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# ROLE OF GENITIC FACTORS IN PATHOGENESIS WITH COMPLICATED DUODENAL ULCER WITH BLEEDING

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## ABSTRACT

**Aim:** Study N-acetyltransferase activity and type of acetylation in patients with and without complication of ulcer disease. **Methods:** N-acetyltransferase activity and type of acetylation were studied in 163 patients; of these 63 had noncomplicated and 65 had complicated ulcer disease, while 35 were healthy (control group). Eighteen patients with complicated ulcer disease had perforation, 18 bleeding, and 29 stenosis. Results: In our studies, in the examination of patients with complicated course of peptic ulcer disease according to the most important clinical symptoms, a relationship was found between the activity of the acetylation process and clinical and laboratory indicators of peptic ulcer complicated by bleeding, perforation, and pyloroduodenal stenosis.

**Conclusion:** Our results suggest that it would be useful to identify acetylation phenotype to aid prediction of the character and clinical course of gastric and duodenal ulcer disease. Peptic ulcer is a chronic recurring polyetiological disease that occurs as a result of the interaction of exogenous and endogenous factors: a hereditary predisposition from 5.5 to 50%, the type of nervous system, endocrine systems, psychoemotional features, metabolic characteristics, biochemical reactions, immune status, cytokine profile and environmental factors, resulting in a violation between the factors of “aggression” and “protection” of the mucous membrane of the gastroduodenal zone. In the etiology of peptic ulcer, a certain role is played by hereditary burden. Therefore, when studying the nature of the hereditary predisposition to peptic ulcer of the stomach and duodenum, an important area is the identification of genetic markers.

**Key words:** Helicobacter pylori, N-acetyltransferase, Gastric ulcer, Duodenal ulcer, Bleeding.

## INTRODUCTION

Many issues of surgical tactics in gastric (GU) and duodenal ulcer (DU) remain controversial. This is due to the variety of options for the clinical course, timing and nature of complications. The development of prognostic criteria makes it possible to choose the most rational treatment tactics, in many patients to prevent relapses and complications, rather than affect the already frolicing severe pathological process.

Peptic ulcers account for 28% to 59% of nonvariceal upper gastrointestinal (GI) hemorrhage with duodenal ulcers responsible for 17% to 37% and gastric ulcers 11% to 24%.1 Peptic ulcer disease has reduced in prevalence, probably owing to improved nonsteroidal antiinflammatory drug prescribing practice, increased testing, and treatment of Helicobacter pylori infection in addition to more widespread use of proton pump inhibitors. However bleeding from peptic ulcers continues to result in significant morbidity and mortality, with the latter reported at 2% to 11%. Mortality for inpatients with upper GI bleeding is higher, owing to the increased comorbidities and older age of these patients. Over the years, endoscopic techniques and therapies have improved the management of peptic ulcer bleeding, with endotherapy becoming more accessible and technologically advanced. A 2007 audit of upper GI bleeding in the UK reported data on 6750 patients, 36% of whom had peptic ulcer bleeding.

Upper gastrointestinal bleeding is a medical condition routinely encountered in clinical practice. Overt upper gastrointestinal bleeding usually presents as melena or hematemesis but can also present as hematochezia in cases of brisk bleeding. The initial evaluation of a patient with suspected upper gastrointestinal bleeding begins with assessment of hemodynamic status, identification of potential risk factors, and appropriate triage of level of care. After resuscitation measures, endoscopic evaluation can be performed to diagnose and potentially treat the source of bleeding. Risk factors that increase the propensity for recurrent bleeding should be identified and addressed.

Upper gastrointestinal bleeding (UGIB) develops in the oesophagus, stomach or duodenum and has an incidence of 47/100,000. Lower GIB (LGIB) develops in the small bowel, colon or anorectum and has an incidence of 33/100,000. Where the incidence of UGIB has fallen, driven by helicobacter pylori eradication and the use of proton pump inhibitors, the incidence of LGIB may be increasing.

Acute upper gastrointestinal bleeding (UGIB) remains a public health burden with a persistent high mortality despite advances in modern day management. Proton pump inhibitors (PPI) as medical therapy is an attractive adjuvant to

endoscopic treatment in UGIB but the method and dose of PPI therapy remains controversial.

