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SHORT COMMUNICATION

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# Association between the Proinflammatory Cytokine IL-17F and *Helicobacter Pylori* Infection in a Sample of Iraqi Patients

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## Abstract

***Background:*** Infection of the gastric mucosa with *Helicobacter pylori (Hp)* is characterized by the induction of a number of proinflammatory cytokines, including IL-8, IL-6, and TNF-α, involved in *Hp*-related gastric inflammation. The functions of members of the IL-17 cytokine family, other than IL-17A, in *Hp* infection remain understudied. *The aim* of our study was to assess the association between the proinflammatory cytokine IL-17F and *Hp* infection in a sample of Iraqi patients.

***Methods and Results*:** This study included 50 Iraqi patients (18 males and 32 females; a mean age of 36±1.74 years) infected with *Hp.* The healthy control group consisted of 16 subjects (3 males and 13 females), with a mean age of 31±2.44 years. For the qualitative detection of antibodies (IgG, IgM, and IgA) against *Hp* in the serum, we used the OnSite H. pylori Ab Combo Rapid Test (CTK Biotech). ELISA was used to detect levels of human IL-17F in serum using ABTS ELISA Development Kit (Pepro Tech, USA). The serum level of IL-17F in patients with *Hp* infection was significantly higher than in the control group (238.9±7.64 pg/mL vs. 114.00±3.66 pg/mL, *P*=0.0001). However, the serum level of IL-17F in *Hp* patients was not significantly different between men and women (237±12.12 pg/mL and 239±9.94 pg/mL, respectively, *P*=0.9015). In addition, no significant difference was found between age subgroups: 240±13.18 pg/mL, 231±10.17 pg/mL, and 252±18.35 pg/mL in age subgroups of <30 years, 30-45 years, and >45 years, respectively, (*P*>0.05).

***Conclusion***: Patients infected with *Hp* were characterized by higher serum levels of IL-17F than non-*Hp* subjects. IL-17F plays an important role in the inflammatory response to *Hp* infection in a sample of Iraqi patients.(**International Journal of Biomedicine. 2023;13(2):338-341.**)

**Keywords:** *Helicobacter pylori* • IL-17F • ELISA

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## Introduction

*Helicobacter pylori (Hp*), a Gram-negative bacterial pathogen, colonizes the gastric epithelium of at least half of the world's population.[1-4] H. pylori isolates possess substantial genotypic diversity, which engenders differential host inflammatory responses. (5) In some individuals, *Hp*-related inflammation contributes to the development of peptic ulcers and gastric cancer.[6] H. pylori strains that possess the cag pathogenicity island and secrete a functional cytotoxin induce more severe gastric injury and further augment the risk for developing distal gastric cancer.[7,8] In 1994, the IARC/WHO identified *Hp* as a Group 1 carcinogen.[9] Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is also closely associated with Helicobacter pylori (HP) infection.[10] Eradication of H pylori infection has the potential to reduce the risk of gastric cancer development.[5,11]

Infection of the gastric mucosa with *Hp* is characterized by the induction of a number of proinflammatory cytokines, including IL-8, IL-6, and TNF-α, involved in *Hp*-related gastric inflammation.[12-14] The functions of members of the IL-17 cytokine family, other than IL-17A,[15-17] in *Hp* infection remain understudied.

IL-17F is a member of the IL-17 cytokine family, which contains six members (IL-17A-F).[18] IL-17F and IL-17A are

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closely related cytokines that exist as homodimers and IL-17A:IL-17F heterodimers.[19] These cytokines play crucial roles in host defense against bacterial infections by recruiting neutrophils through the induction of CXC chemokines and inducing anti-microbial proteins in infected sites.[20,21] IL-17F, first identified in 2001,[22] is mainly expressed by a distinct type of T cells, T helper 17 cells and γδT cells.[23,24] Due to strong sequence homology with IL-17A, IL-17F can induce the production of proinflammatory cytokines (IL-6, granulocyte colony-stimulating factor [G-CSF], and granulocyte-macrophage colony-stimulating factor [GM-CSF]) and chemokines (CXCL1, CXCL2, and CXCL5) and promote granulopoiesis and neutrophil recruitment, albeit less potently than IL-17A.[23-26] Increased levels of Th17 cytokines, including the production of IL-17A and IL-17F, are associated with more detrimental outcomes of *Hp* infection.(28) Data obtained by Dixon et al.[27] showed that IL-17A and IL-17F might have overlapping roles in maintaining the gastric mucosal response to *Hp* infection.

***The aim*** of our study was to assess the association between the proinflammatory cytokine IL-17F and *Hp* infection in a sample of Iraqi patients.

