Original Article
Role of the Lewis and ABO Blood Group Antigens in *Helicobacter pylori* Infection

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Abstract

**Background:** *Helicobacter pylori* (*H. pylori*) infection is a major risk factor for chronic gastritis, and gastric cancer. Some findings show increased frequency of these diseases in O blood group and secretors (expressing Le⁷ antigen), but some other findings have not characterized any relation between blood groups and this infection. The fact that *H. pylori* infection and gastric cancer are common in Iran, the assessment of the pathogenesis of this infection in relation to these blood groups could be valuable.

**Methods:** In a cross sectional study, we determined the ABO and Lewis, Leᵃ and Leᵇ, blood group antigens by the tube method and anti-*H. pylori* IgG by enzyme linked immunosorbent assay in 171 Iranian blood donors, Mashhad, Iran, during 2010. Difference between the Lewis and ABO phenotypes with *H. pylori* infection were tested by chi-square test. A P-value < 0.05 was considered to be significant.

**Results:** *H. pylori* infection was determined in 76.6% of persons (n=131). The most common Phenotype in the ABO blood groups was O (33.9%) and in the Lewis blood groups was Le⁺ (54.7%). The frequencies of the ABO, Lewis and secretion phenotypes didn’t reveal any significant differences between infected and non-infected persons.

**Conclusion:** We didn’t find any significant relationship between the Lewis, ABO and secretion phenotypes with *H. pylori* infection.

**Keywords:** ABO blood groups, Lewis, Helicobacter pylori, secretor phenotype

Introduction

*Helicobacter pylori* (*H. pylori*) infection is a high prevalence infection worldwide; nonetheless, it is more common in underdeveloped and developing countries than developed countries (1-3). Infection is more common in adults with a prevalence of more than 90% in some countries (4). In Iran, Prevalence of this infection in adults has been reported about
80% (5, 6). *H. pylori* Infection is a major risk factor for chronic gastritis, peptic ulcer and gastric cancer (7-9), the most common cancer in north and northwest Iran (6).

Lewis (Le) antigens like ABO blood group antigens are expressed in fluids and tissues such as endothelium, and bowel mucosa. *H. pylori* express several lipopolysaccharides on its outer membrane which cause adhesion of bacteria to gastric epithelium and allow persistent colonization (10). *H. pylori* binds to H and Le\(^b\) antigens in gastric mucosa; this probably explains increased incidence of gastritis and gastric cancer in O blood group and secretors (expressing Le\(^b\) antigen) (11, 12). However, some other findings have not observed any relation between *H. pylori* infection and the Lewis (4) and ABO blood groups (13). Therefore, data shows the associations of the Lewis and ABO blood groups with *H. pylori* infection are controversial. In addition, we have some heterogeneity in expression of the outer membrane protein especially Bab A among different *H. pylori* strains and therefore, in the capacity to bind to Lewis b antigen on the surface of gastric epithelial cells. This may be a factor that describes some differences in clinical outcomes of this infection (14). The fact that *H. pylori* infection and gastric carcinoma are the high prevalence diseases in Iran, the assessment of the pathogenesis of this infection in relation to these blood groups could be valuable.

**Materials and Methods**

This cross sectional study was financially supported and ethically approved by the research vice chancellor, Mashhad university medical sciences, Iran. The study population was 171 adult healthy blood donors Admitted in Imam Reza teaching hospital and blood transfusion center, Mashhad (a large city located in northeast Iran) during 2010 years. The subjects with positive direct globulin test, on treatment of *H. pylori* infection or history of blood transfusion during the last three months before admission were excluded from the study. We also exclude lipaemic, icteric and hemolytic samples. After obtaining informed consent, 2 mL blood with ethylenediaminetetraacetic acid (EDTA) anticoagulant for typing blood groups and 2 mL blood without anticoagulant for serologic evaluation of *H. pylori* were taken from blood donors. Red cell phenotyping was performed using commercial monoclonal antibodies by direct agglutination using tube method according to manufacturer directions (biotest, Germany). Based on whether Le\(^b\) antigen expression or not, persons were divided to secretor and non-secretor group. Because secretary status wasn’t obvious in Le (a-b-) phenotype these cases were ignored in this dividing (11).