Peptic ulcer disease continues to be a source of significant morbidity and mortality worldwide. Approximately two-thirds of patients found to have peptic ulcer disease are asymptomatic. In symptomatic patients, the most common presenting symptom of peptic ulcer disease is epigastric pain, which may be associated with dyspepsia, bloating, abdominal fullness, nausea, or early satiety. Most cases of peptic ulcer disease are associated with Helicobacter *pylori* infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), or both. In this review, we discuss the role of proton pump inhibitors in the management of peptic ulcer disease, highlight the latest guidelines about the diagnosis and management of *H. pylori*, and discuss the latest evidence in the management of complications related to peptic ulcer disease, including endoscopic intervention for peptic ulcer-related bleeding. Timely diagnosis and treatment of peptic ulcer disease and its sequelae are crucial in order to minimize associated morbidity and mortality, as is prevention of peptic ulcer disease among patients at high risk, including those infected with *H. pylori* and users of NSAIDs.

Literature data on the prediction of ulcer complications are scarce. As prognostic criteria, various indicators are used that are associated with the pathogenesis of peptic ulcer. There is evidence that the development of complications is facilitated by the severe course of diseases with frequent relapses, a family ulcerative history, high acid-forming function of the stomach, and a decrease in the level of gastric mucus glycoproteins. The authors recommend clinical endoscopic data as prognostic criteria. In the etiology of peptic ulcer, a certain role is played by hereditary burden. In this regard, the approach to the study of N - acetyltransferase involved in the implementation of genetic information and the clarification of the relationship of hereditarily determined traits with ulcer pathology are fundamentally important. Recently, research has been carried out to obtain real biomodels and the creation of highly specific species primers for the N-acetyltransferase-1 and N-acetyltransferase-2 genes. According to published data, there is a correlation between the process of acetylation and the etiology and pathogenesis of a number of diseases: peptic ulcer of the stomach and duodenum, ulcerative colitis, heart failure, with infertility and peritoneal form of endometriosis, acute coronary syndrome, with pneumonia. And also, when studying the state of the processes of acetylation of a number of diseases, a correlation was revealed between the activity of these processes and the severity of diseases, as well as their progression.

Over the past few years, foreign and domestic gastroenterologies have claimed that peptic ulcer is a local infectious process caused by contamination of the mucous membrane of the stomach or duodenum of H. pylori (HP). In contrast, most scientists studying ulcer consider that the presence of hydrochloric acid in the stomach is one of the prerequisites for the occurrence of a peptic ulcer in the coolant or bulb of the duodenum. In the past and at present, in the treatment of ulcer, drugs that suppress the secretion of hydrochloric acid (antacids, H2 - blockers, proton pump inhibitors), as well as surgical interventions (ranging from various types of vagotomy to gastrectomy) are mainly used.

There are differences in geographical distribution (between West and Asia), time trends, sex and peptic ulcer ratio, seasonal rates and behavioral response. HP is one of the main causes of peptic ulcers; other environmental and genetic factors contribute to ulcer formation. It should be noted that, in addition to genetic factors, the environmental factor claimed an etiological role in peptic ulcer disease: non-steroidal anti-inflammatory drugs, cigarette smoking, stress and dietary factors.

Until the 19th century, ulcerative ulceration was a rarity, whether in the East or the West. The level of infection varies widely between Asians. It is low in Malays and Indonesians, in whom stomach ulcers and stomach cancer are rare. It is very high in India, where a duodenal ulcer is common, but a stomach ulcer and cancer are not. In the Chinese and Japanese, cancer is common, high, but the Chinese have a greater frequency of duodenal ulcer than the Japanese. It is believed that HPi is the main cause of ulcer, other environmental and genetic factors contribute to the formation of ulcers, supporting the concept of etiological heterogeneity.

Proponents of the infectious origin of ulcer consider the use of anti-Helicobacter pills as the main principle of its treatment. At present, numerous researchers have found that the number of patients with HP-negative forms is gradually increasing from 8 - 56%. Epidemiological studies have established that HP infection is widespread in the world: up to 60% of the population of all continents of the planet in all entic groups of the population is infected with HP, starting from childhood. About 70% of them, however, are healthy bacteria carriers, often throughout life. At the same time, gastric and duodenal ulcer affect only 12-15% of those infected with HP. The authors found in the gastric mucosa, in addition to HP and mucous microflora, which have adhesive properties and high virulence. Unfortunately, there is almost no discussion in the literature of the significance of mucosal microflora in the pathogenesis of ulcer and its relapses. Zimmerman et al. believe that the antiulcer drugs used not only act on HP, but also on mucous microflora. Tkachenko E.I. considers HP to be low virulent

