Case-controlled Study

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# Evaluation of *IL-17F* A7488G polymorphism in *Helicobacter pylori*-infected patients: a case–control study

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**Objective:** Interleukin 17 (IL-17) plays an important role in the inflammation of the gastric mucosa and, in severe cases, the development of gastric cancer. Thus, the authors aimed to evaluate the *IL-17F* A7488G polymorphism in *Helicobacter pylori* (*H. pylori*) patients.

**Patients and methods:** A total of 86 adults (in two *H. pylori*-positive and *H. pylori*-negative groups) were included in the study. To identify the infection, rapid urease test and polymerase chain reaction (PCR) were performed. The *cagA* gene was also evaluated as a bacterial virulence factor. PCR–restriction fragment length polymorphism was used to investigate the *IL-17F* A7488G polymorphism in gastric biopsies using the *NlaIII* enzyme.

**Results:** 96.5% of patients in both groups did not show any mutation and had AA genotype, and only three patients infected with *cagA*-carrying *H. pylori* strains had polymorphism in the *IL-17F* A7488G gene, which included AG (one case) and GG (two cases) patterns. No significant relationship was found between these polymorphisms in the two groups of *H. pylori*-positive and *H. pylori*-negative patients, while, interestingly, a significant difference was observed between the polymorphisms and the presence of the *cagA* gene.

**Conclusion:** This report is one of the first to demonstrate the association of *IL-17F* A7488G polymorphism with *H. pylori* infection and the presence of the *cagA* gene. Although no significant association between *IL-17F* polymorphism and *H. pylori* infection was found in the population of this study, the patients with mutated genotypes were positive for the *cagA* gene, which was statistically significant. Therefore, the possibility of the role of pathogenic strains in causing mutations in cytokine genes is more conceivable.

**Keywords:** *cagA*, *Helicobacter pylori*, *IL-17F*, Iran, polymorphism, rs763780

## Introduction

*Helicobacter pylori* (*H. pylori*) is a gram-negative bacterial pathogen that colonizes the gastric epithelium and was identified by Warren and Marshall in 1983[1]. This bacterium is the most common cause of chronic infection in humans worldwide and is usually seen in all age groups[2]. The prevalence of infection caused by this bacterium is different in each country and population and is directly associated with the people's social and economic status[3]. Most people colonized with *H. pylori* have no specific symptoms, while in some cases it can cause various clinical complications from gastritis, gastric atrophy, peptic and duodenal ulcers to finally mucosa-associated lymphoid tissue (MALT) lymphoma and gastric cancer[4,5]. Reports have indicated that less than 3% of patients develop gastric adenocarcinoma and less than 0.1% develop MALT lymphoma[6].

### HIGHLIGHTS

- This study provides the first data on *IL-17F* A7488G gene polymorphisms among individuals with *Helicobacter pylori* infection in Qom.
- This study is the first study on interleukin 17 polymorphism and *cagA*.

*H. pylori* infection and the progression of related diseases are influenced by the heterogeneity of bacterial virulence genes, host genetic susceptibility to infection, regulation of host/pathogen genes expression, and environmental factors[7]. Among *H. pylori* virulence factors, cytotoxin-associated gene A protein (CagA) is well known, and its gene encoding is in a gene region called cagPAI (cag pathogenicity island). This protein plays an important role in pathogenesis, especially in the development of gastric cancer[8].

Chronic *H. pylori* infection can induce innate and acquired immune responses and the overexpression of pro-inflammatory cytokines such as interleukins (ILs), tumor necrosis factor-alpha (TNF-α), and interferons (IFNs), which ultimately leads to gastritis, etc.[9]. Among cytokines, interleukin 17 (IL-17), as a pro-inflammatory cytokine, is a homodimeric glycoprotein consisting

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of 155 amino acids with a molecular weight of 35 kDa produced by a broad spectrum of cell populations, including T helper 17, γδT, NKT cells, etc.[10,11]. This cytokine is a primary factor in inflammatory responses that induce the expression of IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor (GM-CSF), resulting in inflammation[11]. IL-17 family includes isoforms A to F, where IL-17A and IL-17F are located on chromosome 6 (6p12)[12]. Reports have shown that T helper 17 cells and IL-17 are involved in many disorders, including rheumatoid arthritis, psoriasis, multiple sclerosis, inflammatory bowel diseases, lupus erythematosus, etc.[11,13,14].