Serum samples were tested for anti-*H. pylori* IgG by enzyme linked immunosorbent assay using kit supplied by Euroimmun (Lubeck, GE). According to kit instruction this test hasn’t any cross reactivity; however, high lipaemic, icteric and hemolytic samples may influence the results.

**Statistical analysis**

Initially, prevalence of Le\(^a\) and Le\(^b\) antigens, the Lewis phenotypes and *H. pylori* infection were described and then difference between the Lewis antigens and the Lewis and ABO phenotypes with *H. pylori* infection were tested by Fisher’s exact test. A P-value < 0.05 was considered to be significant. All results were analyzed by SPSS (version 16).

**Results**

We evaluated 171 individuals including 94.3% males and 5.7% females with age range of 19-61 years and mean (SD) of 33.8 (1) years. *H. pylori* infection was determined in 76.6% of persons (n=131). No significant difference was observed between sex and *H. pylori* infection. The most common Phenotype in the ABO blood groups was O (33.9%) followed by A (29.5%), B (28.7%) and AB (7.9%) and the most common phenotype in the Lewis blood groups was Le (a-b+) (54.7%) followed by Le (a+b-) (34.9%), Le (a+b+) (8.9%) and Le (a-b-)
(1.6%). Of 169 donors, 106 cases (62.7%) were secretors and secrete Le and ABO substances in secretions.

As showed in the Table 1, the frequencies of the ABO, Lewis and secretion phenotypes didn’t exhibit any significant differences between infected and non-infected persons. Le (a-b-) phenotype was rare (n=2) and also secretion status can’t inferred from it; therefore, it was disregarded in the Lewis and the secretion phenotype analysis.

Discussion

The blood group antigens are important in pathogenesis of some diseases (15, 16). The Lewis antigens are biochemically related to ABO blood groups. The secretor gene (Se), encodes a fucosyltransferase that adds fucose to the terminal galactose of the type 1 precursor chain forming type 1 H chain. The Le gene encodes an enzyme can add fucose to type 1 precursor chains forming the Le\textsuperscript{a} antigen or add fucose to type 1 H chain forming the Le\textsuperscript{b} antigen. Persons with lacking the Se gene, non-secretors, can’t produce type 1H chain and antigens derived from it, Le\textsuperscript{b} (11, 12, 17); therefore, non-secretors can only express the Le\textsuperscript{a} antigen. For this reason we can also use saliva for determination of lewis antigens in adults.

Some findings show \textit{H. pylori} binds to H and Le\textsuperscript{b} antigens (secretors) in gastric mucosa. Blood group antigen b-binding adhesion on the outer membrane of \textit{H. pylori} mediates binding of \textit{H. pylori} to Le\textsuperscript{b} antigens expressed on gastric mucosa (10, 18); this probably cause increased incidence of gastritis and gastric cancer in the O blood group and Le (a-b+) phenotype (12).

Despite it, we didn’t observe any significant differences between the Lewis and ABO blood groups and secretion status with \textit{H. pylori} infection (Table 1). Frequencies of ABO Blood group phenotypes in Iran have been reported in the following order: O in 37.62%, A in 30.25%, B in 24.36% and AB in 7.77% of population (19) that is similar to our result and other research from Iran (20). Heneghan et al. determined the Lewis and ABO blood group phenotypes of 207 patients undergoing upper endoscopy and like our results didn’t observe any significant association between these blood groups and secretor status with \textit{H. pylori} infection (17). Mattos et al. studied the frequencies of the ABO and Lewis blood group phenotypes and secretor status in patients infected or uninfected by \textit{H. pylori} by using breath and urea tests. They showed that \textit{H. pylori} is more common in the O blood group patients but they didn’t characterize a significant differences between the Lewis blood groups and secretor status with this infection (4).