bacteria, distinguishing them from highly virulent surgical infection. The authors of found that the cytotoxic gene is found in patients with ulcer, gastric cancer, gastroduodenal dyspepsia, with chronic gastritis, as well as in healthy bacteria carriers. Zimmerman et al. consider that the pathogenic HP strain has a cytotoxic effect when the body's immunity is reduced. According to the literature and our data, we can conclude that the role and importance of HP in the pathogenesis of ulcer in the literature are discussed debatably, the absence of HP in the gastric mucosa contributes to a deeper change in metabolic processes.

## MATERIAL AND METHODS

Genitic factors were studied in 163 patients; of these 63 had noncomplicated and 65 had complicated ulcer disease, while 35 were healthy (control group). Eighteen patients with complicated ulcer disease had perforation, 18 bleeding, and 29 stenosis. N-acetyltransferase activity and type of acetylation were determined by micromethod modified by Bulovskaya L.N. Following on overnight fast, each subject was given orall sulfadimesin at a dose of 0.5 g for body weight up to 51 kg, 0.75 g for body weight of 51 - 83 kg and -1 g for body weight over 83 kg. The concentration of acetylated sulfademesin was determined in blood samples obtained five hours later with the degree of sulfadimesin acetylation determined by this method showing N-acetyltransferase activity. Subjects with acetylation activity lower than 50% were concidered as slow acetylators, while those who had acetylation activity higher than 50% were termed as fast acetylators. For evaluation of reliable differences, the criteria of nonparametric statistics was used. A thorough history wascollected from all patients and a comprehensive clinicallaboratory, endoscopic, functional examination was carried out. Statistical data processing was performed using Microsoft Office 2016

## METHOD FOR DETERMINING THE PHENOTYPE OF N - ACETYLTRANSFERASE ACTIVITY

Along with the study of clinical and medical history data, all patients who received a complicated gastroduodenal ulcer underwent routine clinical and biochemical studies: a general analysis of blood and urine, residual nitrogen, urea, blood creatinine, total protein and its fractions, sugar, bilirubin (total, direct and indirect), blood enzymes (AST, ALT), electrolytes and blood chlorides, indicators of the coagulation system, diastasis of blood and urine. All patients underwent ECG, fluoroscopy or radiography of the lungs, and other studies as needed. The motor-evacuation function of the stomach (or its stump) was studied by X-ray examination of the stomach using barium sulfate. Esophagogastroduodenofibroscopy was performed for all patients and, if necessary, repeatedly in dynamics.

The acetylation phenotype was determined according to the Evans method in the modification of L. Bulovskaya. The method is based on the oral administration of sulfadimesin as a substrate of N - acetyltransferase, and the determination of reaction products in blood samples after 5 hours. Patients are given sulfadimezin orally on an empty stomach at a rate of 10 mg / kg body weight 2 hours after taking the drug, a light breakfast (1 cup of tea and bread), after 5 hours, take blood from a finger and determine the amount of free, acetylated and total sulfadimesin, then calculating the percentage of free sulfadimesin to total, which is an indicator of the activity of polymorphic N-acetyltransferase . 0.1 ml of whole blood or serum is introduced into a centrifuge tube with 1.4 ml of distilled water and the proteins are precipitated by pouring 0.5 ml of 20% trichloroacetic acid. The precipitate is carefully transferred with a glass rod and left for 5-10 minutes; then centrifuged for 20 minutes at 3000 rpm. 0.5 ml centrifuge in two identical tubes. In both test tubes, 0.1 ml of 4 p. HCL and one of them is placed for 45 minutes. in a boiling water bath for hydrolysis, then cooled at room temperature.

Then both tubes are cooled in the refrigerator at 40 ° C for 30 minutes. After cooling, diazotization and azo coupling are carried out: 0.1 ml of 1% ammonium sulfamic acid is poured into the samples, shaken and after 2 minutes 0.2 ml of 0.1% NED are added. Samples are left in the dark for 60 minutes, periodically shaking, and photometric on a photo-calorimeter - MKPM at a wavelength of 540 nm in a socket with an optical path length of 10 mm. For the calculation, a calibration curve is constructed using a standard solution of sulfadimezin with a concentration of 2.5; 5; 7.5 and 10 mcg. In hydrolyzed samples, total sulfadimesin is determined, and in non-hydrolyzed samples it is determined free, the amount of acetylated sulfadimesin is calculated by the difference. The type of acetylation is determined by the ratio of the activity of the enzyme N-acetyltransferase, expressed as a percentage. The level of N-acetyltransferase activity is determined by the percentage of sulfadimesin acetylation in the blood.

