Research Article

Assessment of the Levels of TGF-β1 and IL-18 in Gastritis Patients Infected with *Helicobacter pylori*

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I N F O

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A B S T R A C T

Background: Gastritis is characterised as an inflammation of the gastric mucosa, the stomach's protective lining, and is divided into two categories: acute and chronic, depending on the severity of the inflammation and the disease's history. This study aims to estimate the levels of transforming growth factor-beta 1 (TGF-β1) and interleukin-18 (IL-18) in gastritis patients infected with Helicobacter pylori.

Material and Method: From September 2022 to June 2023, a cross-sectional study was conducted in the General Hospital and at various private clinics in Balad City, Iraq. Eighty-nine samples (50 patients and 39 healthy individuals as control) were collected from 42 males and 47 females aged 15–85 years from Balad General Hospital, and private upper surgical endoscopy clinic. Blood, stool, and biopsy samples were collected from individuals suffering from complaints such as loss of appetite, weight loss, diarrhoea, vomiting, and dyspepsia.

Results: The study included 89 samples (50 gastritis patients (56.18%) and 39 control (43.82%)). Depending on the diagnosis of gastroenterologists, the gastric patients were divided into four groups: 28 (56%) were gastritis patients, 13 (26%) patients were chronic gastritis patients, 8 (16%) patients were gastritis ulcer patients, and 1 (2%) patient was gastric cancer patient. *H. pylori* was detected by antibody (Ab) and antigen (Ag) in the serum among all 50 patients using the one step test. Among the 50 patients, 26 (52%) showed a positive result for Ab and 24 (48%) showed a negative result, while 20 (40%) were positive and 30 (60%) were negative for Ag. In addition, this research found that the concentration of TGF-β1 and IL-18 in H. pylori-infected patients was significantly (p ≤ 0.05) higher than that in healthy controls.

Conclusion: IL-18 and TGF-β1 levels were elevated in the serum of people with gastritis *H. pylori* infection in this study as compared to the healthy groups. A correlation was found between TGF-β1 and IL-18 serum levels in relation to *H. pylori* and bacterial infection.

Keywords: TGF-β1, IL-18, *H. pylori*, Gastritis

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Introduction

Gastritis is an inflammation of the gastric mucosa, the stomach's protective lining, and is divided into two categories: acute and chronic, depending on the severity of the inflammation and the disease's history.[1] Helicobacter pylori is a human-to-human-transmitted gram-negative microaerophilic bacteria that causes gastroenteritis, ulcers of the stomach, mucosa-associated lymphoid tissue lymphoma and gastric cancer.[2] *H. pylori* has been identified as a group 1 carcinogenic pathogen since 1994,3 according to the International Agency for Research on Cancer. Inhibiting B- and T-lymphocyte proliferation and decreasing macrophage and natural killer cell activity, transforming growth factor-1 (TGF-1) has a crucial function in regulating inflammatory responses.[4] In addition to its role as a regulator of cytokine production by various cell types, TGF-1 also operates as a chemoattractant and activator of monocyte activities.[5] Major autoimmune responses are also seen by developing stomach dysplastic lesions and severe gastric inflammation and ulceration. Mutations in the gastric mucosa of TGF-1 null mice are strikingly comparable to those of H. pylori-associated gastritis. The 192 and 193 amino acids that make up human interleukin-18 (IL-18) proteins have been determined.[6] IL-18 is categorised as an IL-1 cytokine due to the similarity between its amino acid sequence and that of IL-1. Despite sharing a -pleated sheet structure,[7] the sole sequence homology between human IL-18 and IL-1 is 15%. The purpose of this research was to estimate the levels of TGF-β1 and IL-18 in gastritis patients infected with *H. pylori.*

Material and Method

This cross-sectional study was conducted between September 2022 and June 2023 at the Balad General Hospital and private upper surgical endoscopy clinic in Balad City, Iraq. A total of 89 samples were taken (42 men and 47 women) spanning 15–85 years of age (50 patients and 39 healthy persons as controls). Blood, stool, and biopsy samples were collected from individuals suffering from complaints such as loss of appetite, weight loss, diarrhoea, vomiting, and dyspepsia. Blood samples were collected using disposable syringes; 3–5 mL of venous blood was collected from each person's vein. After transferring the blood to gel tubes, it was left to coagulate at room temperature and spun at 1,500 RPM for 15 minutes. The sera were stored at -20ºC until further analyses were performed.[8] A questionnaire was prepared and designed according to the criteria that included study information (age - sex -Pathological case)