Cytokine gene polymorphisms are usually associated with host susceptibility to varying diseases[15,16]. Numerous studies have shown that polymorphisms in pro-inflammatory or anti-inflammatory cytokine genes, including IL-1β, IFN-γ, IL-17, IL-6, and IL-10, are associated with a higher risk of active gastritis and stomach cancer[17–19]. Among these, polymorphisms in *IL-17A* and *IL-17F* genes increased the risk of gastrointestinal diseases, especially in cancers[20–22]. However, limited data are available on these polymorphisms and *H. pylori* infection in the world as well as in Iran. Therefore, the aim of this study was to investigate the association of *IL-17F* A7488G (His161Arg, rs763780) polymorphism with *H. pylori* infection and the presence of the *cagA* virulence gene in Qom, Iran, for the first time.

## Material and methods

### Patients

This case–control study was conducted for 12 months (2020–2021) on patients referred to the endoscopy department of Shahid-Beheshti Hospital in Qom. In fact, the patients included in the study were those who were recommended to perform endoscopy in their treatment process based on the decision of the gastroenterologist. Therefore, no additional endoscopy was performed for the patients.

Based on the researcher's estimates and considering the percentage of polymorphism in two groups equal to 18% and 1% and using the percentage comparison formula, the sample size of 86 people (43 in each group) was calculated. Sampling continued until reaching 43 people in both groups. The case group consisted of patients who were positive for *H. pylori* infection, and the control group was those who were not infected. The main inclusion criteria were patient satisfaction and no history of using anti-*H. pylori* drug regimens during the past 3 weeks prior to sampling.

### Sampling

After recording informed written consent, demographic information, and clinical symptoms of the patients, the endoscopy was performed by a gastroenterologist. One biopsy sample was taken from the incisura angularis of each patient and endoscopic findings were also recorded. The sample was divided into two parts: one for initial infection screening using rapid urease test (RUT) and the other for molecular evaluations using polymerase chain reaction (PCR) for 16S rRNA, *cagA*, and *IL-17F* genes. The last sample was kept in a sterile physiological buffer at – 20°C until genome extraction.

### DNA extraction and PCRs

Total DNA was extracted from biopsy specimens using FavorPrep Tissue Genomic DNA Extraction Mini Kit (Favorgen Biotech, Ping-Tung, Taiwan) according to the manufacturer's instructions. For a definitive diagnosis of *H. pylori* infection, a fragment of the 16S rRNA gene was evaluated using PCR. Next, all positive samples containing the 16S rRNA gene were analyzed for the presence of the *cagA* virulence gene. The final PCR test was carried out to amplify the *IL-17F* gene.

PCRs were performed in a final volume of 25 μl, containing 10 μl of 2× Master Mix (Ampliqon, Denmark), 1 μl of each primer (10 pmol/μl) listed in Table 1 (Metabion, Germany), 5 μl of the extracted genome, and 8 μl of sterile distilled water. The PCR temperature cycling conditions were as follows: initial denaturation (95°C/5 min for one cycle), and then denaturation (94°C/30 s), annealing (54°C/60 s for 16S rRNA, *cagA*, and *IL-17F* genes), extension (72°C/30 s) was performed in 33 cycles, and then 72°C for 10 min in a thermocycler (Eppendorf, Hamburg, Germany). Finally, the PCR products were examined on 1% agarose gel.

### IL-17F A7488G genotyping by PCR–restriction fragment length polymorphism (PCR–RFLP)

Ten microliters of the *IL-17F* PCR product was digested with 1 μl of *NlaIII* restriction enzyme (Thermo Scientific, USA) for 5 h at 37°C in the buffer recommended by the supplier and visualized after separation by electrophoresis on 3% agarose gel. One to three patterns are expected to be observed after digestion by *NlaIII* enzyme and electrophoresis: one fragment of 143 bp (lacking the digestion site, GG genotype); two fragments of 80 and 63 bp (AA genotype); or three fragments of 143, 80, and 63 bp in length (AG genotype)[26].

### Statistical analysis

The relationship between infection, polymorphism, age, gender, and other variables in both groups was calculated by Fisher's exact test, $\chi^2$ test (with exact method), and independent *t*-test. Statistical analysis was performed using the statistical program SPSS version 22 (IBM, New York, USA). A *P*-value of less than 0.05 was considered statistically significant.

## Results

Of the 86 patients participating in this study, 49 (57.0%) and 37 (43.0%) were male and female, respectively, with a mean ± SD age of 47.10 ± 16.83 years. Also, the mean ± SD of height and weight was 167.50 ± 9.76 cm and 72.52 ± 18.03 kg, respectively.

**Table 1**

**Primers used in this study.**

| Target gene | Sequence (5′→3′) | Size of products (bp) | Reference |
|---|---|---|---|
| 16S rRNA | F: CTGGAGAGACTAAGCCCTCC<br>R: ATTACTGACGCTGATTGTGC | 110 | [23] |
| *cagA* | F: CGGTATCAGTGGCTAAAGC<br>R: AGCAACTTGAGCGTAAATG | 377 | [24] |
| *IL-17F* | F: ACCAAGGCTGCTCTGTTTCT<br>R: GGTAAGGAGTGGCATTTCTA | 143 | [25] |

IL-17F A7488G genotyping by PCR–restriction fragment length polymorphism (PCR-RFLP).

