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OPTIMIZING THE DIAGNOSIS AND TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE ASSOCIATED WITH REFLUX

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ANNOTATION OF THE MONOGRAPH

This manual (monograph) is about dedicated to one the major health cake`s problems to the gastroesophageal reflux which videspread in developed countries of the world and cause for disability and mortality are developed by occurred vastly atypical (cardiac, broncho-pulmonary, anemic, dental) symptoms and short – term complications (Barrett's esophagus, esophageal adenocarcinoma). As the result of the research conducted by the author's, the causes of ineffective treatment of gastroesophageal reflux disease are now fully explored. The manual explores the extent to which the clinical and endoscopic manifestations of gastroesophageal reflux disease are linked to the type of reflux environment. A set of clinical-diagnostic measures that provide timely detection of these changes and, most importantly - early prevention, have been developed and implemented.

This manual is intended for medical universities, medical scientific centers, researchers, professors, masters, students, healthcare organizations, gastroenterologists, therapists, and general practitioners.

МОНОГРАФИЯ АННОТАЦИЯСИ

Ушбу қўлланма (монография) ҳозирги даврда дунёнинг ривожланган мамлакатларида кенг тарқалган, хасталикнинг атипик (кардиал, бронхо-пулмонал, анемик, стоматологик) белгиларининг нисбатан кўпроқ кузатилиши ҳамда асоратларининг (Барретт қизилўнгачи, қизилўнгач аденокарциномаси) қисқа муддат ичида ривожланиши натижасида юзага келадиган аҳолининг ногиронлиги ва ўлимига сабаб бўлаётган, соғлиқни сақлашнинг долзарб муаммоларидан бири бўлган гастроэзофагеал рефлюкс касаллигига бағишланади. Асарда муаллиф ўтказган илмий тадқиқотнинг якуни сифатида гастроэзофагеал рефлюкс касалигининг ҳозирги вақтда даволашнинг самарасизлиги сабаби тўлиқ очиб берилган, рефлюксат муҳити ва айнан рефлюксат муҳитига боғлиқ бўлган клиник, эндоскопик манзаралари ва даволаш тамойиллари клиник – инструментал ва лаборатор усуллар орқали таҳлил этилиб, уларнинг қонуниятлари кенг берилган. Монографияда илк бор гастроэзофагеал рефлюкс касаллигида учрайдиган клиник, эндоскопик манзараларининг намоён бўлиш хусусиятлари рефлюксат муҳити турига боғлиқлик даражаси ўрганилган. Ушбу ўзгаришларни вақтли аниқлаш ва энг муҳими – эрта профилактикасини таъминловчи клинико-диагностик чора – тадбирлар мажмуаси яратилган ва амалиётга қўлланилган.

Мазкур қўлланма тиббиёт олий ўқув юртлари, тиббиёт илмий марказлари, илмий изланувчилари, профессор – ўқитувчилари, магистр – талабалари, соғлиқни сақлаш ташкилотлари, гастроэнтерологлар, терапевтлар, умумий амалиёт шифокорлари учун мўлжалланган.

АННОТАЦИЯ МОНОГРАФИИ

Данное руководство (монография) посвящено одной из важнейших проблем здравоохранения - гастроэзофагеальному рефлюксу, который широко распространен в развитых странах мира и является причиной инвалидности и смертности, развивается при крайне атипичных (сердечных, бронхо-легочных, анемических, стоматологические) симптомы и кратковременные осложнения (пищевод Барретта, аденокарцинома пищевода). В результате проведенных автором исследований в настоящее время полностью изучены причины неэффективного лечения гастроэзофагеальной рефлюксной болезни. В пособии исследована степень связи клинических и эндоскопических проявлений гастроэзофагеальной рефлюксной болезни с типом рефлюксной среды. Разработан и внедрен комплекс клинико-диагностических мероприятий, обеспечивающих своевременное выявление этих изменений, а главное - раннюю профилактику.

Настоящее пособие предназначено для медицинских вузов, медицинских научных центров, научных работников, профессоров, магистров, студентов, организаций здравоохранения, гастроэнтерологи, терапевты и врачи общей практики.

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SHORT LIST OF WORDS

MG - main group

BE - Barrett's esophagus

GER - gastroesophageal reflux

GERD - gastroesophageal reflux disease

DGER - duodenogastroesophageal reflux

WHO - World Health Organization

IE - alkaline environment

AcM - acidic environment

ARI - acidic refluxate environment

IRM - alkaline reflux medium

LES - lower esophageal sphincter

CG - control group

NRD - noerosive reflux diseases

GT - gastrointestinal tract

PPI - proton pump inhibitor

RE - reflux esophagitis

BMI - body mass index

ERD - erosive reflux disease

INTRODUCTION

Relevance and necessity of the dissertation topic. Today, gastroesophageal reflux disease (GERD) is one of the urgent problems of medicine in the field of therapy. This disease is recognized as [1]"... the disease of the 21st century..." . In fact, it wasn't long before this prediction began to be confirmed in everyday practice. About 10% of the scientific articles published in the pages of the leading European and American gastroenterology journals in the last 10 years are dedicated to the problems of treatment of GERD. According to the World Health Organization (WHO), "... the occurrence of GERD in developed countries is 20-40%, and the population of the globe is constantly suffering from the feeling of hot flashes, which is the leading clinical sign of this disease..." [2]. The relevance of GERD is determined by its stable distribution on a large scale throughout the world and the tendency of this situation to increase every year. At the moment, GERD occupies one of the leading positions not only in the digestive or gastrointestinal system (GIS), but also in all diseases occurring in the human body. It is noteworthy that GERD is most observed among the population of economically developed countries.

In the world, a number of scientific researches are being carried out in order to achieve the high efficiency of the clinical and endoscopic picture of gastroesophageal reflux disease and the connection of therapy with the reflux environment. In this regard, it is necessary to create a convenient and economical method that allows to determine the type of reflux environment (RE) and to evaluate its possibility, the level of quantitative indicators of the leading clinical signs of the disease, and the level of relevance to the RE. It is of special importance to develop a set of health measures aimed at the comparative assessment of the degree of visibility of signs characteristic of the GERD endoscopic picture, the selection of treatment types based on the parameters of the reflux pH environment, and the comparative assessment of their therapeutic effectiveness.

[1]VI European week of gastroenterologists. Birmingham, 1997
[2]World Health Organization Reports 2014

Today, a number of works are being carried out in our country to adapt the medical field to the requirements of world standards, to prevent and eliminate diseases of the gastrointestinal system among the population. In 2017-2021, the action strategy for the five priority areas of the development of the Republic of Uzbekistan states "... implementation of comprehensive measures aimed at improving and strengthening the health of the population, reducing morbidity rates, increasing the convenience and quality of specialized medical services, improving the system of rapid and emergency medical care tasks such as reform, protection of motherhood and childhood, prevention of somatic diseases and increase of life expectancy... [3]In the performance of these tasks, prevention and diagnosis of various diseases, raising the level of modern medical services to a new level, improving the use of modern technologies in the diagnosis and treatment of diseases of the gastrointestinal system, and reducing the level of various somatic diseases among the population and increasing the level of longevity.

The President of the Republic of Uzbekistan No. PF-4947 of February 7, 2017 "Strategy of Actions on Five Priority Areas of Development of the Republic of Uzbekistan in 2017-2021" and No. PQ-3071 of June 20, 2017 "Increasing the provision of specialized medical care to the population of the Republic of Uzbekistan in 2017-2021 serves to a certain extent in the implementation of the tasks defined in the Decisions on development measures and other regulatory legal documents related to this activity.

[3]of the President of the Republic of Uzbekistan No. PF-4947 " On the Strategy of Actions for Further Development of the Republic of Uzbekistan "

Chapter I. LITERATURE REVIEW.

THE SIGNIFICANCE OF THE TYPE OF REFLUX ENVIRONMENT IN THE DIAGNOSIS AND TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE

§ 1.1. Epidemiology of gastroesophageal reflux disease with different types of reflux

Epidemiological studies indicate that 40-45% of the population of economically developed countries (USA, European countries) suffer from boils, one of the main clinical signs of GERD [20; P.208 23; P.19, 28; P.20-30, 73; P.104-114, 105; P.871-880, P.148; 2-14]. According to the data obtained as a result of other researches in the same direction, the sign of shingles is found in an average of 20-40% of the population [12; P.23-30, 13; P. 46, 21; P.464, 22; 27; P.75-95, 38; P.21, 39; P.11-16, 122; P. 248-252].

About the prevalence of this disease among the population of the countries of the Commonwealth of Independent States, the pages of the field literature show different figures close to each other. In particular, according to the data provided by the famous Russian specialist D.S. Bordin (2014), GERD occurs in 46% of the population of Moscow over the age of 18 [4; P.29, 25; P.20, 27; P.75-95, 76; P.2-9]. According to the data of Russian scientists, the prevalence of GERD among the country's population is increasing year by year. According to published scientific data, the main clinical symptom of GERD is boils in 63.6% of the population of Novosibirsk, 63.6% of residents of St. Petersburg and Krasnoyarsk. 46% were recorded [69; P.2-14,75; P.41,140; P.175].

There is no accurate information about the percentage of GERK occurrence among the population of our republic. Nevertheless, according to the results of some few scientific studies, this disease is increasing year by year among the population over 18 years old [34; P. 27, 41; P. 98-101].

It is known that GERD differs from esophageal diseases and acid (Hcl)-related diseases of neighboring organs (stomach, duodenum) in some respects. It is noteworthy that dysfunctions observed in the functional state of adjacent organs - stomach or duodenum - act as the initial impetus for the development of GERD. As a result of these dysfunctions, gastric or duodenal fluids are intermittently but continuously regurgitated abnormally into the esophageal cavity. If isolated gastric juice is released, this process is called gastroesophageal reflux (GER). If duodenal fluid escapes, it is called duodenogastroesophageal reflux (DGER) [15; P.40–42, 27; P.75, 74; P.104–114, 149; P.537–546].

Both gastric fluid and duodenal fluid are now referred to as refluxate or refluxate. Aggressive reflux and expelled fluid - refluxate form the basis of the pathogenesis of GERD. It should be noted that gastric juice is the basis of the liquid that is thrown into the esophageal cavity during the GER process, and its pH environment is naturally acidic. On the contrary, in the process of DGER, duodenal fluid is released and its pH environment is usually alkaline. It should be noted here that most or all of the fluid ejected during GER is gastric juice. However, the duodenal fluid released during the DGER process is likely to be mixed with gastric juice in one way or another, whether we like it or not. As a result, in these cases, the percentage of duodenal fluid in the mixture must be high (at least 60%) in order for the refluxate pH medium to have an alkaline color. Otherwise, the pH of the refluxate medium may be at least neutral or slightly acidic in nature. Therefore, most experts in the field rely on the pH indicator of the refluxate environment and recognize its two types: acidic and alkaline [44; P.30-34, 66;P.1072, 72; P.14-21, 73; P.104-114-76;P.2–9,84; P.5–9,102; P.1364–1365].

One of the leading experts in the studied field A.S. According to Trukhmanov (2014), 50% of patients with GERD had acid reflux, 39.7% had mixed reflux, and the remaining 10.63% had alkaline reflux [25; P.20,75; P.41, 155; P.290 – 295]. Western scientist M. Fein, during his scientific research, only 30% of patients with GERD caused by DGER had an alkaline reflux [55; P.193 - 197, 132; P.334 - 338]. According to some studies, antisecretory drugs offered to patients with GERD are

ineffective in 40% of cases. Researchers are trying to explain the ineffectiveness of antisecretory drugs by the fact that the reflux component is not only hydrochloric acid (Hcl), but also duodenal fluid components[10; P.42 - 46,31; P.4-13,33; P.24,38 P.21,50; P.1627 - 1631,59;P.281,68;P.113 - 118,86;P.10 - 11,108; P.33 - 38, 123; P.713 - 718].

Based on the research results presented above, it can be noted that GERD belongs to a group of widespread diseases from an epidemiological point of view. However, there is no clear idea about the prevalence of acid or alkaline GERD in the population. There is no reliable information about the spread of GERD among the population of our republic. The epidemiology of GERD, especially when it is divided into types with acid or alkaline reflux, inaccuracies in the prevalence indicators, or these and similar abstract cases, serve as a specific impetus for conducting scientific research in this direction.

1.1.1. Controversial aspects of the effect of acid reflux on the pathogenesis of gastroesophageal reflux disease.

In the early stages of studying the pathogenesis of GERD, almost all experts in the field recognized that only the components of gastric juice serve as the main factor in the development of this disease. It is worth noting that the imbalance between the protective forces of the esophageal mucosa and the aggressive factors in the reflux that are released during the process of GER or DGER is the basis of the pathogenesis of GERD. Of course, this imbalance does not occur during any GER or DGER. In these cases, exposure (duration) of GER or DGER is crucial. Even when the protective forces of the esophageal mucosa have sufficient capacity, aggressive factors in the refluxate in the course of long-term GER or DGER are able to finally break their resistance. Also, in these cases, it is necessary to take into account the possibility that the aggressive properties of the refluxate components can cause injury at the same time. Therefore, this aggressive factor is crucial in the formation of the main clinical, endoscopic and morphological signs that occur during the course of GERD. It is for this reason that GERD has already been

unanimously recognized by experts as an equal member of the group of acid-related diseases (gastric, duodenal ulcer) [7; P.560, 76; P.2-9, 151; P.1900-1920].

It is known that the normal pH of the esophageal mucosa is around 5.5-7.0. When this rN indicator is 4 and below (rN<4.0), the environment begins to take on an extremely acidic tone. That is why, in recent years, specialists in the field have reasonably relied on the opinion "No acid - there is no boil " [6; P.24, 26; P.23, 60; P.24-26, 72; P.14-21, 121; P.170-180].

It should be noted that the components of gastric juice - hydrochloric acid and pepsin form the main pair of aggressive factors that damage the integrity of the esophageal mucosa. In our opinion, the proteolytic effect of pepsin may act as a stimulus that opens the way to the injury of the esophageal mucosa. It is known that proteins form the basis of the framework or structure of the mucous membrane of the esophagus. As a result of the proteolytic effect of pepsin, proteins are initially lysed. This deprives the mucous membrane of the esophagus of reliable protection. As a result, the dynamic balance between protective and aggressive factors begins to break. Aggressive factors are more likely to cause injury. In other words, "the strength of aggressive factors occurs due to the weakening of protective forces." At the same time, the second aggressive factor in gastric juice - hydrochloric acid has a chemical effect on the mucous membrane of the esophagus, which is deprived of protection, causing various injuries [8; P.44, 67; P.64-70, 116; P.47-49].

Thus, an important link in the chain of pathogenesis of GERD is the degree of damage to the esophageal mucosa, not only the anatomical structure of the lower esophageal sphincter and the violation of its closing function, but also the type of reflux environment, the duration of the GER or DGER process, the current state of the force of aggressive factors to cause injury, The activity of chemical and mechanical types of esophageal clearance is assessed by the combined effect of a number of factors, such as the extent of leakage [60; P.24–26, 25; P.20].

1.1.2. Controversial aspects of the effect of alkaline reflux on the pathogenesis of gastroesophageal reflux disease

It is known that the first opinions about the importance of reflux of an alkaline character in the development of GERD can be said to act as a kind of motivation that the traditional treatment method of this disease was ineffective in some patients due to the reasons that are difficult to explain. Because GERD is one of the diseases that develop organically to acid (Hcl), proton pump inhibitors (PPI) form the basis of its traditional treatment. According to the results of the conducted scientific researches, in almost 40% of patients with GERD, the proposed traditional method of treatment was ineffective [19;P.1046, 29; P.71–78,31; P.4–13,38; P.21.85; P. 15–19, P 110; P. 295–309]. For this reason, many scientific researches were carried out by experts in the field. As a result of these studies, it was found that not only GER, but also DGER process exists, and as a result, duodenal fluid is first thrown into the stomach and then into the esophageal cavity, which is mainly alkaline (unlike the refluxate rN environment, which is thrown from the stomach) [38; P.21, 89; P.471-475, 90; P.2333-2342, 91; P.46-54]. It is known that the failure of the closing function of the lower part of the stomach (privratnik), chronic duodenostasis and duodenal hypertension are among the causes of the DGER process. It should be noted that these functional defects usually occur in case of damage to the anatomical integrity of the stomach or adjacent organs (gastric resection, gastrostomy, enterostomy, vagotomy, cholecystectomy). Also, in the occurrence of DGER, the motor-evacuator activity discordance of the upper parts of the OIT can act as a specific impetus [60; P.24–26, 104; P.936–945, 154; P.350–354].

At present, experts in the field unanimously recognize the importance of the following mechanisms that can cause refluxes of an alkaline nature : due to the functional failure of the sphincters (valves) located in the lower part of the pyloric and esophagus, these anatomical structures are deprived of the ability to prevent antiperistaltic movements, and as a result, the duodenal masses resist. first into the stomach and then into the esophageal cavity without encountering it; as a result of the motility disorder [79; P.51] observed in the activity of anatomical structures in

the gastric antral and initial (pars horizontalis superior) parts of the duodenum, which is caused by the discoordination in the activity of the antrum and pyloris, which is important from a physiological point of view ejection of duodenal masses to the stomach; due to the functional failure of the antireflux barrier, the duodenal fluid moves backwards almost without resistance and is thrown into the stomach [7;P.560,93; P.820-828]. It is distinguished by its duration, but also by the influence and extent of the aggressive effect of the components of the duodenal mass (bile fluid and its ingredients - bile acids, lysolecithin, etc., pancreatic juice and its components - lipase, trypsin, chymotrypsin, etc.) [24; P. 84–98, P. 57; P.35–39, 88; P. 80–95, 43; P.281–294].

It is known that the DGER process with the following two consecutive stages can act as an important cause of GERD: due to a sudden increase in pressure in the stomach (intragastric) and duodenal (intraduodenal) spaces, the risk of GERD increases several times; duodenal aggressive factors of the liquid: bile acids, lipolytic (lipase) and proteolytic (trypsin, chymotrypsin) enzymes of the pancreas begin to damage the integrity of the mucous membrane of the esophagus, resulting in inflammation and then even erosion and ulcers. It is worth noting that the components of bile fluid GERD plays an important role in the evolution of pathogenesis. They dramatically increase the synthesis of cytokines, which further deepen the inflammatory process. It can also have a negative effect on the processes of proliferation, differentiation and apoptosis of epitheliocytes of the esophageal mucosa [15; P.40-42, 46; P.20-23, 56; P.548, 91; P.46-54, 101; P.111–114, 138; P.1-3]. The analysis of the data obtained as a result of a number of recent scientific researches shows that an increase in the secretion of express inflammatory cytokines (cyclooxygenase-2, interleukin-8) and prostaglandin E_2 fraction leads to gastric-type metaplasia of the multilayered squamous epithelium of the esophagus. It is known that abnormally formed cylindrical epitheliocytes due to metaplasia serve as the main morphological feature of Barrett's esophagus (BE) [17;P.21–26, 134; P.1266-1268].

