Doctor of Medical Sciences, professor **Alihuseyn Alyshan Hidayatov**

AZƏRBAYCAN RESPUBLİKASI TİBB UNİVERSİTETİ

İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb üzrə fəlsəfə doktoru, dosent
Rəşad Şəmsəddin oğlu Talışınskiy
"08" 04 2025 il

GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the topic. Gastroesophageal reflux disease (GERD) currently occupies an important place in the general structure of gastroenterological pathology. The wide spread of this pathology, the presence of a large number of clinical symptoms, risk factors and complications show its relevance. According to the data of various foreign researchers, the prevalence of GERD fluctuates between 10-50%. Thus, in the US, the prevalence rate of GERD is 18-27%, in Europe-8.8-25.9%, in Australia-11.6%, in Asia – significantly lower-2.5-7.8%. In Azerbaijan, it is 22.7% [1, 2]. Endoscopic Barrett's esophagus, a complication of GERD, is considered a major risk factor for the development of adenocarcinoma[3].

In different countries, the risk factors of GERD are various. Even in the regions of large countries, different risk factors are found[4]. Various risk factors involved in the formation of GERD are reflected in the studies of foreign researchers. In 2018, a study among young nurses in South Korea found significant positive associations between GERD and high BMI, smoking, and mild, moderate, and severe depression[5]. In 2018, the Mayo-Clinical study showed a link between tobacco and Barrett's esophagus[3]. A study of patients with GERD in Nepal found that 50% had non-erosive GERD,

[1] Gyawali CP, et al. Modern diagnosis of GERD: the Lyon Consensus Gut 2018;67:1351–1362. doi:10.1136/gutjnl-2017-314722

[2] Sevda Aghayeva, David Katzka, Nargiz Afandiyeva, Serhat Bor et al. The prevalence of Gastroesophageal Reflux Disease in Azerbaijan: A Population-Based Cross-sectional Study. Turk J Gastroenterol 2023 Nov; 34(11): 1134-1142

[3] Westra WM, Lutzke LS, Mostafavi NS, Roes AL və b. Smokeless tobacco and cigar and/or pipe are risk factors for barrett esophagus in male patients with gastroesophageal reflux disease. Mayo Clin Proc. 2018 Sep. 93(9): 1282- 1289

[4] Vasilevskiy D.İ., Skurihin S.S., Luft A.V., Mednikov S.N., Silantiev D.S., Kulagin V.İ. et al. Prevalence of erosive esophagitis and peptic esophageal strictures // Chirurgia 2015;6:35-37

[5] Kim O, Jang HJ, Kim S, Lee HY, Cho E, Lee JE, Jung H, Kim J. Gastroesophageal reflux disease and its related factors among women of reproductive age: Korea Nurses Health Study. BMC Public Health. 2018 Sep. 21, 18 (1)

45% had erosive esophagitis, 5% had hiatal hernia (HIGH), and 1.6% had Barrett's esophagus[6].

A study conducted in Iran in 2017 showed that GERD is more common among women than among men. During this study, HH was the 2nd risk factor in patients with GERD. 69.2% of patients with GERD were younger than 50 years [7].

The study of risk factors plays an important role, since GERD has a serious negative impact on the patient's quality of life for a long time. In the treatment of GERD, it is very important to eliminate risk factors along with medications. In most cases, long-term various molecular proton pump inhibitors (PPI) are prescribed to patients without determining the nature of reflux in patients with GERD[8]. There are a number of adverse side effects of PPI: osteoporosis, cardiovascular complications, risk of polyps, etc.[9].

Thus, given that GERD is a common pathology, leading to precancerous complications, it becomes clear that timely diagnosis and proper selection of treatment of GERD are very important. The treatment of this pathology leads to great discussion. All those mentioned indicate that our research is relevant.

Object and subject of the study. The subject of the study was patients who presented with complaints of GERD and underwent esophagogastroduodenoscopy (EGDS), impedance pH-metry, and esophageal manometry.

Purpose of the study. To identify risk factors, clinical forms, and improve diagnostic algorithms and treatment for the purpose of timely detection of GERD and prevention of its complications.

---

6. Dewan KR, Patowary BS, Bhattarai S, Shrestha G. Barret s esophagus in patients with gastroesophageal reflux disease. J Nepal Health Res Counc. 2018 Jul 3, 16 (2): 144- 148.

7. Fakhre Yaseri H. Gender is a risk factor in patients with gastroesophageal reflux disease. Med J İslam Repub İran. 2017 Sep 8, 31:58

8. Mei J, Yu Y, Ma J, Yu X. Evaluation of the effectiveness of esomeprazole treatment strategies in the management of patients with gastroesophageal reflux disease symptoms: a meta-analysis. Pharmazie . 2016 May, 71 (5): 285- 91.

9 Jessica Devitt, Corey Lyon, Sarah Beth Swanson, Kristen DeSanto. What are the risks of long- term PPI use for GERD symptoms in patients >65 years? The journal of family practice 2019 April, 68 (3): E18- E19

The tasks of the research:

1. The risk factors and incidence of GERD among patients with complaints related to pathologies of the upper digestive system were studied.

2. The endoscopic features of the esophagus were evaluated in different clinical forms of GERD.

3. The indicators of esophageal manometry and 24-hour impedance Ph-metria were evaluated in the diagnosis of GERD.

4. The diagnostic algorithm of GERD was developed.

5. In reflux of various nature, treatment was applied and its effectiveness was evaluated.

Research methods. In the first part of the study, EGDS examination was carried out to patients (1900 patients) with complaints of pathologies of the upper gastrointestinal tract (heartburn, etc.). The incidence of GERD among these patients was determined. Biopsies were taken from the lower 1/3 of the esophagus of patients diagnosed with GERD, morphologically examined, and the clinical form of GERD was determined. Risk factors were investigated by applying a questionnaire to 231 GERD patients. The relationship between the identified risk factors and the clinical forms and complications of GERD was studied.

In the second part of the study, 24-hour esophageal impedance pH-metry and esophageal manometry were performed on patients with GERD (60 patients), thereby clarifying the type of reflux (acid, weak acid, and weak alkaline), the spectrum of reflux (liquid, gas, and mixed), and the option of reflux (functional, pathological-SAP+, and pathological SAP-). According to the results of impedance pH-metry, we treated 2 groups of patients, and based on the results, comparisons were made between these groups by applying a questionnaire.

The control group (CG) included 35 patients with endoscopic gastroesophageal reflux (GER), who we selected among people applied for the purpose of "check-up (who had no complaints, applied voluntarily) and underwent EGDS.

Statistical processing of data. In our study, statistical analysis was performed in IBM Statistics SPSS-26 and MS EXCEL2019 programs using discriminant, variation, correlation, dispersion methods.

In the analysis of quantitative indicators, the average (M±m, 95% CI (confidence interval)) and average structure (Me, min, max) indicators of the variation series were calculated, for comparison, non-parametric U-Mann-Whitney (2 groups) and KU-Kruskal-Wallis (3 or more groups) criteria were applied. The χ^2-criterion (Chi-square Pearson) was used to compare quality indicators. Dependence between indicators in research groups was determined by correlation analysis. Taking into account that the indicators are both quantitative and qualitative in nature, ρ-Spearman correlation analysis was applied. Factorial analysis-single-factor dispersion analysis (ANOVA test) was performed. The ROC curve was applied to study specificity and sensitivity[10]

Before and after treatment, the GERD – HRQLQ - Gastr-oesophageal Reflux Disease-Health Related Quality of Life Questionnaire (GERD-health-related quality of life) was applied[11].