16S rRNA PCR results confirmed that all 43 RUT-positive samples had *H. pylori* infection and no positive cases were observed in patients with negative urease tests. The positive infection rate in men was significantly higher than in women (69.8% vs. 30.2%). Except for gender ($P$-value = 0.017), there was no significant difference between age, height, weight, etc., and *H. pylori* infection. More information about patients is presented in Table 2.

Based on the recorded findings of all patients, the most clinical symptom was abdominal pain (61.6%), and the least was diarrhea (3.5%). The highest number of endoscopic findings was also duodenal ulcer (23.3%), and the lowest were gastric cancer (1.2%) and hiatal gastric hernia (1.2%).

In the *H. pylori*-positive group, the highest and lowest clinical symptoms were related to abdominal pain (74.4%) and diarrhea (2.3%), while the highest and lowest endoscopic findings were correlated with duodenal ulcer (27.9%) and cancer (0.0%), respectively. No significant correlation was observed between clinical symptoms/endoscopic findings in both *H. pylori*-positive and *H. pylori*-negative groups, except for abdominal pain. Moreover, the results of the frequency of the *cagA* gene in *H. pylori*-infected patients showed that 13 of 43 cases (30.2%) were positive. There was no significant difference between clinical symptoms/endoscopic findings and the presence of the *cagA* gene (Table 3).

Based on *IL-17* enzymatic digestion on 86 samples and the pattern of fragments observed on electrophoresis (Fig. 1), our results showed that 83 samples (96.5%) had AA genotype, two patients had GG genotype, and one case had AG genotype. No significant relationship was found between polymorphisms in the two groups of *H. pylori*-positive and *H. pylori*-negative patients. All three patients with AG and GG patterns belonged to the case group and were positive for the *cagA* gene. Interestingly, a significant difference was observed between the *IL-17F* polymorphism and the presence of the *cagA* gene ($P = 0.003$) (Table 4). Also, more information about the three patients is provided in Table 5.

## Discussion

*H. pylori* is one of the most important causes of gastric diseases worldwide[3]. In studies conducted in Iran, the prevalence of this infection varies between 36 and 90% in different geographical areas[27]. Most infections caused by this bacterium are asymptomatic and can persist for a long time, causing inflammation of the stomach and inducing gastritis, gastric cancer, etc.[6]. Usually, bacterial pathogens alone cannot play a full role in disease progression, and therefore other factors, including host factors, especially those that regulate immune and inflammatory responses, also play an important role in this process[28]. In order to increase knowledge in this field of study, it seems that it is important to evaluate infections and bacterial genetic traits along with host factors among different populations. Thus, this study was conducted to investigate the *IL-17F* polymorphism for the first time in *H. pylori*-positive patients in Qom at the same time as evaluating one of the bacterial virulence factors.

Various methods are used to diagnose *H. pylori* infection, including culture, serological methods, molecular assays, urease tests, etc., among which molecular techniques are more sensitive[29,30]. In this study, 16S rRNA gene was used to confirm the infection, the results of which were similar to the RUT and there were no false positives or negatives. Lu *et al.*'s study compared five molecular PCR assays using 16S rRNA gene, random chromosome sequence, 26-kDa *Helicobacter* species-specific antigen gene, and *ureA* and *ureC* genes (urease A and C) to detect *H. pylori* in gastric tissue. Their results showed that 16S rRNA and *ureC* genes could detect 100% of the *H. pylori*-positive cases with high sensitivity[31].

The mean age of patients in the *H. pylori*-positive group was 45.12 years, which showed a lower rate than the *H. pylori*-negative group. Moreover, there was no statistically significant difference between the *H. pylori*-positive and *H. pylori*-negative patients in terms of age, which is consistent with Bazin's study in France[32]. Some other studies also show the prevalence of *H. pylori* infection depending on age in different countries. For example, a study by Venerando *et al.*[33] in Brazil showed that patients under 10 years of age are 1.3 times more susceptible to *H. pylori* infection. Another study by Mori *et al.*[34] in Malaysia reported that the highest infection rate was in patients aged 30–39 years.

Our results showed that BMI has no significant relationship with *H. pylori* infection, which is consistent or contradictory with some other studies. For example, in a study by Xu *et al.*[35] among the Chinese population, BMI was significantly associated with *H. pylori* infection, while Kyriazanos *et al.*[36] in Greece showed that the presence of obesity was not related to the status of *H. pylori* positivity. Also, the smoking status among our patients in both groups had no significant relationship, which is consistent with the study of Khalifa *et al.*[37].

