GENETIC VARIANTS OF *H.pylori* IN DIFFERENT FORMS OF CHRONIC GASTRITIS

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Abstract. The development of clinical forms of infection and endoscopic changes in the gastric mucosa depends on the *H.pylori* genetic diversity in a given region. The aim of this work was to study the relationship of the genetic profile of *H.pylori* pathogenicity factors with clinical and endoscopic features of *Helicobacter*-associated gastritis in Nizhny Novgorod. A number of *H.pylori* pathogenicity genes of DNA isolates obtained by endoscopy from 151 patients with chronic H.pylori-associated gastritis (non-destructive, erosive, and atrophic) were studied by PCR. Results. In destructive processes in the gastric mucosa, the detection frequency of *cagA*, *vacA* s1 m1 genes and a combination of several pathogenicity factors, including *ice*A A1 and *bab*A was higher than in other forms of gastritis. Atrophic gastritis is characterized by the genetic profile *cagA* and *vacA* s2 m2. Infection with several *H.pylori* strains is determined more often in erosive gastritis and atrophy of the gastric mucosa. Conclusions. In chronic gastritis in Nizhny Novgorod, a predominantly "European" character of the pathogen population structure was revealed - with a moderate content of the most pathogenic *cag*A, *vac*A s1-positive strains. Colonization of the gastric mucosa by *H.pylori* with a genetic structure containing pathogenicity factors *cagA*, *vacA*, *babA*, *ice A2*, in chronic *H.pylori*-associated diseases, it is a factor in increasing the severity, activity and prevalence of the inflammatory process, the appearance of signs of atrophy of the gastric mucosa. The greatest influence on these indicators is exerted by the presence of *cagA* and *vacA* s1 in the microorganism genome, as well as a combination of several pathogenicity factors.

Keywords: *Helicobacter pylori*, genes of pathogenicity, genetic structure, chronic gastritis

List of abbreviations

Helicobacter pylori – *H.pylori*
Polymerase chain reaction – PCR
Pathogenicity island – PAI
Cytotoxin-associated gene – *cag*
Vacuolating associated cytotoxin – *vac*
Blood group associated binding gene – *bab*
Induced by contact with epithelium gene – *ice*

Introduction

H. pylori infection is one of the most common chronic human infections. According to various data, this infection ranges between 85% and 95% in developing countries in Asia and Africa, between 40% and 80% in Eastern Europe and South America, and between 25% and 40% in developed countries in Europe and North America (Maev et al., 2016; Hooi et al., 2017; Mahachai et al., 2018). *H. pylori* can persist in the stomach and areas of gastric metaplasia in the human duodenum, causing various forms of infection from asymptomatic infection up to type B gastritis and peptic ulcer disease, provoking the development of adenocarcinoma or gastric lymphoma (Maev et al., 2016; Hooi et al., 2017; Mahachai et al., 2018; Kpoghomou et al., 2020).

In recent decades, changes in the structure of *H. pylori*-associated pathology have been detected all over the world, and in Russia, there was a significant reduction in both general and primary incidence of gastric and duodenal ulcers (Baranovsky et al., 2019; Malfertheiner et al., 2018). According to the Federal state statistics service of Russia in 2017, the peptic ulcers among Russians decreased from 1047.0 per 100,000 population in 2010 to 848.3 in 2016 (Health in Russia, 2017). 90–95% of stomach ulcer cases and at least 70–75% of duodenal ulcer cases continue to be associated with *H. pylori*. So, according to D. S. Borodin et al., in Moscow by 2016, compared with 1994, the incidence of peptic ulcer disease decreased by 77%, and its prevalence-by 64% (Bordin et al., 2018). At the same time, there was an increase

in the incidence of gastritis and duodenitis (1.2 times), including those associated with *H. pylori* infection (Konovalov & Varenova, 2015; Lazareva & Gordeeva, 2017). In addition, the proportion of more severe and prognostically unfavorable forms (erosive, subatrophic, and atrophific) increased by 2.5 times (Avdeeva et al., 2009; Lazareva & Gordeeva, 2017). Long – term *H. pylori* infection is a risk factor for disruption of regenerative processes in the gastric mucosa, with the development of atrophy manifested in the early stages: 2 years after infection-in 6% of patients, and 10 years later - in 43% of patients (Evsyutina, 2016; Okuda et al., 2016; Nimish et al., 2017).

