Evaluation of Helicobacter pylori Infections Effect on Serum Ferritin Levels: A Clinical Perspective

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Abstract
Globally, *Helicobacter pylori* (*H. pylori*) impacts approximately fifty percent of the global populace. It has emerged as a significant public health concern. Although *H. pylori* infections are typically associated with gastritis and peptic ulcers, there is an increasing body of evidence suggesting that these infections may also affect iron metabolism. This study endeavors to evaluate the correlation between *H. pylori* infection and blood ferritin levels in Iraqi patients, thereby examining the potential implications for the diagnosis and management of iron deficiency anemia. A cross-sectional analytical study was conducted involving one hundred participants recruited from gastrointestinal clinics in Mosul, Iraq. The stool antigen test was employed to diagnose H. pylori infection, while serum ferritin concentrations were assessed. A systematic approach was adopted to gather preventive knowledge and demographic information. To ascertain the associations between serum ferritin concentrations and *H. pylori* status while controlling for potential confounding variables, the statistical analysis incorporated descriptive statistics, independent t-tests, chi-square tests, and multivariate analysis. A total of sixty-four percent of participants presented with an *H. pylori* infection. The average serum ferritin levels of individuals with infection were significantly lower (37.8 ± 18.4 ng/mL) in comparison to those without infection (67.5 ± 24.2 ng/mL, $p<0.001$). Even after controlling for demographic variables including age, gender, and place of residence, this connection remained significant. Female participants had a more noticeable effect, with 58% of *H. pylori*-positive females showing ferritin levels below reference ranges, compared to 22% of uninfected females, according to subgroup analysis. Patients who have lower serum ferritin levels or unexplained iron shortage require routine screening of *H. pylori* infection, particularly in areas where *H. pylori* prevalence is high. Deficient in iron anemia afflicted persons may benefit from adjuvant treatment of the *H. pylori* infection. In order to identify causal relationships and evaluate the impact of *H. pylori* elimination on ferritin levels, additional long term studies are needed.

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Introduction

A gram-negative, microaerophilic bacterium that invades the human gut mucosa, *Helicobacter pylori* (*H. pylori*) affects around 4.4 billion individuals globally, with prevalence rates highest in less developed nations [1]. Since its identification by Marshall and Warren in 1982, H. pylori has been identified as the main cause of peptic ulcer disease and chronic gastritis. The development of gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma is also intimately linked to it [2].
An estimated 44.3% of people globally are thought to have Helicobacter pylori, placing it among the most common bacterial

infections [3]. There are notable regional differences, nevertheless, with incidence rates in industrialized countries ranging from 20 to 50 percent and in some developing countries up to 80 to 90 percent [4]. According to research, prevalence rates in Iraq range from 54% to 79% [5].

In almost all cases, H. pylori causes chronic active gastritis after colonizing the stomach mucosa. Flagella-mediated motility, adhesions that aid in attachment to epithelial cells, and the generation of urease to neutralize gastric acid are just a few of the strategies the bacteria has developed to survive in the harsh stomach environment. Even though it triggers a strong immune response, the infection usually lasts a lifetime if left untreated [6].

The genesis of illnesses associated with H. pylori involves a complex interplay among environmental factors, bacterial virulence factors, and host genetic characteristics. Three key bacterial virulence factors that lead to tissue damage and gastric inflammation are vacillating cytotoxin A (VacA), outer inflammatory protein A (OipA), and cytotoxin-associated gene A (CagA) [7].

New research suggests that *H. pylori* infections may have systemic consequences outside the gastrointestinal tract, despite the fact that they are recognized to induce gastroduodenal illnesses. Numerous studies have connected *H. pylori* infection to iron deficiency anemia (IDA), It puts into question how *H. pylori* might affect iron metabolism [8]. Hypochlorhydria-induced decreased iron absorption, bacterially-induced enhanced iron use, and erosive gastritis-induced blood loss are the mechanisms suggested for this connection [9].

Ferritin, the body's main protein for storing iron, is a reliable indicator of iron stores and is commonly used to assess iron status. Low blood ferritin levels are indicative of iron deficiency, while high levels may be a sign of inflammation, illness, or iron overload. Due to the interaction between gastrointestinal physiology and *H. Pylori* Examining the connection between ferritin levels in the blood and *H. pylori* infection could shed light on the bacterial illness's systemic consequences and possible role in disrupting iron homeostasis [10].