In addition, our findings showed that the most clinical symptoms in *H. pylori*-infected patients were abdominal pain. Lubetzky *et al.*[38] also stated that abdominal pain was the main manifestation in patients infected with this bacterium. Furthermore, in our case group, the most common endoscopic results were duodenal ulcers, which is in agreement with other studies. In the Otero Regino *et al.*[39] study in Colombia, 76 of 104 patients (73%) with duodenal ulcers were positive for *H. pylori*.

Except for abdominal pain, our results showed no significant difference between the two groups of patients in terms of other clinical symptoms as well as endoscopic findings. Various studies have shown that these symptoms and findings may have etiological factors other than *H. pylori* infection. For example, the cause of gastritis and peptic ulcer disease in *H. pylori*-negative patients may be due to smoking, stress, alcohol consumption,

**Table 2**

**Comparison of demographic variables between two groups of patients.**

| | Groups | | | |
|---|---|---|---|---|
| **Variables** | **Total** | **Case** | **Control** | ***P*** |
| Gender, *N* (%) | | | | |
| Male | 49 (57.0) | 30 (69.8) | 19 (44.2) | 0.017 |
| Female | 37 (43.0) | 13 (30.2) | 24 (55.8) | |
| Age (M ± SD), year | 47.10 ± 16.83 | 45.12 ± 14.88 | 49.09 ± 18.55 | 0.276 |
| Height (M ± SD), cm | 167.50 ± 9.76 | 165.91 ± 9.73 | 169.09 ± 9.65 | 0.131 |
| Weight (M ± SD), kg | 72.52 ± 18.03 | 70.42 ± 14.76 | 74.63 ± 20.77 | 0.282 |
| BMI (M ± SD), kg/m$^2$ | 25.76 ± 5.6 | 25.46 ± 4.31 | 26.07 ± 6.70 | 0.621 |
| Smoking, *N* (%) | 5 (5.81) | 3 (7.0) | 2 (4.7) | 0.50 |
| Education level, *N* (%) | | | | |
| Less than Diploma | 60 (69.8) | 28 (65.1) | 32 (74.4) | 0.515 |
| Diploma | 17 (19.8) | 9 (20.9) | 8 (18.6) | |
| Bachelor and higher | 9 (10.5) | 6 (14.0) | 3 (7.0) | |

BMI, body mass index; M ± SD, mean ± standard deviation; *N*, number.

**Table 3**

**Comparison between clinical symptoms and endoscopic findings in two groups of patients and their relationship with the presence of the *cagA* gene.**

| | Groups | | | | | | |
|---|---|---|---|---|---|---|---|
| | | *H. pylori* | | | *cagA* | | |
| Variables | Total, *N* (%) | Positive (*N* = 43), *N* (%) | Negative (*N* = 43), *N* (%) | *P* | Positive (*N* = 13), *N* (%) | Negative (*N* = 30), *N* (%) | *P* |
| Clinical symptoms | | | | | | | |
| Abdominal pain | 53 (61.6) | 32 (74.4) | 21 (48.8) | 0.015 | 12 (92.3) | 20 (66.7) | 0.077 |
| Weight loss | 24 (27.9) | 13 (30.2) | 11 (25.6) | 0.631 | 2 (15.4) | 11 (36.7) | 0.163 |
| Heartburn | 21 (24.4) | 10 (23.3) | 11 (25.6) | 0.802 | 3 (23.1) | 7 (23.33) | 0.985 |
| Decreased appetite | 21 (24.4) | 14 (32.6) | 7 (16.3) | 0.079 | 2 (15.4) | 12 (40.0) | 0.114 |
| Nausea | 39 (45.3) | 19 (44.2) | 20 (46.5) | 0.829 | 5 (38.5) | 14 (46.7) | 0.619 |
| Diarrhea | 3 (3.5) | 1 (2.3) | 2 (4.7) | 0.557 | 0 (0.0) | 1 (3.3) | 0.505 |
| Bloating | 13 (15.1) | 7 (16.3) | 6 (14.0) | 0.763 | 1 (7.7) | 6 (20.0) | 0.315 |
| Endoscopic findings | | | | | | | |
| Duodenal ulcer | 20 (23.3) | 12 (27.9) | 8 (18.6) | 0.307 | 6 (46.1) | 6 (20.0) | 0.079 |
| Gastritis | 12 (14.0) | 3(7.0) | 9 (20.9) | 0.062 | 0 (0.0) | 3 (10.0) | 0.237 |
| Gastroesophageal reflux | 3 (3.5) | 1 (2.3) | 2 (4.7) | 0.557 | 1 (7.7) | 0 (0.0) | 0.124 |
| Gastric ulcer | 4 (4.7) | 1 (2.3) | 3 (7.0) | 0.306 | 0 (0.0) | 1(3.3) | 0.505 |
| Hiatal gastric hernia | 1 (1.2) | 1 (2.3) | 0 (0.0) | 0.314 | 1 (7.7) | 0 (0.0) | 0.124 |
| Gastric cancer | 1 (1.2) | 0 (0.0) | 1 (2.3) | 0.314 | 0 (0.0) | 0 (0.0) | – |