It is known that the *H. pylori* infection is not always associated with clinical manifestations. The development variant of any form of *H. pylori* infection depends on a number of factors, including, first of all, virulent and pathogenic properties of the bacteria strain, immunogenetic characteristics of the host, as well as social and living (Yokota et al., 2015; Mamishi et al., 2016; Hooi, 2017; Bordin et al., 2018; Ofori et al., 2019; Hong-Ming Zhu et al., 2020).

The development, course features, frequency and severity of relapses and success of etiotropic therapy of chronic *H. pylori*-associated pathology may be due to the presence of certain Helicobacter genotypes in humans. For a number of years, intensive studies of *H. pylori* genetic diversity have been conducted abroad, and attempts have been made to identify correlations between infection with certain genotypes of this microorganism and human health indicators (Sedaghat et al., 2014; Dadashzadeh K. et al., 2015; Mamishi, 2016).

The greatest interest is the study of a number of genes encoding the production of toxins – virulence factors of the microorganism. These include *cag*A, *vac*A, *bab*A, *ice*A genes and some others.

In the genome of any strain, there is a *vac*A gene responsible for the production of vacuolating cytotoxin VacA. This toxin increases the production of pepsinogen, reduces the secretion of hydrochloric acid in the stomach and cell proliferation, damages lysosomes and mitochondria, and disrupts the cytoskeleton of gastric epithelial cells. The toxin VacA contributes to the nutrition of the bacterial cell, damaging the intercellular contacts in the stomach epithelium and facilitating the transport of small molecules through the cell membranes. Vacuolating cytotoxin A acts on type 5 ATP-ase and acidifies the internal environment of gastric epithelial cells, which ensures the flow of ammonia and other substances from the extracellular space into the epithelial cells, which attract water. As a result, vacuoles swell, which leads to rupture of the cell membrane and cell death. The formation of a cytotoxin protein depends on the composition of the *vac*A. This gene has three regions: s -signal, i - intermediate and m - middle. Each region includes 2 alleles: the signal s-region - s1 and s2, intermediate i-region – i1 and i2, middle m-region – m1 and m2. The activity of the vacuolating toxin production is determined by the composition of the *vac*A gene and causes differences in cytotoxic activity between strains (Isaeva & Valieva, 2018). *H. pylori* strains containing the region s1*vac*A, depending on the presence of the region m1 and m2, produce the largest and average amount of cytotoxin and have the ability to colonize the gastric mucosa at a high density. The development of peptic ulcer disease, as well as stomach cancer is associated with the infection with *H.pyroli* strains containing *vac*As1m1 variant (Sedaghat et al., 2014; Dadashzadeh, 2015; Maev et al., 2016; Isaeva & Valieva, 2018; Venneman et al., 2018).

The *cag*A gene is found only in *H. pylori*, but is not present in all strains. This gene is one of the main factors of pathogenicity, and indicates the presence of the PAI pathogenicity in this strain. It encodes the CagA protein responsible for the production of pro-inflammatory cytokines, the induction of inflammation and disruption of gastric mucosal epithelium integrity, the induction of uncontrolled proliferation of epithelial and lymphoid cells. The gene has allelic variations that occur in different countries of the world, and depending on the gene subtypes, *H.pylori* pathogenic properties and resistance to gastric acid, and according to some data, to a number of antibiotics vary (Kusters et al., 2006; Sedaghat et al., 2014; Da-

dashzadeh et al., 2015; Isaeva & Valieva, 2018).