The main provisions of the dissertation defended:

1. The incidence of gastroesophageal reflux during endoscopic examination in patients with complaints related to the upper gastrointestinal tract was quite high. It also has an significant relationship with age and gender. Of the risk factors of GERD, the focus should be on increased BMI, HH and fatty food intake.

2. According to the results of endoscopic examination, non-erosive GERD is detected in many cases, and most of the patients' complaints are not related to the degree of esophagitis. This shows the need to use more informative examinations in the diagnosis of GERD.

3. The indicators of impedance pH-metria and manometry showed reliable, honest, significant, high specificity and sensitivity, and the absolute use of these methods in the diagnosis of GER and HH both in patients with or without complaints who have found endoscopic GER by EGDS.

4. The diagnostic algorithm of GERD, developed as a result of the research, shows the sequence and necessity of the performed examinations.

[10] Qafarov I.A. Biostatistika. Bakı: Təbib, 2022, 240 s. ISBN: 978-9952-37-813-9

[11] Velanovich V. The development of the GERD-HRQL symptom severity instrument. Dis Esophagus 2007;130-4

5. As a result of impedance pH-metry, the division of patients into different groups and the application of appropriate treatment increases the effectiveness of the treatment.

Scientific novelty of the research:

For the first time in our country, the incidence of GERD among patients who applied to a multi-profile medical institution with complaints related to pathologies of the upper gastrointestinal tract was studied, and the risk factors in these patients were investigated and clinical forms were determined with the help of complex diagnostic examination methods.

For the first time, new examination methods were applied in patients applied for the purpose of "check-up", esophagogastroduodenoscopy was performed and endoscopic gastroesophageal reflux was detected, their indicators were evaluated, compared with the indicators of new examination methods of patients who applied with complaints and a diagnostic algorithm was developed for endoscopic GERD patients with and without complaints.

For the first time in our study, the specificity and sensitivity of esophageal manometry was determined based on the mutual application of the indicators of the examinations we used in the diagnosis of GERD, using a new statistical method in the diagnosis of the hiatal hernia, which is one of the main risk factors in GERD.

Practical significance of research:

- The developed diagnostic algorithm, evaluation of risk factors and clinical forms opened wide opportunities for prognosis and prevention of complications of patients with GERD.
- Treatment based on indicators of impedance pH-metrian examination had a positive effect on the quality of life of patients with GERD.
- The diagnostic criteria of various clinical forms of GERD, which are often found in the practice of doctors, were determined.
- A new approach to the diagnosis of HH has opened new perspectives in the diagnosis and treatment of this pathology.

Application of research results:

The results of the research were applied in the practical activities of the Educational-Therapeutic Clinic of the Azerbaijan Medical University and the Central Neftchilar Hospital.

Published works: Based on the results of the research, 14 scientific works were published, including 7 articles and 7 theses. 4 articles were published in local journals (1- Scopus), 3 articles were published in journals recommended by the Supreme Attestation Commission (1- Web of Science).

Approbation of research work. The main provisions of the research in the form of an oral report:

– Scientific-practical congress "Actual problems of medicine" dedicated to the 90th anniversary of the Azerbaijan Medical University (Baku, 2020);

– International scientific-practical conference dedicated to the 270th anniversary of Shusha "Actual problems of medicine" (Baku, 2022)

– "I International Medical Forum" (Nakhchivan, 2022)

– International Scientific and Practical Congress of Azerbaijan Medical University "Actual Problems of Medicine" (Baku, 2023) dedicated to the 100th anniversary of the birth of national leader Heydar Aliyev.

The main provisions of the research in the form of a poster report:

– "39th National Gastroenterology Week" (Antalya, 2022)

– "World Congress of Gastroenterology" (Dubai, 2022)

– 40 National Gastroenterology Week" (Antalya, 2023)

The initial discussion of the dissertation work was held on June 21, 2024 at the meeting of "Internal Diseases I", "Internal Diseases II" and "Internal Diseases III" departments of Azerbaijan Medical University (protocol №1).

The scientific seminar of the dissertation was held on December 23, 2024 at the Educational - Therapeutic Clinic of the Azerbaijan Medical University (protocol №4).

The organization in which the dissertation work was carried out. Dissertation work was performed at the Educational-Therapeutic Clinic of Azerbaijan Medical University, Central Neftchilar Hospital and Leyla Medical Center.

Volume and structure of the dissertation. The dissertation work was published and presented on 196 pages (172.900 marks:

introduction – 11.000, chapter I – 57.000, Chapter II – 25.700, Chapter III – 60.000 discussion of the results, conclusions and practical recommendations – 19.200 marks. The dissertation is illustrated with 39 tables, 24 graphics and 20 pictures.The bibliography consists of 197 sources, 17 of which are local authors.

MATERIALS AND METHODS OF RESEARCH

The research work included 1900 patients during the period from January 2019 to February 2021. 1067 (56.2%) of them were men, 833 (43.8%) were women. The age of the patients was between 15 and 80 years. Patients applied with various complaints characteristic for pathologies of the upper gastrointestinal tract: belching, regurgitation, flatulence, dysphagia, etc. All patients underwent an EGDS examination. When we examined the results of EGDS, 662 (35.9%) patients had hiatal hernia, 415 (21.8%) had incompetence of cardia, and 622 (32.7%) had endoscopic GERD. Several pathologies were observed in some patients. GERD predominated in men (35.9% vs. 28.7%; p=0.001). Of these, 500 patients (80.4%) had endoscopic esophagitis, 122 patients (19.6%) had non-erosive GERD. According to the Los Angeles classification, 249 (40.0%) patients had grade A esophagitis, 169 (27.2%) patients had grade B esophagitis, 7 patients (1.1%) had grade C esophagitis, and 75 patients (12.1%) had grade D esophagitis.

Patients with endoscopically detected GERD. Our subsequent study included 231 patients with GERD out of the 622 patients with endoscopic GERD detected among the 1900 patients mentioned above. Inclusion criteria included patients with GERD between the ages of 15 and 80, male and female, with various clinical forms, patients with appropriate degrees of esophagitis, which were found in 622 patients, and patients with daily GERD complaints. Exclusion criteria were active pathologies of the upper digestive tract, severe heart, kidney, or liver failure, oncological diseases, severe diabetes mellitus, immune diseases, generalized and local inflammatory diseases, and taking PPI within the last 2 weeks.

Among the 231 patients included in our study, 121 (52.4%) were men, 110 (47.6%) were women, and their age ranged from 15

to 80. The mean age was 44.7±0.9 years.

Patients were divided into the following groups according to age:15-30 years: 36 patients (15.6%); 31-40 years: 72 patients (31,2%); 41-50 years: 47 patients (20,3%); 51-60 years: 33 patients (14,3%); 61-70 years: 37 patients (16,0%); 71-80 years: 6 patients (2,6%); 51.5% of patients were 31-50 years old.

