H. pylori infection and ABH and Lewis blood groups

Relation between ABH and Lewis blood groups and Helicobacter pylori infection in patients with gastric pathology

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Introduction

Helicobacter pylori (H. pylori) is a gram-negative bacillus, etiologically involved in the gastroduodenal pathogenesis and infecting about 50% of the world population [1–8]. Most infected individuals are asymptomatic, however, only a minority develops severe complications, such as peptic ulcer, gastric adenocarcinoma and mucous-associated lymphoid tissue (MALT) [1, 2, 4–13]. Recent studies associate H. pylori infection with other diseases, such as iron deficiency anemia, coronary heart disease and chronic renal failure [7, 14].

This bacteria establishes a great adaptive relation in the human stomach, in a co-evolutionary environment [1]. Therefore, there are several factors that explain the virulence developed by H. pylori, including urease synthesis in order to neutralize the acid amibience and digestive enzymes in the gastric mucosa [1, 6, 10]. In addition, geographic differences [9], HIV infection, sex, age, nutritional status, alcohol consumption and smoking, as well as socio-economic conditions constitute risk factors for the microorganism infection [5, 8, 15, 16].

In another perspective, different virulence factors are referenced in H. pylori infection, which influence the severity of infection and thus the pathology manifested by the patient. Those virulence factors include cytoxin associated gene A (CagA), vacuolating cytoxin (VacA), blood group antigen-binding adhesion (BabA), protein induced by contact with epithelium (IceA) and outer immunatory protein (OipA). In this context, the CagA protein, when expressed, stimulates the immunatory state of the gastric mucosa through polymorphonuclear cell infiltration and increased production of inflammatory cytokines such as interleukin-8 (IL-8) [6]. CagA also promotes abnormal proliferation and movement of gastric epithelial cells. When VacA is expressed, H. pylori develops vacuoles responsible for the increased intracellular permeability of the gastric epithelium cells membrane, causing apoptosis and release of proinflammatory cytokines, amplifying the effect produced [2, 3, 6, 13].

During the process of human gastric epithelium colonization, H. pylori binds to gastric mucins, in order to avoid the acidity of the gastric epithelium [17]. So, the binding that exhibits greater efficiency occurs at the Lewis b mucin and H antigens type I. From this, arises the adherence as one of the fundamental aspects for the H. pylori virulence, being the same for H and Lewis b (Leb) antigens, from the ABH and Lewis systems, respectively, in gastric epithelium, mediated by BabA, which promotes a solid adherence of the bacteria to gastric epithelium cells. In this context, the functional receptors with promote that some bacterial adhesion include ABH and Lewis b fucosilated antigens and sialic acid-binding adhesin (SabA) [5, 7, 11, 12, 14, 18, 19].

Although several studies have been developed over the last years, the relation between the presence of gastric pathology, infection by H. pylori and the expression of ABH and Lewis antigens is not clarified yet. Therefore, this study intended to associate the expression of these antigens in patients with gastroduodenal pathology, carriers or patients with H. pylori infection, relating them with demographic factors characteristic of each individual studied.

Abstract

Introduction: Helicobacter pylori is a human pathogen that causes chronic gastritis and peptic ulcers. Epidemiological studies demonstrated that individuals with the blood group O and presence of the Lewis b antigen are more likely to develop gastric disease, since they mediate the attachment of H. pylori to human gastric mucosa.

Aim: The aim of this study was to evaluate the interrelation between Lewis phenotype, ABH blood group, H. pylori infection and gastric disease occurrence.

Material and Methods: The population of this study consisted of 114 patients (72 men, 42 women) who attended the Gastroenterology Service of HDEF, E.P.E., and CHC, E.P.E. ABO blood groups and Lewis(a,b) phenotype were determined by gel-test methodology. Antibodies (lgG) against H. pylori were determined by a chemiluminescence method.

Results: In a total of 114 patients included in this study (age: mean 46 ± 18.80; 72 males and 42 females). 69.2% had anti-H. pylori IgG antibodies. The differences between the frequencies of the ABO blood group phenotypes among infected (A 27.2%; B 2.6%; AB 0.9%; 0 36.0%) and uninfected patients (A 16.7%; B 4.4%; AB 0.0%; O 12.3%) are not statistically significant, but indicate a pattern. For the Lewis phenotypes, the differences among infected (Lea–b–) 55.8%; Lea+–b– 4.4%; Lea–b+ 3.5%) and uninfected patients (Lea–b– 19.3%; Lea+–b– 9.6%; Lea–b+ 4.4%) were statistically significant (p-value = 0.001).

Conclusion: These results suggest that H. pylori infection can be related to O and A blood groups and Lea–b+ phenotype, which could be useful to characterize the individual risk to develop gastric disease.

