

Role of Some Immunological Cytokines in *H. pylori*-infected Patients in Relation to Iron Indices Levels

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ABSTRACT

Background: The human stomach is colonized by *Helicobacter pylori* (*H. pylori*), a Gram-negative bacterium. A chronic *H. pylori* infection can lead to a number of gastrointestinal disorders, including gastric cancer.

Objective: The study aimed to investigate serum level IL6, IL1 β , and TNF- α with iron status to assess the severity of infection.

Methods: Case control study design involved 100 participants (50 patients and 50 control), for each groups, rapid *H. pylori* stool antigen test, IgG, serum IL6, IL1 β , and serum TNF- α were estimated along with iron parameters.

Results: Immunological marker concentrations in the patient and control groups. All tested indices, comprising IgG, IL-6, IL-1 β , and TNF- α , showed statistically notable increase in comparison with control ($p < 0.001$). Parameters related to iron were highly skewed such as serum iron, ferritin, total iron binding capacity (TIBC), serum iron, and transferrin value ($p < 0.001$).

Conclusion: These indicators can be used to diagnose and/or monitor the course of an infection since *H. pylori* infection can drastically affect the diagnostic indicators and the markers typically used to measure the degree of inflammation during infection.

KEYWORDS: IL6, IgG, IL1B, TNF-a, *H. pylori*.

INTRODUCTION

Helicobacter pylori (*H. pylori*) is believed to cause peptic ulcers, gastric cancer and chronic gastritis, conditions which affect approximately 50% of the world's population. It is now believed that chronic *H. pylori* infection is answerable to 78% of all instances of gastric cancer, or 89% of non-cardia cancers [1]. Gram-negative bacteria are *Helicobacter pylori* is classified as a pathogen that causes malignancy within class I. *H. pylori* infection is closely associated with gastric conditions such as gastritis, intestinal metaplasia, peptic ulcers, and cancer [2]. When *H. pylori* colonizes the stomach epithelium, inflammatory cytokines such as interleukin-1 β (IL-1 β), IL-6, IL-8, and TNF-alpha are released. Long-term exposure to these cytokines can increase the likelihood of DNA replication errors and cell division by blocking cell autophagy and death [3]. Chronic inflammation and *H. pylori* infection have been proven in both experimental and clinical studies to be important factors in the advancement of stomach cancer [4].

IL-6 is an essential mediator in the inflammation process and has two unique regulatory mechanisms. IL-6 binds to a membrane-associated IL-6 receptor (IL-6R) in the first, which is referred to as classical IL-6 signaling. Tumor necrosis factor-alpha (TNF- α) and other proinflammatory cytokines are the immune system's primary reaction to aggressive infections [5]. Endotoxins create TNF- α , a glycoprotein that belongs to a family of cytokines linked to acute phase response and systemic inflammation. TNF- α is primarily involved in immune cell regulation. Being an endogenous pyrogen, this cytokine can produce fever, inflammation, apoptosis, and fatigue [6].

Innate as well as adaptive immunity are triggered by an *H. pylori* infection, which stimulates immune cells and results in the production and release of several pro-inflammatory mediators [7]. However, atrophic gastritis and duodenal ulcer disease are significantly influenced by the development of a pro-inflammatory response and the volume of stomach acid secreted [8]. One strong cytokine that induces inflammation is IL-1 β . The multimorphic IL-1 β and IL-RN genes are part of an assortment of genes that also generates the IL-1 β cytokine, the most powerful reported blocker of acid release [9].

Therefore, using iron indices, the study sought to assess the levels of pro- and anti-inflammatory cytokines in *H. pylori*-infected people in relation to iron status.