Serum Antibody Test and Stool Antigen Test for Helicobacter pylori Detection: This was performed according to the instructions of the manufacturing company (German-Acon).[9]

Estimation of TGF-β1 and IL-18 by Enzyme-linked Immunosorbent Assay (ELISA) Protocols: This was performed according to the instructions of the manufacturing company (BTLAB).[10]

Statistical Analysis

The common statistical package GraphPad Prism version 7 was used, and the data were summarised using the Mean Stander division format. The degree of association between markers was estimated using correlation coefficients. Mega stat (Version v 10.12) for Excel 2010 was used to calculate descriptive statistics and correlation coefficients.

Results and Discussion

Demographic Study

The current study included 89 samples, which were separated into two groups for further analysis (gastritis patient: 50 (56.18%), and control: 39 (43.82%)). According to the results of the study, the male patients outnumbered the female patients by a margin of 28 (56%) to 22 (44%) for gastritis patients, while males were less than females (15 (38.5%) versus 24 (61.5%)) in the control group as illustrated in Figure 1.
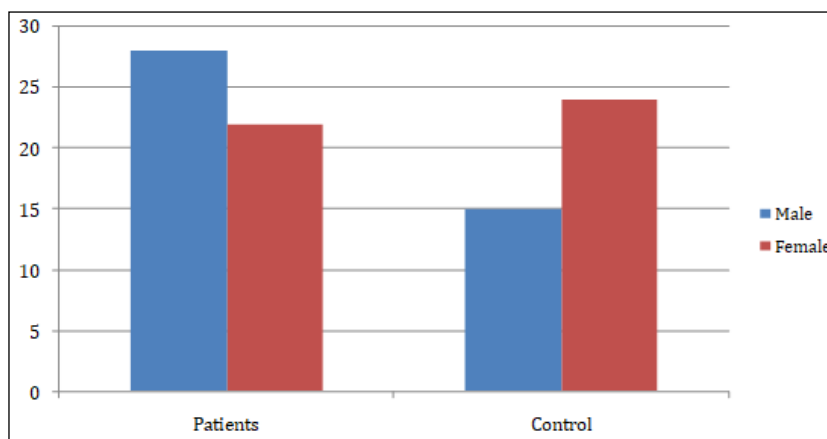

Figure 1.Distribution of Patients and Control According to Gender

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H pylori colonises and thrives in the acidic pH of the stomach. It then enters the stomach's epithelial cell through the mucus layer.11 *H. pylori* needs the urease enzyme to survive in the acidic stomach, since it may neutralise gastric acidity and cause damage to the gastric mucosa via the production of toxins such as CagA and VacA.12 The relationship between *H. pylori* isolation from gastrointestinal patients and many immunological characteristics was investigated, as was the efficacy of molecular versus serological approaches for the identification of H. pylori.

Rapid Diagnostic Test

The result of all 50 patients was tested using the Rapid Diagnostic Test (RDT) to identify *H. pylori* antibody (Ab) and antigen (Ag) in a single step. Table 1 displays the percentages of patients with positive (26, 52%) and negative (24, 48%) Ab test results and positive (20, 40%) and negative (30, 60%) Ag test results.

Table 1.Positive and Negative Results of Stool Antigen and Serum Antibody Test for *H. Pylori*

Method	Tests	Results	n (%)	p Value
Rapid diagnostic test	Ab	Positive	26 (52)	p > 0.05
		Negative	24 (48)	
	Ag	Positive	20 (40)	p > 0.05
		Negative	30 (60)	

The results of the present study showed that rapid diagnostic test helps to identify. *H. pylori* infection as shown in Table 1. Positive results for rapid diagnostic tests for *H. pylori* infection have been shown to vary from 63% to 88% across nations.[13,14] This is because each individual's immune response is unique and the length of time an infection has been present might also have an impact on the outcome.[15] Due to a lack of discrimination between active and latent infections, the test's sensitivity and specificity are reduced and false positives are more likely to occur.[16]

Immunological Study

Evaluation of TGF-β1 in Patients

The present study showed that TGF-β1 (pg/mL) concentration was higher in the patient group as compared to the control group (556.6 ± 44.24 pg/mL and 184.7 ± 12.19 pg/mL, respectively). Significant differences were found between the patient group and control group at $p \leq 0.05$, as shown in Figure 2.