## RESULTS AND DISCUSSION

The distribution of the acetylation phenotype in the control group and in the group of patients under consideration is presented in Table 1. When studying the activity of N-acetyltransferase, the bimodal distribution of the sulfadimesin acetylation phenotype was established in both healthy individuals and patients with uncomplicated peptic ulcer disease. In the control group, 68.6% of slow and 31.4% of fast acetylators were detected.

Among the examined individuals with uncomplicated peptic ulcer disease, patients with a slow type of acetylation predominated, and the ratio of slow and fast acetylators was 87.3 and 12.7%. The enzyme activity in slow acetylators in the control group ranged from 0 to 20%, in fast - from 50% to 60%. (table 1). The

average level of N-acetyltransferase activity in this group for slow acetylators was 15.0%, for fast - 53.3%.

**Table 1.**

**Change in the ratio of slow and fast acetylators and level acetylation in patients with uncomplicated duodenal ulcer (M±m).**

| Researched groups | number of subjects | | Acetylation activity, % | |
|---|---|---|---|---|
| | "slow" | "fast" | "slow" | "fast" |
| Control, n=35 | 24 (68,6%) | 11 (31,4%) | 15,0±1,12 | 53,3±1,8 |
| Noncomplicated ulcer disease, n=63 | 55 (87,3%) | 8 (12,7%) | 22,0 ±1,36* | 63,0 ±2,81* |

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

Results of N-acetyltransferase activity determination showed that gastroduodenal ulcer occurred both among subjects with slow acetylation and those with fast phenotype. However, there were significant differences in frequency of the presence of both phenotypes between the study and control group (table 1). Thus, in the group of healthy subjects, the number of subjects with slow and fast acetylation type accounted for 68.6% and 31.4%, respectively. In patients with noncomplicated ulcer disease, there was a relative increase of slow acetylators by 27.3% and decrease of fast acetylators by 59.6% comparing with the control group (table 2).

During the progress of ulcer disease and development of complications one directional changes were noted in the proportion of slow and fast acetylators. Thus, in patients with nonperforated gastroduodenal ulcers there was increase in slow acetylators of 37.6% and a decrease in fast acetylators of 82.2% in comparison with the control group, - - and of 8.1 and 56.0% respectively, in comparison with noncomplicated ulcer disease. In patients with gastroduodenal ulcer complicated by bleeding, the increase in slow and decrease in fast acetylators was 13.7% and 30.0%, respectively, in comparison with the control group. However, in contrast to the non - perforated group of patients, when comparison with non-complicated ulcer was made, the decrease in the number of slow acetylators was 10.7% and the increase in fast acetylators was 73.2%.

In patients with pyloroduodenal stenosis, an increase in slow acetylators of 20.6% and decrease in fast acetylators of 44.9% was noted in comparison with control subjects, while noncomplicated ulcer disease slow acetylators decreased by 5.3%, and fast acetylators increased by 36.2%.

**Table 2.**

**Percentage of changes between slow and fast acetylators and acetylation level in patients with gastroduodenal ulcer**

| Study groups | number of subjects | | | | Acetylation activity, % (means±SEM) | |
|---|---|---|---|---|---|---|
| | "slow" | | "fast" | | "slow" | "fast" |
| | n | % | N | % | | |
| Control, n=35 | 24 | 68.6 | 11 | 31.4 | 15.0±1.12 | 53.3±1.8 |
| Noncomplicated ulcer disease, n=63 | 55 | 87.3 | 8 | 12.7 | 22.0 ±1.36* | 63.0 ±2.81* |
| - bleeding, n=18 | 14 | 78 | 4 | 22 | 26.0 ± 3.8** | 55.0 ± 3.12 |

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

Along with change in proportion of slow and fast acetylators in noncomplicated and complicated ulcer disease, the increase in N-acetyltransferase activity level was noted at the limits of its phenotype in both slow (by 46.7%) and fast (by 18.2%) acetylators in the group of patients with ulcer disease, complicated with bleeding, the acetylation level of which did not differ from the control group.

