Research Article:
Body Mass Index and the Success of Helicobacter Pylori Eradication Therapy

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ABSTRACT

Background: Helicobacter pylorus (H. pylori) is a Gram-negative spiral bacterium related to several gastric and extra-gastric complications. The effects of H. pylori infection on cardiometabolic diseases such as dyslipidemia, diabetes, and metabolic syndrome have been investigated. The present paper aims to assess the effects of body mass index on the success of Helicobacter pylori eradication therapy for the first time.

Methods and Materials: This study included 198 patients with H. pylori infection. The patients underwent H. pylori eradication using clarithromycin (500 mg, twice daily), pantoprazole (40 mg, twice daily), amoxicillin (500 mg, three times daily), and bismuth substrate (120 mg, twice daily) for 14 days. After that, the success of eradication was assessed through stool antigen within a month following the treatment. The association of eradication success with age, gender, and Body Mass Index (BMI) was evaluated.

Results: H. pylori infection was eradicated in 76.3% (P<0.001) of the patients following the treatment. The rate of response to anti-H. pylori remedy was affected by age (P= 0.29). But it was not affected by gender (P= 0.81) and BMI (P= 0.60).

Conclusion: Based on the study findings, the patients’ response to the H. pylori eradication was not affected by age, gender, and BMI.
peptic ulcer, and Mucosa-Associated Lymphoid Tissue (MALT) lymphoma has been well-established [4, 5]. Although gastric-related complications of \( H. \) pylori infection are apparent, their effect on other organs is still under investigation. Recently studies are in progress to assess the role of \( H. \) pylori infection with neurological, cardiovascular, metabolic, and hematological disorders [1, 6, 7]. Studies have assessed the association of \( H. \) pylori infection with cardiometabolic risk factors such as diabetes, dyslipidemia, and metabolic syndrome [8-11]. Studies regarding body weight and obesity have yielded different outcomes, as some of them presented a significantly higher rate of infection among more obese cases, while others presented no association [12, 13].

To the best of our knowledge, studies in the literature have focused on the association of \( H. \) pylori infection with body weight. The present paper aims to assess the association of response to \( H. \) pylori infection eradication medical treatment with Body Mass Index (BMI).

2. Materials and Methods

The current non-randomized case-series study was conducted on 198 patients positive for \( H. \) pylori infection referred to the outpatient university clinics of AL Zahra and Kashani affiliated to Isfahan University of Medical Sciences from May 2016 to June 2017. Patients with the age range of 18-60 years old who presented their willingness to participate in the study and had the indications for the eradication of \( H. \) pylori based on the American College of Gastroenterology were included [14].

The exclusion criteria were defined as relapse and or resistance to the eradication treatment of \( H. \) pylori, previous history of immunodeficiency and or use of immunosuppressive remedies, history of hypersensitivity to the used antibiotics, addiction, chronic medical diseases requiring specific cares (i.e. diabetes mellitus, end-stage renal disease, and collagen vascular diseases), and history of psychiatric disorders such as psychosis. Any drug-related adverse effects leading to discontinuation of the treatment, failure to comply with the therapeutic schedule, and patients’ failure to refer for follow-up studies were also considered exclusion criteria.

The study was approved by the Ethics Committee of the Isfahan University of Medical Sciences with the code number IR.MUI.REC.1396.3. After that, the study process was explained entirely to the participants, and they were requested to sign the written form of participation in the study. The participants’ demographic information, including age, gender, height, weight, BMI, occupation, and educational status, were recorded in the study checklist. After that, all study samples underwent eradication treatment of \( H. \) pylori based on the therapeutic schedule of 14 days remedy of clarithromycin tablets (500 mg, twice daily) (EXIR, Iran), pantoprazole capsules (40 mg, twice daily) (Abidipharma, Iran), amoxicillin capsules (500 mg, three times daily) (Farabi, Iran), and Bismuth Subcitrate (120 mg, twice daily) (Chemiedarou, Iran).

