Published online 2023 July 9.

Research Article

Association of ABO and Rh Blood Groups with *Helicobacter pylori* Seropositivity in Gonabad City, Iran: A Case-Control Study

Alireza Mohammadzadeh¹, Mohammad Hassan Minooeianhaghighi¹, Mohamad Ghorbani^{2,3}, Behdad Zibaee² and Jafar Hajavi ¹/₀^{4,*}

¹Department of Microbiology, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

²Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

³Department of Pathology, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

⁴Department of Microbiology, Infectious Diseases Research Center, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

* Corresponding author: Department of Microbiology, Infectious Diseases Research Center, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran. Email: hajavi.jaf@gmail.com

Received 2022 February 05; Revised 2022 May 25; Accepted 2022 July 02.

Abstract

Background: *Helicobacter pylori* infection is one of the most common chronic bacterial infections in humans, affecting large populations worldwide.

Objectives: The aim of this study was to investigate the relationship between *H. pylori* infection prevalence with ABO and Rh blood groups.

Methods: This descriptive-analytical study was conducted with a case-control design on individuals with anti-*H. pylori* positive test. Patients with IgG pylori were included in the study based on the inclusion criteria. The individuals were divided into two groups based on antibody titer. The case group included subjects with positive serological results with a titer greater than 12 u/mL IgG, and the control group entailed subjects with negative serological results with a titer less than 8 u/mL IgG. The ABO and Rh blood groups of both groups were examined based on case information. Finally, the data were entered into the SPSS software, and a significance level of 5% was considered for all analyses.

Results: According to the results of this study, there was no significant relationship between the blood group and *H. pylori* infection (P > 0.05). However, the prevalence of blood type A was significantly higher in individuals with positive *H. pylori* IgG test.

Conclusions: The current study suggests no association between ABO and Rh groups, but people with A blood group infected with *H. pylori* need more attention.

Keywords: Blood Group ABO, Rh, Helicobacter pylori, IgG

1. Background

Helicobacter pylori is one of the most common bacterial pathogens in humans. This bacterium lives in the stomach and duodenum. It is one of the most important reasons for gastrointestinal diseases, such as chronic gastritis, peptic ulcer (stomach and duodenum), and gastric tumor (1, 2). The literature shows that around 4.4 billion people worldwide have been infected with *H. pylori*. North America (37.1%) and Australia (24.4%) reported the lowest prevalence rates, while Africa (79.1%), Latin America (63.4%), and Asia (54.7%) described the maximum prevalence of infection (3). The occurrence of *H. pylori* infection in diverse parts of Iran varies from 19.2% in Sari to 74.3% in Tehran (4). Some characteristics of *H. pylori* bacteria play a role in infection, such as the colonization power of bacteria (motion, urease, and adhesion factors) and factors that cause tissue damage. These factors include lipopolysaccharide and cytotoxin vacuoleza A, a gene that codes cytotoxin and heat-sensitive proteins (5). Person-to-person transmission of this bacterium occurs in fecal-oral or oral form, and the prevalence of infections depends on age and economic status (6). Humans are important reservoirs of this bacterium, and the family is considered one of the main sources of infection transmission (7, 8). In many studies, environmental and lifestyle aspects (such as smoking and diet), as well as genetic factors, are considered important factors in increasing susceptibility to *H. pylori* infection (9, 10).

Copyright © 2023, Zahedan Journal of Research in Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

One of the genetic risk factors is the expression of ABO blood group phenotypes in different people (11, 12). These bacteria identify and bind to blood group antigens expressed on the surface of gastric mucosa and play an important role in the stability of infection (13, 14). During colonization, *H. pylori* in the stomach bind to Lewis's antigens and type 1 antigen of the gastric mucosa. H antigen has a carbohydrate structure, leading to the O phenotype in the ABO blood group system (15).

Although, during the last decade, some studies showed the relationship between ABO blood groups and *H. pylori* (16, 17), this association has not been observed in other investigations (13, 18). On the other hand, determining ABO blood groups may effectively assess the risk of *H. pylori* (11). Some studies have revealed a close relationship between the O blood group and duodenal ulcers, as well as blood group A and gastric carcinomas. However, the exact cause of these relations is unknown (19-21).

