

Frequency of *H. Pylori* Genotypes in Patients with Acid-Dependent Diseases

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Annotation: The article presents the results of a scientific study of the frequency of occurrence of genotypic variants of the virulent Ice A gene of *H. pylori* infection in patients with acid-dependent diseases of the digestive system, such as gastroesophageal reflux disease, chronic gastritis, peptic ulcer of the stomach and duodenum and their relationship with the pharmacotherapy of diseases.

Keywords: acid-dependent diseases of the digestive system, gastroesophageal reflux disease, chronic gastritis, peptic ulcer of the stomach and duodenum, virulent Ice A gene of *H.pylori*, *H.pylori* infection.

Relevance

It is known that the world's leading scientists consider *Helicobacter pylori* (*H. pylori*) infection as the main etiopathogenetic factor of acid-dependent diseases (ADD) of the digestive system, such as gastroesophagoreflux disease (GERD), chronic gastritis (CG), peptic ulcer disease (PUD) and duodenal ulcer disease (DU), chronic duodenitis and gastric maltlymphoma [3, 10].

H. pylori bacteria are capable of adhesion to epitheliocytes of the gastric mucosa (GMS), where microorganisms induce cytotoxicity products (pathogenicity factors), creating prerequisites for the realisation of their pathogenic potential [13].

The genome of *H. pylori* infection contains genes associated with increased virulence of bacteria: Cag A, Vac A, Bab A2 and Ice A genes. The protein encoded by the Cag A gene (cytotoxin - associated gene) integrates directly into gastric epitheliocytes, modulating the expression of IL - 8 genes, causing marked inflammatory changes in the gastric mucosa [1, 17]. Bab A protein encoded by Bab A2 gene (blood group antigen - binding adhesin) determines the density of *H. pylori* colonisation on gastric epitheliocytes [2, 6]. The Ice A gene product is induced directly by contact of the bacterium with epithelium (induced by contact with epithelium) and possibly determines the severity of infiltration and epithelial damage of the GI tract, which has an ethnic character [8, 16]. In modern literature, reasonable assumptions have been made about the connection of a number of virulent factors of *H. pylori* with the formation of the clinical course and outcome of the disease, as well as the influence on the development of comorbidities [4, 11].

The aim of this study was to investigate the frequency of genotypic variants of the virulent Ice A gene of *H.pylori* infection in patients with CPH and comparative analysis of pharmacotherapy depending on the presence of *H.pylori* bacterial genotypes.

Materials and Methods

A comprehensive examination of 120 patients with CPZ, including 37 patients with GERD, 43 patients with CH and 40 patients with JD, who were hospitalised in the department of gastroenterology and observation in 1-clinic of Bukhara OMPCB and in the treatment and diagnostic centre 'Mohi Hossa' was carried out. These patients were included in the main group of the study.

The control group included 42 healthy people with no history of GI diseases, who corresponded by sex and age to the main group of the study.

The age of patients with GI disease ranged from 18 to 79 years, men were 74 (62%), women - 46 (38%), i.e. men significantly prevailed in the sample of patients with GI disease.

In the course of molecular genetic studies, biological material was collected from the stomach of patients in the form of a biopsy for isolation of DNA of *H. pylori* bacteria. Real-time PCR amplification was performed. DNA isolation was performed according to the instructions of the DNA/RNA isolation kit (Ribo-prep, Interlabservice, Russia). The isolated DNA was used for real-time polymerase chain reaction. The obtained results were documented in the form of curve growth using two detectors FAM and HEX in graphical mode on the appropriate programme.

Statistical processing of the results of the study was carried out by the generally accepted method using Student's criterion

Results and Discussion

It is well known that the virulent Ice A gene of *H.pylori* infection has 3 genotypes: Ice A1/Ice A1, Ice A1/Ice A2 and Ice A2/Ice A2 [12, 15]. When we studied the comparative characteristic of the occurrence of genotypic variants of *H.pylori* bacteria in patients with CPH, it turned out (Fig. 1) that in patients with GERD, the Ice A1/Ice A1 genotype occurs more - about 66%, while the Ice A1/Ice A2 and Ice A2/Ice A2 genotypes are detected in the range of 15% and 20%. In addition, in patients with CH, the studied genotypic variants of the virulent Ice A gene of the *H.pylori* bacterium were determined in the order: genotype Ice A1/Ice A1 in every second patient, genotype Ice A1/Ice A2 in every seventh patient and genotype Ice A2/Ice A2 in every third patient. Also, the Ice A1/Ice A1 genotype was detected in the highest number of patients with IBD - about 69%, while the Ice A1/Ice A2 genotype was detected in 20% and the Ice A2/Ice A2 genotype in 11% of cases.

