



The Association Between *Helicobacter pylori* Infection and Rosacea

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Abstract

Background: *Helicobacter pylori* (*H. pylori*) is one the most infectious microorganism of human disease found in half of the world's population. Despite intense investigations into the spread of rosacea, the precise etiology remains unclear. There are theories, which suggest *H. pylori* as a predisposing factor for the occurrence. This study aimed at determining the prevalence of *H. pylori* in patients with rosacea.

Methods: This analytical-descriptive study was conducted on patients with rosacea disease attending Tabriz University of Medical Sciences Dermatology Clinics from October 2011 to January 2011. Patients, who were 18- to 65-year-olds with confirmed rosacea diagnosis, were included in the study. All patients were referred to a dermatologist and the severity of rosacea was categorized in 3 grades of mild, moderate and severe. Then *H. pylori* infection was investigated using *H. pylori* stool antigen. P values of less than 0.05 were considered statistically significant.

Results: Out of 63 patients with rosacea, 35 patients (55.55%) were male and 28 patients (44.44%) were female. Based on the rosacea categorization, 11 (17.46%), 32 (50.79%), and 20 (31.74%) patients had respectively severe, moderate, and mild rosacea. There was no statistical significant difference regarding age and gender between different severities ($P = 0.39$). Forty patients (63.4%) out of all 63 were positive for *H. pylori* on stool antigen examination. There was no statistically significant association between *H. pylori* infection and gender ($P = 0.87$) or age ($P = 0.62$). There was a statistically significant difference between patients with *H. pylori* negative and positive test results considering severity ($P = 0.013$).

Conclusions: In conclusion, although no association between rosacea and *H. pylori* infection was seen, there was a significant association between *H. pylori* infection and cases of severe rosacea.

Keywords: Rosacea, Prevalence, Severity, *Helicobacter pylori*

1. Background

Helicobacter pylori are gram-negative spiral-shaped bacteria that colonize the gastric mucosa lining and tend to cause upper GI diseases (1). Although they can be present in 50% of the population worldwide, studies show that in developing countries, *H. pylori* infection is well over twice the population in developed countries (2). Some studies suggest that these bacteria can also be linked to non-gastroenterological diseases, such as ischemic heart disease, idiopathic thrombocytopenic purpura, and iron deficiency anemia (3-9). Risks for the incidence depends on the environment and poor living conditions (10, 11). The risk is higher mostly due to low socioeconomics by the theory of "contagion through society" (12). Epidemiologic reviews show most infections occur during childhood (13). Birth in developing countries is correlated with higher rates of

infection, specifically crowded living conditions and poor socioeconomics (14). It seems that these bacteria are typically transferred through same age groups in families, yet then to the other members (15). Recent evidences suggest the principle role for *H. pylori* in dermatological problems, including Reynaud, rosacea, and urticarial rosacea, which is a chronic skin condition with frequent episodic characteristics, such as flushing, skin erythema, papulopustules, and skin telangiectasias (16, 17).

Helicobacter pylori of the gastric mucosa being considered as a pathogenic factor for rosacea has been controversial. Many reports have been published on the prevalence of *H. pylori* infection among patients with rosacea (11, 18-23), which ranges from studies reporting prevalence of 100% to studies indicating no significant difference between healthy people and the rosacea group (24, 25). De-

spite intense investigations on the spread of rosacea, the precise etiology remains unclear. There are some theories that suggest that *H. pylori* is a predisposing factor for occurrence; nevertheless, different results have been retrieved. Therefore, considering this controversy mentioned in the literature, in the present study, it was aimed to show the incidence of *H. pylori* infection in patients with Rosacea.

2. Methods

This analytical-descriptive study was conducted on patients with rosacea disease attending Tabriz University of Medical Sciences dermatology clinics from October 2011 to January 2011. Patients from age 18 to 65 years with confirmed rosacea diagnosis were included in the study. In the case of any other dermatologic problem, former *H. pylori* eradication treatment, allergies to omeprazole or clarithromycin, topical treatment of rosacea in the past 3 weeks, antibiotic therapy within the past 3 months, and history of hospitalization in the past 6 months, patients were excluded from the study. All included patients, were precisely examined by a dermatologist to estimate the severity of rosacea, and were categorized to 3 grades of mild, moderate, and severe, according to the classification method proposed before (Table 1) (26). All demographic information, such as age, gender, and marital status, was collected at patients' enrollment time.