In this study, researchers found that TGF-1 serum levels were significantly higher in patients as compared to controls. This finding is consistent with that of Serruya and Maor,[17] who discovered a statistically significant rise in TGF-1 serum levels of patients as compared to those of controls.
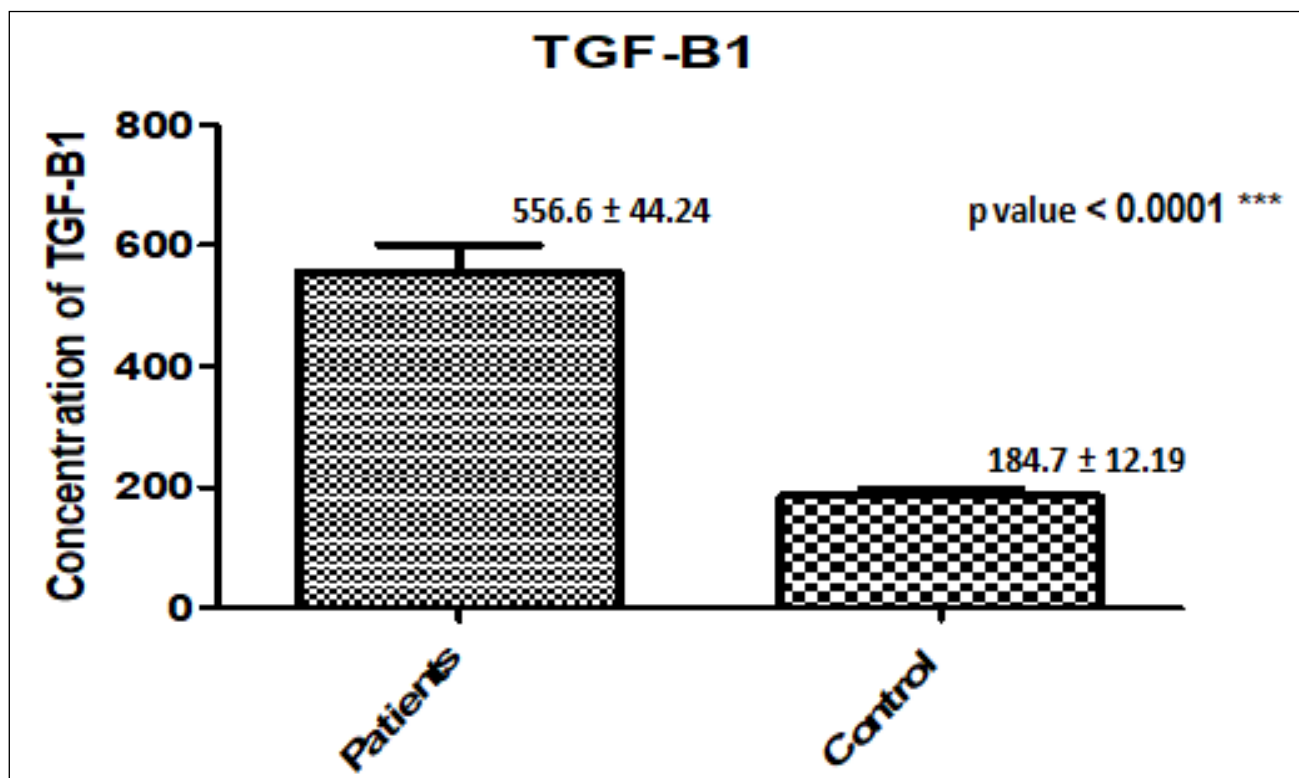

Figure 1 .Distribution of Patients and Control According to Gender

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Treg cell responses in infected patients with gastritis were capable of modulating Th1 and Th17 cell responses that possibly contributed to the persistence of *H. pylori* infection, as shown by the fact that the number of Tregs and the expression of TGF-1 were significantly higher in infected patients who developed gastritis than in control patients.[18]