viral infections, and/or the use of non-steroidal anti-inflammatory drugs (NSAIDs) or steroids, etc.[40–42]. In another study, obesity was associated with a statistically significant increase in the risk of gastroesophageal reflux disease symptoms[43].

Evaluation of the *cagA* gene in the positive samples of *H. pylori* revealed that 30.2% of strains carried this gene. This finding shows a lower prevalence of this gene compared to other studies. In a study in Iran, the prevalence of the *cagA* gene among gastroesophageal reflux disease patients was 44.4%[44]. In Saudi Arabia, 49.2% of *H. pylori*-positive cases were also positive for *cagA*[45]. In addition, a higher prevalence of this gene has been reported in some studies in China, one of which showed that 85.3% of *H. pylori* strains contained the *cagA* gene[46], while the other stated 96.2 and 97.4% positive cases from the antrum and corpus samples, respectively[47]. Overall, these findings show that the presence of this gene is completely different in different geographical areas.

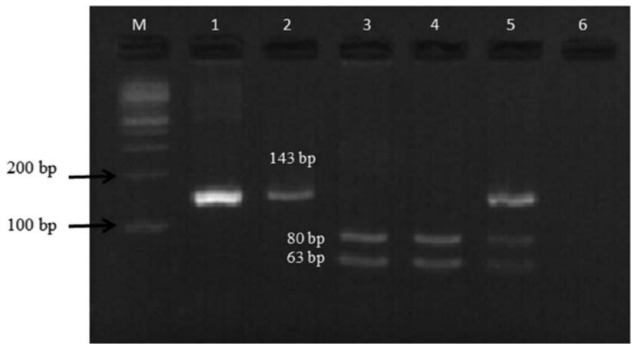


**Figure 1.** PCR–RFLP electrophoresis gel. M: 100 bp marker; lane 1: PCR product of IL-17 (positive control, without enzymatic digestion); lane 2: GG pattern; lanes 3 and 4: AA pattern; lane 5: AG pattern; lane 6: negative control. PCR, polymerase chain reaction; RFLP, restriction fragment length polymorphism.

According to PCR–RFLP results, 83 of the patients in both groups did not show any mutation and had wild AA genotype, and three cases had AG and GG mutant genotypes. No significant relationship was observed between both groups and the *IL-17F* gene polymorphism. There are different published results in this field. Arisawa *et al*. reported genetic polymorphisms in Japanese subjects with functional dyspepsia. They indicated a significant association between *IL-17F* polymorphism and the development of functional dyspepsia, especially epigastric pain syndrome, among *H. pylori*-positive patients[48]. Similar to our study, Ghorbani *et al*.[49] in Sari, northern Iran, found no association between the *IL-17F* A7488G polymorphism and stages/grades of gastric cancer and *H. pylori* infection. In another study conducted in Shahrekord, near the southwest of Iran, Shirzad *et al*.[50] also reported that there was no change in the mucosal pattern of *IL-17F* A7488G in subjects with *H. pylori*-associated gastritis. Compared with these reports, our study was performed on gastric tissue samples from *H. pylori* patients with a wider range of clinical symptoms and endoscopic findings, which seems to be superior to theirs.

Furthermore, in the current study, *IL-17F* A7488G polymorphisms with a virulence factor of *H. pylori* were evaluated for the first time. Our results showed that three patients with AG and

**Table 4**

**Comparison between *IL-17F* polymorphisms according to the *Helicobacter pylori* infection and presence of the *cagA* gene.**

| | Groups | | | | | |
|---|---|---|---|---|---|---|
| | *H. pylori* | | | *cagA* | | |
| Genotypes | Positive (*N* = 43) | Negative (*N* = 43) | *P* | Positive (*N* = 13) | Negative (*N* = 30) | *P* |
| AA, *N* (%) | 40 (93.0) | 43 (100.0) | 0.241 | 10 (76.9) | 30 (100.0) | 0.003 |
| AG, *N* (%) | 1 (2.3) | 0 (0.0) | | 1 (7.7) | 0 (0.0) | |
| GG, *N* (%) | 2 (4.7) | 0 (0.0) | | 2 (15.4) | 0 (0.0) | |