Table 1. Rosacea Classification Used Based on the Clinical Manifestations

Classification	
Mild	1. Intermittent redness on chin, hands, and nose
	2. Visibly broken blood vessels appearing on skin
	3. Foreign body sensation in eyes in some cases, gritty sensation and feeling irritated
Moderate	1. Persistent redness on facial skin
	2. Macules appearing on skin, Acne-like breakouts
	3. Skin begins to thicken, Visible broken blood vessels (spider veins)
Severe	4. Reddish eyes, bloodshot appearance
	1. Progressive skin redness
	2. Erythema swelling and nose edema
	3. Blurred vision, inflamed eyes and orbit

To assess *Helicobacter pylori* infection, an applicator stick of 4 to 5 mm of stool was transferred in a diluent vial, and was vortexed for 20 seconds. Then, 4 drops of the vial was dispensed in ImmunoCard STAT HpSA kit (Meridian Diagnostics, Inc., OH, USA); negative and positive results were interpreted based on the manufacturer's recommendation. Statistical analysis was performed by the

SPSS software package, version 16.0, for Windows (SPSS Inc., Chicago, USA). Quantitative data are presented as the mean \pm standard deviation (SD), while qualitative data are demonstrated as frequency and percentages (%). Student t-test, Fischer's exact and Analysis of Variance (ANOVA) were used for analysis of data. P values of less than 0.05 were considered statistically significant.

3. Results

During 3 months, 63 patients were included in the study. Out of 63 patients with rosacea, 35 patients (55.55%) were male and 28 patients (44.44%) were female. The severity of rosacea among patients based on gender is shown in Table 2. The mean age of the patients was 36.46 ± 9.28 years old. Moreover, patients afflicted with severe forms were 39.9 ± 10.53 years of age, moderate forms had an average age of 35.93 ± 10.00 and those with the mild form were aged 35.4 ± 7.04 years. There was no statistical significant difference according to age, as listed formerly ($P = 0.39$). In addition, 40 patients (63.4%) out of 63 were positive for *H. pylori* on stool antigen examination. Of all *H. pylori* positive patients, 24 patients (38.09%) were male and 16 patients (25.39%) were female. There was no statistically significant association between *H. pylori* infection and gender ($P = 0.87$). The mean age in patients with *H. pylori* positive test results was 37.02 ± 9.84 years old and in those with negative test results, mean age was 35.47 ± 8.28 years old; no statistically significant difference was found between them ($P = 0.62$). The severity and *H. pylori* antigen status are shown in Table 3; there was a statistically significant difference between patients with *H. pylori* negative and positive test results, considering severity ($P = 0.13$). This difference indicated greater *H. pylori* positive results in severe cases and mild cases mostly had *H. pylori* negative test results. Figure 1 shows the *H. pylori* antigen status among patients categorized based on severity.

Table 2. Severity of Rosacea Among Patients Based on Gender^a

	Female	Male	Total
Severe	7 (11.11)	4 (6.34)	11 (17.46)
Moderate	15 (23.8)	17 (26.98)	32 (50.79)
Mild	6 (9.52)	14 (22.22)	20 (31.74)
Total	28 (44.44)	35 (55.55)	63 (100)

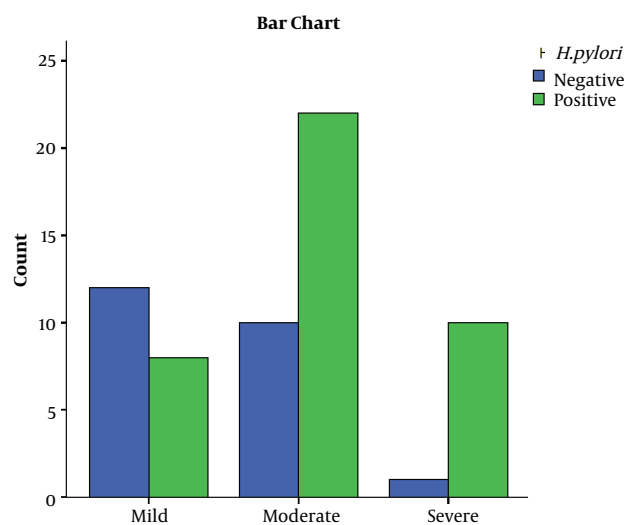
^aValues are expressed as No. (%).