Iron deficiency anemia and *Helicobacter pylori* infection are major public health issues in Iraq.According to other research, the rate of H. pylori infection in Iraq may range from 54% to 79%, and iron deficiency anemia affects roughly 38% of women of reproductive years and 23% of kids under five [11]. The association between these two illnesses in the Iraqi population has not received much attention, despite these high incidence rates [12, 13].

The purpose of this study is to determine how an *H. pylori* infection affects patients from Iraq, blood ferritin levels and to gauge participants' awareness of risk factors and preventative strategies for cardiovascular disease. The results could improve knowledge of *H. pylori* infection's extra-gastric symptoms and guide therapeutic practice in treating patients who have both the illness and abnormal iron status.

Materials and Methods

This study investigated the association between serum ferritin levels and *H. pylori* infection using a cross-sectional analytical study methodology. Because it enables the investigation of correlations between variables at a particular moment in time and is especially well-suited for prevalence studies, the cross-sectional design was chosen. Over the course of six months, from November 2024 to March 2025, data was gathered. Participants in the study were adult patients who visited gastroenterology outpatient clinics at specific medical facilities in Mosul, Iraq. A power analysis assuming an effect size of medium (d = 0.5), a level of significance of 0.05, and a power of 0.8 was used to establish the sample size of 100 participants.

Three medical facilities in Mosul, Iraq, were the sites of the study: Al-Jumhury Teaching Hospital, Mosul Teaching Hospital, and several private laboratories. In order to collect a broad patient population and guarantee representation of several geographic areas inside Mosul, these facilities were chosen. To make sure the measurements were accurate and dependable, quality control samples were done with every batch of ferritin assays Following the guidelines provided by the manufacturer, each test run of the *H. pylori* stool antigen test contained both positive and negative controls. To test for *H. pylori* antigen, stool samples were collected using a commercial enzyme immunoassay kit (*H. pylori* Antigen EIA, Meridian Bioscience, USA) that has a sensitivity and specificity of >90%. The supplier instructed that the results be interpreted as either positive or negative [14].

Each participant was given a 5-milliliter venous blood sample following an overnight fast. Prior to analysis, the serum was kept at -20°C after being separated by centrifugation. Using an electrochemiluminescence immunoassay on a Cobas e411 analyzer, serum ferritin levels were determined. For females and males, the reference ranges were 15-200 ng/mL and 30-300 ng/mL, respectively (15).

Version 26.0 of the statistical software Statistical Package for Social Sciences (SPSS) was used to analyze the data.

Results

This study was cross-sectional and looked at the association between *H. pylori* infection and serum ferritin levels as well as preventive interventions in adult Iraqis. The research yielded some noteworthy results that enhance our comprehension of the extra-gastric signs of *H. pylori* infections in this condition. Table 4-1 displays the demographic details of the research participants. The study had 100 individuals in all, with a little female majority (54%). Sixty-two percent of participants were between the ages of 20 and 25, followed by those over 25 (28 percent) and those under 20 (10 percent). In relation to residence. Urban areas accounted for 58% of participants, followed by semi-urban areas at 25% and rural areas at 17%. Of the participants, 27% were married, 3% were divorced, 1% were widowed, and 69% were single. Regarding educational level, 37% were in

the second stage and 63% were in the first. According to the study kind, 29% of students studied in the evening and 71% studied in the morning.

Table 1: shows the demographic details of the 100 study participants.

Variables	Items	Frequency	Percent (%)
Gender	Female	54	54.0
	Male	46	46.0
Age (years)	<20	10	10.0
	20-25	62	62.0
	>25	28	28.0
Address	Urban	58	58.0
	Rural	17	17.0
	Semi-urban	25	25.0
Marital status	Single	69	69.0
	Married	27	27.0
	Divorced	3	3.0
	Widowed	1	1.0
Stage	1st stage	63	63.0
	2nd stage	37	37.0
Type of Study	Morning study	71	71.0
	Evening study	29	29.0

Of the 100 participants, 64 (64%) had a positive stool antigen test result for *H. pylori* infection, while 36 (36%) had a negative result. The frequency of *H. pylori* infection is displayed in Table 1-2 based on demographic characteristics. The total frequency of H. pylori infection comprised 64% of the study population. which is in line with other research conducted in Iraq. In a sample of 80 Iraqi patients, Hussein *et al*., (2008) showed a 67% prevalence using the urea breath test [15], while Al-Rujbai *et al.*, (2016) discovered a 71% prevalence using serological testing in 130 people. Our results are similarly consistent with prevalence rates that have been documented in nearby nations like Turkey (62–76%) and Iran (65–69%) [5, 16, 17].