Thus, the analysis of the data obtained as a result of modern scientific research shows that the presence of bile acids in the composition of the alkaline refluxate can not only accelerate the proliferation process in the epithelial cells of the mucous layer, but also open a wide path to their unnatural differentiation. As a result, due to this process of metaplasia of the gastric type, cylindrical epithelial cells are formed, which are extremely resistant to the effects of bile acids and components of the pancreatic fluid [115; P.110-118, 124; P.9-16,127; P.1113-1122, 128; P. 200-207].

The evidence presented in the data obtained as a result of a number of other scientific researches in the direction of the category mainly indicates the acceleration of the picture of oxidation processes in the cylindrical epithelial cells caused by gastric-type metaplasia due to the effect of bile acids in the alkaline refluxate. As a result, the amount of free oxygen produced increases uncontrollably, causing oxidative stress. As a result, the DNA molecule undergoes a process of damage that is difficult to reverse . Also, bile acids, which are a component of alkaline refluxate, limit the possibilities of DNA repair process in cylindrical epitheliocytes formed due to metaplasia. It should be noted that this process occurs due to the paralysis of the synthesis of MUTYH and OGG-1 enzymes in the cytoplasm of cylindrical epitheliocytes by bile acids. However, these enzymes are chemical products responsible for DNA molecule repair. Damage to the DNA structure can increase the activity of oncogenic factors. As a result, the activity of suppressor genes decreases, which plays an important role in the development of changes characteristic of dysplasia in cylindrical epithelial cells. As a result, adenocarcinoma of the mucous membrane of the esophagus may develop [16; P.9–16, 116; P.47–49-153; P.431-436].

Thus, based on the analysis of the scientific data obtained as a result of various researches in recent years, it can be said that bile acids, which are one of the main components of alkaline reflux, increase the amount of inflammatory cytokines, cause oxidative stress, and thus damage the DNA structure in the cytoplasm of the epitheliocytes of the esophageal mucosa, as well as the stomach It is possible to open

a wide path to type metaplasia, resulting in the formation of abnormal cylindrical cells and their malignancy.

1.2-§. The significance of the character of the refluxate in the formation of the clinical-endoscopic picture of gastroesophageal reflux disease

The analysis of the data obtained as a result of scientific research carried out in recent years indicates that the type of refluxate pH environment plays an important role in the formation of all clinical, endoscopic and morphological signs characteristic of GERD. However , there are many opinions that cause controversy about which of the clinical, endoscopic and morphological signs that develop in the development of GERD are related to reflux of an alkaline or acid character [84; P.5-9, 85; P.15-19].

It is known that there are differences of opinion about the direct dependence of the manifestation of all clinical signs [24; P.84-98, 89; P.471-475] on the type of reflux pH environment, and there is no definite conclusion in this regard. its absence indicates the presence of significant aspects of the problem.

Heartburn (pyroris), belching (eructatio), discomfort in the epigastric area (discomfortus), pain (dolor), pain behind the bed (odynophagia), swallowing disorders (dysphagia) are typical symptoms of GERD caused by acid reflux [2; P. 144–148, 6; P.24, P.26; P.23, P. 27; P. 75–95, P. 81; P.8–12].

It should be noted that, in terms of diagnostic value, the sign of heartburn is important among them. In most cases, this important clinical sign is manifested as a burning sensation of varying intensity in the chest or behind the sternum (lower 3/1 of the esophagus) or in the epigastric region, according to the literature of the field. observed in 75–83% of patients [45; P.24, 83; P.704, 150; P.4-7]. Undoubtedly, this sign serves as the "clinical face" of GERD.

The leading experts in the field say: "GERD means boiling, and GERD should be understood as boiling." That is why most of the measures used during the treatment of this disease are aimed at early elimination of the sign of boils. The basis of the clinical sign of heartburn is the shift of the pH of the esophageal mucosa towards the acidic side. Due to the long duration of the GER process, the aggressive

effect of the acidic mass in the stomach on the mucous membrane of the esophagus is prolonged. As a result, the pH of the esophageal mucosa begins to shift from the standard 6.8–7.4 to an acidic character (pH<4). It should be noted that the sign of heartburn begins to appear only when the pH of the esophageal mucosa is around this indicator [14; P.90, 23; P.19, 55; P.193 – 197, 145; P.1003 – 1017]. Other clinical signs seen in GERD do not match the sign of boils in terms of prestige or frequency. It is worth saying that clinical signs similar to belching and regurgitation are much less common than the sign of a boil.

The belching sign is a spasm of the gastric outlet (privratnik) and occurs as a result of reflex contraction of the diaphragm and abdominal muscles, resulting in involuntary ejection of excess gases from the stomach through the mouth, and occurs in about 52% of patients with GERD. According to experts in the field, this clinical sign is most often caused by the DGER process due to the release of acidic gastric fluid (relatively small amount) and bitter-tasting duodenal mass (relatively high volume) into the esophagus [33; P.24, 74; P.116-120].

The sign of regurgitation is a special type of the clinical sign of belching, which is manifested by sudden ejection of not only air, but also sour gastric fluid and bitter-tasting gastric masses together with it to the larynx. In most cases, the cause of regurgitation is the DGER process, which occurs violently due to a sharp increase in pressure in the cavities of the duodenum (in relatively many cases) and in the stomach (in relatively few cases). It should be noted that the sign of regurgitation, which is intense and occurs especially at night, can cause an abnormally dry cough (as a result of aspiration of reflux into the upper airways) in patients with GERD [87; P.324,89; P.471-475,158; P.2237 - 2243].

A sign of swallowing disorder is called dysphagia. Dysphagia is one of the hallmarks of GERD. It is based on the fact that a bite of food is blocked or stopped in the esophagus. It should be noted that both organic and functional types of dysphagia can be found in GERD. The first type occurs in reflux esophagitis. It is caused by swelling and narrowing of the mucous membrane of the esophagus due to inflammation. As a result, the passage of food through the esophageal cavity begins

to be disturbed. The second - functional type can be observed when the movement of the esophageal wall is disturbed by nervous regulation. The incidence of dysphagia is lower than other clinical symptoms of GERD, and this indicator is 19-20% according to the literature [3; P. 23, 58; P.11].

Prolonged dysphagia in most cases indicates a narrowing of the esophagus - stricture. If severe transient-progressive dysphagia is observed together with a sharp decrease in body mass, then this condition should be given serious attention. Because this change in the course of GERD can indicate adenocarcinoma of the esophageal mucosa in most cases [98; P.91-102].

Pain sensation behind the sternum - in GERD, it is mainly of a pressing or pressing nature, which can first be located behind the sternum and then spread to the epigastric area or behind the chest. In some cases, the pain behind the chest spreads to the scapula, neck, lower jaw, and even the front surface of the left half of the chest. It can be said that back pain observed in GERD differs from pain caused by diseases of other organs located in the chest in that it is associated with eating, and it is usually eliminated by changing body position, taking alkaline mineral waters and antacids [42; P.58–60, 44; P. 30-34, 59; P.281].

Painful swallowing sensation is usually rare in uncomplicated GERD. But if GERD is complicated, more precisely, if the mucous membrane of the esophagus becomes inflamed and swollen, or if its integrity is damaged, erosion and ulcers occur, then the incidence of this symptom may increase [52;P.6-10]. It should be noted that the sign of pain caused by swallowing in GERD is usually spread over the relatively injured area of the esophageal mucosa. According to the data provided by Xiong et al. (2008) in the research conducted by Xiong and colleagues (2008), the symptom of painful swallowing in the majority of patients with GERD was caused by the damage to the esophageal mucosa as a result of the alkaline reflux effect observed in the process of GERD, and was mainly distributed in the chest area [23; P.19].

According to the analysis of the literature devoted to the field of study, the process of manifestation of GERD clinical symptoms in relation to the environment

of refluxate pH is sufficiently abstract or complicated, and that is why the aspects that need to be clarified remain problematic. In particular, the development of quantitative indicators of the main clinical symptoms of GERD and the study of their aspects related to the nature of the refluxate rN environment, as well as the problems of early diagnosis of this disease and the assessment of the possibility of creating effective types of treatment are considered the main problems facing specialists today.

The endoscopic view of GERD has varied appearances. It should be recognized that among the modern medical and technical examination methods of GERD, the method of fibroesophagogastroduodenoscopy (FEGDS) is the most effective in terms of the effectiveness of the diagnostic possibility [83; P.704]. Therefore, according to industry experts, FEGDS has been the "gold standard" for diagnosing GERD for years. In fact, thanks to the use of this method, the scope of knowledge of specialists about the endoscopic picture of GERD has significantly expanded in recent years. In particular, different types of erosion (linear, point, etc.), visual evaluations of BE, GER, and DGER processes began to be obtained one after another [114; P. 83-93].

Currently, experts in the field have divided the signs characteristic of GERD into different endoscopic groups according to their visual appearance during the FEGDS process. In one of the most common of these distributions, GERD types are distinguished: non-erosive reflux disease (NERD); erosive-ulcerative reflux disease (ERD). According to the statistical data presented in scientific researches, the NERD type of GERD is 60%, ERD is 37%, and BE is only 3%. The NERD type of GERD usually develops during GER due to the frequent and continuous eruption of aggressive factors of gastric juice into the esophageal cavity. Its remarkable endoscopic feature is that when using the FEGDS method, defective substances (erosion, ulcer) are not observed in the mucous membrane of the esophagus, even when GER is noted [47; P.49 –5 2,52; P.6-10,107; P.164]. At the same time, it should be noted that only in some cases, the endoscopic picture characteristic of catarrhal

inflammation in the distal parts of the esophageal mucosa can be shown in the visual field [9;P.830-834].

According to the information obtained as a result of scientific research by experts in the field, the prevalence of ED is extremely wide among the elderly population, on average it is 30-45% [26; P.23].

It should be noted that the aggressive ingredients of gastric juice, especially hydrochloric acid, are continuously released into the esophageal cavity during the course of GER. The evolution of the development of ERD is multi-stage, and according to the extent of the lesions observed in the esophageal mucosa, the following consecutive stages are distinguished: A) damage to one or more parts of the esophageal mucosa, but the size of the lesion does not exceed 5 mm and is within one fold;V) one or more parts of the mucous membrane of the esophagus are covered with wounds over 5 mm in size and do not cross the border of one fold; S) several parts of the mucous membrane are injured at the border of two or more folds, the process occupies up to 75% of the esophageal circulation; D) observed in the mucous membrane the injury occupies more than 75% of the esophageal circulation [14; P.90,23; P.19,79; P.51].

ERD occurs in most cases in men. It should be noted that, among the clinical symptoms, boils are relatively frequent and persistent. Also of particular note is the tendency of this sign to have night attacks. Dysphagia and odynophagia-like clinical signs are also more common in ERD. The duration of the disease is long, most of the patients are overweight and obese [78; P.79-82,103; P.577-582], it is noted that the ES tone decreases in most cases. Characteristic morphological features such as signs of inflammation of various degrees and activity, dystrophic processes, atrophy, leukoplakia and dysplasia of the multi-layered flat epithelium, changes similar to pre-tumor conditions are observed in ERD. In smokers, the disease often recurs, and as a result, the risk of developing an esophageal ulcer increases [16; P.9–16, 17; P.21–26, 94; P.1510–1516].

For the first time in 1950, the British scientist Norman Barrett discovered Barrett's esophagus (BE), abnormally formed epithelial cells in the mucous

membrane of the distal part of the esophagus. It is known that, normally, the mucous membrane of the esophagus is covered with a multi-layered squamous epithelium. During development, the multi-layered squamous epithelium changes into cylindrical epitheliocytes, in other words, undergoes metaplasia of the gastric or duodenal type. As a result, abnormal epithelial cells are formed for the mucous membrane of the distal part of the esophagus [17; P.21–26, 64; P. 200,92;105–120,116; P. 47–49,118; P.373–380, 157; P.2632–2640].

Also, it should not be forgotten that if ERD is accompanied by morphological changes characteristic of BK in the esophageal mucosa, it is necessary to perform FEGDS every year and take a biopsy from the epithelial tissue and study the morphological picture in detail.

Currently, both endoscopic types of GERD - NERD and ERD are recognized as independent nosological units by specialists. However, some specialists recognize NERD and ERD as two types of pathological process, which are related to each other from the point of view of pathogenesis. According to them, if GERD continues for a long time and develops day by day, then NERD can gradually transform into ERD [47;P.49. P.52, 100; P.328].

As can be seen from the above data, there are some abstract and complicated aspects in the questions of the forms and mechanism of origin of the endoscopic changes observed in the esophageal mucosa in GERD, especially in relation to the environment of the refluxate pH. Elucidation of the nature of these complications, of course, requires new and, most importantly, targeted scientific research.

§ 1.3. Relationship of the effectiveness of the treatment of gastroesophageal reflux disease to the nature of the reflux

It is known that from the first days when GERD was recognized as an independent disease of the digestive system, it was included among the pathologies (stomach and duodenal ulcers) that occur in connection with acid, more precisely, hydrochloric acid, which is considered an aggressive component of gastric juice. For this reason, most of the measures used in the treatment of GERD until now are aimed at timely elimination of the possibility of chemical damage of the aggressive factor

of gastric juice - hydrochloric acid. For this purpose, until the beginning of the 21st century, H_2 histamine receptor blockers (cimetidine, ranitidine, etc.) were widely used as the main drugs used in the treatment of GERD [19; P.1046,39; P.11-16,47; P.49.52,136;P.502-507]. But these days, due to certain reasons (blockers of H_2 histamine receptors block only one of the three chains involved in the production of hydrochloric acid - histamine-dependent activity), drugs of this class are rarely used in the treatment of GERD. Another notable drawback of drugs belonging to this group is their extremely wide range of side effects [70; P.4-10, 129; P.584-589,130; P.74-88,137; P.299-311].

Taking into account the above, since the end of the 20th century and the beginning of the 21st century, drugs belonging to the PPI group have been widely used in order to early deprive the main aggressive component in gastric juice - hydrochloric acid of its ability to show chemical damage [31;P.4 -13, 59; P.281, 153; P.431 - 436]. Currently, drugs belonging to the PPI group are widely used in the treatment of GERD [31;P.4-13,108;P.33-38]. However, according to other literature, the use of PPI drugs in the treatment of GERD is ineffective in 40% of cases. Most experts explain the ineffective results of taking PPI drugs as the result of not only gastric juice, but also aggressive factors of duodenal fluid entering the esophagus [42; P.58-60,43; P.1749-1753,50; P.1627-1631,86; P.10-11-109; P.243-251].

It should be noted that almost all of them, regardless of whether they are step up or step down, the main core of the treatment is aimed at the early elimination or at least limitation of the decisive aggressive component of reflux - hydrochloric acid, which can cause chemical damage [23; P.9,155; P.290–295]. From Zim's point of view, any move to neutralize an influential aggressive factor seems to have a logical basis. However, when evaluating this action from the perspective of GERD pathogenesis, it seems appropriate to use a completely different approach. Therapeutic actions aimed at neutralizing the damaging effect of the reflux aggressive factors that occur in the course of GER or DGER are not the cause of the disease, but the consequence [23;P.19,131;P.1-5,133;P.72-81]. However, the

situation requires a type of treatment capable of eliminating the causes that form the basis of the pathogenesis of GERD - GER or DGER.

All specialists working in this field know for sure that the causes of GERD are GER or DGER, and this is a logical conclusion [23; P.19,31; P.4-13, 103; P.577-582,134; P.1266- 1268]. However, in almost all of the proposed treatment methods, PPIs are irrationally used as the base drugs. Undoubtedly, the aggressive effects of some ingredients that are part of the refluxate, including hydrochloric acid, pepsin, bile acids, etc., play an important role in the origin of GERD [25;P.20,28; P.20-30,139; P.45-53]. However, in the absence of GER or DGER or of short duration, the development of GERD remains almost impossible, regardless of the aggressive factors of reflux. That is why the term reflux is included in the list of words in the empirical name of GERD.

Based on the information presented above, it can be said that early application of measures to eliminate the reflux process, and not the activity of the aggressive factors in the refluxate, should be the basis of GERD treatment. Since the slogan "No reflux, no GERD" was announced, most experts in the field have been supporting this position almost unanimously [33; 24p]. Indeed, theoretically, with the elimination of GER or DGER processes, the leading clinical and endoscopic symptoms of GERD should logically disappear by themselves. Naturally, after the disappearance of GER or DGER processes, there is no logical reason to take drugs belonging to the PPI group.

As a result of a comprehensive analysis of the field literature and based on the above-mentioned data, the following controversial opinions can be put forward: quantitative indicators of the main clinical signs of GERD have important aspects in the early diagnosis of this disease; Mechanisms of appearance of the main clinical and endoscopic signs of GERD depending on the reflux character have not been fully elucidated; The effectiveness of GERD treatment, its level of stability in the near and long term, and stable pharmacoeconomic indicators have not been covered in detail.

Thus, until the recent past, the gastric juice component - hydrochloric acid - was unanimously recognized by experts as the main factor causing the injury of the esophageal mucosa and notable clinical and endoscopic symptoms of GERD, while at the same time, it is difficult to identify other types of reflux pH environment (alkaline). Due to the emergence of technical capabilities, the attitude towards this situation began to change radically. The integrity of the esophageal mucosa can be damaged not only by the ingredients of gastric juice [74; P.116-120,77; P. 4-14,137; P. 299-311], but also by various other chemical and physical factors, and every can cause various injuries. Based on the above conclusions, this scientific research was carried out in order to comprehensively illuminate the abstract aspects of the character of reflux, which are related to the manifestation of the main clinical and endoscopic symptoms of GERD, the effectiveness of treatment and the duration of stagnation.