4. Discussion

Helicobacter pylori is one of the most infectious microorganisms of human disease that is found in half of the

Table 3. Severity of Rosacea Among Patients Based on *H. pylori* Status

	Positive <i>H. pylori</i>	Negative <i>H. pylori</i>	Total	P Value
Severe	10 (15.87)	1 (1.58)	11 (17.46)	0.04
Moderate	22 (23.8)	10 (15.87)	32 (50.79)	0.43
Mild	8 (12.69)	12 (19.04)	20 (31.74)	0.01
Total	40 (63.49)	23 (36.5)	63 (100)	

**Figure 1.** *H. pylori* Antigen Status Among Patients Categorized Based on Severity

world's population and proved to have participated in rosacea disease development. Rosacea is a chronic dermatological disease, with an unknown pathogenesis process, which has been the subject of many studies (27). Gastric infection with *H. pylori* is one of the proposed pathogenic sources of rosacea establishment (28), thus many researchers have tried to examine this association by trying to investigate the correlation between *H. pylori* infection and rosacea. This study aimed at showing the prevalence of *H. pylori* in patients with rosacea. In the present study, of 63 patients with rosacea, 40 (63.4%) had positive *H. pylori* stool antigen. Prevalence of *H. pylori* varies worldwide depending on age. In a systematic review study by Eusebi et al. about epidemiology of *H. pylori* infection, it was concluded that in European and North American people, about one-third of adults are infected, yet in South America and Asia, the prevalence of *H. pylori* is often higher than 50% and there was a low prevalence of infection in the younger generations, with the authors suggesting that it may lead to a decline of *H. pylori* prevalence in the coming decades (29). Studies conducted in Iran regarding the prevalence of *H. pylori* have reported rates from 50% to 90% (30-32); thus,

the results presented among patients with rosacea reveals no significant difference with the general population.

In the present study, comparing the 2 groups of *H. pylori* antigen negative and positive reveals a statistically greater number of severe rosacea in patients with *H. pylori* positive results when compared with the *H. pylori*-negative group. Also, the number of mild cases of rosacea in *H. pylori*-negative group was statistically higher than cases of severe rosacea in *H. pylori*-positive group. This indicates a tendency for rosacea progression among *H. pylori* positive rosacea patients, although there were no differences between the 2 groups of *H. pylori* positive and negative when considering age and gender.

In a study by Argenziano et al. the probable association between serological evidence of *H. pylori* infection and rosacea was investigated and it was concluded that there is a significant association between rosacea and *H. pylori* infection (33). However, Abram et al. evaluated several suspected risk factors for rosacea and concluded that there was no statistically significant differences between rosacea patients and those of the control group (34); the present study revealed no association between *H. pylori* and rosacea, while it revealed an association between *H. pylori* infection and severe rosacea. In an interventional study by Utas et al. about effects of *H. pylori* eradication on rosacea, it was shown that although *H. pylori* eradication treatment does not treat rosacea completely, it decreases the severity (35); this study supports the current findings, which indicates existence of an association between *H. pylori* infection and severe rosacea.

In a study by Crawford et al., it was proposed that there is a high probability of repetitive *H. pylori* positive laboratory test results among people with severe rosacea disease (36); this is similar to the current study, where severe rosacea forms were associated with *H. pylori* positive antigen. In a study by Alborzi et al. investigating the prevalence of *H. pylori* infection in children, it was concluded that *H. pylori* prevalence decreases with age (37). Also in developing countries, this pattern of decline has been reported; in a study by Roosendaal et al. studying the prevalence of *H. pylori* from the first months of birth to adolescence rates of about 20% to 10% were reported. This is in contrast with the conclusions of the current study, although the sample

population was chosen among patients with rosacea.

The controversy in this field could have many etiologies. Methods of how *H. pylori* are diagnosed is one factor, which is different amongst various studies; diagnosis methods include *H. pylori* stool antigen, serum *H. pylori* IgG, mucosal biopsy and C-Urea breath test (38, 39). These methods, besides sensitivity and specificity, have greater differences where invasiveness and financial aspects are counted, thus each researcher may choose a method based on the circumstances, while unknowingly creating a bias. Another factor expanding this controversy is population selection; besides significant differences in *H. pylori* prevalence based on location and racial aspects (40, 41), most of the populations are selected in a way that selection bias occurs when including patients attending clinical centers, while most of the patients with *H. pylori* infection are asymptomatic.

4.1. Conclusions

In conclusion, there is no association between rosacea and *H. pylori* infection, although there was a significant association between *H. pylori* infection and severe rosacea. The current study showed no difference between groups considering age and gender. Results of the present study could be an outline for further interventional and cohort studies, which could lead to a more precise conclusion. Further studies are encouraged with a larger population considering other probable confounding covariates.

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