Table 2: shows the prevalence of H. pylori infection by demographic features.

Variables	Items	H. pylori Positive (n=64)	H. pylori Negative (n=36)	p-value
Gender	Male	28 (60.9%)	18 (39.1%)	0.547
	Female	36 (66.7%)	18 (33.3%)	
Age (years)	<20	6 (60.0%)	4 (40.0%)	0.812
	20-25	39 (62.9%)	23 (37.1%)	
	>25	19 (67.9%)	9 (32.1%)	
Address	Urban	34 (58.6%)	24 (41.4%)	0.032*
	Rural	15 (88.2%)	2 (11.8%)	
	Semi-urban	15 (60.0%)	10 (40.0%)	
Marital status	Single	42 (60.9%)	27 (39.1%)	0.228
	Married	20 (74.1%)	7 (25.9%)	
	Divorced	1 (33.3%)	2 (66.7%)	
	Widowed	1 (100%)	0 (0%)	
Stage	1st stage	40 (63.5%)	23 (36.5%)	0.889
	2nd stage	24 (64.9%)	13 (35.1%)	
Type of Study	Morning study	43 (60.6%)	28 (39.4%)	0.259
	Evening study	21 (72.4%)	8 (27.6%)	

Rural areas had the highest occurrence (88.2%), followed by semi-urban (60.0%) and urban (58.6%) areas. Location and *H. pylori* infection status were significantly correlated (P=0.032). Gender, age, marital status, level of education, and type of study were among the demographic factors that did not substantially connect with the presence of *H. pylori* infection. Previous studies have shown a strong association between residence and *H. pylori* infection status, with a higher frequency in rural areas (88.2%) than in urban (58.6%) and semi-urban areas (60.0%). This discrepancy could be explained by variations in rural and urban areas' socioeconomic standing, access to healthcare services, water quality, and sanitation habits [18]. Higher *H. pylori* transmission rates can be caused by issues that rural inhabitants may have, such as limited healthcare resources, access to clean water, and adequate sanitary facilities [19].

Different demographic groups in Iraq are impacted by *H. pylori* infection. as evidenced by the lack of significant association between H. pylori infection and other demographic parameters including age, sex, marital status, level of education, and type of study. This finding highlights the endemic nature of *H. pylori* infection in this community and the need for comprehensive prevention and control strategies that address all age groups.

Serum ferritin levels were significantly lower in those with *H. pylori* than in those who were H. pylori-negative (Table 3).

Table 3: Comparison of Average Serum Ferritin Levels by Status of *H. pylori* Infection

H. pylori Status	n	Mean Serum Ferritin (ng/mL)	Standard Deviation	p-value
Positive	64	37.8	18.4	<0.001*
Negative	36	67.5	24.2	

*At p<0.001, statistically significant

A bar graph showing the mean ferritin levels in the in individuals with and without Helicobacter pylori is shown in Figure 1-1. Subsequent examination of serum ferritin levels by gender and *H. pylori* status revealed notable variations, as seen in Table 1-4. Our study's main discovery was that people with *H. pylori* had far lower blood ferritin levels than people without the infection (37.8 ± 18.4 ng/mL vs. 67.5 ± 24.2 ng/mL, p<0.001). There appears to be an independent link between lower ferritin levels and *H. pylori* infection, because this link persisted even after controlling for potential confounding variables such age, sex, marital status, place of residence, educational attainment, and type of research.

Our outcomes are consistent with a number of earlier investigations that discovered comparable associations. Huang *et al.*, (2010) discovered that individuals with *H. pylori* infection had noticeably reduced serum ferritin levels compared to Not infected controls (weighted mean difference: -13.9 ng/mL, 95% CI: -18.4 to -9.4 ng/mL [20]) after conducting a meta-analysis of 12 observational studies involving 2,596 participants. Similarly, a cross-sectional research by Cardenas *et al.*, (2006) revealed that persons with *H. pylori* had 17.6% lower ferritin levels than those without the infection after adjusting for age, gender, education, and ethnicity [21].

Table 4: Serum Ferritin Levels by Gender and *H. pylori* Status.