According to DI, patients were divided into 3 groups: 50 patients with a disease duration of up to 1 year (21.6%), 101 patients with a duration of 1-5 years (43.7%), for a period of 5 years or more - 80 patients (34.6%).

108 patients (46.8%) noted GERD in their heredity. 49 patients (21.2%) suffered from arterial hypertension. 18 patients (7.8%) had a history of diabetes mellitus. Some patients were taking medications that reduce the tone of the lower esophageal sphincter. Thus, 34 patients (14.7%) were taking angiotensin-converting enzyme (ACE) blockers, and 14 patients (6.1%) were taking antidepressants. 135 patients (58.4%) suffered from nervous tension. 123 patients (53.2%) noted stress.

According to the body-mass index (BMI), the patients were divided into the following groups: patients with low BMI: 5 patients (2,2%); patients with normal BMI: 57 patients (24,7%); patients with excess body weight: 85 patients (36,8%); patients with grade 1 obesity: 55 patients (23,8%); patients with grade 2 obesity: 29 patients (12,6%).

We have studied risk factors in patients with GERD. Several risk factors were noted in some patients. Various degrees of obesity and excess body weight were determined in 169 patients (73.2%), HH was detected in 119 patients (51.5%), nervous tension and stress were recorded in 135 patients (56.4%). Smoking was detected in 69 patients (29.9%), and fatty food intake in 138 patients (59.7%). 94 patients (40.7%) regularly drank carbonated drinks, 91 patients (39.4%) stated that they regularly drank coffee. 66 patients (28.6%) stated that they drink alcohol regularly.

We have investigated the range of complaints of these patients. Several complaints were noted in some patients. Heartburn was detected in the majority of patients (202-87.4%). 144 patients (62.3%) suffered from regurgitation. Dry cough, which is one of the most common complaints, was noted in 83 patients (35.9%), foamy feeling in the

abdomen in 77 patients (33.3%). Suffocation was found in 36 patients (15.6%), dysphagia was in 24 patients (10.4%), hoarseness was in 8 patients (3.5%), pain behind the sternum was in 18 patients (7.8%).

During EGDS, from endoscopic indications, HH was found in 119 patients (51.5%), incompetence of cardia was in 55 patients (23.8%). Non-erosive GERD was determined in 86 patients (37.3%), erosive GERD in 145 patients (62.7%). Among patients with erosive GERD, grade A esophagitis was observed in 71 patients (49%), grade B was observed in 45 patients (31%), grade C and D esophagitis was observed in 4 and 25 patients (2.8% and 17.2%, respectively). As we can see, 80% of the main group of patients had Grade A and B esophagitis, and 20% had grades C and D esophagitis.

During endoscopy, 28 patients (12.1%) had Barrett's esophagus, 13 patients (5.6%) had endoscopic Shatzki's ring. 3 patients (1.3%) had a polyp in the esophagus, only 1 patient (0.4%) had a stricture in the esophagus. Endoscopic examination of 39 patients (16.9%) revealed duodenogastric reflux.

Regarding other endoscopic indicators, gastric ulcer was seen in 57 patients (24.7%), gastric polyp in 28 patients (12.1%), duodenal ulcer in 58 patients (25.1%), duodenal polyp in 8 patients (3.5%). Helicobacter Pylori was positive in 106 patients (45.9%).

In histological examination, biopsies were taken from 32 patients for histological examination. Esophagitis was noted in 22 patients (68.75%), Barrett's esophagus in 7 patients (21.9%), and normal esophagus in 3 patients (9.35%). Intestinal metaplasia was detected in 7 patients and dysplasia in 1 patient.

Impedance pH-metry and EM performed patients. We continued our further study with 60 patients out of 231 patients who underwent impedance pH-metry and EM. Of the 60 patients included in our study, 39 (65%) were men and 21 (35%) were women. The age of the patients was between 15 and 70. The mean age was 41.1±1.6.

We also included 35 people in the control group, who were diagnosed with endoscopic GER, selected from among people who had no complaints, voluntarily applied to our study, and underwent EQDS. We compared these two groups by carrying out impedance pH-metry and EM examinations, which we performed on 60 patients selected

from the main group and on the patients included in the control group. The control group included 21 men (60.0%), 14 women (40%). The mean age was 41.5±2.2.

The age group of patients in the control group is as follows: 15-30 years: 7 patients (20%); 31-40 years: 12 patients (34,3%); 41-50 years: 8 patients (22,9%); 51-60 years: 4 patients (11,4%); 61-70 years: 4 patients (11,4%).

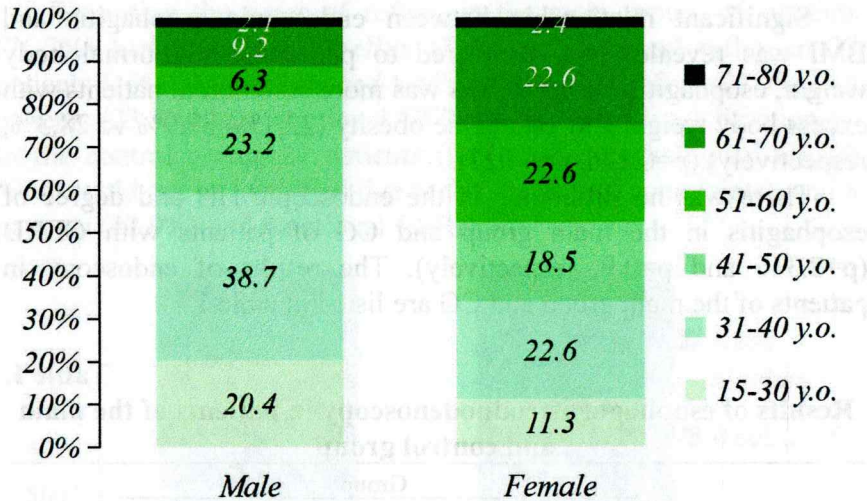
Patients in the control group did not differ statistically from patients in the main group in terms of age group, gender, and endoscopic esophagitis grades ($p\chi2=0.626$, $p\chi2=0.071$, and $p\chi2=0.585$, respectively).

In the main group, a significant relationship was found between the gender of patients and the age and age groups of patients ($\rho=0,333$, $p<0,001$ and $\rho=0,338$, $p<0,001$, respectively). So, 61.9% of men were patients between the ages of 31-40 and 41-50, and 45.2% of women were patients between the ages of 51-60 and 61-70. This is reflected in graph. 1.