Finally, the success of the \( H. \) pylori infection eradication was reassessed through the \( H. \) pylori stool antigen test performed within one month following the therapeutic regimen completion. All of the stool antigen assessments were sent to a single laboratory to avoid biases. The obtained data were entered into the SPSS v. 21 and analyzed. The descriptive data were presented in mean and percentages. For analytics, McNemar’s test was used. A \( P \) value of 0.05 is considered as the significant level.

3. Results

This study included 198 patients with \( H. \) pylori infection. The Mean±SD age of the participants was 36.34±9.06 years, and their mean BMI was 40.79±8.43 kg/m². Most participants were females (81.8%) and had a mean age range of 31-40 years, with a third-degree of obesity (71.2%). The most prevalent educational level and occupational statuses of the patients were Bachelor of Science (36.4%) and housewife (37.9%), respectively. Table 1 presents the demographics in detail.

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All of the studied population was infected with \( H. \) pylori at the study initiation, while in a two-month follow-up study, \( H. \) pylori was successfully eradicated in 76.3% of the cases (\( P<0.001 \)) (Table 2). Table 3 presents the distribution of successful \( H. \) pylori eradication based on age, gender, and BMI. After the medical treatment, 77.8% of males and 75.9% of females were successfully treated. The age-range assessment of \( H. \) pylori eradication showed a positive response to the treatment in 81.7% of under 30-year-old cases, 78.2% of 31- to 40-year-old, 65.9% of 41- to 50-year-old, and 75% of over 50-year-old. The highest eradication rate was found in cases with the first grade of obesity (88.9%), followed by 81.8% in overweight, 78.9% in the second degree obese, 75.2% in the third degree obese, and 57.1% in normal-weight cases. The eradication of \( H. \) pylori was statistically successful in all age groups (\( P<0.05 \)), both genders (\( P<0.05 \)), and all BMI subgroups (\( P<0.05 \)) except in those with normal BMI (\( P=0.12 \)).
In the current study, we assessed the response rate of 198 patients to the medical treatment of *H. pylori* infection. The outcomes of this study showed a remarkable response rate of both genders and all of the age ranges. The primary manifestation of this study evaluated for the first time was the association of BMI with the response to the *H. pylori* eradication treatment. The study revealed significant responses in all BMI subgroups but those with normal BMI. The highest response rate was found among those with the first degree of obesity followed by overweight, the second, and eventually, the third degree of obesity. Further studies showed that the response rate to the eradication was neither influenced by age, nor gender, and nor BMI. Variations in the response rates may occur due to the number of studied people in each subgroup.

Numerous studies in the literature have assessed the association of *H. pylori* infection with different metabolic indices. Although their presentations are not similar, most studies have demonstrated the direct association of *H. pylori* infection with obesity. Insulin resistance, disturbed lipid homeostasis, and metabolism of adipocytokines are entities associated with *H. pylori* infection [15].

### Table 1. Demographic information of the studied population

| Variables                        | No. (%) |
|----------------------------------|---------|
| **Gender**                       |         |
| Female                           | 162 (81.8) |
| Male                             | 36 (18.2) |
| **Age group, y**                 |         |
| <30                              | 60 (30.3) |
| 31-40                            | 78 (39.4) |
| 41-50                            | 44 (22.2) |
| > 50                             | 16 (8.1) |
| **Body mass index (kg/m²)**      |         |
| Normal (18.5-24.9)               | 7 (3.5) |
| Overweight (25-29.9)             | 22 (11.1) |
| The first degree of obesity (30-34.9) | 9 (4.5) |
| The second degree of obesity (35-39.9) | 19 (9.6) |
| The third degree of obesity (> 40) | 141 (71.2) |
| **Educational level**            |         |
| Under diploma                    | 33 (16.7) |
| Diploma                          | 41 (20.7) |
| Associate degree                 | 26 (13.1) |
| Bachelor of sciences             | 72 (36.4) |
| Master of science or higher      | 26 (13.1) |
| **Occupation**                   |         |
| Housewife                        | 75 (37.9) |
| Self-employed                    | 47 (23.7) |
| Jobless                          | 20 (10.1) |
| University student               | 14 (7.1) |
| Worker                           | 1 (0.5) |
| Employee                         | 41 (20.7) |
There are even studies showing increased serum levels of triglycerides, cholesterol, low-density lipoprotein, and apolipoprotein B and decreased levels of high-density lipoprotein and apolipoprotein A among those patients who were positive for *H. pylori* [16, 17]. Studies in this regard assessed the significance of *H. pylori* infection with two aspects. Some studies compared the prevalence of this infection among obese and non-obese cases. Most of these studies reported a remarkably higher rate of infection among obese cases, while others opposed [1, 18, 19]. Other studies tried to investigate the influence of *H. pylori* infection eradication on the patients’ body mass index. These studies almost always declared notifying an increase in the BMI following the eradication therapy and raised the hypothesis that the appetite retrieval following the healing of *H. pylori*-induced dyspepsia is the underlying etiology for the BMI increase following *H. pylori* infection eradication [20-22].