**Table 5**

**Information of three patients with *IL-17F* polymorphisms.**

| Patients | Polymorphism | Age (year) | Gender | Clinical symptoms/endoscopic findings |
|---|---|---|---|---|
| Case 1 | AG | 38 | Female | Abdominal pain, heartburn |
| Case 2 | GG | 44 | Male | Duodenal ulcer |
| Case 3 | GG | 37 | Male | Duodenal ulcer, decreased appetite |

GG mutations were also positive for the *cagA* gene, and there was a significant relationship between the polymorphism of the cytokine and the presence of this gene. In the study of Mizuno *et al.*, IL-17 secretion and IL-17 mRNA expression in *H. pylori*-infected gastric mucosa were investigated. Their results showed that all *H. pylori* strains had *cagA* and *vacA* virulence genes and suggested that IL-17 may play an important role in the inflammatory response to bacterial colonization, which may ultimately affect the outcome of *H. pylori*-related diseases[51].

## Conclusions

This study is one of the first to demonstrate *IL-17F* A7488G polymorphism among subjects with *H. pylori* infection and the presence of the *cagA* virulence gene. The findings show no significant association between *IL-17F* polymorphism and *H. pylori* positivity among our patients. All three patients with AG and GG mutant genotypes were positive for the *cagA* virulence gene, thus it could prove a stronger relationship between pathogenic strains and cytokine polymorphism. However, due to the small number of patients with *IL-17F* polymorphism, statistical inference in this regard may be associated with relatively low accuracy. Therefore, it is recommended to conduct future studies with a larger sample size. In addition, the relationship between *H. pylori* treatment outcomes and cytokine polymorphisms is an interesting topic that is suggested to be investigated in future studies.

## Limitations

Due to financial constraints, it was not possible to study more pathogenic genes of the target bacteria as well as other polymorphisms of *IL-17*. Unfortunately, most of our patients had no information about taking NSAIDs or steroids. Therefore, incomplete information about these cases is not given in our results.

## Ethical approval

The study was reviewed and approved by the Medical Ethics Committees of Islamic Azad University, Qom Branch, and Qom University of Medical Sciences (code: IR.IAU.Qom.REC.1397.006).

## Consent

This study is not a case report.

## Sources of funding

Not applicable.

## Author contribution

A.H. and S.S.: developed and supervised the work; F.S.M.R.: performed the experiments; S.S. and M.A.: drafted the manuscript; A.H., S.S., and M.A.: contributed to data interpretation. All authors reviewed the manuscript. All authors read and approved the final manuscript.

## Conflicts of interest disclosure

The authors declare that there are no conflicts of interest.

## Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: 8807.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):not applicable.

## Guarantor

Saeed Shams.

## Data availability statement

I confirm if any datasets generated during and/or analyzed during the current study are publicly available, available upon reasonable request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

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## References

[1] Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. The Lancet 1983;321:1273–5.
[2] Mehdipour A, Chaboki P, Rasouli Asl F, *et al*. Comparing the prevalence of *Helicobacter pylori* and virulence factors cagA, vacA, and dupA in supra-gingival dental plaques of children with and without dental caries: a case–control study. BMC Oral Health 2022;22:170.
[3] Watari J, Chen N, Amenta PS, *et al*. *Helicobacter pylori* associated chronic gastritis, clinical syndromes, precancerous lesions, and pathogenesis of gastric cancer development. World J Gastroenterol 2014;20:5461.