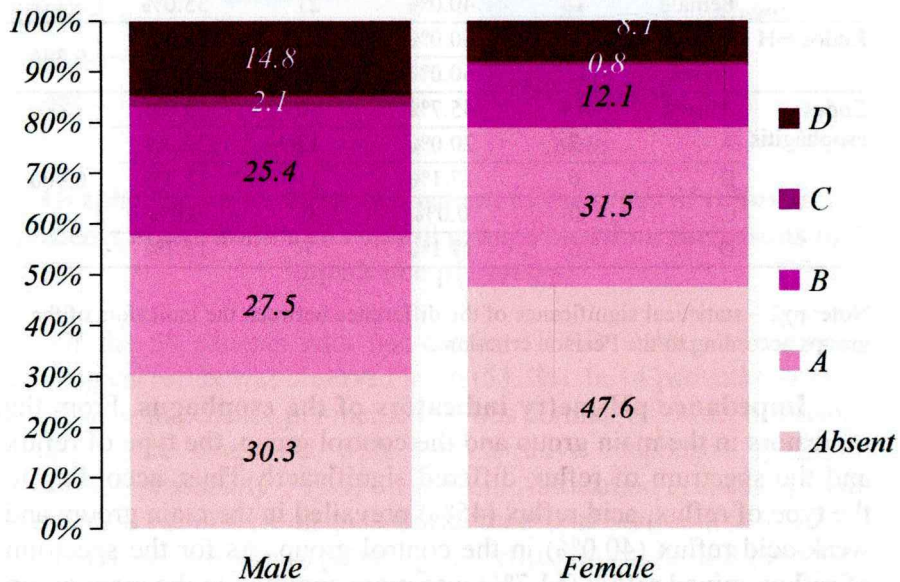
In the main group, a significant relationship was found between endoscopic esophagitis and the gender of patients, since endoscopic esophagitis was more common in men ($\rho=-0,193$, $p=0,003$). A significant relationship was found between the sex of patients and the degree of esophagitis, so Grade A esophagitis was more often found in women (33.6% and 28.1%), B, C and D-grade esophagitis were more often found in men (respectively 25,6% -12,7%, 2,5%- 0,9% and 13,2% - 8,2%) ($\rho=-0,193$, $p=0,003$). This relationship is reflected in graph. 2.

In the main group, the endoscopic Barrette esophagus was more common in the 31-40 age group (22.5%) ($p=0,038$).

A significant relationship was found between the duration of the ilness (DI) and endoscopic esophagitis. So, endoscopic esophagitis was more common in those who were sick for 1-5 years and for more than 5 years than in those who were sick for up to a year. Of the endoscopic esophagitis degrees, C and D degrees of esophagitis were more common in those who were sick for 1-5 years and more than 5 years (0,0%, 8,0%-25%, 32% and 75%, 60%, respectively) than those who were sick for up to 1 years ($\rho=0,201$, $p=0,002$).



Graph.1. Relationship between sex and age groups of patients with GERD



Graph.2. Relationship between esophagitis and gender of patients with GERD

Significant relationship between endoscopic esophagitis and BMI was revealed. So, compared to patients with normal body weight, esophagitis during EGDS was more common in patients with excess body weight and 1st degree obesity (22,1%- 37,9% və 28,3%, respectively) (ρ=0.146, p=0.027).

There was no difference in the endoscopic HH and degree of esophagitis in the main group and CG of patients with GERD (p=0.346 and p=0.9, respectively). The results of endoscopy in patients of the main group and CG are listed in table 1.

Table 1.

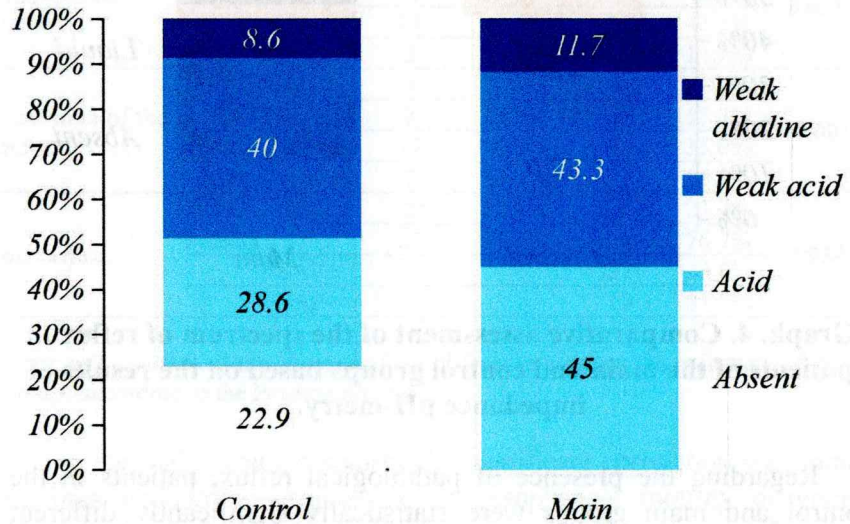
Results of esophagogastroduodenoscopy in patients of the main and control group

		Group				pχ2
		Control		Main		
		N	%	N	%	
Gender	Male	21	60.0%	39	65.0%	0.626
	Female	14	40.0%	21	35.0%	
Endos HH	Absent	14	40.0%	30	50.0%	0.346
	Present	21	60.0%	30	50.0%	
Endos esophagitis	Absent	16	45.7%	30	50.0%	0.900
	A	7	20.0%	12	20.0%	
	B	6	17.1%	11	18.3%	
	C	0	0.0%	0	0.0%	
	D	6	17.1%	7	11.7%	

Note: pχ2 – statistical significance of the difference between the indicators of the groups according to the Pearson criterion

Impedance pH-metry indicators of the esophagus. From the indicators in the main group and the control group, the type of reflux and the spectrum of reflux differed significantly.Thus, according to the type of reflux, acid reflux (45%) prevailed in the main group, and weak-acid reflux (40.0%) in the control group. As for the spectrum of reflux, mixed reflux (51.7%) was more common in the main group, and gas reflux (34.3%) in the control group (pχ2=0.001 and pχ2<0.001, respectively) (graph. 3 and 4).

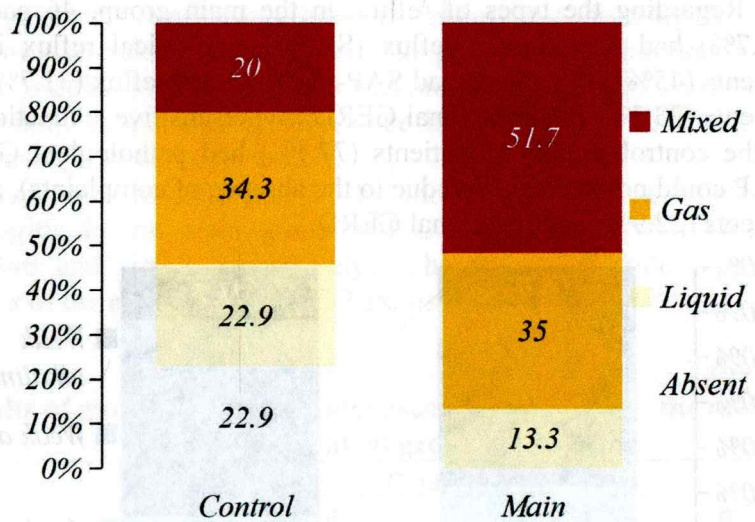
Regarding the types of reflux, in the main group, 46 patients (76.7%) had pathological reflux (SAP+ pathological reflux in 27 patients (45%), 19 patients had SAP- pathological reflux (31.7%), 14 patients (23.3%) had functional GERD (hypersensitive + functional). In the control group, 27 patients (77.1%) had pathological GERD (SAP could not be identified due to the absence of complaints), and 8 patients (22.9%) had functional GERD.



Graph. 3. Comparative assessment of the types of reflux in patients of the main and control groups based on the results of impedance pH-metry.

Of the 30 patients with non-erosive GERD in the main group, pathological reflux was observed in 16 (53.3%). In 14 patients (46,7%), the 24-hour impedance pH-metric test was normal. Of these, 6 patients (42.8%) were diagnosed with hypersensitive esophagus symptom association probability + (SAP- Symptom Association Probability) and 8 patients (57.2%) were diagnosed with functional heartburn (SAP -).