Keywords: Helicobacter pylori; gastric disease; ABH and Lewis blood groups
Table I: Age of patients

<table>
<thead>
<tr>
<th>Age of patients</th>
<th>Mean</th>
<th>Maximum age</th>
<th>Minimum age</th>
<th>Standard Deviation</th>
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<td></td>
<td>64.46</td>
<td>93 years</td>
<td>24 years</td>
<td>18.80</td>
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Material and Methods

Study population
This study was conducted at the District Hospital of Figueira da Foz, E.P.E. (HDDF, E.P.E.), and at the Hospital of Coimbra, E.P.E. (HC, E.P.E.). Sample processing were performed at the Laboratory of the Department Clinical Analysis and Public Health from the College of Health Technology of Coimbra. 114 patients of the Gastroenterology Service of both hospitals were studied.

The study was confidential and done according to the principles of the Declaration of Helsinki.

Determination of the blood group ABO and Lewis phenotype
The determination of the blood group ABO and Lewis phenotype were conducted using a gel-test methodology, from peripheral blood samples collected into tubes with ethylenediaminetetraacetic acid tripotassium (EDTA K3). Each sample was assigned a different and confidential number. This determination was made by using cards DiaClon ABO/D + Reverse grouping for patients and cards DiaClon Anti-Lea/DiaClon Anti-Leb (DiaMed, Cressier, Switzerland).

The evaluation of the parameters age, sex, clinical information of patients, presence or absence of H. pylori infection, as well as pathology gastric associated, were obtained from the clinical diagnosis.

Determination of antibodies IgG anti-H. pylori
The determination of the Immunoglobulin G (IgG) anti-H. pylori was executed by a chemiluminescence method, using the H. pylori test in the equipment IMMULITE 1000 Analyzer (Siemens, Los Angeles, U.S.A.), from the peripheral blood samples collected in tubes with EDTA K3 from each patient. The result is expressed in U/mL. Values less than 0.9 U/mL mean absence of H. pylori; values between 0.9 and 1.1 U/mL are questionable and values above 1.1 U/mL express a positive result.

The results obtained were introduced into a database and the statistical analysis was performed using the software Statistical Package for Social Sciences 18.0 (SPSS Inc., Chicago, E.U.A.) for Windows. We used descriptive statistics and the chi-square test of independence. The results were considered statistically significant when p-value <0.05.

Results
From the universe of patients that attended the Gastroenterology Service of the HDDF, E.P.E., as well as the HC, E.P.E., 114 patients participated in this study, 72 (63.2%) males and 42 (36.8%) females, with a mean age of 64.46 (±18.80) (Tab. 1).

Concerning the ABO blood system, 55 (48.2%) of the patients presented the 0 phenotype, 50 (43.9%) belonged to group A, 8 (7.0%) to group B and, finally, 1 (0.9%) presented the AB phenotype (Fig. 1).

For the Lewis system, 89 (78.1%) of the participants presented the phenotype Le(a–b–). Beyond that, with less frequency, 15 (14.0%) participants had phenotype Le(a+b–) and, finally, 7 (6.9%) had phenotype Le(a–b+) (Fig. 2).

For the presence/absence of colonization by H. pylori in the studied population, 76 (66.7%) of the patients presented positivity for the presence of IgG antibodies anti-H. pylori, while 38 (33.3%) were negative for the research in question (Fig. 3).

When combining the data relative to the presence of H. pylori and ABO phenotypes, we observed 41 (36.0%) cases where the presence of antibodies anti-H. pylori appeared together with the presence of phenotype 0, in 31 (27.2%) cases it appeared together with phenotype A, in 3 (2.6%) cases with phenotype B and 1 (0.9%) case with phenotype AB. In contrast, for the absence of antibodies anti-H. pylori before the different ABO phenotypes, 14 (12.3%) cases emerged with phenotype 0, 19 (16.7%) with phenotype A, 5 (4.4%) with phenotype B and, finally, 0 (0.0%) with phenotype AB (Fig. 4).
In another perspective, evaluating the number of cases that appeared with the presence of antibodies anti-*H. pylori* and Lewis phenotypes, we observed 67 (58.8%) cases with phenotype Le(a−b+), 5 (4.4%) with phenotype Le(a+b−) and finally 4 (3.5%) with phenotype Le(a−b−). For the absence of antibodies anti-*H. pylori*, 22 (19.3%) patients showed phenotype Le(a−b+), 11 (9.6%) phenotype Le(a+b−) and finally 5 (4.4%) phenotype Le(a−b−) (p-value = 0.001) (Fig. 5).

Gathering the various results obtained before the presence/absence of antibodies anti-*H. pylori*, the AB0 phenotype and the Lewis phenotype, it is possible to refer the number of the cases that appeared when combining the three factors in consideration. Therefore, when the presence of antibodies anti-*H. pylori* occurred, there were in total 36 (47.4%) patients with phenotype 0 and Le(a−b+) and 31 (40.8%) of the cohort of group A, B and AB, with the same Lewis phenotype. Furthermore, for the phenotype Le(a−b−), we observed 3 (3.9%) patients with group 0 and 2 (2.6%) of the cohort of group A, B and AB. For the phenotype Le(a−b−), we have 2 (2.6%) with the group 0, as for all A, B and AB (Fig. 6 and Tab. II).