The *bab*A gene encodes the formation of a protein in the blood (the blood group antigen binding adhesion). Sialic acids, glycolipids, sulfogroups of glycoproteins, phospholipids, and fucose Lewis-like antigens are used as adhesion receptors. Due to the interaction of the ligands of the microorganism with the corresponding receptors of the gastric epithelium, adhesion occurs. In addition, microbes can also bind to connective tissue collagen. The *bab*A gene induces the production of interleukin-8, the formation of which increases in proportion to the density of colonization. 3 alleles of the *babA* gene (*bab*A1, *bab*A2, *bab*A3) were detected. The presence of *bab*A1 and *bab*A2 in the genome of *H.pylori* is associated with a higher incidence of duodenal ulcer, and the detection of *bab*A2 – as well as with gastric adenocarcinoma (Sedaghat et al., 2014; Miftahussurur et al., 2015; Dadashzadeh et al., 2015; Isaeva & Valieva, 2018).

The expression of the *iceA* gene (induced by contact with epithelium) was upregulated on contact between *H. pylori* and human epithelial cells. There are at least two alleles of *ice*A: *ice*A1, and *ice*A2. *Ice*A1 gene is more commonly detected in Asian countries, and *iceA2* gene - in Western countries. The role of this gene in the pathogenesis of gastric diseases is not fully understood. Some studies have shown that regardless of *cag*A status in the presence of *ice*A1 neutrophil infiltration of the lamina propria of gastric mucosa and the interleukin-8 expression enhance, acute inflammation up to the gastric ulcer occurs (Sedaghat et al., 2014; Dadashzadeh, 2015; Isaeva & Valieva, 2018).

To determine the virulence genes is important both for deciphering the mechanism for the development of an infectious process, and for studying the ways of spread of *H.pylori* in the population (Ivashkin et al., 2013; Zhebrun et al., 2014). The study of the virulence genes of *H.pylori* isolates from patients living in different regions, their prognostic significance, and the genotypic map creation are regarded as determining directions in epidemiology and the development of indications for the treatment of *H.pylori* infection.

The aim of this work was to study the relationship of the genetic profile of H. pylori pathogenicity factors with clinical and endoscopic features of Helicobacter-associated gastritis in Nizhny Novgorod.

Methods

The work was performed on the basis of the infectious diseases clinic of the Academician I.N. Blokhina Nizhny Novgorod Scientific Research Institute of Epidemiology and Microbiology: including selection, clinical and laboratory instrumental examination and treatment of patients, interpretation and analysis of results. All patients gave informed voluntary consent to the examination and inclusion of the obtained data in scientific work.

The basic comprehensive examination of patients included clinical diagnostics, instrumental and laboratory tests in accordance with the Standards (protocols) for the diagnosis and treatment of patients with digestive diseases (Standard, 2004; Standard, 2012) and clinical recommendations (Ivashkin et al., 2018; Lazebnik et al., 2017).

Instrumental diagnostics included esophagogastroduodenoscopy using Olympus Video endoscopes Gif-E150 and H-180, sampling of biopsy material and gastric juice.

For molecular genetic identification of *H.pylori* (*H.pylori* DNA and *cag*A, *vac*A, *bab*A, *ice*A genes), the PCR method was used, as described earlier (Perfilova et al., 2016). DNA isolates were obtained from the primary biological material. Commercial and experimental test systems (manufactures «LITECH» – Moscow and «Vector-best») were used in the work. In the structure of the *vac*A gene, allelic types were determined: allelic types s1 and s2, as well as m1 and m2, in the structure of the *ice*A gene – allelic types A1 and A2.

In this work, the genetic profile of *H.pylori* DNA isolates obtained from 151 patients (70 men and 81 women aged 18 to 60 years) with different types of diseases of the stomach and duodenum was investigated. Endoscopic examination revealed active gastritis in 76 patients

without violating the gastric mucosa integrity, in 28 patients with single or multiple erosions of the gastric mucosa and / or duodenal ulcer and non-atrophic gastritis, in 11 – duodenal ulcer and non-atrophic gastritis.

Statistical processing of research results was performed using the program «Statistica» version 6.0 and statistical functions of the Exel program according to standard formulas (Glantz, 1998). The significance of differences was evaluated using nonparametric methods of Pearson ($\chi 2$) and Fisher. Differences were considered significant at $p < 0.05$.