Previous research has revealed that TGF facilitates *H. pylori* attachment to and colonisation of host cells.[19] TGF has been linked to gastritis and autoimmune illnesses that *H. pylori* causes in the stomach.[20] Macrophages, lymphocytes, and foam cells are just a few of the cell types that may produce TGF, making it a potentially ubiquitous inflammatory mediator. The degree of H. pylori-associated non-metaplastic atrophic gastritis correlates with the level of TGF-1 expression.[21] *H. pylori* infection is associated with an increase in TGF-1 mRNA expression in human gastric mucosal biopsies, and this effect is positively correlated with the VacA genotype and the grade of chronic inflammation.[22,23]

Evaluation of IL-18 in Patients

The present study showed that IL-18 (pg/mL) concentration was higher in the patient group as compared to the control group (30.73 ± 2.233 pg/mL and 13.11 ± 0.6768 pg/mL, respectively). Significant differences were observed between the patient group and the control group at $p \leq 0.05$ as shown in Figure 3.

IL-18 is a cytokine that plays an important role in the immune response to H.pylori infection, a common cause of gastroenteritis and stomach ulcers. IL-18 is generated by epithelial cells and monocytes/ macrophages in the gastric mucosa, and its levels are associated with the severity of inflammation.[24] IL-18 induction by *H. pylori* depends on the virulence factors of the bacteria, such as the cytotoxin-associated gene A protein (CagA) pathogenicity island and Outer Membrane Inflammatory Protein (Oip) which activate different signalling pathways in the host cells.[25] *H. pylori* can also induce IL-1β production in monocytes, which is regulated by the NLRP3 inflammasome. both IL-1β and IL-18 are members of the IL-1 family of cytokines, which have proinflammatory effects and can modulate Th1/ Th17 responses.[26]

In summary, *H. pylori* infection is associated with increased levels of IL-18. However, the effect of *H. pylori* infection on IL-18 levels specifically varies depending on the study. Some studies have found that IL-18 levels are higher in H. pylori-infected patients than in healthy individuals, while others have found that IL-18 levels in the two groups are similar.

Correlation Between TGF-β1 and IL-18 Serum Level in Patients with H. pylori and Bacterial Infection
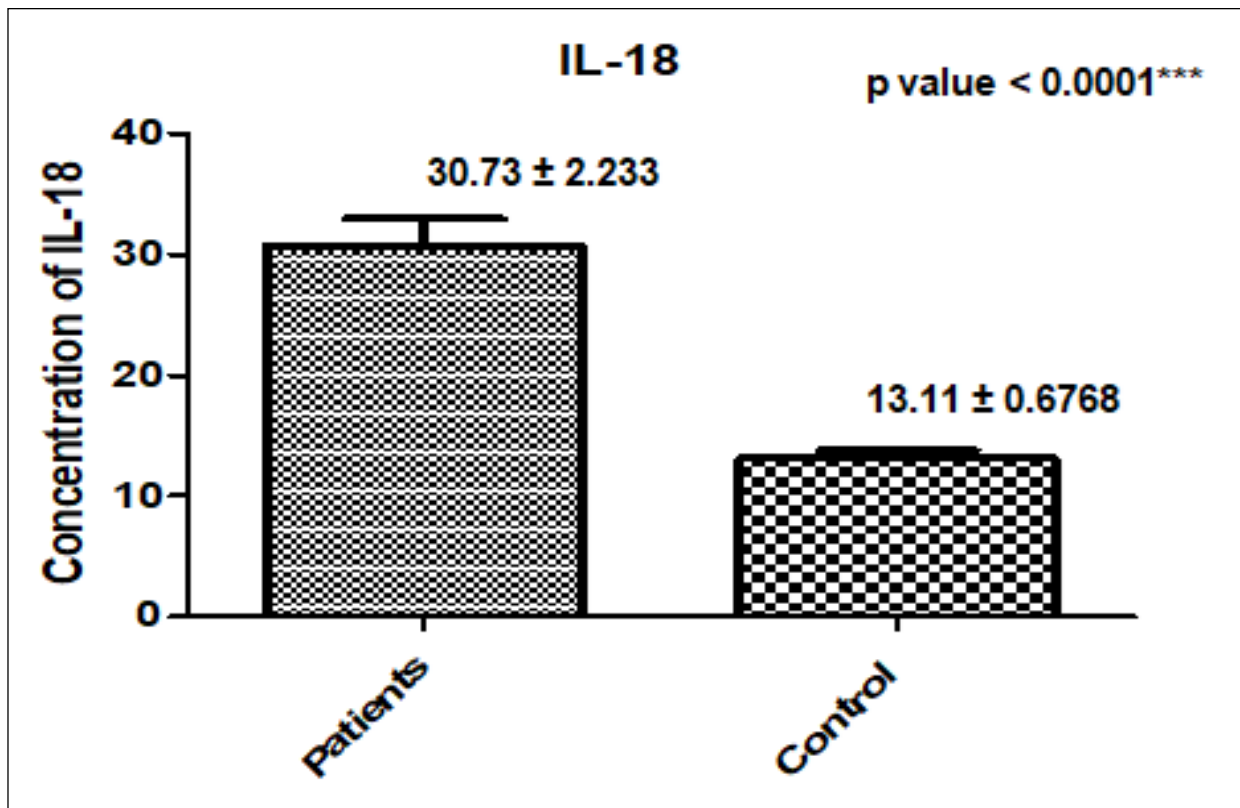