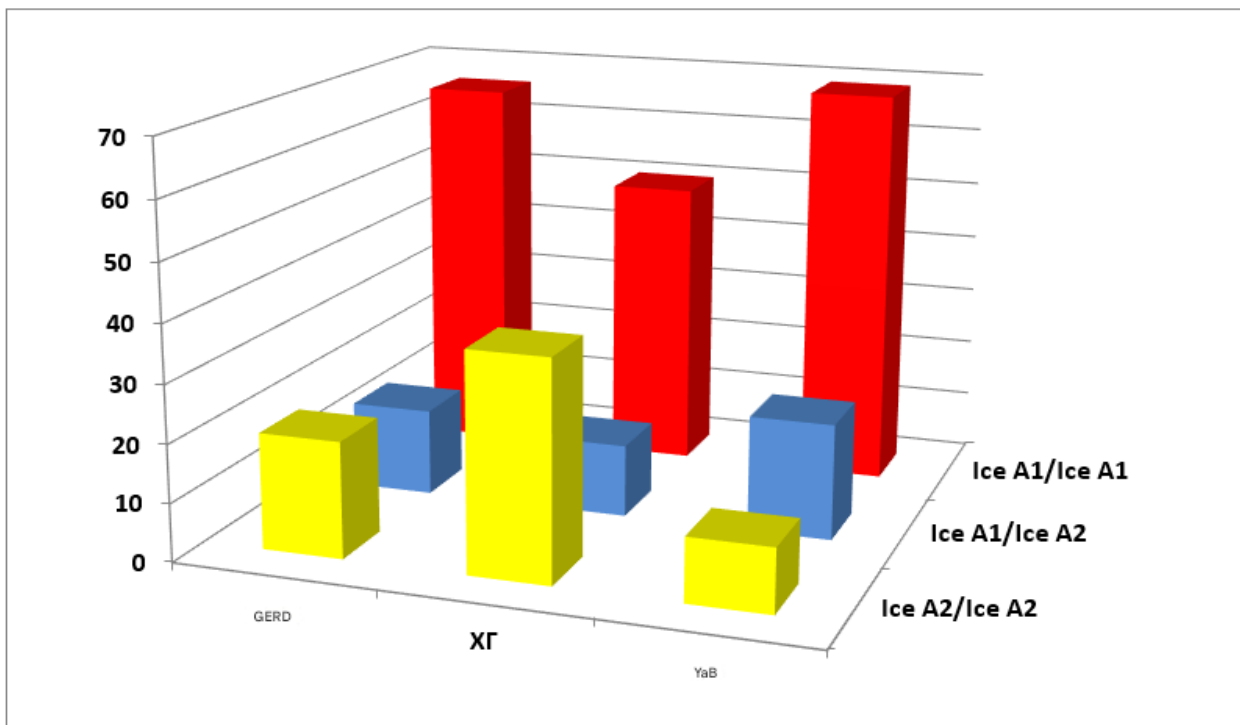


Figure 1: Frequency of genotypes of the virulent Ice A gene of *H.pylori* in patients with CPH (%)

Modern pharmacotherapy of CPD includes eradication therapy, where the first-line drugs are antibacterial agents and proton pump inhibitors (PPIs) [5, 7, 9]. Along with the above, we studied the structure of applied drugs for pharmacotherapy of CPZ depending on the geotypes of virulent gene Ice A of *H.pylori* infection (Fig. 2). Antibacterial drugs in the form of clarithromycin, amoxicillin, levofloxacin, metronidazole, ceftriaxone and cloxacillin were used in the greatest number - from 58% to 100% of cases against *H.pylori* bacteria with Ice A1/Ice A1 genotype, while against other genotypes of infection antibacterial agents were used in the smallest number - up to 28% or were not applied.