The methodology and results were approved by the ethics Committee of the Academician I.N. Blokhina Nizhny Novgorod Scientific Research Institute of Epidemiology and Microbiology.

Results

The study found 22 different combinations of genetic markers of *H.pylori* virulence factors. The proportion of patients from whom *cag*A-positive isolates were obtained was 47.7±4.0%. The *vac*A gene was revealed in different allelic variants in all the examined patients. The proportion of patients with *vac*As1 strains was accounted for 62.2±3.9%, with *vac*As2 strains – for 39.7±3.9%. The frequency of detection of strains with the *vac*Am1 genotype was 29.8±3.7%, the *vac*Am2 genotype was found in 55.6±4.0% of cases. 42.4±3.9% of isolates DNA were *ice*A1 positive, 28.5±3.7% - *ice*A2 positive. The *bab*A-positive genotype was detected in 4.6% of patients, mainly with destructive pathology. The genetic profile of virulence factors in patients with peptic ulcer disease and erosive gastritis and duodenitis was similar, which allowed combining these groups. The results of identifying individual genes and their alleles are shown in table 1.

Only one copy of the vacA gene can be present in the genome, so the registration of genotypes containing alleles m1 and m2 or s1 and s2 at the same time in one patient indicates the presence of more than one strain in the clinical sample.

In the examined patients, mixed *vac*A genotypes of *H.pylori* were detected quite often – 24.8 ± 3.3% in DNA isolates. Of these, 13.2 ± 2.7% were *vac*A m1 + m2 variants, and 11.9 + 2.6% were *vac*A s1 + s2 variants. In general, the *vac*Am2 and *vac*As1 genes were most frequently detected in the group, and *cag*A and *ice*A1 were slightly less frequently detected. All 4 allelic variants of the *vac*A gene were found in 5 patients (4.8%). The detection frequency of *cag*A, *vac*A s1 and *vac*A m2, in peptic ulcer disease and erosive gastritis was higher than in non-destructive gastritis. The *vac*A m1 and *ice*A2 genes were detected almost 2 times more often in patients with erosive and ulcerative pathology. However, there were no statistically significant differences in the frequency of detection of certain genes in the examined groups of patients at the present stage of research.

In most cases of destructive gastroduodenal pathology, the *cag*A *vac*A s1 m1 genotype was detected, as well as high frequency of infection with at least two strains, and a combination of more than two virulence factor genes. According to the literature, *H.pylori* with the *cag*A *vac*A s1 m1 genome is considered highly pathogenic and has the greatest ability to produce toxins (Sedaghat et al., 2014; Dadashzadeh et al., 2015; Maev et al., 2016; Isaeva & Valieva, 2018). In this study, clinical and endoscopic manifestations of the disease were compared in 2 groups of patients: the first group (main group)-32 patients with gastroduodenal diseases associated with highly pathogenic *H. pylori*, the second group - 35 patients with *H. pylori* associated gastroduodenitis, in the genome of which only virulence factors *vac*A s2 and m2 were found. Statistically significant intergroup differences in the endoscopic picture of the gastric and duodenal mucosa were obtained (table 2).

It was found that colonization of the gastric mucosa by highly pathogenic *H. pylori* strains leads to the damage area extension. Chronic inflammation in the subcardia was registered in 25% of the main group against 8.6% in the comparison group ($p < 0.05$), and pangastritis was detected in them more than 4 times more often (34.4% against 8.6%, $p < 0.01$). Macroscopically, inflammation in the gastric mucosa

Table 1

Genetic profile of *H.pylori* in examined groups (%)