MATERIALS & METHOD

Study design & Subjects:

Fifty patients who visited the Specialized Hospital for Gastrointestinal and Hepatic Diseases in the Al-Najaf governorate of Iraq between June and August of 2025 were included in the case control study. The patients' ages varied from 22 to 75, and all of them (28 men and 22 females) had positive *H. pylori* stool antigen tests, which were verified by a specialist physician using clinical data (signs & symptoms). Additionally, 50 healthy individuals (33 men and 17 females) with negative *H. pylori* stool antigen tests, ranging in age from 25 to 70, were included in the research as control groups. They responded to questions on their age, sex, place of residence, prescription drugs, chronic illnesses, etc.

Sample collection:

Two types of samples included in this study:

- **Stool samples for *H. pylori* antigens:**

Using the immunochromatographic method, *H. pylori* antigen may be quickly identified (Zybio cassette, China). In addition to a pink line in the control line sections, a characteristic pink band may be seen in the test line regions as a positive result. The test line region is empty, despite being negative.

- **Blood samples:**

Five milliliters of venous blood were drawn, two milliliters were transferred to an EDTA tube for hematological estimate (CBC), and three milliliters were transferred to plain tubes. The serum samples were then separated for biochemical and immunological analyses by centrifuging them for ten minutes at 3000 rpm. After that, the serum samples were moved to Eppendorf tubes and stored at -20°C until every sample was obtained.

Biochemical parameters:

Iron parameters such as total serum iron, transferrin and TIBC levels were determined by a fully automated biochemistry analyzer (Beckman Coulter, USA). While the VIDAS instrument was used to assess serum ferritin (bioMérieux, France).

Immunological markers:

Serum IgG, IL-1 β , IL-6, and TNF- α were quantitatively assessed using sandwich enzyme linked immunosorbent test (ELISA) (MyBiosource, USA) for both patients and control groups.

Statistical analysis:

Statistic analysis of the social science was done using IBM version 26 statistical package and the statistical parameters used to determine the mean and standard deviation (mean $\pm$ SD) across groups was analysis of variance (t. test). The chi-square test was used to find discrepancies between the analytical and qualitative data. P values less than 0.05 are considered as statistically significant, P values more than 0.05 as non-statistically considerable, and P values less than 0.001 as very statistically noteworthy.

Exclusion criteria

Patients on prolonged, constant non-steroidal anti-inflammatory medication therapy, patients with a history of *H. pylori* antibiotic cure, and patients with a earlier *H. pylori* infection who had been getting treated for it.

RESULTS & DISCUSSION

Results:

Sociodemographic and general features of study people:

Table (1) provides an overview of the patient and control groups demographics. No significant age distribution difference was found between the patient and the control groups ($\chi^2 = 3.46$, $p = 0.486$). While the largest amount of patients (28%) were among the ages of 41 and 50, the largest percentage of control participants (30%) were across the ages of 31 and 40. In terms of sex, men made up 56% of the infected and 66% of the healthy group, while females made up 34% and 44%, respectively. A statistically significant difference was found ($\chi^2 = 2.90$, $p = 0.043$). Additionally, there was no discernible difference in educational achievement across groups ($\chi^2 = 2.64$, $p = 0.267$). Alternatively, smoking status displayed a statistically noteworthy variance ($\chi^2 = 3.92$, $p = 0.048$). There is also a significant difference between the groups in occupation ($\chi^2 = 5.28$, $p = 0.022$).

Table (1): general features of study participant's.

Variables		Groups				Statistical evaluation	
		Patients n=50		Control n=50			
		N	%	N	%	χ^2	<i>p. value</i>
Age (year)	<30	14	28	9	18	3.46	0.486 NS
	31-40	12	24	15	30		
	41-50	8	16	10	20		
	51-60	10	20	7	14		
	>60	6	12	9	18		
Sex	Male	28	56	33	66	2.90	0.043
	Female	22	44	17	34		
Education level	Primary	22	44	18	36	2.64	0.267 NS
	Secondary	15	30	12	24		
	University	12	24	20	40		
Smoking	Yes	22	44	32	64	3.92	0.048
	No	28	56	18	36		
Residence	Urban	17	34	28	56	5.28	0.022
	Rural	33	66	22	44		
χ^2 : chi-square test; NS: non-significant.							