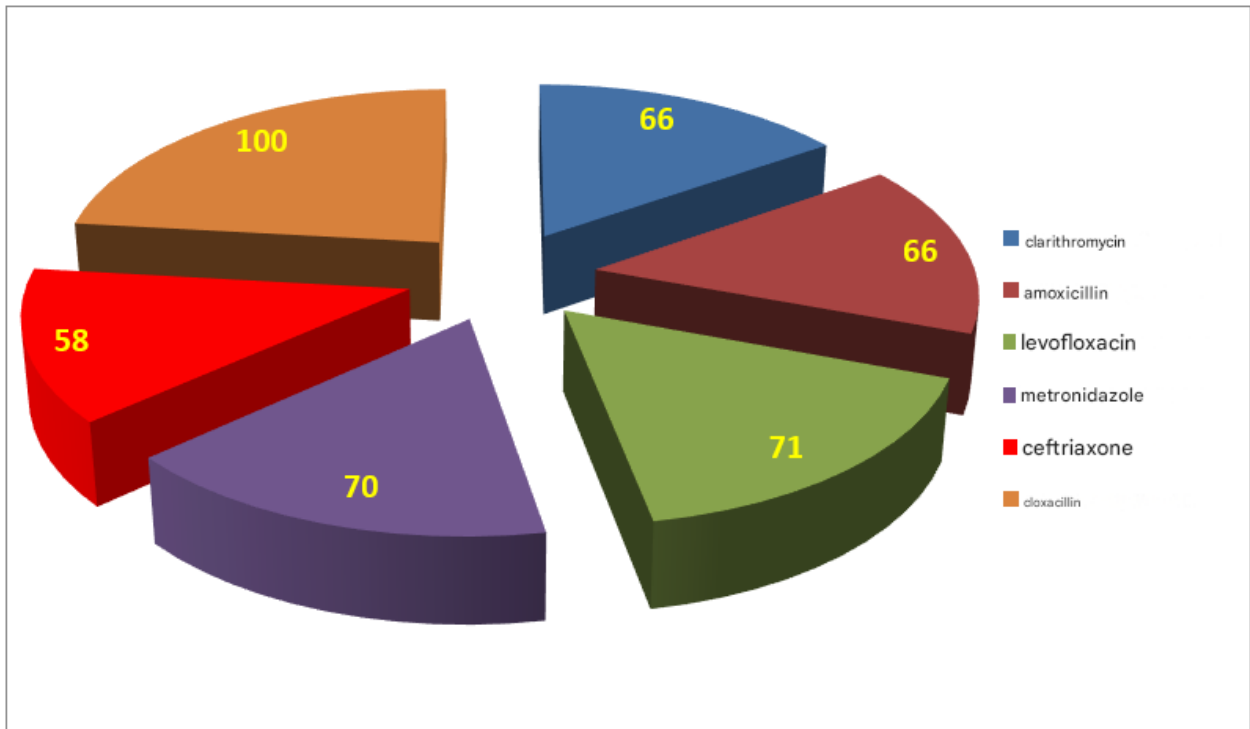


Figure 2: Frequency of antibacterial use in the presence of Ice A1/Ice A1 genotype of H.pylori bacteria (%)

Along with antibacterial drugs, the pharmacotherapy of CPZ includes drugs from the PPI group [14], in which the drugs omeprozole, pantaprozole and lansoprazole were used (Fig. 3).