[4] Ailloud F, Didelot X, Woltemate S, *et al*. Within-host evolution of *Helicobacter pylori* shaped by niche-specific adaptation, intragastric migrations and selective sweeps. Nat Commun 2019;10:1–13.
[5] Ghoddoosi M, Teymoori M, Mirtalebi Roknabadi FS, *et al*. Evaluation of *Helicobacter pylori* and NapA gene in paraffin blocks of gastric adenocarcinoma tissues from pathology bank of Shahid Beheshti Hospital, Qom, Iran (2011-2017). Gazi Med J 2021;32:40–4.
[6] Wroblewski LE, Peek RM Jr, Wilson KT. *Helicobacter pylori* and gastric cancer: factors that modulate disease risk. Clin Microbiol Rev 2010;23:713–39.
[7] Cadamuro ACT, Rossi AFT, Maniezzo NM, *et al*. *Helicobacter pylori* infection: host immune response, implications on gene expression and microRNAs. World J Gastroenterol 2014;20:1424.
[8] Yong X, Tang B, Li B-S, *et al*. *Helicobacter pylori* virulence factor CagA promotes tumorigenesis of gastric cancer via multiple signaling pathways. Cell Commun Signal 2015;13:1–13.
[9] Abdollahi H, Shams S, Zahedi MJ, *et al*. IL-10, TNF-α and IFN-γ levels in serum and stomach mucosa of *Helicobacter pylori*-infected patients. Iran J Allergy Asthma Immunol 2011;10:267–71.
[10] Xu S, Cao X. Interleukin-17 and its expanding biological functions. Cellular Mol Immunol 2010;7:164–74.
[11] Ge Y, Huang M, Yao Y-m. Biology of interleukin-17 and its pathophysiological significance in sepsis. Front Immunol 2020;11:1558.
[12] Domanski L, Kłoda K, Patrzyk M, *et al*. IL17A and IL17F genes polymorphisms are associated with histopathological changes in transplanted kidney. BMC Nephrol 2019;20:1–9.
[13] Yamada H. Current perspectives on the role of IL-17 in autoimmune disease. J Inflamm Res 2010;3:33.
[14] Koga T, Ichinose K, Kawakami A, *et al*. Current insights and future prospects for targeting IL-17 to treat patients with systemic lupus erythematosus. Front Immunol 2021;11:3720.
[15] Bakr NM, Hashim NA, El-Baz HAE-D, *et al*. Polymorphisms in proinflammatory cytokines genes and susceptibility to multiple sclerosis. Mult Scler Relat Disord 2021;47:102654.
[16] Tabatabaei-Panah P-S, Moravvej H, Delpasand S, *et al*. IL12B and IL23R polymorphisms are associated with alopecia areata. Genes Immun 2020;21:203–10.
[17] El-Omar EM, Rabkin CS, Gammon MD, *et al*. Increased risk of noncardia gastric cancer associated with proinflammatory cytokine gene polymorphisms. Gastroenterology 2003;124:1193–201.
[18] Savage SA, Abnet CC, Mark SD, *et al*. Variants of the IL8 and IL8RB genes and risk for gastric cardia adenocarcinoma and esophageal squamous cell carcinoma. Cancer Epidemiol Biomarkers Prev 2004;13:2251–7.
[19] Sánchez-Zauco N, Torres J, Gómez A, *et al*. Circulating blood levels of IL-6, IFN-γ, and IL-10 as potential diagnostic biomarkers in gastric cancer: a controlled study. BMC Cancer 2017;17:1–10.
[20] Dai Z-M, Zhang T-S, Lin S, *et al*. Role of IL-17A rs2275913 and IL-17F rs763780 polymorphisms in risk of cancer development: an updated meta-analysis. Sci Rep 2016;6:1–12.
[21] Arisawa T, Tahara T, Shibata T, *et al*. The influence of polymorphisms of interleukin-17A and interleukin-17F genes on the susceptibility to ulcerative colitis. J Clin Immunol 2008;28:44–9.
[22] Al Obeed OA, Vaali-Mohamed M-A, Alkhayal KA, *et al*. IL-17 and colorectal cancer risk in the Middle East: gene polymorphisms and expression. Cancer Manag Res 2018;10:2653.
[23] Ho S-A, Hoyle JA, Lewis FA, *et al*. Direct polymerase chain reaction test for detection of *Helicobacter pylori* in humans and animals. J Clin Microbiol 1991;29:2543–9.
[24] Mirtalebi Roknabadi FS, Teymoori M, Shams S, *et al*. Presence of cagA gene in patients with gastric cancer and gastritis with *Helicobacter pylori* infection. J Maz Univ Med Sci 2019;29:214–21.
[25] Zacarias JMV, Sippert EÂ, Tsuneto PY, *et al*. The influence of interleukin 17A and IL17F polymorphisms on chronic periodontitis disease in Brazilian patients. Mediators Inflamm 2015;2015:147056.
[26] Samiei G, Yip WK, Leong PP, *et al*. Association between polymorphisms of interleukin-17A G197A and interleukin-17F A7488G and risk of colorectal cancer. J Cancer Res Ther 2018;14(Suppl 2):S299–305.
[27] Fakheri H, Firoozi MS, Bari Z. Eradication of *Helicobacter pylori* in Iran: a review. Middle East J Dig Dis 2018;10:5.