Hematological parameters among the studied groups:

Table (2) showed that a number of hematological parameters including hemoglobin, hematocrit, red blood cells, white blood cells, mean corpuscular hemoglobin and mean corpuscular volume showed a highly significant difference ($p < 0.001$). However, there were no statistically notable variations in mean corpuscular hemoglobin concentration or platelet count across the groups ($p > 0.05$). While platelet counts were $272.7 \pm 79.6 \times 10^9/L$ in patients and $260.2 \pm 69.4 \times 10^9/L$ in controls ($t = 1.543$), the MCHC values were 32.78 ± 1.60 g/dl in patients and 34.30 ± 1.33 g/dl in controls ($t = 1.982$).

Table (2): hematological parameters in patients and control groups.

Hematological parameters	Groups				Statistical evaluation	
	Patients (n=50)		Control (n=50)		t. test	<i>p. value</i>
	Mean	SD*	Mean	SD*		
Hb g/dl	12.23	3.25	15.33	2.1	12.88	<0.001
HCT %	33.43	4.7	44.16	6.2	14.846	<0.001
RBCs X10⁹/L	4.46	0.98	5.88	2.3	5.348	<0.001
WBCs X10¹²/L	11.65	1.7	6.02	0.99	-7.209	<0.001
MCV(fl)	65.43	5.8	87.55	7.9	24.754	<0.001
MCH (pg)	24.11	3.04	32.13	6.2	12.308	<0.001
MCHC (g/dl)	32.78	1.60	34.30	1.33	1.982	>0.05 NS
PLT (×10⁹/L)	272.7	79.6	260.2	69.4	1.543	>0.05 NS

Iron indices parameters:

Table (3) displays the levels of iron variables for the patient and control groups. All iron-associated markers, such as serum iron, ferritin, total iron binding capacity(TIBC) and transferrin levels, showed extremely substantial variance ($p < 0.001$).

Table (3): iron parameters among studied groups.

Iron indices	Groups				Statistical evaluation	
	Patients (n=50)		Control (n=50)		t. test	<i>p. value</i>
	Mean	SD*	Mean	SD*		
Iron µg/dl	55.87	13.92	69.12	22.10	10.872	<0.001
Ferritin ng/ml	113.77	45.6	250.76	67.14	32.25	<0.001
TIBC mg/dl	362.89	69.02	277.8	54.32	9.876	<0.001
Transferrin µmol/	326.32	89.4	45.95	13.6	22.453	<0.001
SD: standard deviation; TIBC: total iron-binding capacity; p. value <0.05 considered significant.						

Immunological markers among patient and control groups:

Table (4) summarizes the immunological marker concentrations in the patient and control groups. All tested indices, comprising immunoglobulin G (IgG), interleukin-6(IL-6), interleukin-1 β (IL-1 β), and tumor necrosis factor-alpha α (TNF- α), showed statistically notable variations ($p < 0.001$).

Table (4): immunological markers among studied groups.

Immunological markers	Groups				Statistical evaluation	
	Patients (n=50)		Control (n=50)		t. test	<i>p. value</i>
	Mean	SD*	Mean	SD*		
IgG	170.82	12.4	15.4	3.2	24.771	<0.001
IL6 (pg/ml)	55.48	8.68	2.33	0.96	8.552	<0.001
IL1 β (pg/ml)	85.21	13.54	23.44	3.66	13.30	<0.001
TNF- α (ng/ml)	88.65	23.02	34.77	8.09	23.187	<0.001

SD: standard deviation; IL6: interleukin6; IL1 β : interleukin1 beta; TNF- α : tumor necrotic factor alpha; p. value lower than <0.05 reflected significant.