In patients with gastro-duodenal ulcer complicated by perforation, acetylation activi-ty was 26.7% hiqher in slow acetylators and 50.7% hiqher in fast acetylators than control subjects. However, it should be noted that in comparison with indicators in patients with noncomplicated ulcer disease, the acetylation level in slow acetylation type patients with perforated ulcer was 13.6% lower. At the same time, the average level of N-acetyltransferase activity in fast acetylators in this group was the highest, exceeding the acetylation le-vel of noncomplicated ulcer disease patients by 27.5%. The average level of enzyme activity in slow acetylator patients with ulcer disease complicated by bleeding, was also highest, ex-ceeding control levels by 73.3%, and noncomplicated ulcer disease levels by 18.2%. Acetylation activity was 40.0% higher in slow acetylators with pyloroduodenal stenosis than control pati-ents and 17.3% higher in fast acetylators, but levels were stable in uncomplicated ulcer disease.

Results showed changes in levels of N-acetyltransferase activity associated with in-dividual fluctuations of sulfadimesin acetylation activity in patients with noncomplicated and complicated ulcer disease, ranging from 0% -49.0% in slow phenotypes, significantly higher than changes in healthy subjects (from 0% to 20%). In fast acetylators, healthy subjects activity changes ranged from 50% -

59%, whilst they were significantly higher (50% - 80%) ($p<0.05$ by Rosenbaum Q criteria) in patients with ulcer disease.

Fluctuations in individual levels of sulfadimesin acetylation activity in patients with complicated ulcer disease showed an interrelationship between the development of complica-tions of ulcerative pathology and change of N-acetyltransferase activity.

According to the literature, individual levels of N-acetyltransferase activity in humans are stabilized by control of gene-modifiers [11]. On the basis of this evidence, it may be suggested that an increase in levels of N-acetyltransferase activity in progressive ulcera-tive pathology, reflects a change in the control of gene-modifiers.

Differences and changes of acetilation actyvity in slow and fast acetylators, leads us to conclude that patients with complicated ulcer disease and fast phenotype of acetylation have a different predisposition to the complications of ulcer disease. Current evidence suggest that fast acetylators are heterogeneous and those with heterozygote heredity acetylate slower than homozygotes [11,12]. It may therefore be concluded that heterozygotes prevailed in the group of patients with complicated ulcer. In this context it is clear why, in spite of an increase in N-acetyltransferase activity during the development of complicated ulcer disease, enzyme activity in patients with bleeding does not exceed control levels.

An increase in the average level of N-acetyltransferase activity in the group of patients due to the appearance of individuals with an “intermediate” phenotype. The results obtained suggest the pathogenetic role of acetylation in the pathogenesis of uncomplicated peptic ulcer of the stomach and duodenum.

When studying the state of the processes of acetylation of a number of diseases, a correlation was revealed between the activity of these processes and the severity of diseases, as well as their progression. An increase in N-acetyltransferase activity was observed within its phenotype as the tumor process progressed [17], an increase in the adhesion process was noted in women with high activity of the N-acetyltransferase enzyme [3,4,7,18], and an increase in acetylation with the progression of lymphogranulomatosis in children [4,7,11,15,16].

Based on literature data, we investigated the activity of acetylation processes in patients with peptic ulcer disease with complications of bleeding, perforations, and pyloroduodenal stenoses.

The results of the study showed (table 3) unidirectional changes in the ratio of slow and fast acetylators in the group of patients with gastroduodenal bleeding

compared with those in the group of patients with uncomplicated peptic ulcer disease.

**Table 3.**

**Change in the ratio of slow and fast acetylators and acetylation levels in patients with bleeding gastroduodenal ulcer (M±m).**

| Study groups | number of subjects | | Acetylation activity, % | |
|---|---|---|---|---|
| | "slow" | "fast" | "slow" | "fast" |
| Control, n=35 | 24 (68,6%) | 11 (31,4%) | 15,0±1,12 | 53,3±1,8 |
| Noncomplicated ulcer disease, n=63 | 55 (87,3%) | 8 (12,7%) | 22,0 ±1,36* | 63,0 ±2,81* |
| Complicated ulcer disease: - perforated, n=18 | 14 (78,0%) | 4 (22,0%) | 26,0 ± 3,8** | 55,0 ± 3,12 |

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

There was also an increase in the number of slow and a decrease in fast acetylators in this group compared with the control, which amounted to 13.7 and 29.9%, respectively. The change in the average level of N-acetyltransferase activity is associated with significant individual fluctuations in sulfadimesin acetylation activity in patients with bleeding and slow acetylators (from 0 to 49%), which is significantly ($p < 0.01$) higher than the fluctuations in the group of healthy individuals (from 0 to twenty%). In the fast type, the indicators of acetylation activity were at the level of control data.