Chapter II. § 2.1. EVALUATION OF THE POSSIBILITY OF A COMPLEX METHOD THAT ALLOWS TO DETERMINE THE TYPE OF REFLUXATE PH MEDIUM

It is known that in determining the pH of endogenous biological fluids, the pH-metric methods developed by the company "Gastroskan-IAM" (ZAO NPP "Istok-Sistema", Rossiya) or the "Bravo" capsule developed by Medtronic (USA) are currently the "golden standard" [26; P.23, 27; P.75-95]. Taking into account the existing technical shortage and the high cost of pH-metric tests performed by the above-mentioned equipment, an alternative complex method was developed and put into practice, which allows to determine the type of refluxate environment. This complex method consists of direct (directly indicating the type of refluxate pH environment) and indirect (biochemical assessment of the type of refluxate pH environment and comparing its consistency with clinical symptoms). The direct method, on the other hand, consists of such components as ph-metry of saliva and in vitro ph -metry of refluxate absorbed during FEGDS. Also, the indirect method, in turn, has components such as biochemical (spectrophotometric study of the biochemical composition of the refluxate collected during the FEGDS process) and clinical (in - depth analysis of the clinical signs of GERD).

that the methods capable of indicating the type of reflux (acidic or alkaline) were used in a certain sequence . First, pH -metry of saliva, then in vitro pH - metry of the refluxate absorbed during FEGDS, then the biochemical composition of the refluxate absorbed as a result of endoscopic research (in order to determine the ingredients of the herb) was studied using a spectrophotometric method, and finally, after an in-depth analysis of the clinical symptoms of GERD, acidification of the refluxate was performed. or note the signs characteristic of the alkaline type.

Salivary pH - metry was performed dynamically on all 18 healthy (CG) and 136 GERD patients (MG) involved in the scientific research process. In the implementation of the method, the persons involved in the examination should collect 4-5 ml of the portion of saliva from the morning meal in a special plastic

container (test tube) with a tightly closed mouth . Then, in vitro conditions, using a universal pH - meter device, one - to-one pH - metry method was implemented, and the obtained data were recorded in special medical documents. Scientifically significant results were obtained in the course of research conducted in order to clarify the indicators of oral fluid pH -metry. Table 2.1 shows the data of saliva pH -metry, which was initially performed in 18 CG individuals with the intention of obtaining reference indicators.

Table 2.1

Results of pH -metry indicators of the oral fluid of the individuals involved in the study

Group r	Salivary pH - metric indicators, in conditional units (ShB)			R
	Minimum	Maximum	M±m	
CG (n= 18)	6.7	7.0	6.8±0.03	
MG (AlR) (n=28)	7, 4	9.4	8.4 ±0.12	<0.0 01
MG (AcR)(n=108)	4.7	5, 7	5, 2 ±0.03	<0.0 01

The average value of pH -metric index of oral fluid of CG individuals was 6.8 ± 0.03, and this condition was considered a neutral environment . It should be noted that the lowest (minimum) indicator of CG including CG was 6.7 pH, the highest (maximum) indicator was 7.0 pH at the limit of the neutral medium interval.

It should be noted that studying the value of pH -metric indicators of the oral fluid of patients with GERD was one of the tasks planned on the eve of the scientific research implementation process. In order to achieve the goal set before this task, saliva pH -metry, performed in 171 patients with GERD, showed the following results (Table 2.1): in 8 patients, these indicators indicated the type of reflux environment (pH - in vitro conditions of reflux) metry, spectrophotometric determination of the refluxate content did not correspond with the clinical data. Therefore, these patients were included in the group of patients with GERD (total of

35 people) with inconsistent results recorded during the use of other methods, and for obvious reasons were excluded from further stages of the study.

Results of pH - metric examination of the oral cavity of patients with GERD (MG) were clearly different from the same indicators of CG. It should be noted that this difference had a polar direction. During pH -metric analysis of the saliva of CG patients, ¼ of the results were higher (alkaline environment), and ¾ of the results were lower (acidic environment). It can be said that the difference between the values of these indicators of CG and MG was around the reliable limit during the statistical selection process ($P<0.05$) .

The value of the pH indicators of the oral fluid of patients with GERD in relation to the age group of the patients, and as a result, the following data were recorded: in patients with GERD, the environment of the oral cavity fluid is acidic, compared to low values of 5.93±0.43 pH (highly acidic environment) were observed in individuals aged 18-29 and, on the contrary, high values of 6.18±0.51 pH (relatively low acidic environment) were observed in individuals aged 40-57 years. According to the information presented on the pages of the field literature, the parameters of the oral cavity liquid pH of patients with GERD are significantly acidic [1; P.57–59,46; P.20–23]. The process of GER is often repeated serves as the cause of this situation. According to A.Gindzienski (2003), the pH of the saliva of patients with GERD is acidic in most cases. This, in turn , indicates a weakening of the antireflux barrier. It should be noted that the results obtained in the scientific research process are consistent with the information recorded in the literature pages of the specialists working in the field.

Can be the reason for coming to the opinion that the value of the pH values of the oral cavity fluid of these patients has an unnaturally acidic color due to the pH of the refluxate, which is thrown towards the mucous layer during the GER process relation to the age of patients is understandable. It is known that as the age increases, the secretory activity of the gastric mucosa, including hydrochloric acid and pepsin products, decreases somewhat. As a result, the amount of aggressive ingredients in the refluxate is relatively reduced. It is self-evident that due to this condition, the

ability to change the value of the oral cavity water q lig pH of the refluxate depending on this or that environment is significantly limited.

The pH -metric value of saliva increased with increasing age in patients with GERD, in which the pH environment of the oral cavity fluid was alkaline. The average value of oral cavity fluid pH - metric index in patients aged 18-29 was 8.2±0.62. At the moment, it was noted that the average value of saliva analog indicators of patients aged between 4 0 and 5 7 is around 8.9±0.65 pH.

Thus, at this stage of the conducted research, the following conclusion can be put forward : the pH of the oral fluid of patients with GERD is significantly different from the same parameters of healthy individuals. It should be noted separately that in some patients the environment of saliva pH is abnormally acidic, and in others it is alkaline. As a result of logical analysis, it is possible to think that this observed difference in refluxate pH is related to the type of environment (acidic or alkaline) .

Table 2.2

The result of pH-metric tests of reflux of patients with GERD

Group r	of patients (n)	Reflux pH -metry indicators, in conventional unit			P
		Minimum	Maximum	M±m	
Acidic	108	2.8	6.3	4 , 5 ±0.09	<0.0 0 1
Alkaline	28	6, 8	11.0	8, 8 ±0.23	

*Note: *** p<0.001 reliable difference between acidic and alkaline media.*

Reflux pH - metric All patients of CG involved in the scientific research process were evaluated dynamically, and 136 of them were selected to participate in the next stages. During the implementation of the method, 4-6 ml of the refluxate, which was ejected into the esophageal cavity during the implementation of the

FEGDS method, was sucked and transferred to a special plastic container (test tube) with a tightly closed mouth. Then, in vitro conditions, using a universal pH -meter, one - to-one pH -metry method was implemented, and the obtained data were recorded in special medical documents. During the analysis of reflux liquid pH -metric indicators, the results that require attention were obtained (Table 2.2) .

Indicators of the reflux fluid injected into the esophagus of patients with GERD was one of the tasks planned on the eve of the research. In order to fulfill the conditions set for this task, pH -metry of reflux fluid was performed in 171 patients with GERD and the following results were obtained (Table 2.2): in 11 of them, these indicators were higher than other methods used in parallel (saliva pH -metry, refluxate determination of its composition using spectrophotometric method, clinical) did not agree with similar data. Therefore, these patients were included in the group of patients with GERD (total of 35 patients) with inconsistent results recorded during the use of other methods, and were excluded from further stages of the study for obvious reasons.

The data obtained from pH-metric examination of the reflux fluid injected into the esophageal cavity of GERD patients (MG) have different views with their value. According to the results of the analysis , it can be noted that these changes are directed towards two opposite poles in terms of value. 28 (20.6 %) of 136 GERD patients were alkaline (8.8 ±0.23) and 108 (79.4 %) were acidic (4.5±0.09) indicator

was noted . Note it should be noted that the difference determined when the values of these indicators of MG patients with GERD were statistically sorted confidence limit was around P<0.01 .

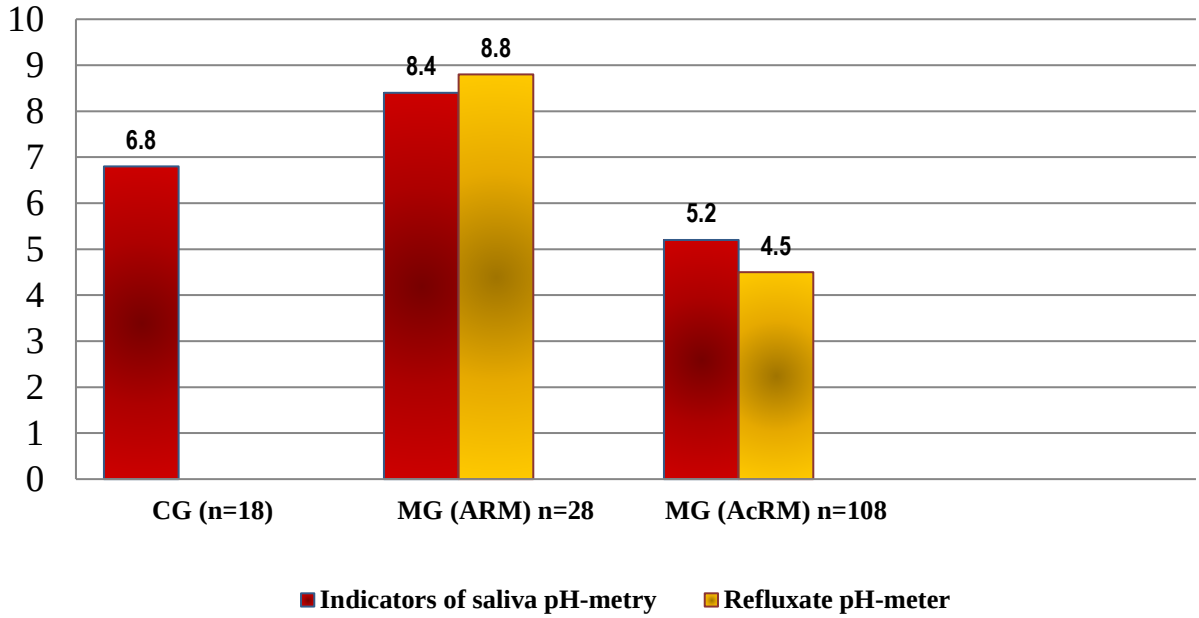


Figure 2.1. Correlation results between salivary and refluxate pH metrics in the examined groups

It can be seen from Figure 2.1 that when the results of pH-metry of saliva and refluxate are compared, the environment is shifted to the acidic side in patients with CRD, and on the contrary, to the alkaline side in patients with GRD. This directly indicates that the reflux changes depending on the environment, the values of pH values of reflux fluid pH of patients with GERD were analyzed in relation to age, and the following conclusions were reached: there is a correlation between pH of reflux fluid (acidic or alkaline) and age of pH patients involved in the test. signs of dependence were observed. A total of 28 patients with GERD who had an alkaline color (8.8 ± 0.23) of the refluxate pH environment were young.

Indicators were around 25-57, and the average value was 42.0 ± 2.0 years. On the contrary, the refluxate pH environment was acidic (4.5±0.09) in patients aged 18-56, and the average value was 34.4 ± 2.2 years (see Figure 2.2).

From the obtained data, it can be seen that the difference between the age indicators of patients with GERD, which passes on the reflux floor with an alkaline

or acidic pH environment, was almost twofold (in favor of the first). In the statistical analysis, it was noted that the level of reliability of this difference is around P<0.01 .

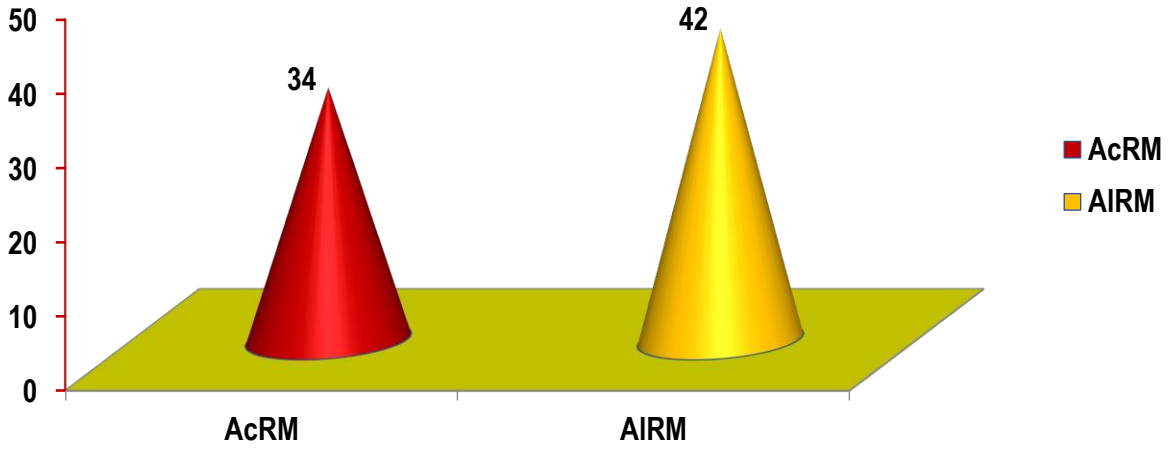


Figure 2.2. Age characteristics of patients with acid and alkaline pH reflux.

The results achieved during the research essentially corresponded with the information reported in the field literature [39; P.11-16,78; P.79-82]. In fact, the secretory capacity of the gastroduodenal mucosa decreases with age. As a result, the ability of aggressive reflux factors (hydrochloric acid, pepsin) to cause damage to the esophageal cavity during GER is significantly weakened. That is probably why GERD disease with acid reflux in elderly people is less common [39; P.11-16].

The preliminary results of this stage of the study indicate that the percentage of total occurrence of acid reflux in patients with GERD is almost twice as high as in alkaline, and it mainly occurs in young people. In contrast, GERD with an alkaline pH environment is much less common and occurs mainly in individuals with a high age index value.

The results of a qualitative study of the presence of bile ingredients (bilirubin, cholesterol) in the refluxate. Bilirubin pigment, which is one of the main components of bile ingredients, was qualitatively studied in the reflux fluid of all 171 GERD patients involved in the study . It is known that there are many signs that indicate the alkaline type of reflux acid. In particular, during FEGDS, the

duodenal liquid is thrown towards the stomach cavity, the abnormal presence of bile ingredients in the refluxate, and it is recorded using a laboratory method, etc. k . It should be noted that bile pigment (bilirubin) is not able to affect biological fluids and the environment. Currently, determination of bilirubin absorption spectrum by fiberoptic spectrophotometry method serves as the "golden standard" of qualitative diagnosis of bile pigment in biological fluids. This method was registered in 1993 under the name Bilitec 2000.

In all 136 GERD patients involved in the study, qualitative indicators of bile pigment bilirubin in the reflux fluid were determined and the data presented in Table 3.3 were obtained. From the analysis of these data, it can be seen that 28 out of 136 GERD patients (20.5%) had positive results of fiber optic spectrometry of bile pigment in reflux. This, in turn, indicates that the reflux fluid of these patients is mixed with bile pigments due to DGER, and therefore its pH medium has an alkaline type . In a large part of the patients involved in this study, more precisely, 108 (79.4 %) of the patients, the results of the study of qualitative indicators of bile pigments in the composition of Fluxat by the method of fiberoptic spectrometry turned out to be negative. It goes without saying that this evidence suggests that the patient's reflux was caused by GER and therefore that his pH was acidic. In 35 out of 171 patients (20.5%), the results of fiberoptic spectrometry of bile pigments in reflux water were of a doubtful (unreliable)nature. Therefore, for obvious reasons, these patients were excluded from the next stages of the study.

Table 2.3

Results of determination of quality indicators of bilirubin in reflux fluid of patients with GERD

Number of patients	Results of qualitative index of bile pigment in refluxate liquid			
	Positive		Negative	
	Abs	%	Abs	%
n = 136	28	20.5	108	79.4

The following data were obtained during the scientific research analysis carried out in order to determine the general diagnostic possibility of this contrast complex method in determining the reflux pH environment (see table 2.4): 136 patients out of 171 patients (79.5%) were also part of the proposed complex method the results obtained with the help of the method turned out to be proportional, in 35 (20.5%) patients, the results of the data indicating the type of refluxate pH environment, obtained with the help of the components of the complex method, were inconsistent with each other.

It should be noted that data with a disproportionate indicator were observed as a result of the data indicating the type of refluxate pH environment obtained by all the methods that made up the component of the complex method. It should also be noted that, in some cases, inconsistent results were observed in the results of two or more methods used to indicate the type of reflux pH environment of the same patient (in order to avoid possible artificial confounding), these indicators are only from the series of data sets of one method took place.

Table 2.4

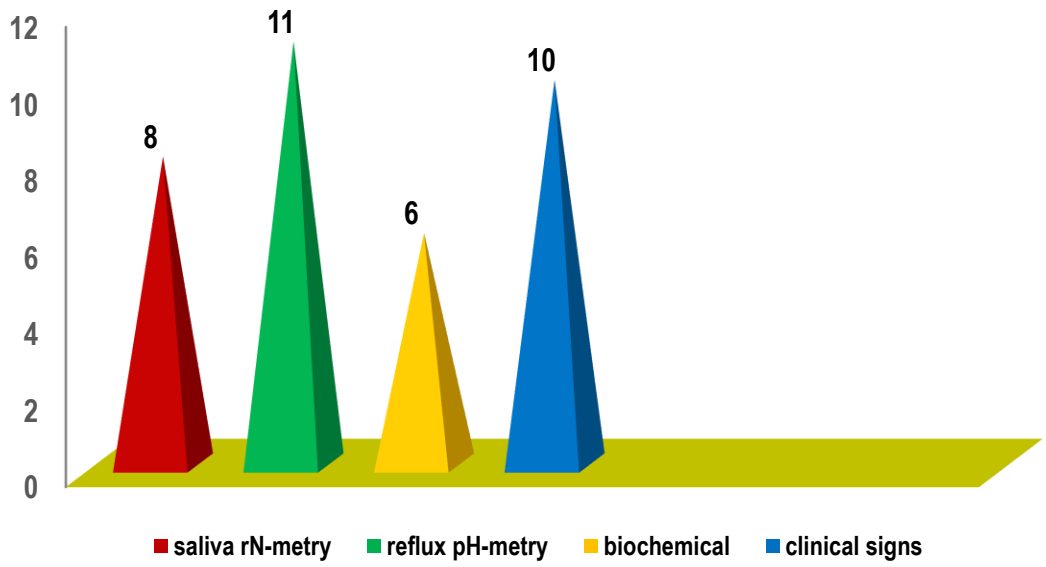
The results of the gross assessment, which allow to determine the type of refluxate RN medium

Method type and name	CG (n=18)	MG (n=171)		
		Proportionate (n=136)		Disproportionate (n=35)
I. Directly:				
Saliva pH -metry	6.8±0.03	5.0 ± 0.03 * (n=108)	8.4 ±0.12 ** (n=28)	6.9±0.5 6 (n= 8)
Refluxate pH-meter	–	4.2 ± 0.09 *** (n=108)	8.8 ± 0.23 *** (n=28)	8.7±0.48** (n=11)
II. Indirectly:				
Biochemical (herb ingredients in refluxate)	–	–	+	– (n=6)

Clinical: a) burning sensation, sour taste in the mouth; b) belching, bitter taste in the mouth;	– –	+ –	– +	+ (n=4) – (n=6)
Overall evaluation results	Neutral	Acidic	Alkaline	Artifact

Note: ** – differences are significant compared to the indicators of the control group (* – P<0.05; ** – P<0.01; *** – P<0.001).*

For example, if both saliva pH-metry and biochemical test results in the same patient had inconsistent indicators, only one of the above-mentioned methods was included in the current data set.