## Materials and Methods

This study included 50 Iraqi patients (18 males and 32 females; a mean age of 36±1.74 years) infected with *Hp*, who were admitted to Baquba Teaching Hospital and some city outpatient departments during the period from January to June 2022. The healthy control group consisted of 16 subjects (3 males and 13 females), with a mean age of 31±2.44 years.

*Serum Samples*

We collected 5 mL of venous blood samples in a plain tube and left for 30 min to allow clotting at room temperature (20-25C°). Samples were centrifuged for 15 min at 3000rpm. After that, the serum was collected in polypropylene microfuge tubes and stored at −20°C for further analysis.

*Immunological Tests*

For the qualitative detection of antibodies (IgG, IgM, and IgA) against *Hp* in the serum, we used the OnSite H. pylori Ab Combo Rapid Test (CTK Biotech).

ELISA was used to detect levels of human IL-17F in serum using ABTS ELISA Development Kit (Pepro Tech, USA) following the manufacturer's instructions. These kits contain the key components necessary for quantitative measurement of human IL-17F in a sandwich ELISA format within the range of 6–2000 pg/ml.

Statistical analysis was performed using statistical software package SPSS version 26.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as the mean and standard error of the mean (SEM) for continuous variables. For data with normal distribution, inter-group comparisons were performed using Student's t-test. Multiple comparisons were performed with one-way ANOVA and Tukey's HSD Post-hoc Test. A probability value of $P<0.05$ was considered statistically significant.

The study was approved by the Ethics Committee of the Technical Institute Baquba. All participants provided written informed consent.

## Results

The serum level of IL-17F in patients with *Hp* infection was significantly higher than in the control group (238.9±7.64 pg/mL vs. 114.00±3.66 pg/mL, $P=0.0001$). However, the serum level of IL-17F in *Hp* patients was not significantly different between men and women (237±12.12 pg/mL and 239±9.94 pg/mL, respectively, $P=0.9015$). In addition, no significant difference was found between age subgroups: 240±13.18 pg/mL, 231±10.17 pg/mL, and 252±18.35 pg/mL in age subgroups of <30 years, 30-45 years, and >45 years, respectively (Table 1).

***Table 1.***

***The serum level of IL-17F (pg/mL) in the study groups.***

| Group | n | Mean ± SEM | *P*-value |
|---|---|---|---|
| Main group | 50 | 238.90±7.64 | 0.0001 |
| Control group | 16 | 114.00±3.66 | |
| | | | |
| Main group | n | Mean ± SEM | *P*-value |
| Male | 18 | 237±12.12 | 0.9015 |
| Female | 32 | 239±9.94 | |
| | | | |
| Main group | n | Mean ± SEM | *P*-value |
| Age group of <30 years | 13 | 240±13.18 | 0.5267 |
| Age group of 30-45 years | 17 | 231 ±10.17 | |
| Age group of >45 years | 20 | 252±18.35 | |

## Discussion

*Hp* is the dominant member of the gastric microbiota and has infected more than half of the human population, of whom 5%–15% develop gastric diseases ranging from gastritis and metaplasia to gastric cancer.[28]

In a study by Fraser et al.,[29] the relative risk of *Hp* infection significantly increased with age, lower socio-economic status, and lower household income, but was not significantly associated with gender. Joshi et al.[30] showed that among the 418 patients diagnosed with peptic ulcer diseases, 213 patients were positive for *Hp* by rapid urease test. Among the positive cases, over half were male patients, and the majority of the patients were in the age group of 35-44 years.

*Hp*-associated gastritis is characterized by an increased number of acute and chronic inflammatory cells secreting cytokines that contribute to maintaining and expanding the local inflammation.[31] Studies have reported that *Hp*-specific gastric mucosal T cell responses are usually Th1 predominant,

but recently, Th17—markedly IL-17—is believed to be one of the driving immune cells in *Hp* infection.[17,32]

Arisawa et al.[33] investigated the associations between the *IL-17F* 7488T/C (rs763780) polymorphism in association with the development of inflammatory changes in the gastric mucosa in *Hp*-infected Japanese subjects. The authors found that in *Hp*-infected cases, the carriage of the T allele and TT genotype increased the risk of the development of epigastric pain syndrome (OR=11.3, 95% CI: 1.23-103.2, *P*=0.032 and OR=0.4, 95% CI:1.17-92.3, *P*=0.036, respectively).

Data obtained by Luzza et al.[31] indicate that biologically active IL-17 production is increased during *Hp* infection, suggesting that this cytokine may play an important role in the inflammatory response to *Hp* colonization.

In our study, patients infected with *Hp* were characterized by higher serum levels of IL-17F than non-*Hp* subjects. IL-17F plays an important role in the inflammatory response to *Hp* infection in a sample of Iraqi patients.

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## Competing Interests

The authors declare that they have no competing interests.

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