In the control group, pathological reflux was seen in 8 (50%) of 16 patients with non-erosive GERD, impedance pH-metry test was normal in 8 patients (50%). In this group, SAP was not prescribed because the patients had no complaints.



Graph. 4. Comparative assessment of the spectrum of reflux in patients of the main and control groups based on the results of impedance pH-metry.

Regarding the presence of pathological reflux, patients in the control and main groups were statistically significantly different (p=0.958). All these mentioned are reflected in table 2.

According to the results of statistical analysis, patients in the MG and CG groups did not differ in terms of impedance pH-metry indicators. For all indicators, p>0.05.

Esophagus manometry indicators. In manometry, esophageal motility disorders were found in the main group as follows: normal - 34 patients (56,7%); ineffective esophagus - 11 patients (18,3%); fragmentary peristalsis - 6 patients (10,0%); hypercontractile esophagus - 6 patients (10,0%); achalasia type I - 2 patients (3,3%); mechanical obstruction - 1 patient (1,7%).

The motility disorders in patients of the CG are as follows: normal- 25 patients (71,4%); ineffective esophagus - 7 patients (20,0%); fragmentary peristalsis - 3 patients (8,6%).

Table 2.

Statistically significant difference according to certain indicators between patients of control and main groups

		Group				$P_{\chi 2}$
		control		main		
		N	%	N	%	
Type of the reflux	Absent	8	22.9%	0	0.0%	0.001
	Acid	10	28.6%	27	45.0%	
	Weak acid	14	40.0%	26	43.3%	
	Weak alkaline	3	8.6%	7	11.7%	
Spectrum of the reflux	Absent	8	22.9%	0	0.0%	<0.001
	Liquid	8	22.9%	8	13.3%	
	Gas	12	34.3%	21	35.0%	
	Mixed	7	20.0%	31	51.7%	
pH reflux	Absent	8	22.9%	14	23.3%	0.958
	Present	27	77.1%	46	76.7%	
	– SAP+			27	45.0%	
	– SAP-			19	31.7%	

Note: $p\chi 2$ – statistical significance of the difference between the indicators of the groups according to the Pearson criterion

In the main group, a statistically significant correlation was found between endoscopic esophagitis and esophageal motility disorders. Thus, ineffective esophageal and fragmentary peristalsis were found in 57.2% of patients with esophagitis D ($p\chi 2=0.023$).

A statistically significant relationship between endoscopic esophagitis and esophageal motility disorders was also found in CG. Thus, 66.7% of patients with grade B esophagitis had ineffective esophagus, 83.3% of patients with D esophagitis had ineffective esophagus and fragmented peristalsis ($p\chi 2<0.001$). From this, we can conclude that esophageal motility disorders is more common in severe esophagitis.

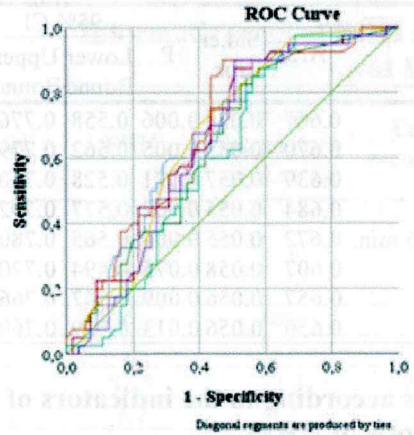
According to the Student-Bonferroni and ANOVA criteria, patients in the control and main groups did not differ in terms of esophageal manometry indicators. According to the Mann-Whitney criterion, patients in the main and CG differed in lower esophageal sphincter pressure (LESP) ($p<0.001$). But the average number of this indicator in both groups was within the norm.

When we examined the relationship between the type of reflux and other pH-metry indicators, it was found that in the main group, between the type of reflux and total reflux time (r=-0.523, p<0.001), standing reflux time (r=-0.565, p<0.001), lying reflux time (r=-0.376, p=0.003), the number of reflux periods (r=-0.507, p<0.001), the number of reflux lasting more than 5 min (r=-0.448, p<0.001), the longest reflux (r=-0.350, p=0.006) and DeMeester score (r=-0.505, p<0.001) were significant correlations. So, the indicators mentioned by us are significantly higher in acid and weak-alkaline reflux than in weak-acid reflux.

When examining the relationship between the reflux spectrum and the parameters of the esophagus impedance pH-metry in the main group, it was found that between reflux spectrum and total reflux time (P_H=0.003), standing reflux time (P_H=0.002), the number of reflux periods (P_H =0.007), the number of reflux periods lasting more than 5 min. (P_H=0.014), and DeMeester score (P_H =0.003) revealed a statistically significant relationship. Thus, in liquid reflux, the total reflux time was 3.2 times higher than in gas reflux, 2 times higher than in mixed reflux, and the DeMeester score was 3.4 times higher than in gas reflux, and 2.1 times higher than in mixed reflux.

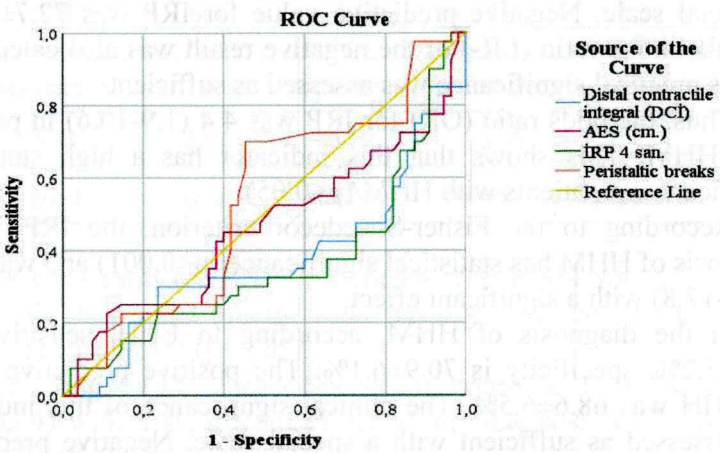
We investigated the specificity and sensitivity of the EM examination in the diagnosis of HH. The area of the ROC (Receiver operating characteristic) curve, which is an integral parameter of sensitivity and specificity in the diagnosis of HHM, is shown in figure 11 for 24-hour esophageal pH-metry indicators. So, for the total reflux time (with pH<4-%), this indicator is 0.667±0.056 (p=0.006), standing reflux time (min.) and lying reflux time (min.), respectively, 0.670±0.055 and 0.639±0.057 (p=0.005 and p=0.021, respectively). For the number of reflux periods, this indicator was calculated as 0.684±0.055 (p=0.002), for the number of reflux periods lasting more than 5 minutes, 0.672±0.055 (p=0.004), for the DeMeester score, 0.657±0.056 (p=0.009).

If we pay attention to the results of the ROC curve for the EM indicators in the diagnosis of HHM, we will see that this indicator was calculated as 0.371±0.061 (p=0.032) for the distal contractile integral, and 0.357±0.060 (p=0.018) for the discharge pressure-IRP-4s. The results are shown in graph. 5 and 6.