2. Objectives

This study was conducted to determine the association of ABO and Rh blood groups with *H. pylori* infection in patients referred to medical diagnostic centers in Gonabad city, Iran.

3. Methods

This cross-sectional retrospective, case-control study was performed after the approval of the proposal and after receiving the code of ethics. According to the study plan, people were referred to diagnostic centers in Gonabad in 2019 with positive anti-H. pylori IgG test results were included in the research. By reviewing the records of patients referred to medical diagnostic centers in Gonabad city with IgG serological test of H. pylori in 2019, based on previous studies (22), considering 95% reliability and 80% test power, and using G*Power software, the sample size in each group was obtained 115. The case group was patients with H. pylori-positive IgG test (titer greater than 12 u/mL), and the control group entailed people with H. pylori-negative IgG test (titer less than 8u/mL IgG). Due to the possible loss of the sample, the sample size was considered to be 240 people. The phenotypes of blood groups ABO and Rh (determined by direct hemagglutination using commercial monoclonal antibodies) were studied in two groups. Furthermore, the checklist for demographic information was completed.

3.1. Statically Analysis

After collecting and entering the data into the SPSS software, mean, standard deviation, frequency, and

percentage of frequency were used to describe the variables. In analytical analysis, a chi-square statistical test was used to investigate the relationship between qualitative variables. Moreover, to compare quantitative variables, independent samples *t*-test, and Mann-Whitney test were used if the distribution was normal or not normal, respectively.

4. Results

This descriptive-analytical retrospective study was performed on 240 patients referred to Allameh Bohlool Laboratory of Gonabad University of Medical Sciences for an IgG test. Individuals in the case group had *H. pylori* positive tests, and those in the control group were negative for *H. pylori* IgG. In the case group, 52.5% (63) were female, and 47.5% (57) were male, and in the control group, 62.5% (75) were female, and 37.5% (45) were male. The mean age in the case and control groups was 8.21 ± 47.1 and 7.12 ± 49.07 years, respectively. The chi-square test indicated no significant difference between the groups in terms of gender (P > 0.05) and age (P > 0.05).

The percentage of frequency was higher only in groups A and O in the case group than in the control group, but the chi-square test showed no significant difference between the ABO blood groups in the two groups (P > 0.05) (Table 1).

Fable 1. Comparison of Case and Control Groups by Blood Group				
Blood Groups	Case Group (%)	Control Group (%)	P-Value	
Α	39.16	36.66	> 0.05	
В	30.83	35.00		
AB	19.16	21.66		
0	10.83	6.66		

The chi-square test showed no significant difference between the number of Rh-positive and Rh-negative people in each group (P = 0.085). We found a significant relationship between smoking and *H. pylori* (P = 0.015), as the incidence of *H. pylori* was higher in smokers than in non-smokers. On the other hand, no significant relationship was detected between the place of residence and *H. pylori* infection (P > 0.05) (Table 2). However, the prevalence of *H. pylori* was higher in the villagers. Statistical analysis displayed a significant relationship between marital status and infection with *H. pylori* (P = 0.037), so the prevalence of *H. pylori* was higher in married people.

Table 2. Comparison of Case and Control Groups in Terms of Kit				
Rh	Case Group (%)	Control Group (%)	P-Value	
\mathbf{Rh}^+	71.66	79.16	> 0.05	
Rh [°]	28.33	20.83		

Table 2. Comparison of Case and Control Groups in Terms of Rh

5. Discussion

The results of the present study showed that the frequency percentage of *H. pylori* infection was higher in blood groups A and O in the case group. However, no significant difference was observed between the ABO blood groups of the two groups. In addition, there was no significant difference between Rh-positive and Rh-negative blood groups. In recent decades, some studies have expressed a conflicting relationship between ABO blood groups and *H. pylori* (13, 16-18).

Keller et al. and Sharara et al. investigated the association between upper gastrointestinal diseases, ABO blood groups, and *H. pylori* infection in patients with a positive outcome of *H. pylori* infection based on the endoscopic outcome. They did not observe any significant relationship between different types of blood groups and the prevalence of infection with this bacterium (22, 23). The findings of the present study were similar to our study.