2.3 . Reflux pH in methods indicating the type of environment disproportionate results observed

Taking into account the above, it can be said that the number of cases of disproportion (more than 60) observed in the results of the data obtained using the methods indicating the indicator of the type of reflux pH environment is actually due to this indicator, the last research it was supposed to be more than the number of patients (35 people) excluded from the stages for obvious reasons, and it turned out to be so.

These inconsistent data were shown as follows in the cross-section of the used testing methods (see Figure 3.3) : from the picture presented in Figure 3.3, it can be seen that the inconsistent results compared to the data obtained during the application of the pH - metry method conducted in vitro in order to determine the type of refluxate pH medium. observed a lot. In 11 (6.4%) of 171 patients with GER K in MG, the results of the pH-metry method performed in vitro were inconsistent with the data obtained using other methods. Among patients with GERD with such a disproportionate outcome, 5 were men and the rest were women. It is worth noting that the results with the disproportionate position of the index of the refluxate pH environment were recognized as an artifact, and all GERD patients with these data were excluded from the next stages of the scientific research.

It is worth noting that the artifact indicators appeared in the following order: in the results of reflux pH-metry conducted under in vitro conditions, 11 cases were noted, in saliva pH-metry indicators, 8 cases, during the analysis of clinical signs, 10 cases, and as a result of biochemical examination of the contents of the reflux liquid, 6 imbalance cases were noted. Inconsistent results were observed in the in vitro pH measurement of the reflux fluid. Results of this type were recorded in 11 of 171 patients with GERD (6.4%). At the same time, similar indicators were observed in 8 (4.7%) of the gross results of saliva pH-metry. Also, the analysis of GERD-specific clinical signs in 10 patients (5.8%) and the results of chemical examination of the reflux fluid content in 6 patients (3.5%) were inconsistent with similar data from other methods used. in 35 patients (20.4%), the results of the methods that are components of the complex method on the refluxate pH environment were inconsistent, and the patients were excluded from the next stages of the research for obvious reasons.

Thus, the used complex method provides a wide opportunity to determine the type of reflux pH environment, and the possibility of the information obtained through it does not lag behind the same indicators of other modern methods.

III . SYMPTOMS COMPOSING THE CLINICAL AND ENDOSCOPIC VIEW OF GASTROESOPHAGEAL REFLUX DISEASE AND THE RELATIONSHIP TO THE TYPE OF REFLUX ENVIRONMENT

3.1 . Clinical description of patients with gastroesophageal reflux disease with different reflux environment

136 patients with GERD were involved in the investigation in order to fulfill the tasks set before this stage of the research. GERD patients were divided into two representative groups based on age, gender, body mass (Kettle) index, average disease duration, and similar characteristics. The only difference was in type of reflux medium (TRM) indicators. Based on this, all patients were divided into two groups. In 108 patients of the 1st group, the reflux environment is acidic (AcR= 4.5±0.09) and in 28 patients (group 2) it is alkaline (AlR= 8.8 ±0.23). Clinical and anamnestic characteristics of both groups of patients are presented in Table 3.1.

It can be seen from the data presented in the table that the patients of both groups are close to each other with most of their indicators. Patients with GERD were divided into two groups, based on the predominant indicators of the type of reflux rN environment, and patients with MG. There were 108 patients with acid reflux type of environment. 46 of these patients (42.6%) are men, 62 (57.4 %) are women, their age ranges from 18 to 56 years. Both groups of patients have indicators close to each other in terms of age and body mass (Ketle) index results (see Table 3.1).

Table 3.1

Clinical parameters of patients involved in the study

Parameters	Reflux pH is an indicator of the environment			
	Alkaline (n=28)	Acidic (n= 108)		
Age averages	39.3±3.34	3 0 .4 ± 1 .42		
of disease progression (in years)	4.7 ± 0.40	4.5 ± 0.47	x^2	R
Gender indicators (A: E)	1 : 1,4	1 : 1.3		

Number of patients according to body mass index (according to Ketle):	abs	%	abs	%		
< 25 kg/m²	14	50.0	40	37.03	0.95	0.33
25.1 – 29.9 kg/m²	10	35.7	44	40.7	0.15	0.69
≥ 30 kg/m²	4	14.3	24	22.2	0.57	0.44
Number of smokers	8	28.6	34	31.4	0.05	0.82
Number of alcoholic beverages	6	21.4	27	25.0	0.11	0.74
There are many recurrences of GERD	3	10.7	13	12.03	0.05	0.83

The average age at the onset of GERD in patients with an acid reflux type of environment was 24 [20, 28, 4]. In male patients, the disease is relatively early -34 [30.7; 37.9] years old, while women are 38 [34.2; 42.3] was found to occur around age. Based on the duration of GERD-specific complaints in patients with an acidic reflux environment , it can be said that the duration of the disease is in a wide range (from 8 months to 8 years), on average 6 [4,7;8] formed the year. Are 28 patients with GERD with an alkaline type of reflux pH medium, aged 23-54, 17 of them (60.7%) are women, 11 (39.3%) are men. During the analysis of the age and body mass index (Ketle) average indicators of this group of patients, data similar to the same results of patients with acid reflux type of environment were noted. It should be noted that the number of overweight and obese patients in both groups was low and almost equal, so the difference between them was not statistically sorted.

When comparing the clinical parameters of both groups of patients with GERD, the percentage of cases with high body mass index in individuals with acid reflux environment was not significantly higher than the same data of patients with TRM alkaline. Due to the small number of smokers and alcohol drinkers recorded among both groups of patients, the observed difference between them did not have a statistically reliable value appeared.

3.2 - §. Correlation of clinical signs of gastroesophageal reflux disease with the type of reflux environment.

Likert's 5 -point social scale (R. Likert . 1932; ed. 1977) was used in order to evaluate the quantitative indicators of the main clinical signs specific to this pathology, which were included in the scope of scientific investigation.

Was to determine how TRM is related to the quantitative indicators of the main clinical symptoms in patients with typical GERD. That is why, initially, the features of the main clinical signs encountered in these patients were studied separately . In order to comprehensively describe the manifestation of clinical symptoms, it was necessary to first calculate the most important medical indicators of the clinical features of this disease.

Table3.2

Procedure for quantitative assessment of GERK main symptoms

Evaluation criteria	Allocated points
GERD-specific symptoms are absent	1 point
Symptoms of GERD are subtle (unnoticed)	2 points l
Symptoms characteristic of GERD are moderate (it is impossible not to feel, but it does not disturb daytime activity and sleep) and constantly bothers the patient.	3 points l
Severe symptoms of GERD (disruption of daytime activity and sleep)	4 points
Presence of highly visible GERD symptoms (significant disruption of daytime activity and sleep)	5 honey l

The following are considered to be the main clinical signs of GERD: sore throat; regurgitation; stuttering bitter taste in the mouth; sour taste in the mouth; dysphagia; odynophagia.

Table 3.3 presents the main clinical symptoms in GERD patients with different reflux conditions. Based on the information in this table, it was determined that some clinical signs typical of GERD are relatively frequent regardless of the type of refluxate pH environment (acidic or alkaline). Among the clinical signs of such a characteristic, the place of boiling, regurgitation and belching took place. The

most commonly reported complaint among patients in both groups was hives. There was no statistically significant difference in the prevalence of this clinical symptom between the two groups of patients included in the study.

Table 3.3

of GERD symptom prevalence coverage with TRM (n=136)

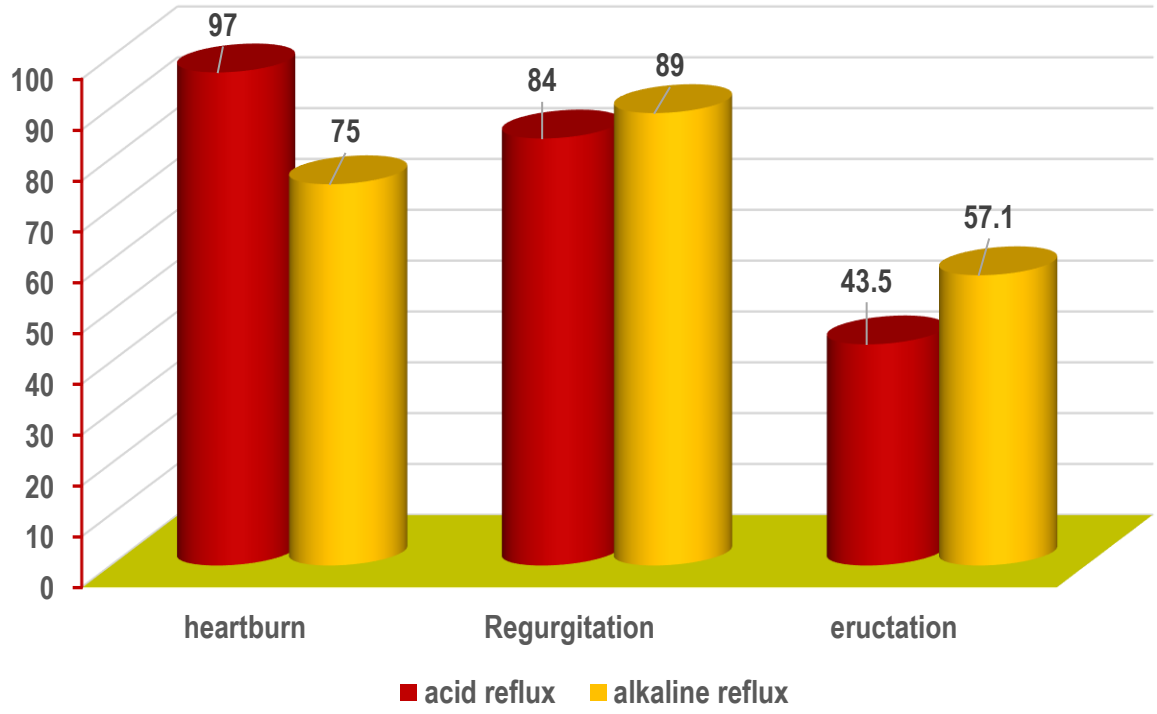
Main clinical signs	Type of refluxate pH medium					
	Acidic (n= 108)		Alkaline (n=28)			
	Clinical symptoms					
	a bs.	%	a bs.	%	ch2	R
Heartburn	105	97	21	75.0	0.82	0.365
Regurgitation	91	84	25	89	0.08	0.782
Eructation	47	43, 5	16	57.1	1.07	0.301
Bitter taste in the mouth	17	15.7	26	93	9.68	0.002
Sour taste in the mouth	100	92	4	14.3	9.90	0.002
Dysphagia	24	22, 2	6	21.4	0.00	0.967
Odynophagia	17	15, 7	4	14.3	0.02	0.885

the symptom of scurvy had a significant negative effect on the night sleep of both groups of patients. This symptom was observed in 62.4% of patients with an acidic pH environment , and in 53.5% of patients with an alkaline pH environment. The difference was not statistically significant.

Refluxate pH was detected in 97 % of GERD patients with an acidic environment, regurgitation in 43.5 %, and regurgitation in 84 %, on the contrary, refluxate pH was found in 75.0% of patients with an alkaline environment. 57.1% had the second and 89 % the third symptom (see Figure 3.1).

Symptoms characteristic of GERD are related to the type of reflux pH environment at the next stages of the case analysis. According to the manifestation of this characteristic, all the main clinical signs can be divided into two large groups : the first group of clinical signs is to note that the refluxate is manifested in some

relation to the type of environment, such as gurgling, belching, bitter or sour taste in the mouth possible



3.1- fig. Comparative description of GERD clinical symptoms in patients with acid and alkaline reflux.

In the second group, it was noted that symptoms such as boils and sour taste in the mouth are more frequent in patients with acid reflux pH (see Figure 3.2).

These symptoms was 97% (this indicator was 75.0% in patients with pH-alkaline reflux) and regurgitation was 84% (89% in patients with pH -alkaline). Also, at the same time, clinical symptoms such as stuttering and a bitter taste in the mouth , on the contrary, are more common in patients with reflux with an alkaline pH environment. 57.1% of patients of this group had stuttering symptom (in 43.5% cases in patients with acidic pH environment) and 93% had a bitter taste sensation in the mouth (in 15.7 % cases in patients with acidic pH environment).

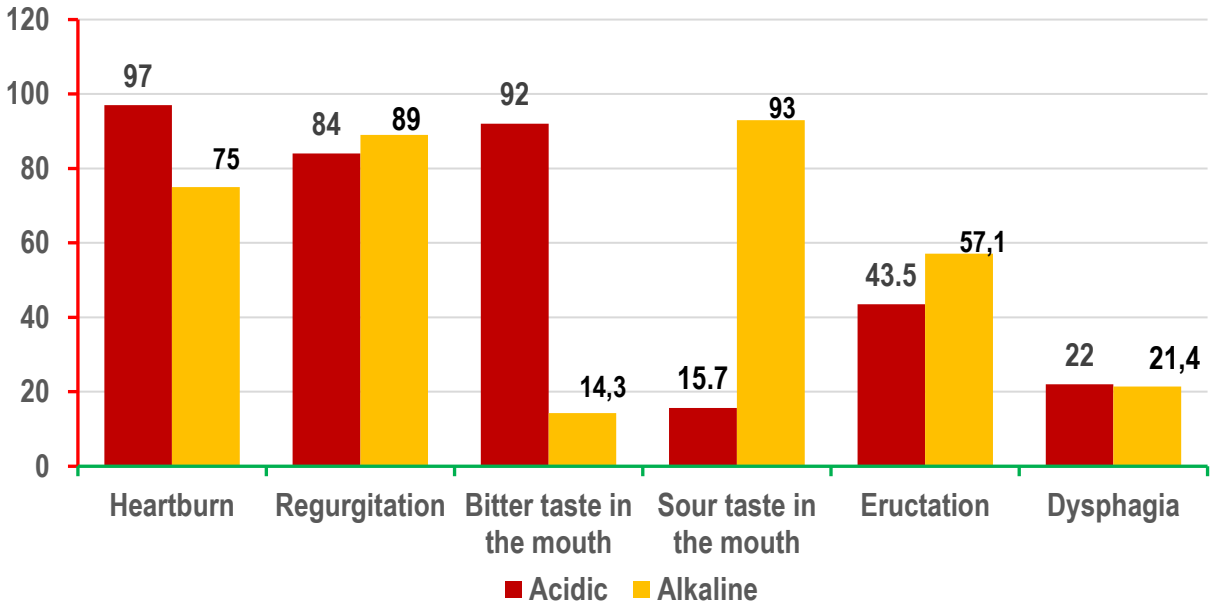


Fig. 3.2. GERD clinical signs related to the type of refluxate pH environment.

The clinical sign of regurgitation was analyzed, it was observed in 25 out of 28 patients (89%) with alkaline TRM and 91 out of 108 patients (84%) with acidic TRM. These numbers indicate that GERD-specific regurgitation in patients with TRM, although small, is clinically significant. Therefore, it is appropriate to take into account the measures to eliminate the clinical signs of regurgitation when creating a treatment plan for GERD. Out of 28 patients (57.1%) with GERD and TRM alkalosis involved in the study had the symptom of stuttering, and almost 15 of them (93.8%) had an unexpected feeling of lightness similar to this clinical symptom passed as soon as it arrived. On the contrary, these indicators were significantly lower in patients with acid TRM. In particular, 47 (43.5%) of the 108 patients with TRM acidity who were involved in the study had stuttering symptoms, while only 27 (57%) of them had this clinical symptom with a feeling of lightness. It should be noted that both groups no significant difference was found in the level of clinical symptoms such as dysphagia, odynophagia and regurgitation in patients.

Thus, briefly summarizing the level of clinical symptoms specific to GERD, it is necessary to note the following:

1. GERD-specific clinical signs is different and it largely depends on the type of reflux pH environment.

2. The sign heartburn is relatively common, regardless of TRM.

3. The level of boils, sour taste in the mouth, stuttering and bitter taste in the mouth were directly related to TRM, the first two of which were observed more when the reflux pH was acidic, and the last two were more alkaline.

3.3 - §. Quantitative indicators of clinical signs of gastroesophageal reflux disease reflux is related to the type of environment

Of scientific research, there was the task of detailed analysis of quantitative indicators of GERD -specific clinical signs. In order to do this , based on the intensity of manifestation of GERD clinical signs, quantitative assessments were given using a 5-point Likert social scale (see Table 3.4). It can be seen that the quantitative indicators of the main clinical signs characteristic of GERD have different views in terms of value. Quantitative indicators of these clinical symptoms, even when considered superficially, it is noticeable that the intensity of their manifestation is related to TRM. The value of the quantitative indicators of clinical symptoms such as burning sensation, sour taste in the mouth, belching, and bitter taste in the mouth, which are mentioned below, are clearly related to TRM got up It should be said that the intensity of visibility of 4 out of 7 (57.1%) of the clinical symptoms of GERD included in the scientific analysis and the value of the quantitative indicators allocated for this reason were clearly related to TRM.