Figure 2.Comparative Concentrations of TGF-β1 Between Study Groups

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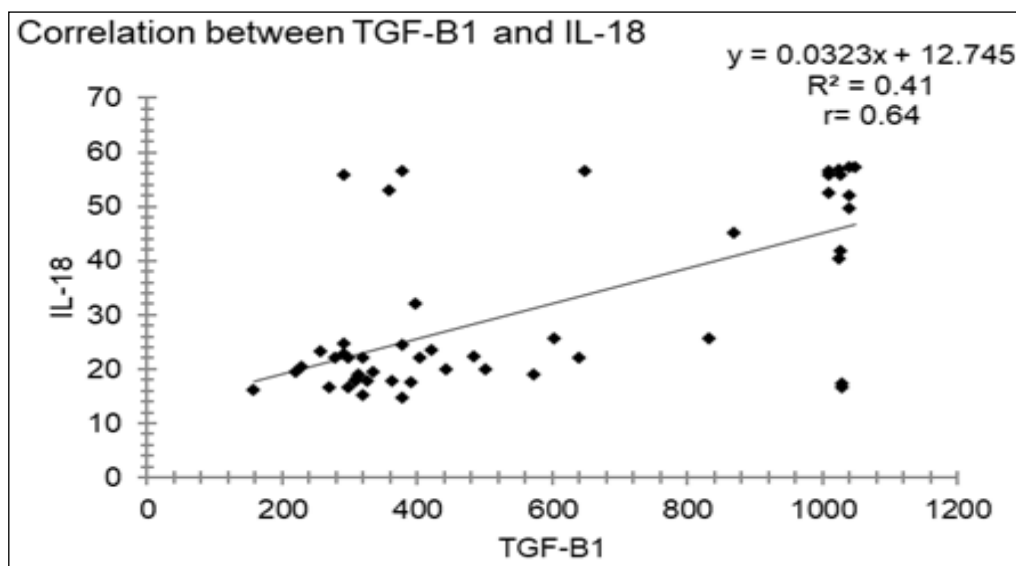*J. Commun. Dis. 2024; 56(1)*

Figure 4. Correlation between TGF-β1 and IL-18 Serum Levels

There are several studies that have investigated the correlation between TGF-β1 and IL-18 serum levels in relation to *H. pylori* and bacterial infections. One such study showed that TNF-alpha and TGF-β1 influence IL-18-induced IFN-γ production through the regulation of IL-18 receptor and T-bet expression.[27] It is recommended to employ the molecular technique to measure the level of cytokines against pathogens; this technique such as PCR was applied in different topics of the medical field.[28–39]

In summary, TGF-β1 and IL-18 are cytokines that play important roles in the immune system, including the regulation of immune responses against bacterial pathogens.

Conclusion

IL-18 and TGF-β1 levels were elevated in the serum of people with gastritis *H. pylori* infection in this study as compared to the healthy groups. A correlation was found between TGF-β1 and IL-18 serum levels in relation to *H. pylori* and bacterial infection.

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Conflict of Interest: None

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