Inoue et al. (24) and Chakrani et al. (11) investigated the association between H. pylori infection and ABO blood groups. They reported that Helicobacter infection in blood group O was higher than in other blood groups. In our study, the infection rate was higher in groups A and O, but there was no significant difference. Reiisi et al. investigated the relationship between ABO/Rh blood groups. They compared the severity of H. pylori infection in patients who were Rh-positive and those who were Rh-negative. These authors found no relationship between bacterial infection and ABO blood groups (25). In line with this study, we observed no correlation between the Rh blood group and H. pylori infection. Aryana et al. assessed the relation of *H. pylori* infection with the prevalence of ABO and Lewis-synthesized blood groups. In line with our study, they did not indicate any significant relationship between H. pylori infection and ABO or Lewis blood groups (13).

Unlike our study, Kanbay et al. showed that people with blood groups A and O were statistically more susceptible to *H. pylori* infection and had a lower chance of developing an infection than people with the AB blood group (26). de Mattos et al. investigated the association of *H. pylori* infection with the ABO blood group and Lewis in 128 subjects. The results of their study were inconsistent with the present research and indicated that the prevalence of *H. pylori* infection was higher in patients with O blood group (27). Heneghan et al., in another study on 287 patients, similar to the present investigation, did not find any relationship between ABO blood group phenotypes and *H. pylori* infection (28). Moreover, in a study conducted by Loffeld and Stobberingh on 782 healthy blood donors, no significant association was detected to confirm that people with the O blood group were infected with *H. pylori*, which was similar to our results (29).

In the Loffeld and Stobberingh (29) survey, the prevalence of H. pylori infection among men and women was evaluated, and no significant difference was observed in the prevalence of infection with gender nor between infection with ABO and Rh blood group phenotypes. No significant difference was observed between genders in terms of infection prevalence and serological status of this infection with ABO and Rh blood group phenotypes, which was in line with our study. In a study conducted by Tadege et al., similar to our study, there was no statistically significant relationship between the serum prevalence of this infection and the phenotype of ABO blood groups (30). The contradiction between the results of different studies can be due to other factors that may also play a role in infection with H. pylori. The health status of the living environment, place of residence, age, lifestyle, number of family members, and any factors contributing to this infection should be studied alongside blood group phenotypes to generate more comprehensive results.

The results of the current study indicated that smoking can increase the risk of bacterial infection. Zeng et al., similar to the current study, reported a significant relationship between smoking and the severity of contamination. In addition, age and aging can exacerbate inflammation and bacterial localization (31). Monjamzadeh et al. observed no significant relationship between age and infection with this bacterium (32). Shahi et al. (33) and Li et al. (34) found no significant relationship between age and infection with H. pylori. The latter results were similar to the present study. On the other hand, Kim et al. observed a significant relationship between age and infection with this bacterium, which was contrary to our findings (35). The mentioned research, in line with our study, showed that smoking and pathogenic bacteria factors could increase the risk of infection with H. pylori.

5.1. Conclusions

Although some studies have indicated a relationship between blood groups and *H. pylori* infection, our findings did not show such a relationship. This may be due to the role of genetic and demographic factors that require further evaluation. Other influential factors may include lifestyle and the type of diet. Moreover, infection rates can vary due to differences in *H. pylori* strains.

Acknowledgments

This article was extracted from the Behdad Zibaee M.D. thesis. The authors thank the vice chancellor for research of Gonabad University of Medical Sciences, Allameh Bohlool Hospital of Gonabad University of Medical Sciences, and all the participants.

Footnotes

Authors' Contribution: A. M.: Study concept and design, drafting the manuscript, and critical revision of the manuscript, and statistical analysis; M. H. M.: Study concept and design, critical revision of the manuscript, and study supervision; M. G.: Study concept and design, drafting of the manuscript, and critical revision of the manuscript; B. Z.: Acquisition of data and drafting of the manuscript; J. H.: Study concept and design, acquisition of data, analysis, and interpretation of data, drafting of the manuscript, critical revision of the manuscript, statistical analysis, study supervision, as well as administrative, technical, and material support.