3. 4 - table

Quantitative assessment of GERD-specific clinical signs and their relationship to TRM

Main characters	Reflux pH is a type of medium				R
	Acidic (n= 108)		Alkaline (n=28)		
	%	on a Likert scale	%	on a Likert scale	
Heartburn	105 (97%)	4.6 ± 0.01	21 (75%)	3, 6 ±0, 18	< 0.001
Regurgitation	91(84%)	4, 0 ± 0, 02	25 (89%)	4.2 ± 0.02	> 0.05
Eructation	47 (43.5%)	2.1 ± 0.10	16 (57.1)	2, 7 ±0, 14	< 0.001

Bitter taste in the mouth	17 (15.7%)	0.75 ± 0.03	26 (93%)	4.4 ± 0.02	< 0.001
The food tastes sour	100 (92%)	4,4 ±0, 02	4 (14.3%)	0.66 ± 0.05	< 0.001
Dysphagia	24 (22%)	1, 04 ±0, 05	6 (21.4%)	1, 02 ±0, 05	> 0.05

*Note: * – p<0.05; ** – p<0.001 reliable difference compared to indicators of acidic and alkaline environments.*

The value of the quantitative indicators of the listed GERD-specific clinical signs was relatively high in patients whose TRM was acidic in the first pair, and alkaline in the next pair (see Table 3. 4).

An important clinical sign, such as a boil, had the highest value in patients with acidic RMT and was 4.6 ± 0.01 points , while a relatively low indicator was recorded in patients with alkaline TRM, 3.6 ± 0.18 The score consisted of l . The difference between the value of these quantitative indicators was in the statistically reliable (P>0.001) range. The difference between the indicators of the degree of occurrence of an important symptom of GERD, such as heartburn, in TRM with acidic and alkaline patients, was relatively low, in contrast to the quantitative evaluation of this symptom. In conclusion, although the occurrence of the clinical sign of gingivitis is almost equal in patients with acidic and alkaline TRM, the intensity of its manifestation is much higher in patients with acidic TRM, this priority is more than 1.5 times.

According to the consensus adopted in Montreal (Canada) (2006), the weekly level of the boil sign is recognized as one of its important features. In the course of this scientific research, the symptom of gingivitis was observed in 59 (56.1 %) of patients with two or more acid-base tumors (56.1%), and in 8 (3.8 %) patients with acid-base cysts. It should be noted that such an important clinical symptom as feverishness during the week was observed in connection with TRM.

It should be noted that among all the symptoms observed in GERD, the scurvy fever took the leading position in terms of both the level of occurrence and the intensity of manifestation. The sign of Jigildon's boil was observed in patients with

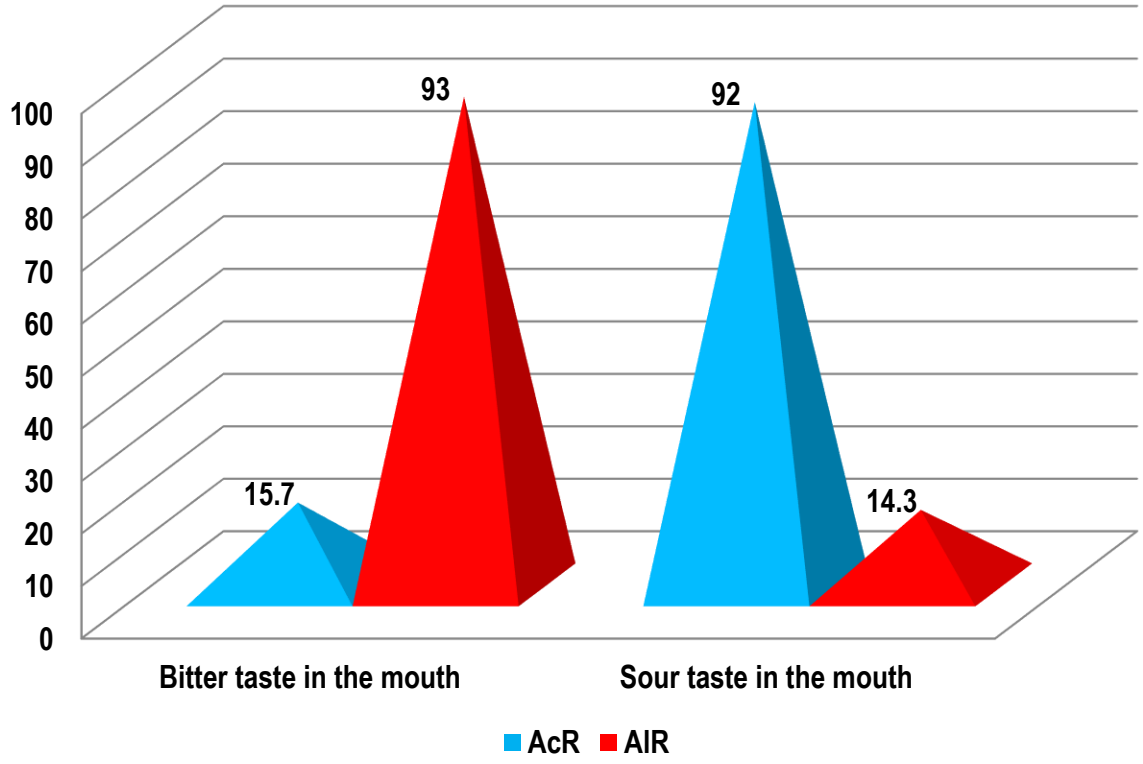
acidosis of TRM. Signs characteristic of GERD, the next place in terms of the value of the quantitative assessment, allocated to the level of visibility, is the feeling of sour taste in the mouth. It is known that the appearance of a sour taste in the mouth often indicates the presence of GER and, therefore, the presence of an acidic indicator of TRM. Based on the above opinion, it should be noted that the clinical significance of the appearance of a sour taste in the mouth can be important in some cases. It has a rightful place among a group of signs that are important in terms of clinical appearance and have a high diagnostic potential: boils in the throat, stuttering, and a bitter taste in the mouth. The important advantage of the sign of sour taste in the mouth is that if its clinically visible features are used rationally and efficiently, it will be possible to make a real assessment of TRM in many cases.

It should be noted that although the clinical symptom such as the appearance of a sour taste in the mouth was recorded in patients with both acidic and alkaline RMT, but, naturally, the value of the estimates allocated to the extent of its occurrence and the intensity of manifestation differed (see Fig.3.3). For example, only 104 (76%) of 136 GERD patients involved in the research process had a sour taste in the mouth. It should be noted separately that this clinical sign is more common in patients with TRM acidity. Also, the intensity of manifestation was relatively higher than the value aspect of the isolated quantitative assessment in these patients. In particular, the average indicator of the isolated quantitative assessment of the degree of manifestation of the symptom of sour taste in the mouth in patients with GERD with acidic TRM was 4.4 ± 0.02 points. formed l.

On the contrary, the value of the quantitative assessment index allocated to the degree of visibility of this clinical symptom in patients with TRM alkalosis was 0.66 ± 0.05 points . When both quantitative scores were compared, it was found that this superiority is also in patients with acidosis.

Also, the sour taste sensation in the mouth of patients with GERD was analyzed according to a number of parameters. In particular, based on gender, body mass (Ketle) index values, the quantitative evaluations divided into the scale of clinical manifestations of sour taste in the mouth were comparatively studied and

the following data were obtained: a total of 136 patients were included in the appropriate control group at this stage of the study.



3. 3 - Fig. Correlation of the value of quantitative evaluations allocated to the degree of clinical visibility of sour taste sensation in the mouth to ng RMT .

The sensation of sour taste in the mouth was noted in 61 of 79 women with GERD (77 %). Among them, 59 (96.7%) patients have acidic TRM, 2 patients (3.3 %) have alkaline. A sour taste in the mouth was noted in 43 of the 57 men involved in the study (75%). It can be seen that the scope of coverage of clinical manifestations of this symptom and the value of quantitative assessments assigned to it did not differ from the same indicators of female patients. 41 out of 43 male patients with symptoms of sour taste in the mouth (95 %) TRM are acidic, and 2 (5 %) are alkaline. It is worth noting that during the study, it was found that there is a significant correlation between the clinical sign of sour taste in the mouth and the value of the body mass index (Ketle) quantitative indicators of GERD patients.

Before this stage of the scientific research, 41 (30%) of 136 patients with GERD, included in the control group, had various abnormal indicators of body mass (indicative of weight gain), 23 of them (56 %) and 18 of them (44%) are male. 23 (56%) of these patients were overweight, 11 (27%) had I degree and 7 (17%) had II degree. A sour taste in the mouth was noted in 18 of 23 overweight women with GERD (78%). When these parameters were compared , it was found that the extent of sour taste in the mouth in female patients with GERD and abnormal values of body mass index is almost 1.6 times higher than the same parameters in male patients.

Clinical signs characteristic of GERD, the next place in terms of the value of the quantitative assessment separated by the level of manifestation was taken by the bitter taste in the mouth. It is known that the appearance of a bitter taste in the mouth is one of the important signs that occurs as a clinical impression of DGER in most cases and therefore has a high diagnostic status. Naturally, the character of the refluxate that occurs in the process of DGER is formed in direct relation to the pH of the duodenal fluid, and in most cases it begins to acquire an alkaline color for obvious reasons. It can be noted that in the course of DGER, a bitter taste in the mouth is a symptom, and in turn, this clinical symptom indicates that TRM is alkaline . Based on the above considerations, DGER and the bitter taste in the mouth associated with it may in most cases indicate that TRM has an alkaline index. Therefore, it is necessary not to forget that the appearance of a bitter taste in the mouth occupies an important position in some cases in terms of clinical significance. Due to this feature, a group of symptoms with a high clinical diagnostic potential is included in the list of symptoms such as heartburn, belching, sour taste in the mouth . When the sensation of bitter taste appears in the mouth, if its clinically manifested features are subjected to a rational and realistic analysis process, it becomes possible to make an accurate assessment in a number of cases.

It should be noted that bitter taste in the mouth has been reported in GERD patients with both acidic and alkaline TRM, but the quantitative evaluations of its occurrence and intensity have varied . In particular, the clinical sign of bitter taste in

the mouth was noted in 43 of the 136 GERD patients involved in the research process (31.6 %). It can be noted that the same clinical sign is found in relative abundance in patients with TRM alkalinity. In the analysis of the data obtained in this regard, it was found that the feeling of bitter taste in the mouth is more common in GERD patients with alkaline TRM than in patients with acidic TRM.

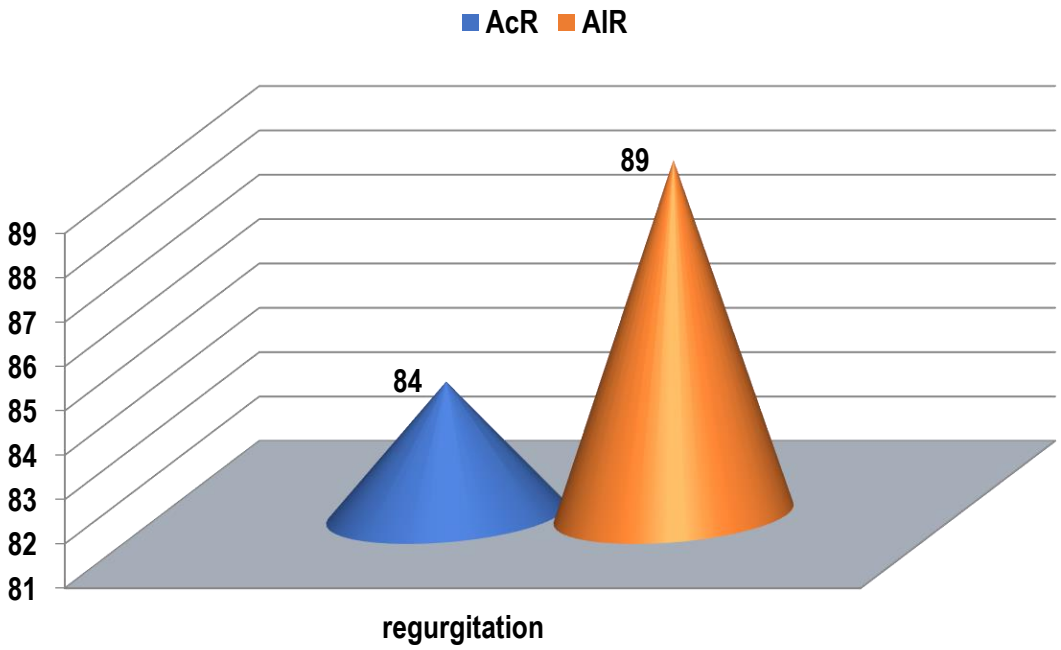
Also, the value indicators of the quantitative assessment divided into the scale of clinical manifestation features were relatively high in patients with GERD, whose TRM was alkaline in color (see Figure 3.3). In particular, the average indicator of the quantitative assessment of the degree of manifestation of the symptom of bitter taste in the mouth in GERD patients with acidic TRM was 0.75±0.03 points. On the contrary, the manifestation of this clinical symptom in patients with alkaline TRM The value of the quantitative assessment index divided by the division level was 4.4±0.02 points. When the values of both quantitative assessments were compared, the difference between them was almost 2-fold, and this advantage was found in patients with alkaline TRM.

Clinical sign of bitter taste in the mouth in patients with GERD underwent a thorough analysis process in terms of a number of other noteworthy aspects. In particular, the following data were obtained by comparing the value of quantitative evaluations divided into the scale of clinical manifestations of bitter taste in the mouth based on specific values of gender, body mass index (Ketle) indicators : at this stage, a total of 136 79 patients (58 %) were female, and 57 (42 %) were male. Bitter taste in the mouth was observed in 43 patients in total, 17 of them (15.7%) had TRM with acidity, 26 93% of people have an alkaline index. Based on these indicators, it was found that the sensation of bitter taste in the mouth is more than 6 times higher in GERD patients with an alkaline TRM index than in patients with an acidic TRM.

It should be noted that in the course of the research, it was found that there is a significant correlation between the bitter taste sensation in the mouth and the value of body mass index (Ketle) quantitative indicators of GERD patients. In order to solve the tasks set before this stage of the scientific research, 36 (26.4 %) of the 136

patients with GERD included in the control group had various abnormal indicators of body mass (indicative of weight gain)say, 20 of them 1 (55, 5 %) are female and 16 (44,4%) are male. 18 of these patients (50.0%) were overweight, 11 (31.3%) were obese, and the remaining 7 (19.4 %) were obese. Out of 20 overweight women, 16 patients with GERD (80%) experienced a bitter taste sensation in the mouth. For example, 7 of 16 male patients with subnormal body mass index A bitter taste in the mouth was found in 44 % of patients. When these parameters were compared, it was found that the coverage of the symptom of bitter taste in the mouth in female patients with GERD and abnormal values of body mass index is almost 2 times more than the same indicators in male patients.

Symptoms specific to GERD, regurgitation takes the next place after the above-mentioned clinical symptoms in terms of the value of its quantitative indicators, and the grade allocated to the intensity of visibility is 4.0±0.02 and, on the contrary, TRM was 4.2 ±0.02 points in patients with alkaline indicators. During the analysis of the above data, it was found that the indicators of the quantitative evaluations of the intensity of the clinical manifestation of regurgitation in both groups of patients are almost equal in terms of value (see Fig.3.4).



3.4 . Comparative value of quantitative indicators of the degree of regurgitation sign in acidic and alkaline TRM

It is known that GERD symptoms, such as stuttering and regurgitation, are essentially the same process, but manifest in different clinical manifestations. Even the group of factors or causes that cause them is unlikely to be the same in most cases. Only these signs may differ slightly in terms of the characteristics of clinical manifestations. If the regurgitation sign is accompanied by the ejection of only air mass to the larynx, in regurgitation, not only air, but also sour or bitter liquid and in some cases even the remnants of recently ingested food mass can return to the oral cavity. Clinical manifestations of both signs it can be said that the difference in the process of digestion depends on the current indicators of the existing pressure in the cavity of the stomach or duodenum. If the air pressure inside the above-mentioned organs is low, then stuttering, on the contrary, regurgitation may occur in cases where it is high [20;P.208].

It should be noted that in terms of the quantitative indicators of the intensity of manifestation of the clinical sign of regurgitation, TRM patients with GERD were almost equally manifested in both groups of alkaline and acidic patients. If in the first of them the quantitative value of this indicator was around 4.0± 0.02 points, in the second it was 4.2 ± 0.02 points.

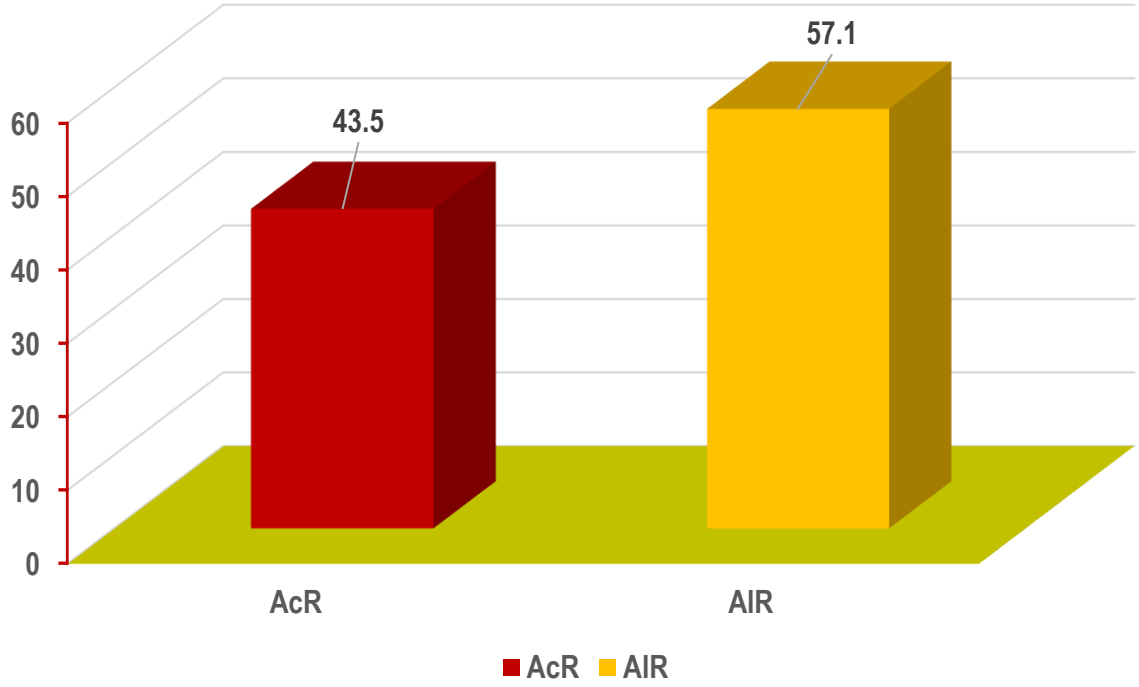
Is the number of times it appears separately, but one after the other, during the process of clinical manifestation. If the symptom of regurgitation occurs as an outbreak, and the number of its appearance is 3 or more during this period, then it is recognized as a symptom that can negatively affect the quality of life of the patient, and a package of measures to eliminate it in time should be developed.