Inversely, when the antibodies anti-*H. pylori* are absent, we observed a total of 9 (23.7%) individuals with group 0 and 13 (34.2%) of the cohort A, B and AB, all with phenotype Le(a−b+). In addition, for phenotype Le(a+b−) there were 4 (10.5%) patients with group 0 and 7 (18.4%) of the cohort A, B and AB. Finally, relatively to the phenotype Le(a−b−), we observed 1 (2.6%) with the group 0 and 4 (10.5%) from the cohort A, B and AB (Fig. 7 and Tab. III).

**Discussion**

The comparison of the results obtained in this study with other similar should be made carefully, since it is necessary to take into account the differences in the populations studied, once investigations in different populations have shown remarkable genomic diversity by *H. pylori*.

The prevalence of antibodies IgG for *H. pylori* among the study population was 66.7%. It was found that the prevalence of cases of individuals who attended the Gastroenterology Service increases with age, with age mean 64.46 years. Furthermore, in relation to the sex of patients, there was a high incidence in males (63.2%; 72) compared to females (36.8%; 42). Similar results have been reported by Moges et al, indicating a high frequency of infection in the older population [5].

When the Lewis system was evaluated, there was a high number of cases in which the individu-
als presented phenotype Le(a−b+), representing 78.1% (89). The percentage of cases with phenotype Le(a+b−) and Le(a−b−) is located in 14.0% (16) and 7.9% (9), respectively. This reveals, in this context, a clear predominance of the phenotype Le(a−b+) in the study population. Moreover, when correlated with the presence/absence of H.pylori, it was found that the presence of phenotype Le(a−b+) revealed a positive result to H. pylori – 58.8% (67) of 78.1% (89) –, which was statistically significant (p-value = 0.001). As reported in several studies, these observations support the hypothesis that patients with phenotype Le(a−b+) have high susceptibility to infection by H. pylori [1, 15].

The ABO blood group system of the 114 patients who participated in the study was also evaluated. It’s possible to verify a prevalence of individuals in group O and A, representing 48.2% (55) and 43.9% (50), respectively, of all subjects. However, the highest percentage is represented for individuals with phenotype O. When these values are associated with the presence of antibodies anti-H. pylori, the data showed a higher percentage for the phenotypes 0 and A, with 74.5% for phenotype 0, in a total of 55 cases of individuals with this phenotype and 62.0% for the phenotype A, in a total of 50 patients who had group A. For the phenotypes B and AB, the number of cases, either for the presence or absence of H. pylori, was reduced, so it is not possible to have the same power of discrimination for the same blood groups. Given this, it is possible to infer a higher prevalence of the phenotype 0 and A in the study population and also establish a relation between the presence of antibodies anti-H. pylori and the susceptibility of these individuals to that same infection.

Therefore, as reported by de Mattos et al., the basis of several investigations initially appears as the hypothesis that individuals with group 0 show high prevalence of infection at a gastric level, promoted by H. pylori [1, 18]. However, due to the results obtained, either in this study or in others, an increased risk for the existence of gastric pathology in patients with group A, in addition to individuals with group 0 was verified [5, 11, 17].

Although the ABH and Lewis antigens were evaluated separately in several observations [11, 12, 18], this study became possible through the combination of these factors with the presence of infection by the gram-negative bacilli. For the presence of antibodies anti-H. pylori, there were in total 36 (47.4%) patients with phenotype 0 and phenotype Le(a−b+) and 31 (40.8%) of the cohort of group A, B and AB, with the same Lewis phenotype. Furthermore, for the phenotype Le(a+b−), we observed 3 (3.9%) patients with group 0 and 2 (2.6%) of the cohort of group A, B and AB. For the phenotype Le(a−b−), we have 2 (2.6%) with the group 0, as for all A, B and AB. So, although it’s possible to describe the number of cases, there isn’t a pattern associated.

However, when the antibodies anti-H. pylori were absent, we observed a total of 9 (23.7%) individuals with group 0 and 13 (34.2%) of the cohort A, B and AB, both with phenotype Le(a−b+). In addition, for phenotype Le(a+b−) there were 4 (10.5%) patients with group 0 and 7 (18.4%) of the cohort A, B and AB. Finally, in relation to the phenotype Le(a−b−), were observed 1 (2.6%) and 4 (10.5%) for the group 0 and to the cohort A, B and AB, respectively. As it occurs in this context for positive H. pylori, it is possible to describe the number of cases, but there is no pattern of association.

**Conclusion**

Based on the results obtained, we conclude that both O and A phenotype for the blood group ABO, as well as the presence of the Le(a−b+) phenotype for the Lewis system constitute risk factors that favor the colonization of the gastric mucosa, promoted by H. pylori.
To answer some discrepancies and to find solutions to issues that remain open, future investigations should evaluate other aspects, in addition with these factors considered, such as social status, geographic factors, environmental factors, host immune status, as well as the virulence factors of *H. pylori*.

**References**