Contrary to the numerous studies assessing the association of *H. pylori* infection with BMI, few studies examined the relationship of BMI with the response to antibiotic eradication therapy. Obesity has become a remarkable concern worldwide, and demands for bariatric surgeries have increased during recent decades. It has been proven that successful *H. pylori* eradication can reduce postoperative complications such as marginal ulcerations and gastric-related symptoms. Besides, a gastric study following bariatric surgery is significantly limited [23, 24]. Therefore, some authors have recommended that assessment of *H. pylori* infection and its eradication should be a routine schedule before the surgeries [25, 26].

Table 2. The status of *H. pylori* Infection at the study initiation and within one month after the medical treatment

| *H. Pylori* Infection Status | Time          | No. (%)          | P       |
|-----------------------------|---------------|------------------|---------|
|                             | Study Initiation | Within one Month |         |
| Negative                    | 0(0)          | 151(76.3)        | <0.001  |
| Positive                    | 198(100)      | 47(23.7)         |         |

Table 3. The distribution of *H. pylori* eradication following medical therapy based on age, gender, and body mass index

| Variables                  | No. (%)     | P       | P       |
|----------------------------|-------------|---------|---------|
|                            | At the Study Initiation | Following Two Months |
|                            | Negative   | Positive | Negative | Positive |         |         |
| Gender                     | Male        | 0(0)    | 36(100) | 28(77.8) | 8(22.2) | <0.001  |         |
|                            | Female      | 0(0)    | 162(100)| 123(75.9)| 39(24.1)| <0.001  | 0.81    |
| Age (y)                    | <30         | 0(0)    | 60(100) | 49(81.7) | 11(18.3)| <0.001  |         |
|                            | 31-40       | 0(0)    | 78(100) | 61(78.2) | 17(21.8)| <0.001  | 0.29    |
|                            | 41-50       | 0(0)    | 44(100) | 29(65.9) | 15(34.1)| <0.001  |         |
|                            | >50         | 0(0)    | 16(100) | 12(75)   | 4(25)  | <0.001  |         |
| Body Mass Index (kg/m²)    | Normal      | 0(0)    | 7(100)  | 4(57.1)  | 3(42.9)| 0.12    |         |
|                            | Overweight  | 0(0)    | 22(100) | 18(81.8) | 4(18.2)| <0.001  |         |
|                            | First degree of obesity | 0(0) | 9(100) | 8(88.9) | 1(11.1) | 0.008 | 0.60 |
|                            | Second degree of obesity | 0(0) | 19(100) | 15(78.9) | 4(21.1) | <0.001 |
|                            | Third degree of obesity | 0(0) | 141(100)| 106(75.2)| 35(24.8)| <0.001 |
The findings of our study are in contrast with the study of Abdullahi et al. that reported a remarkable association between BMI and response to anti-\textit{H. pylori} treatment. They argued that those with more severe obesity status presented more unsatisfactory responses to anti-\textit{H. pylori} agents [27]. Besides, they raised the theory about dose adjustment requirement for more obese patients because of adipose tissue distribution, and thus the hydrophilic and distribution of the agents in their body [27-29]. Another theory about the probable etiology of inadequate response among more obese people is immune system poor antibody response to antigens. Ramaswamy et al. reported that leptin resistance among obese people interrupts T cell-mediated actions [30]. The other theory targets delayed gastric emptying in obese people. This theory believes that as obese people prefer fatty diets, the delayed gastric emptying makes an inappropriate condition for drug absorption [31].