Genes and alleles		Total n = 151	Ulcer disease/erosive gastritis n = 39	Non-destrictive antral gastritis/duodenitis n = 76	Atrophic gastritis n = 36
Cag A		47,7 ± 4,0	66,7 ± 7,5	38,2 ± 5,6	47,2 ± 8,3
*vac*A	s1	62,2 ± 3,9	71,8 ± 7,2	63,1 ± 5,5	50,0 ± 8,3
	s2	39,7 ± 3,9	43,6 ± 6,2	31,6 ± 5,3	52,8 ± 8,3
	s1 + s2	11,9 ± 2,6	20,5 ± 6,4	5,3 ± 2,5	16,7 ± 6,2
	m1	29,8 ± 3,7	53,8 ± 7,9	21,1 ± 4,6	25,0 ± 7,2
	m2	55,6 ± 4,0	46,1 ± 8,0	61,8 ± 5,6	52,8 ± 8,3
	m1 + m2	13,2 ± 2,7	15,4 ± 5,7	9,2 ± 3,3	19,4 ± 6,6
ice	A1	42,4 ± 3,9	48,7 ± 8,0	36,8 ± 5,5	47,2 ± 8,3
	A2	28,5 ± 3,7	41,0 ± 7,8	25,0 ± 4,9	22,2 ± 6,9
bab A		4,6 ± 1,7	10,3 ± 4,8	3,4 ± 2,0	0

Table 2

Comparative characteristics of the clinical and endoscopic picture in patients with the identification of highly pathogenic and weakly pathogenic *H.pylori*

Severity of chronic inflammation of the gastric mucosa	1st group (*H.pylori cag* A, *vac*A s1m1, *ice*A) n = 32		2nd group (*H.pylori vac*A s2 m2) n = 35		Criterion χ2 as amended by Yeats	Normalized value of Pearson's coefficient (C')
Inflammation degree in the body of the stomach	**Absolute value**	**%**	**Absolute value**	**%**		
Initial	12	37,5	28	80,0	2,571	0,243**
Pronouced	11	34,4	1	2,9	6,238	0,427*
Inflammation degree in the antrum						
Medium	2	6,2	16	45,7	6.487	0.413*
Pronounced	21	65,6	8	22,8	4,027	0,314**
Phenomena of hyperplasia	16	50,0	3	8,5	5,832	0,374**
Erosions of the mucous membrane	18	56,2	1	2,9	6,512	0,445*
Lymphoid duodenitis	11	34,4	3	8,5	2,841	0,256**

Connection strength: * – strong; ** – medium; *** – weak; **** – insignificant

caused by highly pathogenic *H. pylori* strains is characterized by the following features: almost every second patient (46.9%) has a pronounced process: in most cases (78.1%) hyperplastic, 25.0% of them show visual signs of atrophy. In patients of group 2, on the contrary, moderate or minor inflammation prevails (82.9%), more often superficial (54.3%), manifestations of the atrophic process are recorded in isolated cases (5.7%, $p < 0.05$). Macroscopic signs of severe duodenitis were significantly more often recorded in the main group (68.7% vs. 25.7%,

$p < 0.005$); lymphoid follicular bulbitis (21.9% vs. 5.7%, $p < 0.05$). The high severity and activity of the inflammatory process in patients of the main group was confirmed by a high frequency of detection of erosions in them (34.4% vs. 14.3%, $p<0.05$) and duodenal lymphoid follicles (37.5% vs. 12.5%, $p<0.01$). Correlation analysis showed that the presence of the cagA gene has the strongest effect on the inflammation severity in the mucous membrane of both the stomach body and the antrum. The presence of this virulence factor positively correlates with all indicators of the inflammatory process: severity ($R=+0.42$, $p< 0.001$), activity ($R=0.35$, $p<0.01$), signs of atrophy ($R=+0.35$, $p< 0.001$), erosions ($R =+0.34$, $p<0.001$) and lymphoid follicles ($R= +0.32$, $p<0.01$). The presence of other virulence factors in the H.pylori genome also directly correlates with the degree of chronic inflammation in the gastric mucosa. Simultaneously, the presence of several virulence factors increases the closeness of this relationship: the value of the Pearson's correlation coefficient increases to +0.45.

Thus, in destructive processes in the gastric mucosa, the detection frequency of H.pylori genes cagA, vacA s1 m1 is higher, and the presence of more than two genes of pathogenicity. The detection of mixed vacA genotypes indicates the infection with several H.pylori strains is more common in destructive gastritis and atrophy of the gastric mucosa, which suggests an increase in the pathogenic potential of the microorganism and the possibility of its genetic changes with prolonged persistence of infection.