When comparing indicators with a group of patients with uncomplicated ulcers, a difference was found in the ratio of phenotypes: a decrease in the number of slow acetylators by 10.7% and an increase in fast ones by 73.2%. The average level of enzyme activity in slow acetylators among patients with peptic ulcer complicated by bleeding exceeded the control level in uncomplicated ulcers by 18.2% ($p < 0.01$).

Thus, acetylation processes play a role in the development of complications of peptic ulcer bleeding: a large predisposition of fast acetylators to the development of bleeding and the appearance of individuals with an "intermediate" phenotype.

Along with a change in the phenotype ratio, a slight increase in the average level of N-acetyltransferase activity was noted in this group compared with the control data. Among slow acetylators, the enzyme activity did not differ from that in the group of patients with uncomplicated ulcers, and among fast acetylators, a significant increase in enzyme activity was noted compared with the

uncomplicated course of peptic ulcer disease ($p < 0.01$). When analyzing individual fluctuations in acetylation activity in slow acetylators, it should be noted that 52.9% of patients had activity ranging from 0 to 9%, and 47.1% patients had activity ranging from 20% up to 49%, i.e. had an intermediate phenotype.

Thus, as the results showed, a perforated ulcer developed mainly in slow acetylators. However, its development is not excluded also in fast acetylators, but, apparently, with a very high level of activity of acetylation processes. The development of perforated ulcers in slow acetylators is more characteristic of patients with the lowest enzyme activity (from 0 to 9%) and with an "intermediate" phenotype, the enzyme activity of which ranged from 20% to 49%

It is known that numerous factors can significantly change the intensity of acetylation, including the treatment of diseases. Thus, according to [12,17], a decrease in N-acetyltransferase activity was observed with successful chemotherapy in patients with malignant lymphomas and after radical surgery in patients with lung and gastrointestinal tract cancer, and with successful treatment and improvement of the condition of sick children with lymphogranulomatosis, a decrease in N- acetyltransferase activity [8,12].

The results of studying the activity of acetylation after traditional therapy for patients with peptic ulcer disease showed that the average level of enzyme activity decreased by 53%.

Thus, traditional therapy and surgical intervention contribute to a decrease in the level of N-acetyltransferase activity in patients with gastroduodenal ulcer. In some cases, in the course of all types of treatment, the acetylation phenotype changes: fast to slow and slow to fast.

It is known that the majority of diseases are based on changes in the chemical homeostasis of the body, the causes of which are metabolic disorders in chemical compounds. A very important enzyme system supporting internal chemical homeostasis is the N-acetylation system. Violation of the metabolic function of this system leads to serious negative consequences. This is confirmed by data on the close relationship between the activity of acetylation processes and clinical indicators of the course of individual pathological conditions [8,10].

In our studies, in the examination of patients with complicated course of peptic ulcer disease according to the most important clinical symptoms, a relationship was found between the activity of the acetylation process and clinical and laboratory indicators of peptic ulcer complicated by bleeding, perforation, and pyloroduodenal stenosis [7].

## CONCLUSIONS

1. This study showed that noncomplicated and complicated gastro-duodenal ulcer occur-red in patients with both slow and fast phenotype of acetylation, and that the incidence of both phenotypes differs from healthy controls (increase in slow acetylators and decrease in fast acetylators). Moreover, there an increase in the average level of acetylation was noted in the study group patients.

2. Moreover, there an increase in the average level of acetylation was noted in the study group patients.

3. A more significant increase in levels of N-acetyltransferase activity in slow acetylators was found in patients with ulcer disease complicated by bleeding, than among fast acetylators in patients with perforated ulcer.

4. In conclusion, our results suggest that it would be useful to identify acetylation phenotype to aid prediction of the character and clinical course of gastric and duodenal ulcer disease.

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