Gender and age were other aspects that revealed no association with the response rate to the \textit{H. pylori} eradication treatment. Despite the study of Abdullahi et al. that confirmed our findings [27], Chen et al. reported that younger cases (less than 50 years) were prone to infection with \textit{H. pylori} [22]. In general, we have found no association between BMI and the response to the \textit{H. pylori} standard eradication treatment. Because of few studies in this regard and the distribution of the study population in the current study, further studies are recommended.

5. Conclusion

Based on the study findings, the patients’ response to the \textit{H. pylori} eradication was not affected by age, gender, and BMI.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of the Isfahan University of Medical Sciences approved this study (Code: IR.MUI.REC.1396.3). All ethical principles are considered in this article. The participants were informed about the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information. They were free to leave the study whenever they wished, and if desired, the research results would be available to them.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors’ contributions

Conceptualization and supervision: Masoud Sayadishahraki and Hossein Bahrami Samani; Methodology: Mahsa Khodadoostan; Data collection: Flora Mazaheri; Data analysis: Somayeh Haghighat; Writing, review and editing: All authors.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Xu C, Yan M, Sun Y, Joo J, Wan X, Yu C, et al. Prevalence of Helicobacter pylori infection and its relation with body mass index in a Chinese population. Helicobacter. 2014; 19(6):437-42. [DOI:10.1111/hel.12153] [PMID]

[2] Ponder RE, Ng D. The prevalence of Helicobacter pylori infection in different countries. Alimentary Pharmacology & Therapeutics. 1995; 9 (Suppl 2):33-9. [PMID]

[3] Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, et al. Global prevalence of Helicobacter pylori infection: Systematic review and meta-analysis. Gastroenterology. 2017; 153(2):420-9. [DOI:10.1053/j.gastro.2017.04.022] [PMID]

[4] Wong BCY, Lam SK, Wong WM, Chen JS, Zheng TT, Feng RE, et al. Helicobacter pylori eradication to prevent gastric cancer in a high-risk region of China: A randomized controlled trial. JAMA. 2004; 291(2):187-94. [DOI:10.1001/jama.291.2.187] [PMID]

[5] Siddiqui B, Yakoob J, Abtas Z, Azmat R, Fatima SS, Awan S. Distribution of Helicobacter pylori infection and abnormal Body-Mass Index (BMI) in a developing country. The Journal of Infection in Developing Countries. 2018; 12(5):342-6. [DOI:10.3855/jidc.10051] [PMID]

[6] Figura N, Franceschi F, Santucci A, Bernardini G, Gasbarrini G, Gasbarrini A. Extragastric manifestations of Helicobacter pylori infection. Helicobacter. 2010; 15(Suppl 1):60-8. [DOI:10.1111/j.1523-5378.2010.00778.x] [PMID]

[7] Roubaud Baudron C, Franceschi F, Salles N, Gasbarrini A. Extragastric diseases and \textit{H. eli}cobacter pylori. Helicobacter. 2013; 18(Suppl 1):44-51. [DOI:10.1111/hel.12077] [PMID]

[8] Satoh H, Saijo Y, Yoshioka E, Tsutsui H. Helicobacter Pylori infection is a significant risk for modified lipid profile in Japanese male subjects. Journal of Atherosclerosis and Thrombosis. 2010; 17(10):1041-8. [DOI:10.5551/jat.5157] [PMID]
[9] Chen Y, Blaser MJ. Association between gastric Helicobacter pylori colonization and glycated hemoglobin levels. Journal of Infectious Diseases. 2012; 205(8):1195-202. [DOI:10.1093/infdis/jys106] [PMID] [PMCID]