[28] Bhat N, Gaensbauer J, Peek RM, *et al*. Local and systemic immune and inflammatory responses to *Helicobacter pylori* strains. Clin Diagn Lab Immunol 2005;12:1393–400.
[29] Clayton C, Kleanthous H, Coates P, *et al*. Sensitive detection of *Helicobacter pylori* by using polymerase chain reaction. J Clin Microbiol 1992;30:192–200.
[30] Gastli N, Allain M, Lamarque D, *et al*. Diagnosis of *Helicobacter pylori* infection in a routine testing workflow: effect of bacterial load and virulence factors. J Clin Med 2021;10:2755.
[31] Lu J-J, Perng C-L, Shyu R-Y, *et al*. Comparison of five PCR methods for detection of *Helicobacter pylori* DNA in gastric tissues. J Clin Microbiol 1999;37:772–4.
[32] Bazin T, Nchare Mfondi A, Julie C, *et al*. Contribution of genetic amplification by PCR for the diagnosis of Helicobacter pylori infection in patients receiving proton pump inhibitors. United European Gastroenterol J 2018;6:1267–73.
[33] Venerando R, Rasmussen LT, de Labio R, *et al*. Relationship between *Helicobacter pylori* detection and an increased risk of infection in childhood. J Venom Anim Toxins Incl Trop Dis 2012;18:369–74.
[34] Mori D, John JL, Sabri SIB, *et al*. Seroepidemiological survey of the prevalence of *Helicobacter pylori* infection in Sabah, Malaysia. IJID Reg 2022;2:126–9.
[35] Xu C, Yan M, Sun Y, *et al*. Prevalence of *Helicobacter pylori* infection and its relation with body mass index in a Chinese population. Helicobacter 2014;19:437–42.
[36] Kyriazanos ID, Sfiniadakis I, Gizaris V, *et al*. The incidence of *Helicobacter pylori* infection is not increased among obese young individuals in Greece. J Clin Gastroenterol 2002;34:541–6.
[37] Khalifa MAAA, EL-fadly Khodiar S, Abd Almaksoud A. Cigarette smoking status and *Helicobacter pylori* infection in non-ulcer dyspepsia patients. Egypt J Chest Dis Tuberc 2014;63:695–9.
[38] Lubetzky R, Mandel D, Reif S, *et al*. Special clinical manifestations of *Helicobacter pylori* infection in children and adolescents. Harefuah 2004;143:554–6; 624.
[39] Otero Regino W, Gómez Zuleta M, Ruiz Lobo X. Etiology of duodenal ulcers in a Colombian population. Rev Colomb Gastroenterol 2009;24:266–71.
[40] Azer SA, Akhondi H, Gastritis. StatPearls. StatPearls Knowledge Base; 2019:1–11.
[41] Malik TF, Gnanapandithan K, Singh K. Peptic Ulcer Disease, StatPearls, StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC., Treasure Island (FL); 2023.
[42] Cárdenas-Mondragón MG, Torres J, Flores-Luna L, *et al*. Epstein–Barr virus association with peptic ulcer disease. Anal Cell Pathol 2015;2015:164840.
[43] Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. Ann Intern Med 2005;143:199–211.
[44] Shavalipour A, Malekpour H, Dabiri H, *et al*. Prevalence of cytotoxin-associated genes of *Helicobacter pylori* among Iranian GERD patients. Gastroenterol Hepatol Bed Bench 2017;10:178.
[45] Akeel M, Shehata A, Elhafey A, *et al*. *Helicobacter pylori* vacA, cagA and iceA genotypes in dyspeptic patients from southwestern region, Saudi Arabia: distribution and association with clinical outcomes and histopathological changes. BMC Gastroenterol 2019;19:1–11.
[46] He Y, Hu P-j, He X-x, *et al*. Prevalence of cagA and vacA subtypes of *Helicobacter pylori* in Guangzhou. Zhonghua Nei Ke Za Zhi 2000;39:818–20.
[47] Chen X-J, Yan J, Shen Y-f. Dominant cagA/vacA genotypes and coinfection frequency of *H. pylori* in peptic ulcer or chronic gastritis patients in Zhejiang Province and correlations among different genotypes, coinfection and severity of the diseases. Chin Med J 2005;118:460–7.
[48] Arisawa T, Tahara T, Shibata T, *et al*. Genetic polymorphisms of molecules associated with inflammation and immune response in Japanese subjects with functional dyspepsia. Int J Mol Med 2007;20:717–23.
[49] Ghorbani A, Hosseini V, Ajami A, *et al*. Association between polymorphism of interleukin 17 (IL-17F) and increased susceptibility to gastric cancer. J Maz Univ Med Sci 2012;22:11–20.
[50] Shirzad H, Bagheri N, Azadegan-Dehkordi F, *et al*. New insight to IL-23/IL-17 axis in Iranian infected adult patients with gastritis: effects of genes polymorphisms on expression of cytokines. Acta Gastroenterol Belg 2015;78:212–8.
[51] Mizuno T, Ando T, Nobata K, *et al*. Interleukin-17 levels in *Helicobacter pylori*-infected gastric mucosa and pathologic sequelae of colonization. World J Gastroenterol 2005;11:6305–11.