Area Under the Curve

Test Result Variable(s)	Area	Std.error	p	95% CI Lower Bound	95% CI Upper Bound
Distal contractile integral (DCI)	0.371	0.061	0.032	0.252	0.490
AES (cm)	0.461	0.063	0.522	0.338	0.584
IRP 4 sec.	0.357	0.060	0.018	0.239	0.476
Peristaltic breaks	0.531	0.061	0.606	0.412	0.650



Graph. 5.. Results of ROC analysis according to the indicators of 24-hour esophageal pH-metry in the diagnosis of HHM.

Area Under the Curve

Test Result Variable(s)	Area	Std.error	P	95% CI	
				Lower Bound	Upper Bound
Total reflux time (pH<4)- %	0.667	0.056	0.006	0.558	0.776
Standing reflux time (min.)	0.670	0.055	0.005	0.562	0.779
Lying reflux time (min.)	0.639	0.057	0.021	0.528	0.750
Number of reflux periods	0.684	0.055	0.002	0.577	0.792
Number of reflux periods lasting more than 5 min.	0.672	0.055	0.004	0.565	0.780
Longest reflux (min.)	0.607	0.058	0.075	0.494	0.720
DeMeester score	0.657	0.056	0.009	0.547	0.766
Adult score	0.650	0.056	0.013	0.539	0.760

Graph. 6. Results of ROC-analysis according to the indicators of EM in the diagnosis of HHM.

The cut-off point for IRP-4s in patients with HHM is 9.6 (sensitivity 62.5±7.7%, specificity 75.5±5.9%).

The positive predictive value (pPV) of IRP-4s was 65.8±7.7%. The likelihood ratio (LR+) of a positive result was calculated to determine its practical significance. True correlations of positive results were calculated to determine their practical significance. The clinical significance of this indicator was assessed as sufficient with a special scale. Negative predictive value for IRP was 72.7±6.0%. The likelihood ratio (LR-) of the negative result was also calculated, and its practical significance was assessed as sufficient.

Thus, the odds ratio (OR) for IRP was 4.4 (1.9-10.6) in patients with HHM. This shows that this indicator has a high statistical significance in patients with HHM ($p<0.05$).

According to the Fisher-Sneedecor criterion, the IRP in the diagnosis of HHM has statistical significance ($p<0.001$) and was 15.4 (10.5-17.8) with a significant effect.

In the diagnosis of HHM, according to EHH, sensitivity is 87.5±5.2%, specificity is 70.9±6.1%. The positive predictive value for EHH was 68.6±6.5%. The clinical significance of this indicator was assessed as sufficient with a special scale. Negative predictive value (nPV) for IRP was 88.6±4.8%. The practical significance of this result was evaluated as good in accordance to LR- (table 3).

Table 3.

Informativeness of EHH and biopsy in the diagnosis of MHH

NN	EHH	Endos incompetence of cardia	Endos esophagitis	IRP 4 sec.	Endos Barret Esoph	Bx
Cut off point	> 0	< 1	> 2	< 9.5	> 0	> 0
n+	40	40	40	40	40	9
++	35	37	10	25	8	8
Sn	87.5	92.5	25.0	62.5	20.0	88.9
±mp	5.2	4.2	6.8	7.7	6.3	10.5
n-	55	55	55	53	55	2
--	39	24	52	40	53	2
Sp	70.9	43.6	94.5	75.5	96.4	100.0
±mp	6.1	6.7	3.1	5.9	2.5	0.0
ÜDD	74	61	62	65	61	10
%	77.9	64.2	65.3	68.4	64.2	90.9
±mp	4.3	4.9	4.9	4.8	4.9	8.7
pPV	68.6	54.4	76.9	65.8	80.0	100.0
±mp	6.5	6.0	11.7	7.7	12.6	0.0
nPV	88.6	88.9	63.4	72.7	62.4	66.7
±mp	4.8	6.0	5.3	6.0	5.3	27.2
LR+	3.01	1.64	4.58	2.55	5.50	99999
	satisfactory	inapprop.	satisfactory	satisfactory	good	excellent
LR-	0.18	0.17	0.79	0.50	0.83	0.11
	good	good	inapprop	satisfactory	inapprop	good

The odds ratio for EHH in patients with HHM was 17.1 (5.7-51.4). This shows that this indicator has high statistical significance in patients with HHM ($p<0.05$).

According to the Fisher-Sneedecor criterion, EHH was 94.0 (48.1-52.4) with a significant effect on the diagnosis of HHM and was statistically significant ($p<0.001$).

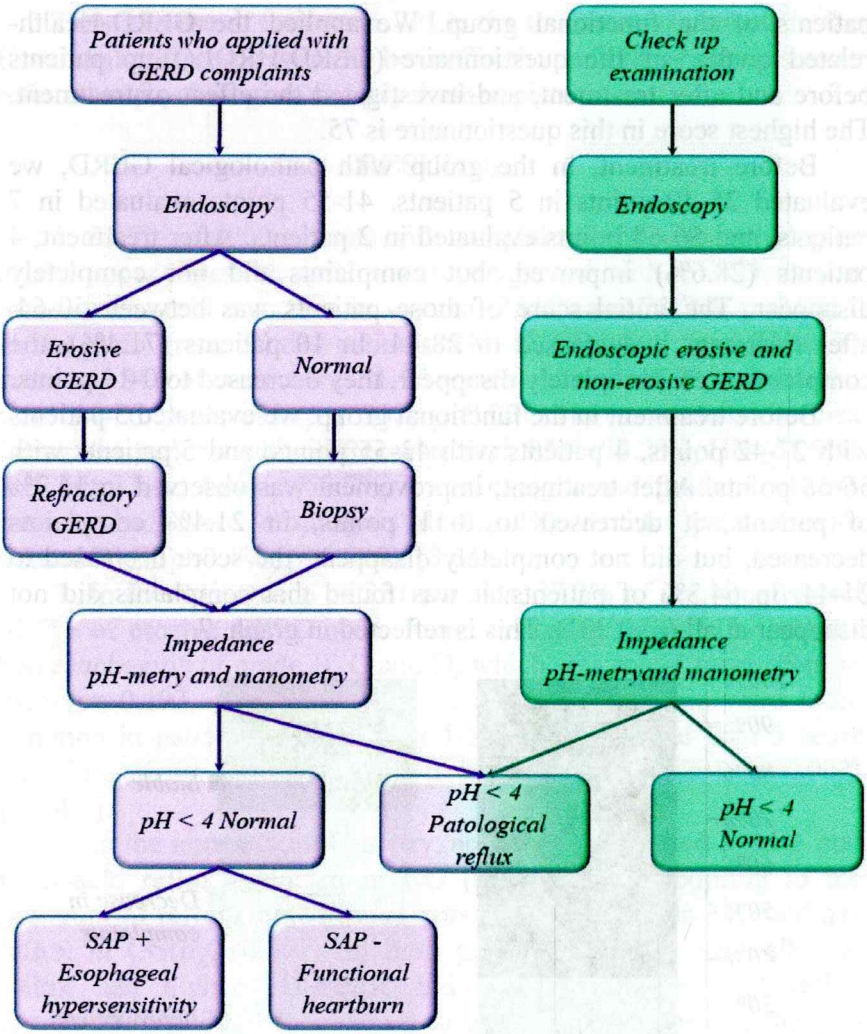
In the diagnosis of HHM, the sensitivity for biopsy of the esophagus is 88.9±10.5%, and the specificity is 100.0±0.0%.The positive predictive value for esophageal biopsy was 100.0±0.0%. The LR+ was calculated to determine their practical significance. The clinical significance of this indicator was assessed as excellent with a special scale. The negative predictive value for esophageal biopsy was 66.7±27.2%. The practical significance of this result was assessed as good according to LR-(table 3).