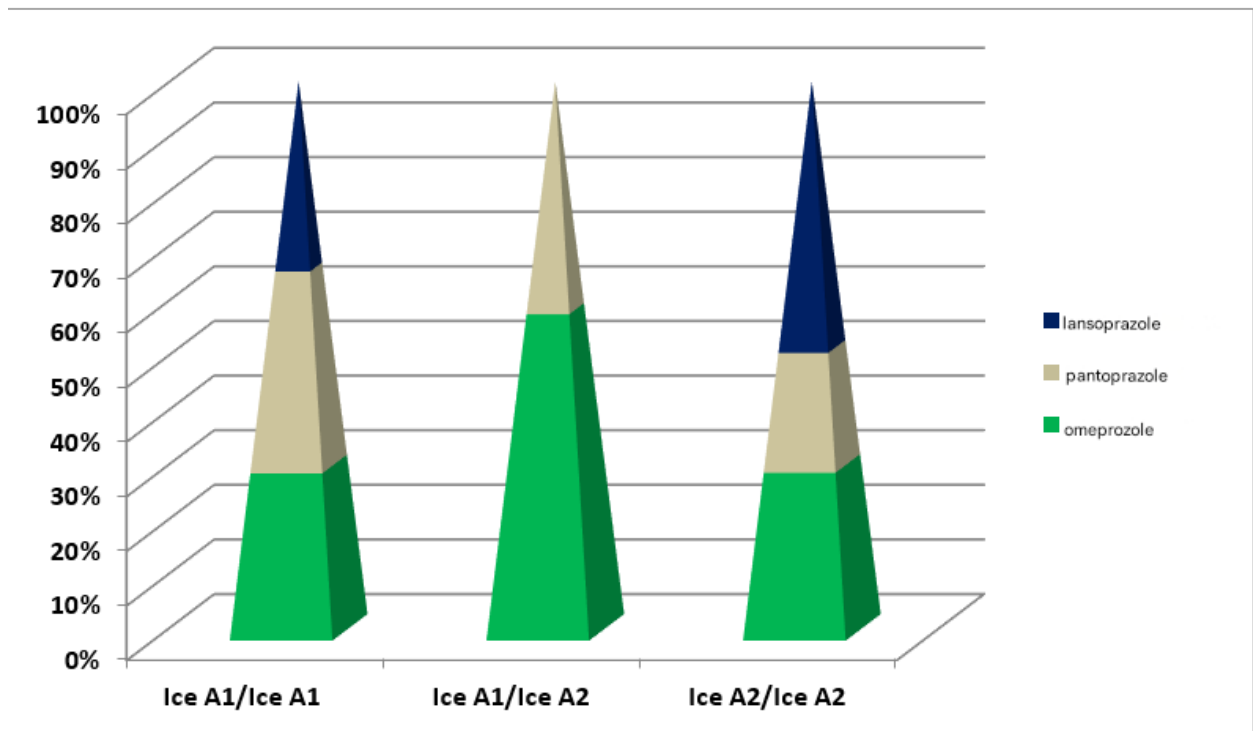


Figure 3: Relationship between frequency of PPI use and genotypes of the virulent Ice A gene of H.pylori in patients with CPH

When studying the relationship between the use of PPIs and genotypes of microorganisms it was revealed that in the presence of Ice A1/Ice A1 genotype of H.pylori infection about 71% of patients with CPZ received pantoprazole, about 67% received lansoprazole and about 59% of patients with CPZ received omeprozole, while in the presence of other genotypic variants PPIs were used in the

least amount. It should be noted that in the presence of Ice A2/Ice A1 genotype of H.pylori infection PPI lansoprazole was used in single cases or was not used.

Conclusion

Thus, it should be noted that the Ice A1/Ice A1 genotype of the virulent Ice A gene of H.pylori infection is more often detected in patients with GERD and JD. It can be assumed that Ice A1/Ice A1 genotype of H.pylori bacteria contribute to the progression of CPP.

In addition, eradication therapy in the greatest number was carried out in patients with the presence of Ice A1/Ice A1 genotype of H.pylori, which indicates a rapid clinical course of CPP in patients with Helicobacteriosis.

We think that identification of the presence of H.pylori infection genotypes contributes to the most optimised treatment of CPP in the form of personalisation of pharmacotherapy, to improve the efficacy and safety of treatment.