Is a clinical manifestation of complex compensatory mechanisms that inevitably occur during their peristaltic movements due to excessive air pressure inside the stomach and duodenum. If, for one reason or another, the pressure within the stomach and duodenum tends to increase, then in order to prevent or eliminate this abnormal condition which may occur in the above-mentioned organs, the sign of regurgitation begins to appear, and the patients feel relief from this [38; P. 21, 146; P. 255-264].

In conclusion, it should be said that the process of clinical appearance of regurgitation sign has a unique appearance, and the in-depth analysis of the quantitative evaluations given to them is of great diagnostic importance. It was also noted that the formation and emergence of these characteristics is often related to TRM.

Stuttering took the next place in terms of the value of quantitative indicators among GERD - specific clinical signs , and the assessment allocated to the intensity of manifestation was 2.7 ± 0.14 points. It is known that during the process of clinical manifestation of stuttering sign, solitary air must be pushed towards the larynx. If, not only air, but also sour or bitter-tasting liquid and the remains of ingested food, then this clinical condition is recognized as regurgitation [14;P.90,148;P.2-14].

It can be said that stuttering was observed in patients with alkaline TRM in terms of both the degree of occurrence and the value of the quantitative indicators of the intensity of manifestation. Below, for comparison, we found it necessary to present the value of the quantitative indicator of the intensity of stuttering symptoms in patients with TRM acidity. The value assigned to the manifestation of this clinical sign was 2.1 ±0.1 points (see Figure 3.5). When both indicators were compared, it was observed that the intensity of stuttering in patients with alkaline TRM was twice as high as in patients with acid reflux environment. At this point, it should be mentioned that the difference between the indicators of stuttering symptoms in patients with acid and alkaline TRM was not within the scope of the superiority mentioned above.



3. 5 - fig. Comparative assessment of the quantitative indicators of the intensity of the stuttering symptom in patients with acidic and alkaline TRM

Sign characteristic of GERD is the frequency of its appearance. If the sign of stuttering occurs as an outbreak, and the number of its appearance during this period is 5 or more, then it is recognized as a clinically significant sign. From this point of view, stuttering sensation was observed in 16 of 28 patients (57.1%) with alkaline TRM, and only 47 of 108 patients (43.5 %) with acidic TRM. and was determined. These numbers indicate that an important clinical sign such as GERD-like stuttering is clinically important in patients with TRM. Therefore, it is appropriate to take into account the measures to eliminate the sign of stuttering when creating a treatment plan for GERD.

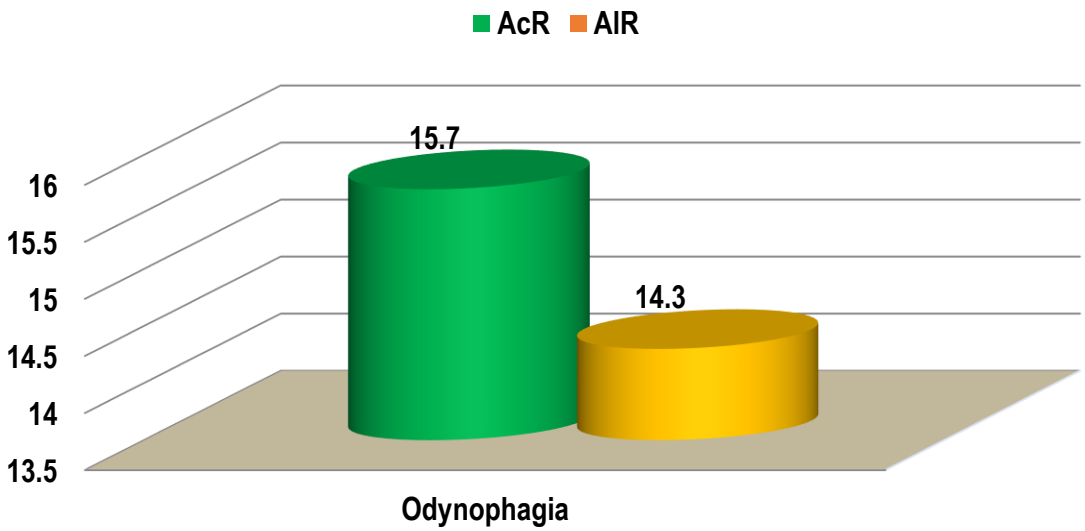
It is known that belching is a clinical reflection of complex compensatory mechanisms that occur during peristaltic movements of the stomach and duodenum. If, for one reason or another, there is a tendency for the pressure in the stomach and duodenum to increase, then in order to prevent or eliminate this abnormal condition that may occur in the above-mentioned organs, the sign of burping begins to appear, and the patients feels an unexpected lightness [44; P.30-34, 4 5; P.24].

A total of 28 patients with GERD with RMT alkalosis involved in the study had stuttering in 16 (57.1%), and almost 15 of them (93.8%) had an unexpected feeling of lightness as this clinical sign. On the contrary, these indicators were significantly lower in patients with acid TRM. In particular, stuttering was observed in 47 (43.5 %) of 108 patients with TRM acidosis involved in the study, and only 27 of them (57.1%) experienced this clinical symptom.

It should be noted that the process of clinical manifestation of stuttering in patients with GERD, who were under systematic control, took different forms. In patients included in the control group , snoring was mainly manifested in two clinical forms: intermittent and paroxysmal. If the number of this symptom that occurs in the process of stuttering is up to 5, and the interval between them does not exceed 3 0-60 seconds, then the condition that meets this requirement is recognized as oktin-oktin. On the contrary, if the number of consecutive occurrences of this symptom during stuttering is 10 or more, and the time between them is about 3-5 seconds, then the manifestation of the symptom in this way is considered as an attack [57; 35-39 p].

Among them, 40 (63.5 %) had symptoms of stuttering, and 23 (36.5 %) had symptoms of stuttering - the arrow became visible is worth noting that the clinical manifestation of stuttering occurred in patients with relatively high TRM alkalinity of the paroxysmal type. For example, stuttering was noted in 16 (57.1%) of 28 patients included in the group , and 1 patient (6.2%) had a case of snoring 47 (43.5%) of 108 patients with GERD and TRM acidosis included in the study had stuttering, only 7 of them (14.8 %) had paroxysmal stuttering, and the remaining 40 (85%) had stuttering cases were recorded.

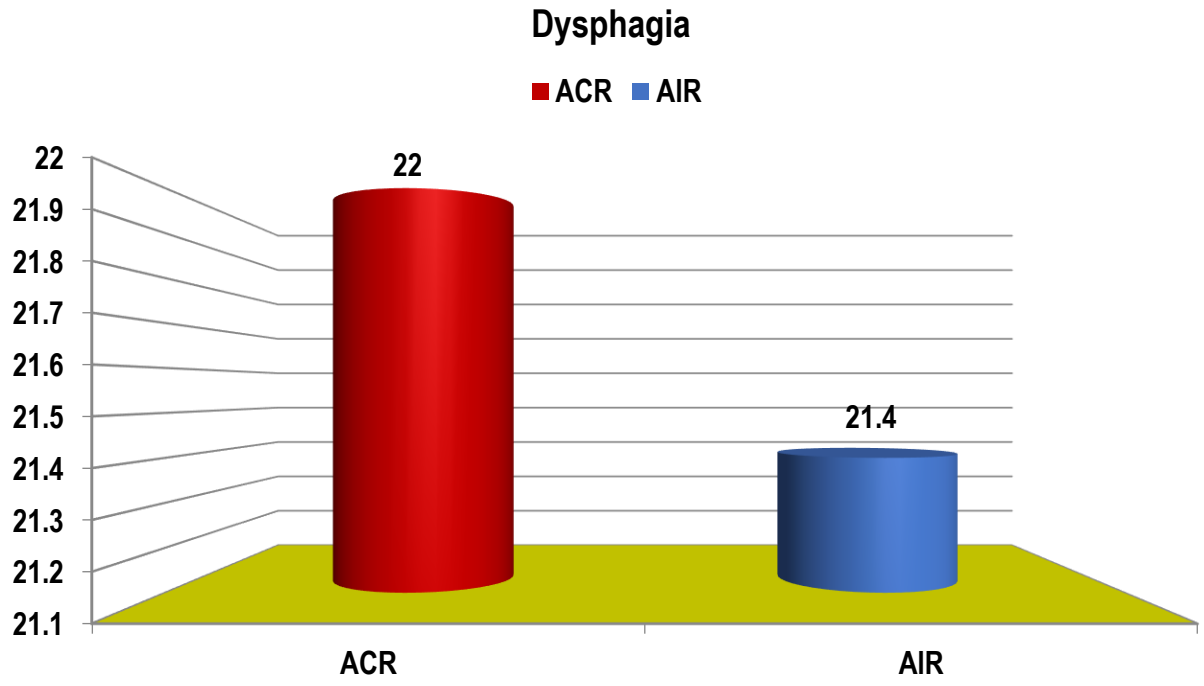
Thus, in conclusion, it can be said that the process of appearance of the stuttering sign from a clinical point of view has some important and noteworthy features, and it was noted that their formation and emergence are often related to TRM.



3. 6 - fig. Quantitative evaluations of the degree of clinical manifestation of the odynophagia symptom in patients with different TRM

Symptoms characteristic of GERD, in terms of the value of quantitative indicators, odynophagia took the next place after the above-mentioned symptoms, and in the first of the symptoms divided by the intensity of visibility, the TRM was 0,75 ± 0,03 in acidic patients and, on the contrary, the RMT was 0 , 68 ± 0 in alkaline patients. , 0 formed 3 points (see Fig .4.6).

At the moment, the quantitative index of the clinical sign of dysphagia was 1.04 ± 0.05 in patients with acid uric acid and 1.02 ± 0.05 in patients with alkaline uric acid (see Figure 3.7).



3. 7 - fig. Quantitative evaluations of the degree of clinical manifestation of dysphagia in patients with different TRM

17 of the patients with GERD with acid RMT (15.7 %) and 4 patients with alkaline RMT (14.3%) had odynophagia (pain in the esophagus during the process of swallowing a bite of food) complained that the sign periodically disturbs him . However, the observed difference between the quantitative assessment value assigned to the clinical sign of odynophagia in both groups of patients was not statistically significant (R>0.05).

The analysis of the extent of clinical manifestation of the odynophagia symptom gave the following results: the odynophagia symptom was manifested once a week or less in most patients with GERD. However, TRM occurred almost daily in two (6.3%) patients with acidosis, observed when swallowing a bite of food. The observed difference between the clinical sign of odynophagia in both groups of patients involved in the research process is not statistically significant (R>0.05).

Dysphagia was noted in 30 of 136 GERD patients (22 %). The index of quantitative evaluations divided into the scale of clinical manifestation of this sign was 1.04 ± 0.05 in patients with TRM acid and 1.02 ± 0.05 points in patients with an alkaline appearance of TRM. Most patients suffering from dysphagia report a

sensation that passes through the esophagus when swallowing a bite of solid food. Also, 4 of the patients with TRM acid color reported that they felt signs of dysphagia even when taking liquid food. None of the control patients had persistent symptoms of dysphagia or daily progression.

As a result of the analysis of the data obtained at this stage of the scientific work, the following conclusions can be made:

symptoms of patients with GERD, in terms of the extent of occurrence, symptoms such as burning sensation, sour or bitter taste in the mouth, and stuttering stood out. The extent of meeting these clinical signs to TRM appeared in relation. It was found that the first pair of clinical signs is relatively high in patients whose TRM is acidic, and the second is alkaline.

It was noted that the value of quantitative evaluations allocated to the intensity of clinical manifestations of GERD symptoms has different indicators and depends on the type of TRM.

symptom of shingles is an important symptom that can negatively affect the quality of life of patients, and it is mainly associated with the risk of disturbing their night sleep.

4. Symptoms such as nausea, regurgitation of bitter-tasting liquid up to the larynx, and pain in the area of the right rib cage were noted in most cases in patients with GERD with an alkaline color of TRM. If the patient has the above complaints specific to GERD, then in these cases, it is necessary to refer to the treating specialist for investigations suspecting that the base of the refluxate component consists of duodenal fluid.

3.4 - §. Endoscopic appearance of gastroesophageal reflux disease is related to the type of reflux environment

136 patients with GERD and 18 individuals with CG underwent endoscopic examination of the esophagus, and the following data were obtained: the first group of pathological changes detected during the endoscopy procedure was limited to the

mucous membrane of the esophagus, while the second group was characteristic of neighboring organs. Diaphragmatic esophageal hiatal hernia (DEH) accounted for the majority of endoscopic changes involving adjacent organs. Details of these changes are provided below. In turn, the endoscopic changes related to the esophagus were distinguished by their location in the mucous membrane of the distal part of the organ . Some types of these endoscopic changes were observed only in the mucous layer of the esophagus (erosions), while others (ulcers) spread to deeper layers.

According to the results of FEGDS examinations, 97 (71.3%) of 136 patients with GERD involved in the research process had catarrhal inflammation - esophagitis-specific endoscopic changes in the mucous membrane of the distal part of the esophagus. Currently, endoscopic changes of this type are called non-erosive reflux disease (NER). In the remaining 39 patients (28.7%), the results were erosions and ulcers, which are among the serious manifestations of endoscopic changes. If these endoscopic changes are noted in the esophageal mucosa of patients with GERD, it is referred to as erosive ulcerative reflux disease (ERD). The following results were obtained in the analysis of the shape, number, localization, etc. of erosions and ulcers in the esophageal mucosa of patients with GERD: endoscopic changes in the distal part of the esophagus due to damage to the integrity of the mucous membrane were detected in 30 of the 39 patients with GERD (76.9%) erosions and 9 (2 3.1 %) wounds were detected. Isolated types of erosions were noted in 1 7 (56.6%) patients, their manifestations in the majority state were noted in 13 (43, 3%) patients done. A number of remarkable data were noted in the process of superficial analysis of erosion and ulceration in the esophageal mucosa of patients with GERD. The comparative assessment of the figures given above showed that the rate of erosion is more than 3 times higher than the characteristics of the wounds. 5 (83.3 %) of the total identified erosions were found in patients with acidic TRM, and the remaining 5 (16.6 %) were found in patients with an alkaline color in TRM. 20 patients (66.6%) were women and 10 (33.3%) were men. When analyzing the erosions recorded in the mucous membrane of the distal part of the esophagus the

following results were recorded: when using the FEGDS method, pointy, linear and oval or round forms of erosions were found. Among the erosions recorded on the esophageal mucosa of patients with ERD, their pointy appearance was relatively common. 17 out of 30 patients had erosions on the esophageal mucosa 8 In one of them (2 6.6 %), linear and in 5 (16.6%) oval or round forms were determined. By comparing these indicators, it was observed that the point shape of erosions has more than 1.5 times the advantage of the sum of linear and oval or round forms in terms of its degree of occurrence. No important information was obtained when analyzing the degree of occurrence of studied forms of erosions in the section of patients' gender indicators . None of the 30 GERD patients with erosive changes in the esophageal mucosa had any bleeding symptoms during the follow-up period or in the near and long term (2 years). 2 (22.2%) of the total ulcers detected in the esophageal mucosa of patients with GERD were found in patients with alkaline TRM, 7 (77,7%) in patients with an acidic tone in TRM. 6 (66.6 %) of GERD patients were male and 3 (33.3%) were female. During the analysis, the following results were noted in terms of the shape of the wounds noted on the mucous membrane of the distal part of the esophagus: among the wounds noted on the mucous membrane of the esophagus of patients, their oval-shaped appearance was relatively common. Out of 9 patients with lesions on the esophageal mucosa, 5 patients (55.5 %) had oval, 3 patients (33. 3%), round and 1 patient (11.1%) had a linear form. When these indicators were compared, it was observed that the oval shape of the wounds with its meeting level has an advantage of almost 1.5 times more than the quantitative value of the sum of the linear and circular forms. No significant aspects were found when analyzing the extent of the studied formal manifestations of wounds in terms of gender indicators of patients. None of the 9 GERD patients with ulcerative changes in the esophageal mucosa had any signs of bleeding during the near or long follow-up period (2 years).

In the endoscopic examination, no pathological changes were detected in the mucous membrane of all 18 people who were treated with CG.

Based on the analysis of the data obtained during endoscopic examinations, catarrhal esophagitis or NERD TRM was found at a relatively high rate in patients with alkalinity and consisted of 75%. The same indicator was 70 % in patients with TRM acidosis. The difference between these indicators was at the statistically reliable limit ($R<0.05$). Thus, GERD patients with alkaline TRM develop correspondingly more NERD due to the fact that the refluxate caused by DGER is not acidic in nature and occurs in the postprandial period.

Based on the analysis of the data obtained at this stage of the research, it can be said that: patients with GERD have more frequent erosions and ulcers on the esophageal mucosa in patients with TRM acidosis, because the period of acidification in the above-mentioned organ is much longer in them, and between this condition and the injury of the esophageal mucosa the existence of an organic link is a proof that does not require proof; on the other hand, NERD was observed more in TRM alkaline patients.

IV. THE EFFICACY OF A STEP -OPTIMIZED GASTROESOPHAGEAL REFLUX DISEASE TREATMENT METHOD RELATIONSHIP TO THE TYPE OF NG REFLUX ENVIRONMENT

4.1. Principle differences in the method of treatment of gastroesophageal reflux disease, with steps optimized according to the logical need

Been less than a quarter of a century since GERD was recognized as an independent disease of the digestive tract. Despite the fact that it is the youngest of all familiar diseases related to the digestive system, it has come forward in terms of prevalence at the moment [13;P.46,3 4; P.27]. In the early stages of studying the pathogenesis of GERD, almost all experts in the field believe that only the components of the gastric juice serve as the main factor in the development of this disease , according to him, "this aggressive factor plays a decisive role in the formation of the main clinical, endoscopic and morphological signs that occur during the course of GERD", they considered [38;P.21].