Conflict of Interests: There are no relevant financial or non-financial competing interests to report.

Ethical Approval: The Ethics Committee of Gonabad University of Medical Sciences approved this research (ethical code: IR.GMU.REC.1399.071).

Funding/Support: This study was supported entirely by grant A-10-1976-1 by the vice chancellor for research of Gonabad University of Medical Sciences.

References

- Wong F, Rayner-Hartley E, Byrne MF. Extraintestinal manifestations of Helicobacter pylori: a concise review. World J Gastroenterol. 2014;20(34):11950–61. [PubMed ID: 25232230]. [PubMed Central ID: PMC4161781]. https://doi.org/10.3748/wjg.v20.i34.11950.
- Sugizaki K, Tari A, Kitadai Y, Oda I, Nakamura S, Yoshino T, et al. Anti-Helicobacter pylori therapy in localized gastric mucosa-associated lymphoid tissue lymphoma: A prospective, nationwide, multicenter study in Japan. *Helicobacter*. 2018;23(2):e12474. [PubMed ID: 29504247]. [PubMed Central ID: PMC5900897]. https://doi.org/10.1111/hel.12474.
- Ghotaslou R, Leylabadlo HE, Asl YM. Prevalence of antibiotic resistance in Helicobacter pylori: A recent literature review. World J Methodol. 2015;5(3):164–74. [PubMed ID: 26413490]. [PubMed Central ID: PMC4572030]. https://doi.org/10.5662/wjm.v5.i3.164.
- 4. Sayehmiri F, Darvishi Z, Sayehmiri K, Soroush S, Emaneini M, Zarrilli R, et al. A Systematic Review and Meta-Analysis Study to Investigate the Prevalence of Helicobacter pylori and the Sensitivity of its Diagnostic Methods in Iran. *Iran Red Crescent Med J.* 2014;16(6):e12581. [PubMed ID: 25068041]. [PubMed Central ID: PMC4102974]. https://doi.org/10.5812/ircmj.12581.
- Backert S, Clyne M. Pathogenesis of Helicobacter pylori infection. Helicobacter. 2011;16 Suppl 1:19–25. [PubMed ID: 21896081]. https://doi.org/10.1111/j1.1523-5378.2011.00876.x.