Discussion

Research aimed at studying the *H.pylori* pathogenesis has shown that the degree of risk of disease is due to specific interactions between the pathogen itself (*H.pylori*) and the host organism. These interactions, in turn, are directly dependent on strain-specific bacterial factors and effects induced in the host (Chattopadhyay et al., 2015; Zhebrun, 2015; Maev et al., 2016; Venneman et al., 2018; Khan et al,2019; Bakhti, 2020). The *H.pylori* genome contains about 1600 genes and 62 of them are classified as "virulence genes" (Tkachenko & Suvorov, 2009; Maev et al., 2016).

Numerous studies conducted worldwide show a significant diversity in the frequency of *H.pylori* pathogenicity genes in people in different countries and ethnic groups, depending, in addition, on the diagnosis in the examined groups. So, cag genes in Central Europe are detected in 80.0% of those surveyed, in the Russian Federation in 81.5%, and in a number of countries in Asia and Latin America - only in 50.0% (Leanza et al., 2004; Cellini et al., 2006; Dharne et al., 2007; Basso et al., 2008; Daribi et al., 2009; Chattopadhyay et al., 2015; Orlov et al., 2015; Lucero et al., 2017). Belarusian researchers found a high incidence of *cag*A in diseases of the stomach and duodenum, which was 93.7% in duodenal ulcer and 78.8% in chronic gastritis (Yanovich et al., 2019). In Japan and Korea, the proportion of *cag*A-positive *H.pylori* strains is more than 90.0% (Kim et al., 2009). The prevalence of this gene is associated with a high incidence of stomach cancer in the population. Infection with *cag*A-positive strains other than distal gastric cancer is associated with an increased risk of severe atrophic gastritis. A variety of genetic variants of the bacterium is observed in various ethnic populations of the Russian Federation. Thus, *cagA*-positive *H.pylori* strains were diagnosed in 60.1% of Tuvans, in 59.8% of East Siberian Caucasians, in 43.8% of Evenks, and in 36.5% of the indigenous population of the Republic of Khakassia (Polivanova &Vshivkov, 2017; Grishchenko E.G. et al., 2017). However, there is evidence that each ethnic group has a specific type of *H.pylori cag* gene (Ageyeva et al., 2009; Muraviova, 2014).

VacA gene in the Asian population occurs only in 40.0-65.0% of cases, while in Latin America - in 75.0%. Detection of the vacAs1 allele varies slightly from 63.3% (in Asian countries) and 64.0% (in the Russian Federation) to 73.6% (in Latin America). In Northern and southern America, Central Europe and Australia, dominates *H.pylori* with the *vacA*s1, *ice*A genotype. The *ice*A1 genotype is found more often in the Russian Federation (71.5%), Europe (67.6%), and Asia (52.0%) than in Latin

America (36.5%). The *iceA* genotype, on the contrary, is almost 2 times more often detected in the Latin American population than in residents of Asian and European countries (52.0% and 67.6% respectively) (Leanza et al., 2004; Erzin et al., 2006; Basso et al., 2008; Homan M. Et al., 2009; Zhou et al., 2010; Vega et al., 2010; Chattopadhyay et al., 2015; Orlov et al., 2015). *H.pylori* strains predominate in Cuba – *vac*As1-positive (73.5%), *ice*A2-positive (53.3%), *cag*A-positive (55.9%) (Feliciano et al., 2015). Studies conducted in China have shown that there is a relationship between duodenal ulcer disease and the *ice*A gene, but no significant relationship was found between *ice*A2 and the clinical manifestations of the disease (Chung et al., 2010). In Russia, the distribution of *vac*Am1 is fairly uniform across all regions and varies from 20.0% in Kazan to 33.0% in Krasnoyarsk and Ufa (Orlov et al., 2015). The most common *H.pylori* genotype in Russia is *vac*As1m1. The association of infection with peptic ulcer disease was registered in the populations of Khakassia: it was found that in Caucasians the peptic ulcer disease is associated with s1 and s2 subtypes of *vac*A-positive *H.pylori* strains, and in khakasians with-*cag*A-positive *H.pylori* strains (Ageyeva et al., 2009).