It is known that normally the pH of the esophageal mucosa is around 5.5-7.0. In GERD, this pH indicator of the esophageal mucosa is 4 and below (pH<4.0), which means that the environment begins to take on an extremely acidic hue [1; P 57–59,10,5; P.871–880]. That is why, in recent years, experts in the field have been relying more on the opinion: "If there is no No acid - no boiling" [85; P.15–19, 141; P.585-591, 142; P.631-642].

At that time, not enough information was collected about the importance of alkaline or mixed reflux in the development of GERD. That is probably why most experts without hesitation assigned GERD to the group of diseases (gastric and duodenal ulcers) that develop in relation to gastric juice acid (Hcl). entered [83; P.704,147;P.47-51]. Because of this step, which does not always turn out to be correct, all GERD treatments proposed so far focus on eliminating or at least neutralizing the effect of reflux s at aggressive factors (Hcl). Over the past period, various methods of GERD therapy based on the above-mentioned approach have

been proposed. Most of them, including when they are used in a step up or step down manner, the main effect of the treatment is aimed at eliminating or neutralizing the aggressive potential of the refluxate components [68; P.113-118,70;P.4-10].

Analyzed based on the personal experience gathered over the years, different conclusions are made in this regard than the currently prevailing opinions. It should be recognized that the aggressive factors of gastric juice or duodenal fluid do not play the role of the primary factor in the pathogenesis of GERD, as it is currently recognized. It is known that these factors do not acquire the color of aggressiveness when they enter the esophageal cavity, but this characteristic is present even when they are active within the limits of their natural territory (stomach or duodenum). In these natural spaces, normally, there are no protective factors capable of neutralizing their aggressive forces. But the possibility of protective forces in the esophageal cavity does not have the power to completely eliminate the aggressive features in them. Therefore, when gastric juice or duodenal fluid is thrown towards the esophagus cavity, their aggressive properties begin to manifest. Therefore, it is unequivocal evidence that the primary factor in the pathogenesis of GERD is not the aggressive potential of gastric or duodenal fluids, but their discharge into the esophagus (GER or DGER flow). Most experts in the field theoretically recognize this [31; P.4-13, 44; P.30-34, 113; P.13].

It is well known that refluxate is a foreign substance whose natural habitat must be the empty stomach or duodenum. It is abnormally released into the esophagus during GER or DGER processes. Manifestation of aggressive effects of refluctate liquid components directly depends on the level of occurrence of GER or DGER processes within a unit of time and their duration [44;P.30-34]. Also, during the process of GERD formation, it is important whether TRM is acidic or alkaline.

Aggressive properties of components of biological fluids, which make up the component of the effluent, play an important role in the emergence of the disease . But this, in turn, is an axiom directly related to the scale of intensity of manifestation of GER or DGER processes. So, the time has come to push forward the motto "No reflux, no GERD". Viewing the problem in this way, it is correct to ask " is it correct

to eliminate the effects of aggressive factors or GER and DGER processes during the treatment of GERD?" , the question arose. Logically correct understanding of the problem, of course, encourages to take the second one. Therefore, it is logical that the main focus of innovative types of GERD treatment (unlike the current ones) is not to neutralize the effect of aggressive factors, but to eliminate the reflux process.

China probably interpret this attitude to the problem in a theoretically correct way. Unfortunately, there is still a logic that is difficult to understand in the recognized methods of treatment of GERD that are used in practice. In most of them PPI manifestations are recommended as the main (base) drug [55; P.193-197, 152; P.1815–1823]. Everyone knows that they can only reduce the process of hydrochloric acid formation to the required level. This situation is the same as the elimination of the existing pathological process in the esophagus. But the same situation can cause the imbalance of the homeostatic parameters of an important organ like the stomach and, in connection with it, various inappropriate deviations in the digestive process.

Therefore, in our opinion, it would be logical to recommend drugs capable of eliminating GER or DGER as the main source of treatment in modern schemes of GERD treatment, for example, prokinetic groups. But despite this, in almost all modern treatment methods of GERD, prokinetic agents are unreasonably assigned a secondary position. However, from the point of view of the pathogenesis of GERD, it should be recognized that it is more appropriate to use prokinetic agents than PPI drugs in its treatment.

" If there was no reflux, there would be no GERD " also requires the use of prokinetics, which immediately eliminate GER or DGER, among the first. It goes without saying that complete resolution of reflux paves the way for significant clinical signs of GERD, including heartburn, to disappear. Therefore, if the various manifestations of reflux are successfully eliminated , there is no need to use PPI methods. Because the need to limit the process of acid formation disappears by itself. Also, the process of acid suppression does not always go as intended. In some cases,

it can unreasonably disturb the existing stable balance of indicators of gastric homeostasis.

the proposed situation may fundamentally contradict some of the points specified in the standards of modern treatment of GERD. But the results of the modern interpretation of the pathogenesis of GERD indicate that there are significant steps in the proposed guidelines. It is important that the proponents of this guideline direct their future scientific research not to eliminate the process of hydrochloric acid formation, which is not always appropriate, but to restore the impaired motor activity of the upper parts of the gastrointestinal tract. The method of treatment of GERD proposed by a group of employees of the Department of Internal Diseases propaedeutics, including the author of the dissertation, who has been working in this field, is presented below. The main difference of this method from others: the treatment consists of steps that come and go; The steps can be improved based on the instructions given above.

Schematic representation of the proposed GERD treatment method

	Indications and optimal sequence of GERD treatment method
I.	**I. Treatment without drugs**
II.	- which can be eliminated quickly (rejection of tea, coffee, alcoholic beverages, some medicines, etc.);
III.	-measures performed slowly (reducing weight, giving up smoking and the like).
	IV. Drug treatment
	1) prokinetics;
	2) PPI samples.
	V. Surgical treatment

The proposed GERD treatment method consists of 3 steps, the order of which is first of all to eliminate reflux of various forms and, at the same time, to achieve the effectiveness of the pre-planned treatment. Therefore, her medication

regimen begins with taking prokinetics rather than the usual PPI side effects. It is important to remember that when using this scheme of treatment, it is necessary to strictly follow the sequence of steps. Because this procedure is one of the principal distinguishing aspects of the proposed method of treatment.

The proposed treatment approach for GERD is termed non-drug, and includes a number of conservative measures that have the potential to reverse GER or DGER processes . According to the advantages of being able to use them in practice, they can be divided into two groups, which are interrelated in content, but independent in form: 1) which can be eliminated quickly (rejection of taking tea, coffee, alcohol, some drugs, etc.) ; 2) measures performed slowly (reducing weight, quitting smoking) can be divided into t measures. Stage II is called medication and it is recommended to take drugs belonging to different groups effective in the treatment of GERD. Medicines must be taken in a strict sequence . In contrast to the widely used GERD treatment methods, the treatment should be started with the use of prokinetics as a monopreparation. Prokinetics should be the main part of the treatment plan even when other group drugs (PPI drugs, etc.) are recommended. It should be noted that it is reasonable to recommend PPI side effects only when the TRM is acidic or when nocturnal attacks of hot flashes are observed. Stage III requires the use of surgery. We remind you that it is appropriate to use the surgical procedure when there are indications for it.

Is recommended on the basis of recognition and proper evaluation of the importance of GER and DGER process in the development of this disease and the fact that prokinetics are taken as the main drug. The application of step treatment method in personal practice has confirmed that many of its aspects are natural and appropriate. These conclusions are the personal opinions expressed by those seeking a controversial opinion.

4.2 -§. Comparative effectiveness of conventional and countermeasures used in the treatment of gastroesophageal reflux disease

It is known that GERD is the youngest among all known diseases not only of the esophagus, but also of the digestive system. From the first days when it was recognized as an independent disease, it was recognized by most experts in the field as a disease (stomach and duodenal ulcer) caused by hydrochloric acid in gastric juice [145;P.1003-1007,152;P.1815 -1823]. As a result of this conclusion, which is not always confirmed in practice (because there is also alkaline reflux), GERD forms the basis of modern treatment methods, sometimes inappropriately, in our opinion, IPP manifestations.

Hydrochloric acid in gastric juice is of great importance in the formation of some clinical variants of GERK. But this phenomenon can occur only because of GER. Therefore, the importance of the reflux process in the pathogenesis of GERD is much higher than the properties of hydrochloric acid [113; P.13]. Therefore, the word reflux was included in the list of words used in the empirical naming of GERD. In our opinion, taking into account the above points, it is appropriate to recognize GERD as a disease related to the reflux process rather than acid. For the same reason, the basis of drugs used in its treatment is not IPP, but on the contrary, it is appropriate to organize prokinetics. Taking this into account, at this stage of scientific research , the task was to dynamically study the results of the therapeutic effectiveness of traditional and alternative methods proposed by the author (step by step) in the treatment of GERD. In order to perform this task, the dynamic results of the data obtained as a result of the use of the above-mentioned treatment methods in 76 patients with NERD type of GERD with an acidic appearance of TRM were systematically and comparatively studied. The life indicators of the patients included in the scope of the audit were around 18-56 years, and the average age was 3 4.4 ± 4.2 years. Out of a total of 76 patients, 42 (55.3%) were male and 34 (44.7%) were female. All patients were divided into two groups representative of a number of clinical parameters: age, gender, body mass (Kettle) index, mean duration of GERD,

relapses, number of treatments received so far, etc. The first group (CG) of patients consisted of 37 (48.7%) individuals, and they were mainly offered the traditional (A) method of GERD treatment. Its components are mainly pantoprazole or pantoprazole (pharmaceutical company " Nobel", a joint venture of the Republics of Uzbekistan and Turkey) , which is a PPI , 40 mg per tablet and itomed or itopride hydrochloride (pharmaceutical company" Promed", Czech Republic) 50 mg per tablet. Among these drugs, it was recommended to take 1 tablet of pantap 40-60 minutes before breakfast and 1 tablet of itomed every day at 7:00 , 13:00 and 19:00 20-30 minutes before eating. The duration of taking both drugs is 20–24 (average 22.4±3.6) days.

The remaining 39 patients (51.3%) were included in the second (AG) group, and they were offered an alternative (A) method as a means of treatment. This method consisted of steps without drugs and with drugs . The drug-free step included immediate measures (ceasing tea, coffee, alcohol, certain medications, etc.) and slow measures (ceasing weight, smoking, etc.) . In the drug phase, trimedate or trimebutin (De Han New Pharmaceutical Company, Seoul, Korea) were used individually, as universal types of prokinetic agents are shown. It is mainly developed in pill form and in 100mg or 200mg dosage. Group patients received trimedat 200 mg at 7:00 , 1:00, and 7:00 p.m. 20–30 minutes before meals. Effective K indicators of the proposed treatment methods were dynamically analyzed every 10–12 days. The obtained data are presented in table 5.1.

From the data presented in Table 4.1, it is clear that the results of therapeutic efficiency of methods A and M used in the treatment of patients with GERD were different as expected.

these methods: the dynamics of the main clinical symptoms (%); Positive changes in the quantitative value (in points) of important signs of GERD; The number of times the main clinical symptoms of GERD are encountered during the day; number of nocturnal attacks of hot flashes; the scale of positive changes in quality of life indicators of patients and similar factors were used as criteria. Individual questionnaires prepared in advance were distributed to each of the

patients involved in the audit in order to record the chronology of the changes to be observed in the indicators of these criteria.

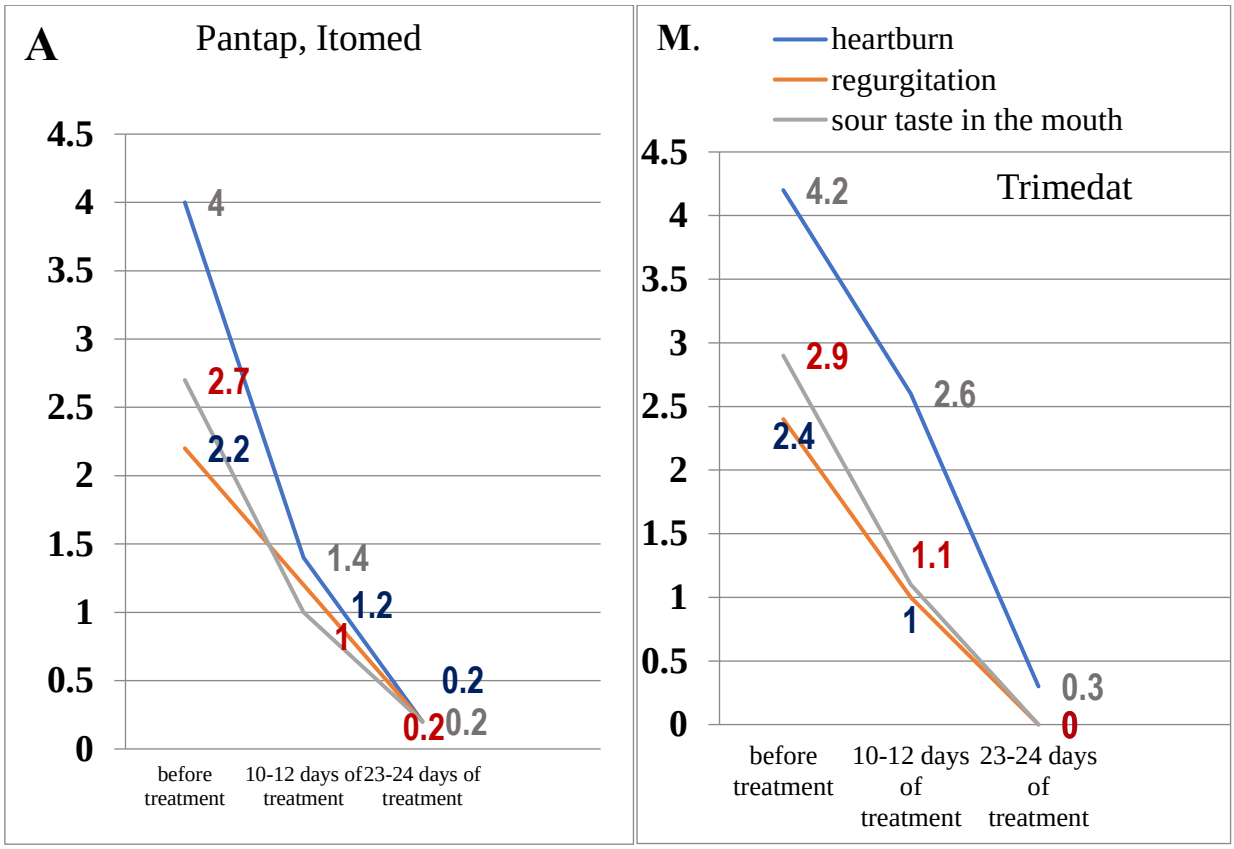
Table 4.1

Dynamics of the therapeutic effectiveness of the M and A methods used in the treatment of GERD

Main clinical b handles	Alternative treatment (n=39)					
	From the treatment:					
	you have		(in days)			
	abs	%	10-12		23-24	
			abs	%	abs	%
Heartburn	33	84.6	21	53.8**	3	7.7***
Regurgitation	19	48.7	8	20.5**	0	0.0
Eructation	15	38.5	6	15.4*	1	2.6***
Bitter taste in the mouth	7	17.9	3	7.7	0	0.0
Sour in the mouth t am	23	59.0	9	23.1***	0	0.0
Dysphagia	8	20.5	3	7.7	0	0.0
Odynophagia	7	17.9	4	10.3	1	2.6*
	CG (n=37)					
Main clinical b handles	you have		days (in days)			
			10-12		23-24	
	abs	%	abs	%	abs	%
Heartburn	30	81.1	11	29.7***	2	5.4***
Regurgitation	17	45.9	9	24.3*	2	5.4***
Eructation	14	37.8	5	13.5*	3	8.1**
Bitter taste in the mouth	6	16.2	3	8.1	1	2.7*
Sour in the mouth T	20	54.1	8	21.6**	2	5.4***
Dysphagia	8	21.6	4	10.8	0	0.0
Odynophagia	7	18.9	3	8.1	1	2.7*

** – differences are significant compared to the group before treatment (* – P<0.05; ** – P<0.01; *** – P<0.001).*

When analyzing the dynamics of the results of the therapeutic effectiveness of the therapeutically used M and A methods, the following important results were obtained: 33 cases (84.6%) of this symptom before treatment in patients with hypertension , when evaluating the amount on the Lykert scale (4.2±0.2) points were noted in the patient , in the first ten days of the treatment it was 21 times 53.9 % , by the end of the second ten days (2.6±0.1) this sign was only 3 times. in a far (7.8%) it occurred only when evaluating the quantity (0.3±0.01) on the Lykert scale.



4.1Dynamics of therapeutic efficiency of M and A methods used in GERD treatment (likert scale, points)

In the same clinical sign in NG patients were different. If before the treatment this symptom was noted in 30 out of 37 patients (81.1 %) , with a Likert scale rating of (4.0 ± 0.2) points , after the first decade of treatment it was 11 29.7 % (1.4±0.07) by the end of the second ten days, only 2 patients (5.4%) had this symptom when evaluating the amount on the Likert scale (0.2 ± 0.01) also happened.

These positive changes reported by K were relatively more pronounced in the results of the first decade. Strong positive changes noted in NG patients (in contrast

to AG patients) in the dynamics of the boil can be explained by the effect of PPI manifestations in method A applied to them. The fact that the results of the therapeutic efficiency of method A are much better in patients with nocturnal attacks of symptoms of hot flashes indicates that it is related to the effect of PPI side effects, there was no significant difference between the dynamic changes observed in other GERD-specific symptoms (apart from the symptom of a boil) of MG and CG patients. In the same way, the results of the criteria that allow to adequately evaluate the therapeutic effectiveness of the M and A treatment methods also gave results corresponding to the above- mentioned conclusion.

Thus, based on the data obtained at this stage of scientific research, the extent of the therapeutic effectiveness of the M method used in the treatment of GERD was competitively visible compared to the current indicators of the A treatment measures This competitive therapeutic efficiency was more clearly observed in patients who did not have nocturnal symptoms of hives. Also, a number of stable aspects of the alternative method compared to A were identified:

1) measures involved in each step of the alternative treatment method of GERD are aimed at logically eliminating the process of reflux (GER or DGER), which is the generator of this disease;

2) the range of drugs used in the medicinal stage of the alternative treatment method is narrow (mainly prokinetics used individually), its level of therapeutic efficiency was noted to be fully competitive with the same indicators of method A;

3) of types of drugs (mainly, universal prokinetics) involved in the use of the opposite method , the cost of the treatment is reduced by 20 %, and at the same time, its pharmacoeconomic indicators have increased significantly.