- Mezmale L, Coelho LG, Bordin D, Leja M. Review: Epidemiology of Helicobacter pylori. *Helicobacter*. 2020;25 Suppl 1:e12734. [PubMed ID: 32918344]. https://doi.org/10.1111/hel.12734.
- Furesz J, Lakatos S, Nemeth K, Fritz P, Simon L, Kacserka K. The prevalence and incidence of Helicobacter pylori infections among young recruits during service in the Hungarian Army. *Helicobacter*. 2004;9(1):77-80. [PubMed ID: 15156907]. https://doi.org/10.1111/j.1083-4389.2004.00200.x.
- Roesler BM, Rabelo-Goncalves EM, Zeitune JM. Virulence Factors of Helicobacter pylori: A Review. *Clin Med Insights Gastroenterol.* 2014;7:9–17. [PubMed ID: 24833944]. [PubMed Central ID: PMC4019226]. https://doi.org/10.4137/CGast.S13760.
- Camilo V, Sugiyama T, Touati E. Pathogenesis of Helicobacter pylori infection. *Helicobacter*. 2017;22 Suppl 1:e12405. [PubMed ID: 28891130]. https://doi.org/10.1111/hel.12405.
- Shiota S, Suzuki R, Yamaoka Y. The significance of virulence factors in Helicobacter pylori. J Dig Dis. 2013;14(7):341–9. [PubMed ID: 23452293]. [PubMed Central ID: PMC3721066]. https://doi.org/10.1111/1751-2980.12054.
- Chakrani Z, Robinson K, Taye B. Association Between ABO Blood Groups and Helicobacter pylori Infection: A Meta-Analysis. *Sci Rep.* 2018;8(1):17604. [PubMed ID: 30514875]. [PubMed Central ID: PMC6279815]. https://doi.org/10.1038/s41598-018-36006-x.
- Nakao M, Matsuo K, Ito H, Shitara K, Hosono S, Watanabe M, et al. ABO genotype and the risk of gastric cancer, atrophic gastritis, and Helicobacter pylori infection. *Cancer Epidemiol Biomarkers Prev.* 2011;20(8):1665-72. [PubMed ID: 21680535]. https://doi.org/10.1158/1055-9965.EPI-11-0213.
- Aryana K, Keramati MR, Zakavi SR, Sadeghian MH, Akbari H. Association of Helicobacter pylori infection with the Lewis and ABO blood groups in dyspeptic patients. *Niger Med J.* 2013;54(3):196–9. [PubMed ID: 23901182]. [PubMed Central ID: PMC3719247]. https://doi.org/10.4103/0300-1652.114583.
- Rizzato C, Kato I, Plummer M, Munoz N, Stein A, Jan van Doorn L, et al. Risk of advanced gastric precancerous lesions in Helicobacter pylori infected subjects is influenced by ABO blood group and cagA status. *Int J Cancer*. 2013;**133**(2):315–22. [PubMed ID: 23319424]. [PubMed Central ID: PMC3656130]. https://doi.org/10.1002/ijc.28019.
- Kominato Y, Sano R, Takahashi Y, Hayakawa A, Ogasawara K. Human ABO gene transcriptional regulation. *Transfusion*. 2020;60(4):860–9. [PubMed ID: 32216153]. [PubMed Central ID: PMC7187371]. https://doi.org/10.1111/trf.15760.
- Franchini M, Favaloro EJ, Targher G, Lippi G. ABO blood group, hypercoagulability, and cardiovascular and cancer risk. *Crit Rev Clin Lab Sci.* 2012;49(4):137-49. [PubMed ID: 22856614]. https://doi.org/10.3109/10408363.2012.708647.
- Iodice S, Maisonneuve P, Botteri E, Sandri MT, Lowenfels AB. ABO blood group and cancer. *Eur J Cancer*. 2010;46(18):3345–50. [PubMed ID: 20833034]. https://doi.org/10.1016/j.ejca.2010.08.009.
- Keramati MR, Sadeghian MH, Ayatollahi H, Badiee Z, Shakibayi H, Moghimi-Roudi A. Role of the Lewis and ABO Blood Group Antigens in Helicobacter pylori Infection. *Malays J Med Sci.* 2012;**19**(3):17–21. [PubMed ID: 23610545]. [PubMed Central ID: PMC3629660].
- Abdulridha MK. The Relationship between ABO Blood Group Distribution and the incidence of Upper Gastric and Duodenal Ulcer in Iraqi Patients. Iraqi J Pharm Sci. 2013;22(1):97-103. https://doi.org/10.31351/vol22iss1pp97-103.
- Teshome Y, Mekonen W, Birhanu Y, Sisay T. The association between ABO blood group distribution and peptic ulcer disease: a cross-sectional study from Ethiopia. J Blood Med. 2019;10:193-7. [PubMed ID: 31308778]. [PubMed Central ID: PMC6613600]. https://doi.org/10.2147/[BM.S209416.
- Wang Z, Liu L, Ji J, Zhang J, Yan M, Zhang J, et al. ABO blood group system and gastric cancer: a case-control study and meta-analysis. *Int J Mol Sci.* 2012;**13**(10):13308–21. [PubMed ID: 23202954]. [PubMed Central ID: PMC3497328]. https://doi.org/10.3390/ijms131013308.