Reference:

1. Baryshnikova N.V., Suvorov A.N., Tkachenko E.I., Uspensky Yu.P. The role of genetic features of Helicobacter pylori in the pathogenesis of digestive system diseases: from theory to practice // EIKG. 2008. No. 6. URL: <https://cyberleninka.ru/article/n/rol-geneticheskikh-osobennostey-helicobacter-pylori-v-patogeneze-zabolevaniy-organov-pischevareniya-ot-teorii-k-praktike-1>.
2. Isaeva G.Sh., Valieva R.I. Biological properties and virulence of Helicobacter pylori // KMAKH. 2018. No. 1. URL: <https://cyberleninka.ru/article/n/biologicheskie-svoystva-i-virulentnost-helicobacter-pylori>.
3. Klichova F.K., Mavlyanov I.R., Musaeva D.M. Influence of genes on pharmacotherapy of ulcer disease // New Day in Medicine. – 2020. – No. 2. – P. 147–150.
4. Maksimov M.L. et al. General issues of clinical pharmacology and pharmacotherapy. – 2020.
5. Maksimov M.L. et al. Clinical pharmacology and rational pharmacotherapy for practicing doctors. – 2021.
6. Mishkina T.V., Aleksandrova V.A., Suvorov A.N. Influence of various H. pylori genotypes on clinical-endoscopic and morphological manifestations of chronic gastroduodenal diseases in children and adolescents. Pediatrics 2007, 86(5):28-32.
7. Musaeva D.M. Personalization of pharmacotherapy – a demand of the times // ISCHLH. 2022. No. 1. URL: <https://cyberleninka.ru/article/n/personifikatsiya-farmakoterapii-trebovanie-vremeni>.
8. Musaeva D.M., Sagdullaeva G.U. Helicobacter pylori and its significance in the onset and course of gastroduodenal diseases // Integrative Dentistry and Maxillofacial Surgery. – 2022. – Vol. 1. – No. 2. – P. 69–74.
9. Musaeva D.M., Ochilova G.S. Personalized pharmacotherapy of chronic gastritis // Pharmacology of Different Countries. – 2020. – P. 116–119.
10. Nizhevich A.A., Ahmadiyeva E.N., Kuchina E.S., Tuigunov M.M., Sataev V.U. Regional genotypes of Helicobacter pylori among children with gastroduodenal diseases in the Republic of Bashkortostan // Medical Bulletin of the South of Russia. 2013. No. 2. URL: <https://cyberleninka.ru/article/n/regionalnye-genotipy-helicobacter-pylori-sredi-detey-s-gastroduodenalnymi-zabolevaniyami-v-respublike-bashkortostan>.
11. Ochilova G.S. Patient genotype as the main indicator for choosing effective and safe pharmacotherapy for chronic gastritis // Bulletin of Science and Education. – 2021. – No. 13-1 (116). – P. 99–104.
12. Fayzullina R.A., Abdullina E.V. Pathogenicity and virulence factors of Helicobacter pylori and their role in the development of Helicobacter-associated gastroduodenal pathology // PM. 2011.

- No. 48. URL: <https://cyberleninka.ru/article/n/factory-patogennosti-i-virulentnosti-helicobacter-pylori-i-ih-rol-v-razviti-helikobakter-assotsirovannoy-gastroduodenalnoy-patologii>.
13. Faydenko G.D. Helicobacter pylori infection: results of 20 years of studying its pathogenicity // Bulletin of KhNU named after V.N. Karazin. Series Medicine. 2004. No. 7 (614). URL: <https://cyberleninka.ru/article/n/infektsiya-helicobacter-pylori-itogi-20-letnego-izucheniya-ee-patogennosti>.
 14. Kamilovich O.A. Features of the relationship of the carrier of allelic-genotype variants of the CYP2C19 gene in patients with chronic gastritis // Journal of Innovation, Creativity, and Art. – 2022. – Vol. 1. – P. 20–26.
 15. Kusters J.G., Arnoud H.M. van Vliet, Kuipers E.J. Pathogenesis of Helicobacter pylori Infection. Clin Microbiol Rev. 2006 July; 19(3): 449–490.
 16. Tham K.T., Peek R.M.Jr., Atherton J. et al. Helicobacter pylori genotypes, host factors, and gastric mucosal histopathology in peptic ulcer disease. Hum. Pathol. 2001, 32(3):264–273.
 17. Umit H., Tezel A., Bukavaz S., et al. The relationship between virulence factors of Helicobacter pylori and severity of gastritis in infected patients. Dig. Dis. Sci. 2009, 54(1):103–110.