THE END

Despite numerous studies, GERD remains one of the urgent problems of modern gastroenterology. This is explained not only by the prevalence of this disease, but also by the high rate of death due to its dangerous complications (Barrett's esophagus, esophageal adenocarcinoma).

This research work was carried out at the department of internal medicine propaedeutics of the Bukhara State Medical Institute , the gastroenterology, functional diagnostics and clinical laboratory of the Bukhara Regional Multidisciplinary Medical Center and the Bukhara City Medical Association during the years 2010-2015.

During the years 2010-2015, 136 patients diagnosed with GERD in the gastroenterology department of the multidisciplinary medical center of Bukhara region, analysis of clinical, laboratory and instrumental (roentgenoscopy and imaging, fibroesophagogastroduodenoscopy, etc.), pH-metry results of salivary and aspiration reflux fluids. complex was studied. Among them, group 1 has 108 patients with acid reflux environment and group 2 has 28 patients with alkaline reflux environment. Dynamically acquired medical data of individuals aged 18 to 56 years (mean 34.2±4.2) and a control group of 18 healthy individuals served as the basis.

All patients under observation underwent a complete clinical examination in the conditions of the above-mentioned medical facilities. GERD was diagnosed based on subjective feelings, anamnesis, clinical and additional examination methods.

It is known that GERD has been recognized as an independent disease by experts in the field for almost a quarter of a century. From the point of view of its occurrence in the population, it overtook not only digestive diseases, but also other diseases in a short period of time. Since the early days when GERD was recognized as an independent disease, it has been included in the list of diseases related to gastric ulcer (stomach and duodenal ulcer). Because until now, the important aspects of the pathogenesis of the disease are the aggressive factors of the gastric juice (chloric

acid, pepsin) that are thrown into the erythrocyte cavity and damage its mucous layer as a result of GER [75; P. 41, p. 98; P.91-102]. For the same reason, antisecretory drugs form the basis of the plan of traditional types of GERD treatment [22; 48; P.2000, 49; P.2-7, 61; P. 69-89, 97; P.115-117]. The fact that the word GER forms the basis of the well-known empirical name of this disease means that this process plays an important role in the development of GERD.

However, it is now known that approximately 20–25% of GERD cases result from DGER. The main aspects of its pathogenesis develop depending on aggressive factors of duodenal fluid - bile acids, pancreatic enzymes [60;P.24-26,77; P.4-14,81;P.8-12,155;P.290-295]. In our opinion, this is the reason why the name GERD has lost its importance and rightfully causes various disputes. Because the development of this disease is related not only to GER, but also to DGER , there is no doubt among experts in the field. Therefore, it would be appropriate if the name of this disease is called esophageal reflux disease.

It is worth noting that the resistance of most patients with GERD to the proposed treatment, the decrease in their quality of life due to the failure to eliminate the specific symptoms of the disease, the increase in GERD complications, and the increase in the number of deaths from esophageal adenocarcinoma encourage researchers to find ways to study new aspects of GERD pathogenesis [53; P. 32 – 41, 99; P. 714– 721,127; P. 1113–1122]. At the moment, the goal of finding ways to solve this serious puzzle can be achieved only through the practical implementation of verification methods that allow for an adequate assessment of TRM. Impedanceometry method to patients with GERD, which was first implemented in foreign countries, the pH environment of the refluxate turned out to have an alkaline color, contrary to expectations. Antisecretory therapy offered to patients with GERD presenting with typical and atypical clinical signs of this disease does not result in the expected results in most cases [49;2-7-P,117;10-P,119; 1267–1273-P,120;365-2982-P]. The main reason for resistance to this treatment appears to be the presence of refluxes with an alkaline environment. Also, the results of many scientific studies indicate the development of serious complications of GERD:

Barrett's esophagus, esophageal adenocarcinoma TRM is not only acidic, but also alkaline [3;23,4; P. 29,5; P. 3-5,8 ; 44-P, 11; P. 24, 14; P. 90, 17; P. 21-26, 56; P. 548, 109; P. 243-251].

Taking into account the current shortage of equipment and the high cost of pH data obtained through intraesophageal pH -metry or pH -impedancemetry methods introduced in most Western countries, an alternative comprehensive method was developed and implemented to allow determination of TRM. This complex method consists of direct (directly indicating the type of refluxate pH environment) and indirect (indirectly indicating the type of refluxate pH environment) components. The direct method, on the other hand, consists of components such as pH-metry of saliva and in vitro pH-metry of refluxate absorbed during FEGDS. Also, the indirect method, in turn, consists of components such as biochemical (spectrophotometric study of the biochemical composition of the refluxate absorbed during the FEGDS process) and clinical (in-depth analysis of the clinical signs of GERD).

In order to determine the general diagnostic possibility of this alternative complex method in determining the reflux pH environment, the following information was obtained during the scientific research: in 136 (79.5%) of 171 patients with GERD, the results obtained using the components of the proposed complex method turned out to be proportionate. In the remaining 35 (20.5%) patients with GERD, the results of the data indicating the type of refluxate pH medium, obtained using the components of the complex method, were inconsistent. It should be noted that the data with a disproportional indicator were observed as a result of the data indicating the type of refluxate pH medium obtained by all the methods that made up the component of the complex method. Although in some cases discrepant results were observed in the results of two or more test methods used to indicate the type of reflux pH environment in the same patient (in order to avoid possible artificial confounding), these results were obtained from the series of data sets of only one method. For example, if the results of both saliva pH - metry and biochemical examination in the same patient have inconsistent indicators, only one of the above-mentioned methods was used in the same data set. The results of pH-

metric analysis of the reflux fluid injected into the esophageal cavity of GERD patients (MG) showed different values. When carefully analyzed, it was noted that these changes were directed towards two opposite poles in terms of value. 28 (20.5%) of 136 patients with GERD had alkaline (8.8 ± 0.23) and 108 (79.5%) acidic (4.5 ± 0.09) reflux media the indicator was observed. The confidence limit of the difference determined in the process of statistical selection of the values of these indicators of MG patients with GERD was around $P<0.01$. The research, one of the important tasks was to determine how the degree of manifestation of the main clinical symptoms in patients with a typical form of GERD is related to TRM. Some clinical signs characteristic of GERD appeared to be relatively common regardless of the type of refluxate pH environment (acidic or alkaline). Among the clinical signs with this characteristic, the place of boiling, regurgitation and belching took place. The most common complaint among patients in both groups was a rash. The prevalence of this clinical symptom was not statistically significantly different between the two groups of patients (groups of patients with acidic and alkaline TRM). Also, boils had a significant negative effect on the night's sleep of both groups of patients. If this symptom disturbed 62.4% of patients with an acidic environment, this condition was observed in 53.5% of patients with an alkaline environment. The mentioned difference was not statistically significant ($R >0.05$). Regurgitation was detected in 97% of GERD patients with an acidic reflux environment, belching in 43.5 % and regurgitation in 84%, on the contrary, in 75.0% of patients with an alkaline reflux environment, 57.1% in second and third in 89%. Symptoms such as heartburn, sour taste in the mouth were noted to occur relatively often in patients with an acidic reflux environment. Also, at the same time, clinical symptoms such as burping and bitter taste in the mouth, on the contrary, were relatively common in reflux patients with an alkaline pH environment. There was no significant difference in the level of clinical symptoms such as dysphagia, odynophagia and regurgitation in both groups of patients.

Quantitative indicators of clinical signs, even when considered superficially, showed that the intensity of their manifestation is related to TRM. Quantitative index

of an important clinical sign , such as shingles, had the highest value in patients with acidic TRM and was 4.6 ± 0.01 points, while it was relatively low in patients with alkaline TRM libemors and was 3.6 ±0.18 points. The difference between the values of these quantitative indicators was in the statistically reliable ($p>0.001$) range. It is worth noting that although the occurrence of the sign of gingivitis is almost equal in patients with acidic and alkaline TRM, the intensity of its manifestation is much higher in patients with acidic TRM, and this priority is more than 1.5 percent. Among all the symptoms observed in GERD, it occupied the leadership position with the indicators of both the level of occurrence and the intensity of manifestation. These features of the sign were observed with a clear advantage in patients with TRM acidosis.

Among the set of clinical symptoms characteristic of GERD, the next place in terms of the value of the quantitative assessment, allocated to the level of visibility, was occupied by the sign of feeling a sour taste in the mouth. It is known that the clinical sign of the appearance of a sour taste in the mouth often indicates the presence of GER and, therefore, the presence of an acidic indicator of TRM. Based on the opinion expressed above, it can be said that the sensation of the appearance of a sour taste in the mouth can have a very high clinical significance in some cases. It is a sign that has a rightful place among a group of symptoms that are important from the point of view of clinical visibility and have a high diagnostic potential: boils in the throat, stuttering, and a bitter taste in the mouth. The important stability of sour taste in the mouth is that if its clinically visible features are used rationally and efficiently, then in many cases it will be possible to realistically assess TRM.

Among GERD-specific clinical signs, stuttering took the next place in terms of the value of quantitative indicators, and the grade allocated to the intensity of manifestation was 2.1 ±0.10 points. It is known that during the clinical manifestation of the stuttering symptom, only air must be thrown towards the larynx. If it passes with sour or bitter-tasting liquid and the remnants of food taken in the recent past, then this clinical condition is recognized as regurgitation.

The clinical symptom such as stuttering was significantly observed in patients with RMT-alcoholism in terms of the quantitative indicators of both the degree of occurrence and the intensity of visibility. One of the important characteristics describing the clinical significance of GERD-specific stuttering sign is the frequency of its appearance. If the symptom of stuttering occurs as an outbreak, and the number of its appearance during this period is 5 or more, then it is recognized as a sign of clinical significance. Analyzing the sign of stuttering from this point of view, it was observed in 16 of 28 patients (57.1%) with alkaline TRM and 47 (43.5%) of 108 patients with acidic TRM. These numbers indicate a clinically significant change in GERD-specific stuttering in patients with TRM. Therefore, it is advisable to take into account the measures to eliminate the stuttering symptom when creating a treatment plan for GERD.

It is known that GERD symptoms, such as stuttering and regurgitation, are symptoms that reflect the same process in content, but manifest in different clinical manifestations. Even the group of factors or causes that cause them is inevitable in most cases. The difference in the clinical manifestation of both symptoms depends on the current indicators of the existing pressure in the stomach or duodenal cavity. If the indicators of air pressure in the above-mentioned organs are low, then stuttering, on the contrary, if it is high, rapid stuttering - a sign of regurgitation may occur [36; P.184, 71; P. 24].

A total of 136 patients with GERD and 18 subjects with CG were all included in the study and underwent esophageal endoscopic examination, resulting in the following significant data. According to the results of FEGDS examinations, catarrhal inflammation - esophagitis-specific endoscopic changes were noted in 97 (71.3%) of 136 GERD patients included in the research process. Currently, endoscopic changes of this type are called NERD [23; P.19]. In the remaining 39 patients (28.7%), the results were erosions and ulcers, which are serious manifestations of endoscopic changes. If these endoscopic changes are noted in the esophageal mucosa of GERD patients, it is referred to as ERD [31;P.4-13].

Form, number, localization, etc. of erosions and ulcers in the esophageal mucosa of patients with GERD. During the analysis, the following results were obtained: 30 of the 39 GERD patients (76.9%) had endoscopic changes due to damage to the integrity of the mucous membrane of the distal part of the esophagus, erosion and 9 (23.1%) Wounds were identified. Isolated types of erosions were recorded in 17 (56.6%) patients, multiple forms were recorded in 13 (43.3%) patients. A number of remarkable data were noted in the process of superficial analysis of erosion and ulceration in the esophageal mucosa of patients with GERD . The comparative assessment of the above numbers, it was noticed that the indicators of the occurrence of erosions are more than 3 times higher than the characteristics of the wounds. Of the total identified erosions (83.3 %) were found in patients with acidic TRM, and the remaining 5 (16.6 %) were found in patients with an alkaline tone in TRM. 20 patients (66.6%) were women and 10 (33.3%) were men.

The following results were noted when analyzing the erosions recorded in the mucous membrane of the distal part of the esophagus: when using the FEGDS method, pointy, linear and oval or round erosions were found.

2 (22.2%) of the total ulcers detected in the esophageal mucosa of patients with GERD were found in patients with alkaline TRM, 7 (77,7%) in patients with an acidic tone in TRM. 6 (66.6 %) of GERD patients were male and 3 (33.3 %) were female. Based on the analysis of the data obtained during endoscopic examinations, catarrhal esophagitis or NERD TRM was found at a relatively high rate in patients with alkalinity and consisted of 75%. The same indicator was 70 % in patients with TRM acidosis. The difference between these indicators was at the statistically reliable limit ($R<0.05$). Thus, GERD patients with alkaline TRM develop correspondingly more NERD due to the fact that the refluxate caused by DGER is not acidic in nature and occurs in the postprandial period.

Strengthening the role of aggressive factors of gastric juice in the pathogenesis of GERD has become important in the formation of its proposed treatment schemes. Because of this step, which does not always turn out to be correct, the main focus of

all GERD treatment methods proposed so far is to eliminate or at least neutralize the effect of refluxate aggressive factors (Hcl). Over the past period, various methods of GERD therapy based on the above-mentioned approach have been proposed. Most of them, including when they are used in a step up or step down order, the main effect of the treatment is aimed at eliminating or neutralizing the aggressive potential of the refluxate components [35 ; P.11-13, 37; P.4-10, 56; P.548, 65; 29, 96; P.1506-1512, 111; P.180-186].

Analyzed based on the personal experience gathered over the years, different conclusions are made in this regard than the currently prevailing opinions. Evidence that the primary factor in the pathogenesis of GERD is not the aggressive potential of gastric or duodenal fluids, but their discharge into the esophageal cavity (GER or DGER flow) does not require confirmation.

It is well known that refluxate is a foreign substance whose natural habitat must be the empty stomach or duodenum. It is abnormally released into the esophagus during GER or DGER processes. Aggressive properties of the components of biological fluids, which are part of the refluxate, play an important role in the emergence of this disease [5; 3-5, 11; P.24, 26; P.23, 62; P.9, 63; P.20]. But this, in turn, is an axiom directly related to the scale of intensity of manifestation of GER or DGER processes. Manifestation of aggressive effects of the components of the reflux liquid directly depends on the degree of occurrence of GER or DGER processes in a unit of time and their duration. Also, during the process of GERD formation, it is important whether TRM is acidic or alkaline. The time has come to advance the slogan "No reflux, no GERD". Therefore, the word reflux was included in the list of words used in the empirical naming of GERD.

In our opinion, taking into account the above points, it is appropriate to recognize GERD as a disease related to the reflux process rather than acid. For the same reason, it is appropriate that the basis of drugs used in its treatment is not PPI manifestations, but on the contrary, prokinetics. This into account, at this stage of scientific research, the task of dynamic study of the therapeutically effective results of traditional and counter-methods proposed by the author in the treatment of GERD

was taken. In order to adequately evaluate the therapeutic effectiveness of the M and A methods used in the treatment of GERD: the dynamics of the main clinical symptoms (%); Positive changes in the quantitative value (points) of leading GERD clinical signs; The number of times the main clinical symptoms of GERD are encountered during the day; the number of nocturnal occurrences of an important sign, such as a chirping bird; the extent of positive changes in the quality of life of patients and similar factors were used as criteria.

When analyzing the dynamics of the results of the therapeutic effectiveness of the therapeutically used M and A methods, the following important results were obtained: 33 out of 39 patients (84.6%) in the M group before the treatment of this symptom, L If the quantity was evaluated on the monthly scale , it was recorded as (4.2±0.2) points , at the end of the first decade of the treatment , 53.9% of them were 21, and (2.6 ± 0.1) at the end of the second ten days. this sign occurs only in 3 cases (7.8%) when evaluating the quantity on the Lykert scale (0.3 ±0.01) . Group A patients with the same clinical signs were different. If before the treatment this symptom was noted in 30 out of 37 patients (81.1 %) , with a Likert scale rating of (4.0 ± 0.2) points, after the first decade of treatment it was 11 29.7 % (1.4±0.07) had this symptom at the end of the second ten days , and only 2 (5.4%) had this symptom when evaluating the severity on the Likert scale (0.2 ±0.01)also happened. Changes noted in NG patients (in contrast to AG patients) in the dynamics of the symptoms of the boil can be explained by the effect of the PPI components of method A applied to them. The fact that the results of the therapeutic efficiency of method A are much better in patients with nocturnal attacks of hot flashes indicates that it is related to the effect of PPI side effects.

M and A, there was no significant difference between the dynamic changes observed in other GERD-specific symptoms (apart from the symptom of a boil) of AG and CG patients. In the same way, the results of the criteria that allow to adequately evaluate the therapeutic effectiveness of the M and A treatment methods also gave results corresponding to the above- mentioned conclusion.

Thus, based on the obtained data, it was observed that the level of therapeutic effectiveness of the M method used in the treatment of GERD is competitive with the same indicators of the A treatment measures. This competitive therapeutic effect was more pronounced, especially in patients who did not have nocturnal episodes of hives.

As a result of the analysis of the data obtained during the scientific research, the clinical and endoscopic symptoms observed in patients with GERD, as well as the therapeutic efficiency noted in the treatment, are to a certain extent related to RMT. The magnitude of the observed association was relatively pronounced in patients with RMT acidosis. Therefore, it is appropriate to take this feature into account in the diagnosis and treatment of GERD.

CONCLUSION

1. The data obtained as a result of the application of the complex method, which allows to determine the pH index in the diagnosis of GERD, are equal to the modern methods of investigation (pH-metry and pH-impedancemetry).

2. Among the clinical symptoms of patients with GERD, in terms of the indicators of the scale of occurrence, it was 97%, sour taste in the mouth was 97% in patients with AcRM. In patients with IRM, it was distinguished by the presence of burning sensation in 75%, and the appearance of bitter taste in the mouth in 93%.

3. During the endoscopic analysis of GERD, it was noted that ERD was more common in patients with NERD was more common in patients with AlRM.

Of the p -cell treatment method, which takes into account the type of refluxate pH environment, significantly increased the effectiveness of GERD therapy and at the same time led to a significant decrease in the cost of drugs used for this purpose. The range of manifestations of clinical and endoscopic symptoms observed in patients with GERD and the therapeutic efficacy noted in the treatment are to some extent related to TRM. Therefore, it is appropriate to take into account this feature in the diagnosis and treatment of GERD.

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