- Keller R, Dinkel KC, Christl SU, Fischbach W. Interrelation between ABH blood group 0, Lewis(B) blood group antigen, Helicobacter pylori infection, and occurrence of peptic ulcer. *Z Gastroenterol.* 2002;40(5):273–6. [PubMed ID: 12016560]. https://doi.org/10.1055/s-2002-30115.
- Sharara AI, Abdul-Baki H, ElHajj I, Kreidieh N, Kfoury Baz EM. Association of gastroduodenal disease phenotype with ABO blood group and Helicobacter pylori virulence-specific serotypes. *Dig Liver Dis.* 2006;**38**(11):829–33. [PubMed ID: 16931196]. https://doi.org/10.1016/j.dld.2006.06.040.
- Inoue T, Suzuki K, Hamajima T, Watarai R, Kimura A, Ichino N, et al. Association between Helicobacter pylori infection and ABO blood groups: a cross-sectional study in Hokkaido, Japan. Int J Anal Bio Sci. 2014;2(2):72–6.
- Reiisi S, Shahi H, Shahi S, Damavandi MS. [Determination of ABO/Rh blood group, sex and age with severity of Helicobacter pylori infection in Iranian gastrointestinal patients]. *Iran J Med Microbiol.* 2017;11(2):81–6. Persian.
- Kanbay M, Gur G, Arslan H, Yilmaz U, Boyacioglu S. The relationship of ABO blood group, age, gender, smoking, and Helicobacter pylori infection. *Dig Dis Sci.* 2005;**50**(7):1214-7. [PubMed ID: 16047462]. https://doi.org/10.1007/s10620-005-2762-y.
- de Mattos LC, Rodrigues Cintra J, Sanches FE, Alves da Silva Rde C, Ruiz MA, Moreira HW. ABO, Lewis, secretor and non-secretor phenotypes in patients infected or uninfected by the Helicobacter pylori bacillus. Sao Paulo Med J. 2002;120(2):55–8. [PubMed ID: 11994774]. https://doi.org/10.1590/s1516-31802002000200006.
- Heneghan MA, Moran AP, Feeley KM, Egan EL, Goulding J, Connolly CE, et al. Effect of host Lewis and ABO blood group antigen expression on Helicobacter pylori colonisation density and the consequent inflammatory response. *FEMS Immunol Med Microbiol.* 1998;20(4):257-66. [PubMed ID: 9626930].

https://doi.org/10.1111/j.1574-695X.1998.tb01135.x.

- Loffeld RJ, Stobberingh E. Helicobacter pylori and ABO blood groups. J Clin Pathol. 1991;44(6):516–7. [PubMed ID: 2066433]. [PubMed Central ID: PMC496837]. https://doi.org/10.1136/jcp.44.6.516.
- Tadege T, Mengistu Y, Desta K, Asrat D. Serioprevalence of Helicobacter pylori Infection in and its Relationship with ABO Blood Groups. *Ethiop J Health Dev.* 2005;19(1):55–9. https://doi.org/10.4314/ejhd.v19i1.9972.
- 31. Zeng HM, Pan KF, Zhang Y, Zhang L, Ma JL, Zhou T, et al. Genetic variants of toll-like receptor 2 and 5, helicobacter pylori infection, and risk of gastric cancer and its precursors in a chinese population. *Cancer Epidemiol Biomarkers Prev.* 2011;20(12):2594–602. [PubMed ID: 21994405]. https://doi.org/10.1158/1055-9965.EPI-11-0702.
- Monajemzadeh M, Abbasi A, Tanzifi P, Taba Taba Vakili S, Irani H, Kashi L. The Relation between Helicobacter pylori Infection and Acute Bacterial Diarrhea in Children. Int J Pediatr. 2014;2014:191643.
 [PubMed ID: 24696690]. [PubMed Central ID: PMC3950475]. https://doi.org/10.1155/2014/191643.
- Shahi H, Moghni M, Shirzad H. [The relation between severe density of Helicobacter pylori in biopsy with cigarette smoking and age in infected patients]. *Iran J Med Microbiol.* 2015;9(1):1–5. Persian.
- 34. Li M, Huang L, Qiu H, Fu Q, Li W, Yu Q, et al. Helicobacter pylori infection synergizes with three inflammation-related genetic variants in the GWASs to increase risk of gastric cancer in a Chinese population. *PLoS One*. 2013;8(9):e74976. [PubMed ID: 24069371]. [PubMed Central ID: PMC3777913]. https://doi.org/10.1371/journal.pone.0074976.
- Kim HL, Jeon HH, Park IY, Choi JM, Kang JS, Min KW. Helicobacter pylori infection is associated with elevated low density lipoprotein cholesterol levels in elderly Koreans. *J Korean Med Sci.* 2011;26(5):654–8. [PubMed ID: 21532857]. [PubMed Central ID: PMC3082118]. https://doi.org/10.3346/jkms.2011.26.5.654.