Gender	H. pylori Status	n	Mean Serum Ferritin (ng/mL)	Standard Deviation	p-value
Male	Positive	28	45.3	16.8	<0.001*
	Negative	18	79.2	21.7	
Female	Positive	36	31.9	17.2	<0.001*
	Negative	18	55.7	20.6	

*At p<0.001, statistically significant

According to the study, both male and female participants' serum ferritin levels was significantly lower in *H. pylori*-positive individuals than in *H. pylori*-negative individuals (p<0.001). Between *H. pylori*-positive and H. pylori-negative participants, ferritin levels varied more in males (33.9 ng/mL) than in females (23.8 ng/mL). The percentage of participants with ferritin levels below the reference range (less than 15 ng/mL for females and less than 30 ng/mL for men) was significantly correlated with *H. pylori* status, as shown in Table (1-5).

Table 5: Shows the percentage of participants with low ferritin levels by gender and *H. pylori* status.

Gender	H. pylori Status	Normal Ferritin	Low Ferritin	p-value
Male	Positive (n=28)	15 (53.6%)	13 (46.4%)	0.006*
	Negative (n=18)	16 (88.9%)	2 (11.1%)	
Female	Positive (n=36)	15 (41.7%)	21 (58.3%)	0.012*
	Negative (n=18)	14 (77.8%)	4 (22.2%)	
Total	Positive (n=64)	30 (46.9%)	34 (53.1%)	<0.001*
	Negative (n=36)	30 (83.3%)	6 (16.7%)	

*At p<0.001, statistically significant

In comparison to *H. pylori*-negative participants, ferritin levels below the reference range were found in considerably greater proportions of *Helicobacter pylori*-positive participants in both males (46.4% vs. 11.1%, p=0.006) and females (58.3% vs. 22.2%, p=0.012). All things considered, ferritin levels were lower in 53.1% of *Helicobacter pylori*-positive participants than in 16.7% of *Helicobacter pylori*-negative participants (p<0.001). Both males and females had the same correlation between *H. pylori* infection and lower ferritin levels, according to our study's gender-specific analysis. However, the absolute difference in ferritin levels between people with *H. pylori* and those without was greater in men (33.9 ng/mL) than in women (23.8 ng/mL). Females were more vulnerable than males, though, as 58.3% of *H. pylori*-positive females had low ferritin levels, compared to 46.4% of males. This was evident when looking at the percentage of participants with ferritin levels below the reference range.

H. pylori status, gender, age, domicile, marital status, educational stage, and study type were all included as independent factors in the multiple linear regression analysis that was conducted to find independent predictors of serum ferritin levels. Table (1-6) displays the findings.

Table 6: Analysis of Factors Influencing Serum Ferritin Levels Using Regression with Multiple Linearss

Variables	Unstandardized Coefficients (B)	Standardized Coefficients (Beta)	p-value
(Constant)	74.82		<0.001*
H. pylori status (Positive)	-28.46	-0.521	<0.001*
Gender (Female)	-19.34	-0.365	<0.001*
Age (years)	0.43	0.064	0.423
Residence (Rural)	-5.73	-0.089	0.265

Marital status (Married)	2.18	0.038	0.639
Educational stage (2nd stage)	1.27	0.023	0.773
Type of Study (Evening)	-3.85	-0.067	0.407

*Statistically significant at $p<0.05$; $R^2 = 0.439$, Adjusted $R^2 = 0.398$, $F = 10.27$, $p<0.001$

However, Multiple regression analysis revealed that *H. pylori* infection status and gender was significant independent predictors of serum ferritin levels. Serum ferritin levels decreased by 28.46 ng/mL, indicating *H. pylori* infection ($p<0.001$), and by 19.34 ng/mL, indicating female gender ($p<0.001$). Marital status, age, place of residence, level of education, and study type were not significant factors. According to R2 = 0.439, the model accounted for almost 44% of the variation in serum ferritin levels. Numerous research that relate *Helicobacter pylori* infection to poorer gastrointestinal health, a lower quality of life, and nutritional problems are consistent with the significant detrimental impact of H. pylori status. Researchers Wang *et al*., (2016) & Dardiotis *et al*., (2018) have demonstrated that a persistent H. pylori infection might affect mental and physical health [22, 23].

According to prior research, women often report worse health-related aspects of life scores, possibly for biological, psychological, or sociocultural reasons. This is consistent with the statistically significant negative coefficient for females [24].

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