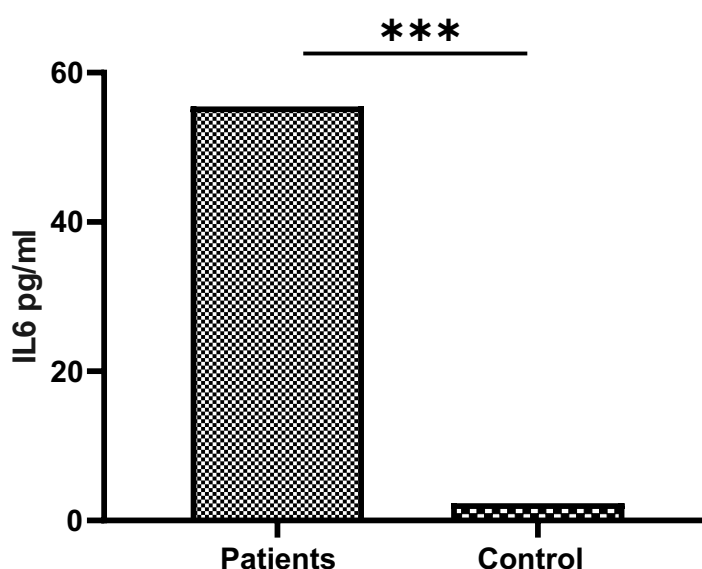


Figure (1): serum IL6 level among studied groups.

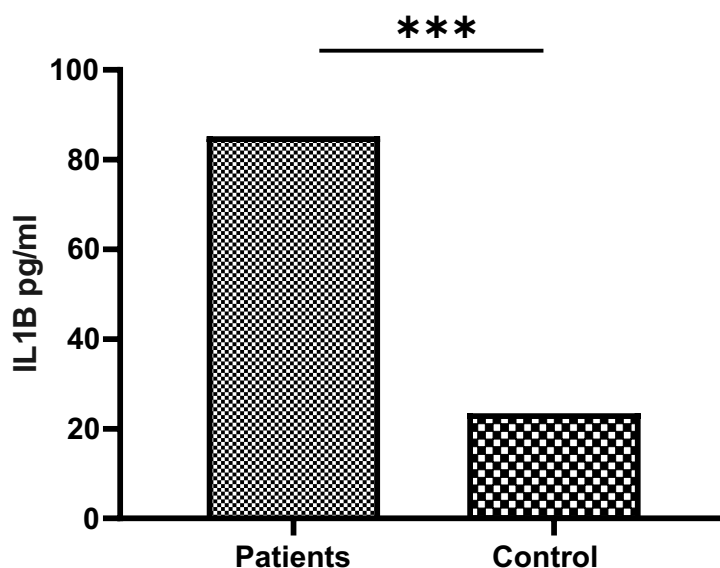


Figure (2): serum IL1B level among studied groups.

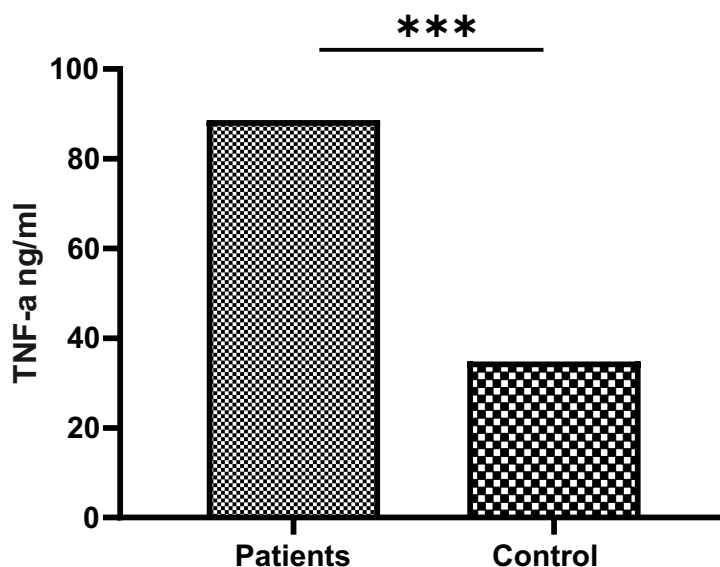


Figure (3): serum TNF-a level among studied groups.