As esophageal biopsies were not performed in all of our patients, larger studies can be performed by increasing the number of biopsies in the future.

Based on all these mentioned, it can be concluded that the sensitivity and specificity of EM is higher in the diagnosis of HH.

Diagnostic algorithm. Based on the obtained impedance pH-metry and esophagus manometry results, we designed the following diagnostic algorithm (Scheme). According to the algorithm, EGDS is performed for patients with a complaint of GERD. During EGDS, erosive and non-erosive forms of GERD are distinguished. Esophageal biopsy is performed in patients with non-erosive GERD because the mucosa of the esophagus is normal during EGDS. Then, these patients are involved in EM and impedance pH-metry examination (Scheme).

Impedance pH-metry reveals a group with normal pH<4 and pathological reflux. In the group with normal pH<4, depending on the presence of SAP+ and SAP-, functional heartburn and esophageal hypersensitivity are revealed. Also, EGDS is performed for patients without complaints and who applied voluntarily. Erosive and non-erosive forms of GERD are distinguished in patients with endoscopic GERD during EGDS. Esophageal biopsy is performed on patients with non-erosive GERD, as the mucosa of the esophagus is normal during EGDS. Then, these patients are involved in EM and impedance pH-metry examination. During impedance pH-metry, a group with pH<4 normal and pathological reflux is distinguished.



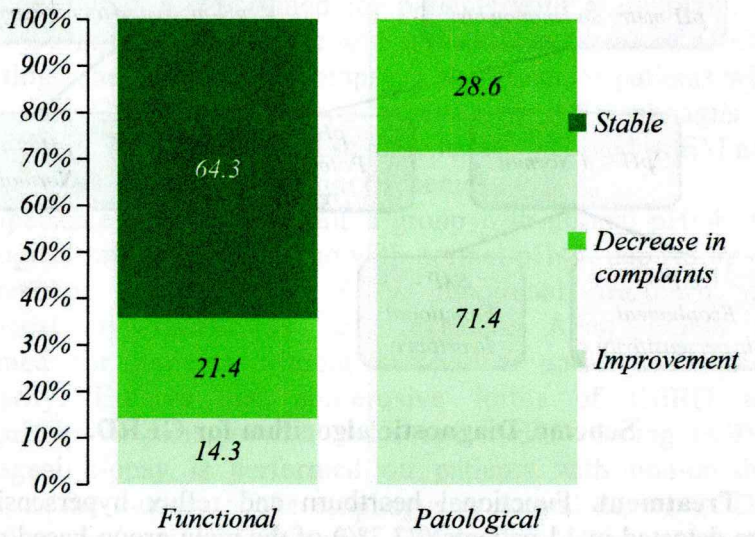
Scheme. Diagnostic algorithm for GERD.

Treatment. Functional heartburn and reflux hypersensitivity were detected in 14 patients (23.3%) of the main group based on the results of impedance pH-metry. We prescribed Ulseblock 20 mg from PPI, containing Rabeprazole, for 4 weeks to 14 patients and 14

patients of the functional group. We applied the GERD-Health-related quality of life questionnaire (GERD-HRQLQ) to patients before and after treatment, and investigated the effect of treatment. The highest score in this questionnaire is 75.

Before treatment, in the group with pathological GERD, we evaluated 25-40 points in 5 patients, 41-55 points evaluated in 7 patients, and 56-64 points evaluated in 2 patients. After treatment, 4 patients (28.6%) improved, but complaints did not completely disappear. The initial score of those patients was between 50-64, after treatment it decreased to 28-44. In 10 patients (71.4%), the complaints were completely disappear, they decreased to 0-11 points.

Before treatment in the functional group, we evaluated 5 patients with 27-42 points, 4 patients with 43-55 points, and 5 patients with 56-68 points. After treatment, improvement was observed in 14.3% of patients, it decreased to 0-11 points, in 21.4% complaints decreased, but did not completely disappear, the score decreased to 24-44. In 64.3% of patients, it was found that complaints did not disappear at all (p=0.001). This is reflected in graph. 7.



Graph. 7. Comparative assessment of the effect of treatment in the group with functional and pathological GERD

Thus, the use of long-term PPI in the treatment of patients in the functional group was found to be ineffective, and these patients were referred to psychologists and psychotherapists.

RESULTS

1. 32.7% of 1900 patients with complaints related to pathologies of the upper digestive system were diagnosed with GERD. It was more common in men than in women (35,9% and 28,7%; p=0,001). In the main group 51,5% patients with GERD were aged 31 to 50 years. 61.9% of men were 31-50 years old and 45.2% of women were 51-70 years old (ρ=0,338, p<0,001).The most common risk factors for patients with GERD were high BMI (73.2%), HH (51.5%), and fatty food intake (59.7%). Overweight and grade 1 obesity patients had more esophagitis during EQDS than patients with normal BMI (ρ=0.146, p=0.027). [3,6].

2. In the main group of 231 patients, 37.2% of non-erosive and 62.7% of erosive GERD were found endoscopically. 51% patients had esophagitis of grade B, C and D, which was found more often in men (ρ=-0,193, p=0,003). Grade C and D esophagitis were more common in patients with a DI of 1-5 years and more than 5 years than in patients with a DI of up to 1 year (ρ=0,201, p=0,002) [1,2,4,5].

3. In the impedance pH-metry, acid reflux prevailed in MG, and weak-acid reflux prevailed in CG ($p\chi2$=0.001). According to the spectrum of reflux, mixed reflux was more common in MG and gas reflux in CG($p\chi2$<0.001). In both groups, acid and weak-alkaline reflux had higher pH-metric indicators than weak-acid reflux (ρ=-0.523, p<0.001). In contrast to gas and mixed reflux, the pH-metric indicators were high (pH=0.003) in the liquid reflux spectrum. In patients with D esophagitis in the MG and CG, ineffective esophagus and fragmented peristalsis prevailed in EM ($p\chi2$=0.023 and $p\chi2$<0.001, respectively). 87.5±5.2% sensitivity and 70.9±6.1 specificity of EM examination according to EGDS diagnosis, 62.5±7.7% sensitivity and 75.5±5.9% specificity according to IRP-4s [4,7,8,9,10,11,13].

No correlation between patient complaints and 24-hour esophageal impedance pH-metry results was found. Pathological reflux was seen in 76.7% of patients in the main group. 24-hour impedance pH-metry test was normal (functional heartburn) in 23.3% of patients. In the control group, 22.9% of patients did not have reflux, and 77.1% of patients had pathological reflux ($p=0.958$). Based on the results of Ph-metry, a diagnostic algorithm was developed for patients with GERD [9,10,11,12].

4. As a result of 4 weeks of standard treatment applied to patients, symptoms disappeared in 71.4% of patients in the pathological reflux group and in 14.3% in the functional group ($p=0.001$) [2,14].