[10] Chen LW, Chien CY, Yang KJ, Ku SF, Chen CH, Chien RN. Helicobacter pylori infection increases insulin resistance and metabolic syndrome in residents younger than 50 years old: A community-based study. PLoS One. 2015; 10(5):e0128671. [DOI:10.1371/journal.pone.0128671] [PMID] [PMCID]

[11] Chen TP, Hung HF, Chen MK, Lai HH, Hsu WF, Huang KC, et al. Helicobacter pylori infection is positively associated with metabolic syndrome in Taiwanese adults: A cross-sectional study. Helicobacter. 2015; 20(3):184-91. [DOI:10.1111/he1.12190] [PMID]

[12] Cho I, Blaser MJ, Francois F, Mathew JP, Ye XY, Goldberg JD, et al. Helicobacter pylori and overweight status in the United States: Data from the Third National Health and Nutrition Examination Survey. American Journal of Epidemiology. 2005; 162(6):579-84. [DOI:10.1093/aje/kwi237] [PMID]

[13] Ioannou GN, Weiss NS, Kearney DJ. Is helicobacter pylori seropositivity related to body mass index in the United States? Alimentary Pharmacology & Therapeutics. 2005; 21(6):765-72. [DOI:10.1038/sj/apt.4700521] [PMID]

[14] Chey WD, Wong BCY, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. American Journal of Gastroenterology. 2007; 102(8):1808-25. [DOI:10.1111/j.1572-0241.2007.01393.x] [PMID]

[15] Ohara H, Suzuki T, Nakagawa T, Yoneshima M, Yamamoto M, Tsujino D, et al. 13C-UBT using an infrared spectrometer for detection of Helicobacter pylori and for monitoring the effects of lansoprazole. Journal of Clinical Gastroenterology. 1995; 20:S115-7. [DOI:10.1097/00004836-199506002-00031] [PMID]

[16] Crabtree JE, Shallcross TM, Heatley RV, Wyatt JL. Mucosal tumour necrosis factor alpha and interleukin-6 in patients with Helicobacter pylori associated gastritis. Gut. 1991; 32(12):1473-7. [DOI:10.1136/gut.32.12.1473] [PMID] [PMCID]

[17] Gunji T, Matsuhashi N, Sato H, Fujibayashi K, Okumura M, Sasabe N, et al. Helicobacter pylori infection significantly increases insulin resistance in the asymptomatic Japanese population. Helicobacter. 2009; 14(5):496-502. [DOI:10.1111/j.1522-5378.2009.00935.x] [PMID]

[18] Gerig R, Ernst B, Wilms B, Thurnheer M, Schultes B. Preoperative nutritional deficiencies in severely obese bariatric candidates are not linked to gastric Helicobacter pylori infection. Obesity Surgery. 2013; 23(5):698-702. [DOI:10.1007/s11695-013-0878-2] [PMID]

[19] Suki M, Leibovici Weissman Y, Bolton D, Itskoviz D, Tsadok Perets T, Comanescu D, et al. Helicobacter pylori infection is positively associated with an increased BMI, irrespective of socioeconomic status and other confounders: A cohort study. European Journal of Gastroenterology & Hepatology. 2018; 30(2):143-8. [DOI:10.1097/MEG.0000000000001014] [PMID]

[20] Azuma T, Suto H, Ito Y, Muramatsu A, Ohtani M, Dojo M, et al. Eradication of Helicobacter pylori infection induces an increase in body mass index. Alimentary Pharmacology & Therapeutics. 2015; 41(Suppl 2):240-4. [DOI:10.1007/s11686-016-3231-x] [PMID]

[21] Lane JA, Murray JJ, Harvey IM, Donovan JL, Nair P, Harvey RF. Randomised clinical trial: Helicobacter pylori eradication is associated with a significantly increased body mass index in a placebo-controlled study. Alimentary Pharmacology & Therapeutics. 2011; 33(8):922-9. [DOI:10.1111/j.1365-205x.2011.04610.x] [PMID]