A study by Rothenbacher et al. investigated role of the Lewis antigens on current \textit{H. pylori} infection on 712 women with different nationality admitted in obstetric clinic department of Gynecology and Obstetrics at the University of Ulm (Germany) between November 2000 and November 2001; in contrast to many other reports, they showed higher frequency of \textit{H. pylori} infection in Le (a+b-) phenotype compared with Le (a-b+). Therefore, they presented this hypothesis that individuals with a Le (a+b-) phenotype secrete only Le\textsuperscript{a}, and no other ABH substances, in secretion such as gastric fluids; In contrast, individuals with a Le (a–b+) phenotype (secretors) secrete Le\textsuperscript{a} as well as Le\textsuperscript{b} and ABH substances in body fluids, so it is possible that Le\textsuperscript{b} present in other body secretions such as gastric mucus may bind to specific glycoproteins of \textit{H. pylori} and hinder the binding of \textit{H. pylori} to the gastric mucosa (10).

Recent findings on strains of \textit{H. pylori} from different areas of the world have revealed that Strains differed about 1500-fold in binding affinities, and diversity in related to babA gene sequences (14, 16, 21). Not all strains are so specific for O and Le\textsuperscript{b}; many strains from outside South America having binding capabilities for A and Le\textsuperscript{b} in addition to O and Le\textsuperscript{b}. For example, Peruvian strains are related to Spanish but not to Asian strains (16, 21). A study by Con et al. (2010) by genotyping of 95 Costa Rican and 95 Japanese \textit{H. pylori} isolates revealed a higher frequency of babA2 in Japan (96.8%) than in Costa Rica (73.7%). In comparison, babA2/B was higher in Costa Rica (11.6%) than in Japan (1.1%). They suggest
that babA2 and babA2/B have geographic differences (22). Another virulence factor characterized recently in \textit{H. pylori} is a sialic acid-binding adhesin, SabA. It also has geographic difference and is more common in European than Japanese \textit{H. pylori} isolates (23, 24). As a result, this diversity in \textit{H. pylori} strains maybe explains why our findings were different from the results of some other reports from different geographic area. We suggest in another study in addition to ABO and Lewis blood groups, strains of \textit{H. pylori} also characterize.

In conclusion, we didn't observe any significant relationship between the Lewis, ABO and secretion phenotypes with \textit{H. pylori} infection.

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Authors' Contributions

Conception and design, analysis and interpretation of the data, statistical expertise: MRK
Obtaining of funding, collection and assembly of the data: AMR
Provision of study materials, drafting of the article: MHS
Critical revision of the article: HA
Final approval of the article: ZB
Administrative, technical, or logistic support: HS

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References


Table 1: Comparison of the distribution of ABO, Lewis and secretion phenotypes in the patients between two groups (infected and non-infected by H. pylori)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-infected n (%)</th>
<th>Infected n (%)</th>
<th>P-value</th>
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<tr>
<td><strong>ABO phenotypes</strong> (n=171)</td>
<td></td>
<td></td>
<td>0.669</td>
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<tr>
<td>O (n=15)</td>
<td>15 (37.5)</td>
<td>48 (36.6)</td>
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<tr>
<td>A (n=10)</td>
<td>10 (25.0)</td>
<td>38 (29.0)</td>
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<td>B (n=11)</td>
<td>11 (27.5)</td>
<td>31 (23.7)</td>
<td></td>
</tr>
<tr>
<td>AB (n=4)</td>
<td>4 (10.0)</td>
<td>14 (10.7)</td>
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</tr>
<tr>
<td><strong>Lewis phenotypes</strong> (n=169)</td>
<td></td>
<td></td>
<td>0.945</td>
</tr>
<tr>
<td>Le (a^b^-) (n=16)</td>
<td>16 (41.0)</td>
<td>47 (36.2)</td>
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<tr>
<td>Le (a^b^+) (n=21)</td>
<td>21 (53.8)</td>
<td>71 (54.6)</td>
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<tr>
<td>Le (a^b^+) (n=2)</td>
<td>2 (5.1)</td>
<td>12 (9.2)</td>
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<tr>
<td><strong>Secretion phenotypes</strong> (n=169)</td>
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<td>0.581</td>
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<td>Secretor (n=23)</td>
<td>23 (59.0)</td>
<td>83 (63.8)</td>
<td></td>
</tr>
<tr>
<td>Non-Secretor (n=16)</td>
<td>16 (41.0)</td>
<td>47 (36.2)</td>
<td></td>
</tr>
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</table>

1. P-value