PRACTICAL RECOMMENDATIONS

1. The absence of relationship between complaints and impedance pH-metry indicators and at the same time the pathological reflux detected during the pH-metry examination in the control group, which we selected from the people without complaints who applied voluntarily, showed the role of pH-metry in the diagnosis of GERD and made it necessary to use the developed algorithm.

2. Impedance pH-metry and manometry examinations, which are recommended as a complex diagnosis for the correct treatment and prevention of complications of GERD, allow the detection of various clinical variants of the disease. As a result, the advice of a psychologist or psychotherapist is recommended as appropriate treatment for patients in the functional group, and correctly applied treatment both increases the quality of life of patients and reduces the use of unnecessary drugs.

3. Because Barrett's esophagus, which is a precancerous condition of the esophagus, is more common in the 31-40 age group, practitioners should advise people to undergo endoscopy after the age of 30.

4. Esophageal manometry and esophageal biopsy must be performed together for prognosis in patients with HH detected during EGDS examination, and it is also recommended for the selection of future treatment of these patients.

List of scientific publications on the subject of the research:

1. İmanlı G.A. Qastroezofageal reflyuks xəstəliyinin müasir müalicəsi / G.A.İmanlı, İ.Ç.Əlixanova // – Bakı: Sağlamlıq jurnalı, – 2020. №4, – s. 37-42.
2. İmanlı G.A. Qastroezofageal reflyuks xəstəliyinin müasir diaqnostikası / G.A.İmanlı, Hidayətov Ə.A., İ.Ç.Əlixanova // – Bakı: Sağlamlıq jurnalı, – 2020. №5, – s. 37-42.
3. İmanlı G.A., Əlixanova İ,Ç. Qastroezofageal reflyuks xəstələrində risk faktorlarının endoskopik ezofagitlə əlaqəsi // Şuşa ilinə həsr olunmuş "Təbabətin aktual problemləri" adlı konqresin materialları. – Bakı, – 2022, – s. 156-157.
4. İmanlı G.A., Əlixanova İ,Ç. Qastroezofageal reflyuks xəstələrində endoskopik əlamətlərin 24-saatlıq qida borusu pH-metriyasının göstəriciləri ilə əlaqəsi. // Şuşa ilinə həsr olunmuş "Təbabətin aktual problemləri" adlı konqresin materialları. – Bakı, – 2022, – s. 156-157.
5. İmanlı G. Qastroezofageal reflyuks xəstələrində şikayətlərin endoskopik ezofagitlə əlaqəsi // Akademik M.A.Topçubaşov adına Elmi Cərrahiyyə Mərkəzinin 60 illik yubileyinə həsr olunmuş elmi-praktik konfransın materialları. – Bakı, – 2022, – s. 63.
6. İmanlı G.A. Qastroezofageal reflyuks xəstəliyinin endoskopik əlamətlərinin risk faktorları və onların xəstəliyin şikayətləri ilə əlaqəsi / G.A. İmanlı // – Bakı: Azərbaycan Tibb Jurnalı, – 2022. №2, – s. 35-40.
7. Иманлы Г. Связь показателей 24-часовой импеданс pH-метрии с эндоскопическим эзофагитом у пациентов с гастроэзофагеальным рефлюксом /Иманлы Г. // – Минск: Медицинские новости – 2022. №11, – s. 52-56.
8. Imanli G. Gastroözofageal reflü şiddeti ile hiatus hernisi korelasyonunun özofagus manometrisi ile gösterilmesi / G.Imanli, I.Alikhanova // 39. Ulusal gastroenteroloji haftası. Bildiri Kitabı, Antalya, Türkiye, – 2022, – 22-27 kasım, – PP-063, – s. 520-521.
9. Imanli G. Diagnostic utility of the 24-hour esophageal impedance pH-metry indicators of gastroesofageal reflux patients. / G.Imanli // World Congress of Gastroenterology. Abstract book-Poster. Dubai: 2022, – 12-14 December, PP-074.

10. Imanli G., Alikhanova I. Diagnostic significance of the spectrum of reflux of gastroesophageal reflux patients / Ümumilli lider Heydər Əliyevin anadan olmasının 100 illiyinə həsr olunmuş "Təbabətin aktual problemləri" adlı beynəlxalq elmi-praktiki konqresin materialları. – Bakı, – 2023, – s. 303.

11. Imanli G. Assessment of hiatal hernia diagnosed in patients with gastroesophageal reflux disease by esophageal manometry / G.A.Imanli, I.Ch.Alikhanova, I.A.Gafarov // – Киев: World of Medicine and Biology – 2023. №2, – s. 78-83.

12. Иманлы Г. Взаимосвязь между показателями 24-часовой пищеводной импеданс-pH-метрии с данными манометрии пищевода и эндоскопии / Иманлы Г. Алиханова // – Минск: Медицинские новости – 2023. №10, – s. 59-62.

13. Imanli G. Diagnosis of hiatal hernia in patients with gastroesophageal Reflux Disease / G.Imanli, I.Alikhanova // Turkish Journal of Gastroenterology. Proceedings of the 40th National Gastroenterology Week and 11th Congress of Gastrointestinal Surgery, Antalya, Turkish, –November 2023; 34(Supp 4): – GP1 – s. 53-54.

14. İmanlı G.A. Qastroezofageal reflyuks xəstəliyi: müalicəyə yeni baxış. / G.A.İmanlı, İ.Ç.Əlixanova // – Bakı: Sağlamlıq jurnalı, – 2024. №4, – s. 55-61.

List of conventional abbreviations

ACE- Angiotensin converting enzyme
BMI- Body-mass index
CG- Control group
Check-up – A voluntary, non-complaint referral (a set of regular medical examinations)
DCI – Distal Contractile Integral
DI- Duration of illness
EGDS- Esophagogastroduodenoscopy
EHH- Endoscopic hiatal hernia
EM- Esophageal manometry
EMD - esophageal motility disorders
GER- Gastroesophageal reflux
GERD- Gastroesophageal reflux disease
GERD-HRQLQ- Gastroesophageal Reflux Disease- Health Related Quality of Life Questionnary (GERD- Health-related quality of life questionnaire)
HH- Hiatal hernia
HHM- Hiatal hernia in manometry
IRP- Integrated Relaxation Pressure (discharge pressure)
LESP- Low esophageal sphincter pressure
LR- – likelihood ratio for negative results
LR+ – likelihood ratio for positive results
MG- main group
nPV – negative predictive value
OR – Odds ratio
PPI- Proton pump inhibitors
pPV – positive predictive value
ROC- Receiver operating characteristic
SAP – Symptom Association Probability
Sn – sensitivity
Sp – specificity

The defense will be held on "14" may 2025 at "14⁰⁰" at the meeting of the Dissertation Council ED 2.27 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the Azerbaijan Medical University/

Address: AZ 1022, Baku city, A. Gasimzade St., 14.

Dissertation is accessible at the Library of the Azerbaijan Medical University.

Electronic versions of the dissertation and its abstract are available on the official website of the Azerbaijan Medical University (www.amu.edu.az).

Abstract was sent to the required addresses on "08" april 2025.

Signed for print: 01.04.2025
Paper format: 60x84 1/16
Volume: 32.800 characters
Number of hard copies: 20
Order: 222
"Tabib" publishing house