The results of a study conducted in children in the Republic of Bashkortostan showed that the majority of patients with chronic gastritis were positive for the *ice*A gene, and the development of ulcers in childhood was associated with the *cag*A gene. The combination of *cag*A+*vac*As1+*bab*A2 genes was obligate for duodenal ulcer (Nijevitch et al., 2013).

The *bab*A2 gene is more common in patients with peptic ulcer disease and stomach cancer. According to a meta-analysis summarizing the results of 38 studies, it turned out that in Western countries, babA2 may contribute to an increased risk of developing duodenal ulcers. In contrast, in the Asian population, the presence of *bab*A2 has a slight association with the risk of stomach cancer, which requires further study (Chen et al., 2013; Kpoghomou et al., 2020). In Bulgaria and Turkey, the *bab*A gene was detected in the same percentage, while in Brazilian end Mexico, the detection rate of this gene is low (Erzin et al., 2006; Gatti et al., 2006; Boyanova et al., 2010; Román-Román, et al., 2017). In Russia, the *bab*A2 genotype was detected in 51.5% of clinical *H.pylori* isolates in the Rostov region, slightly less frequently in Ufa and Kazan (33.0%), and in Krasnoyarsk - in 100.0% of isolates (Orlov et al., 2015; Bereznyak et al., 2013; Akhtereeva et al, 2017; Sorokin et al., 2018). In our study, the *bab*A gene was detected in isolated cases and was associated with the most pronounced phenomena of inflammation of the gastric mucosa.

It should be noted that the outcomes of pathology depend not only on the pathogenicity factors of the bacterium, but also on the population-geographical zones, as well as the genetic features of macroorganism. However, despite the available data, the question of what factors or their combination induce *H.pylori* pathogenicity is still open.

Our study established certain features of the H.pylori genetic composition have been established in different forms of gastroduodenal pathology. The cagA vacAs1m1 or m2 genotypes were more often associated with erosive and ulcerative pathology, and for non-erosive gastroduodenitis, the *H.pylori vac*As1 or s2 genotype in conjunction with m2 was characteristic. In atrophic gastritis, *vac*As1 m2 variants and the mixed *vac*A s1/s2 genotype in conjunction with m2 are more often found. Probably, several H.pylori strains existed in patients with an atrophic process for many years. In the absence of visual signs of mucosal inflammation, *H.pylori cag*A *vac*A s2 m1 variants were found. Mixed *H.pylori vac*As1/s2 and *vac*Am1/m2 genotypes were more often identified in the older age (45-60 years).

Assessment of the relationship between the detection frequency of *H.pylori* genes responsible for the development of virulence factors with the clinical and endoscopic manifestations of the disease can contribute to understanding the mechanisms of pathogenesis of helicobacteriosis and help optimize the treatment of *H.pylori* - infection. The study of the genetic *H.pylori* variant will make it possible to identify persons infected with a microorganism with the highest pathogenic cytotoxic potential, who

need mandatory eradication therapy, regardless of clinical manifestations and endoscopic picture.

The results of this work serve as the basis for further research on epidemiological features and clinical variants of the *H.pylori* - infection.

Conclusions

Thus, in patients of a large city of Central Russia - Nizhny Novgorod, a predominantly "European" character of the pathogen population structure with a moderate content of the most pathogenic cagA, vacAs1-positive strains was detected. Colonization of the gastric mucosa by *H.pylori* strains with a genetic structure containing pathogenicity factors *cagA, vacA, babA, iceA* in chronic *H.pylori*-associated diseases is a factor in increasing the severity, activity and prevalence of the inflammatory process, the appearance of signs of atrophy of the gastric mucosa. The greatest influence on these indicators is exerted by the presence of *cag*A and *vac*As1 in the genome of the microorganism, as well as a combination of several pathogenicity factors.

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