DISCUSSION

H. pylori infection causes chronic gastritis, which may progress to severe gastroduodenal diseases, apart from stomach cancer and gastric mucosa-associated lymphoid tissue lymphoma (MALT) and peptic ulcers. Breath, stool, and serological tests are among the invasive, endoscopy-based, and noninvasive techniques used to detect *H. pylori* infection. Their application is contingent upon local availability and the unique medical history of each patient [10].

This investigation's findings are similar to those from another study by a group of scientists [11] who found that males (54%) were generally more likely to be infected with *H. pylori* than females (46%). Also, a similar observation was made that 51.7% of

the infected were males, while females accounted for 48.3% of all infected [12]. These outcomes may contribute to the understanding of whether adult *H. pylori*-related diseases such as duodenal ulcers and stomach cancer are more prevalent in males [13].

The results of the present research corroborate earlier studies that demonstrated a marked increase in sickness occurrence in adolescence compared to other age categories. The risk of *H. pylori* infection in middle-aged individuals is increased by a number of factors, such as lifestyle decisions, immune system alterations, and repeated contact over a prolonged period [14].

Variations in RBC indicators in adult *H. pylori*-infected individuals are associated with a number of processes, including iron intake by *H. pylori*, reduced iron uptake due to atrophic and chronic gastritis, iron losses due to hemorrhagic gastritis and active bleeding peptic ulcers, and iron and vitamin B12 depletion due to neither, which may cause changes in blood and iron parameters in *H. pylori*-infected patients compared to controls [15]. This outcome is in agreement with other studies on adult patients with *H. pylori* infection [16-18]. Iron uptake by *H. pylori*, reduced iron absorption because of chronic gastritis, iron loss because of hemorrhagic gastritis, and active bleeding peptic ulcer disease may contribute to the decrease in blood and iron concentrations in those infected with *H. pylori* [19].

Since elevated blood immunoglobulin values frequently reflect the host immunological response to *H. pylori* infection, they may be disregarded as likely markers for sickness diagnosis and observation [20]. According to [21], *H. pylori* induces both systemic and localized cytokine signaling, which can impede the progress of cancer, duodenal or stomach bursting, and recovery. The results of the current study are similar to previous studies that have found a higher blood concentration of TNF- α in *H. pylori*-infected people. This bacterium produces excessive amounts of this cytokine, which is connected with cancer and gastric neoplasia [22]. A previous study indicated that inflammatory markers such as IL-6 were increased in *H. pylori*-affected patients as compared with their healthy counterparts. This suggests that chronic inflammation might worsen deterioration of tissue, which could result in disorders linked to *H. pylori* [23].

In *H. pylori*-infected people, the expression of pro-inflammatory cytokine IL-1 β is tightly linked to stomach cancer development [24]. This association can be attributed to its ability to decrease stomach acid secretion and increase inflammation, which leads to gastritis, atrophy, intestinal metaplasia, and gastric cancer [25].

CONCLUSION

In conclusion, *H. pylori* infection can drastically change the investigative indicators and markers frequently accustomed assess the inflammatory reaction following infection; as a result, those markers can be used to diagnose and/or monitor the progression of infection.

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Cite this Article: Abdulateef Ali, Z.H., Abbas, M. (2026). Role of Some Immunological Cytokines in *H. pylori*-infected Patients in Relation to Iron Indices Levels. *International Journal of Current Science Research and Review*, 9(10), pp. 5376-5384. DOI: <https://doi.org/10.47191/ijcsrr/V9-i10-14>