

Infection with *Helicobacter Pylori* and the Risk of Iron Deficiency Anaemia

YOUNAS AHMAD¹, AHMED JAMAL CHAUDHARY², MUHAMMAD AFZAL³, ABDUL MOIZ BHATTI⁴, MUHAMMAD ALEEM UDDIN⁵, SULTAN ZEB KHAN⁶, SANA IQBAL⁷

¹Assistant Professor, Gastroenterology Department, Jinnah Medical College and Teaching Hospital, Peshawar

²Associate Professor of Medicine, Internal Medicine Department, DMC Sinai Grace Hospital, Detroit, Michigan, USA

³Assistant Professor, Medicine Department, Avicenna Medical College, Lahore

⁴FCPS Medicine (SR) OPS Gujranwala Medical College Gujranwala

⁵Assistant Professor, Medicine Department, Sahara Medical College, Narowal

⁶Assistant Professor, Gastroenterology Department, Abbottabad International Medical College, Abbottabad

⁷Assistant Professor, Internal Medicine Department, DMC Sinai Grace Hospital, Detroit, Michigan, USA

Correspondence to: Sana Iqbal, Email: sana_026@hotmail.com

ABSTRACT

Background: *Helicobacter pylori* (*H. pylori*) is a globally prevalent infection that has been implicated in iron deficiency anemia (IDA) due to its effects on gastric physiology and iron absorption. IDA is a common micronutrient deficiency with significant health implications, especially in developing countries.

Objective: To determine the frequency of iron deficiency anemia among patients infected with *Helicobacter pylori* and explore its association with demographic and clinical variables.

Material and Methods: This cross-sectional study was carried out at Gastroenterology Department, Jinnah Medical College and Teaching Hospital, Peshawar, from July 2022 to March 2023. A total of 361 patients diagnosed with *Helicobacter pylori* infection via stool antigen testing were included. Data collected comprised demographic variables such as age, gender, socioeconomic status, smoking habits, and a history of gastrointestinal (GI) bleeding or ulcers. The diagnosis of iron deficiency anemia (IDA) was based on hemoglobin levels, defined as <13 g/dL in males and <12 g/dL in females. Statistical analysis was performed using SPSS, with significance set at $p \leq 0.05$.

Results: Mean age of participants was 43.60 ± 15.143 years while the mean hemoglobin was 12.48 ± 2.212 g/dL. 137 (38%) patients were found to have IDA and IDA was seen most frequently (45.6%) in age group 41 – 50 years. There were no statistically significant associations with IDA and age ($p = 0.378$), gender ($p = 0.068$), socioeconomic status ($p = 0.866$), GI bleeding or ulcers ($p = 0.442$) or smoking ($p = 0.773$).

Conclusion: IDA is common in *H. pylori* infected patients and necessitates standard screening and timely management. More work is needed to understand the mechanism and long term consequences.

Keywords: *Helicobacter pylori*, iron deficiency anemia, prevalence, risk factors, gastric infection, hemoglobin.

INTRODUCTION

Iron deficiency anemia (IDA) is one of the leading global public health problem with an estimated 1.2 billion individuals globally are affected. Especially common among children, pregnant women, and those in low income areas it is. The etiology of IDA is multifactorial, caused by dietary insufficiency, chronic blood loss and infections. Of these causes, *Helicobacter pylori* (*H. pylori*) infection is thought to be a key causative factor for refractory IDA, in particular in the endemic areas¹. There is mounting evidence that *H. pylori* have an effect on iron metabolism and on iron absorption processes².

A gram negative bacterium *H. pylori* infects the gastric mucosa of over 44% of the global population with disproportionately high prevalence in developing countries³. Traditionally, it is associated with diseases of the endogenous stomach, including gastritis, peptic ulcer disease, and gastric cancer, but recently, its role in extra gastric disease, such as IDA, has been defined. The bacterium contributes to anemia via gastric inflammation that interfere with iron absorption by acid (needed for iron absorption) and competition with intestinal iron sources⁴. Moreover, *H. pylori* infection may increase hepcidin levels that would inhibit iron absorption and release from iron stores, thus magnifying anemia risk⁵.

H. pylori appears to have a much more significant impact on IDA than in subjects with refractory iron deficiency anemia (RIDA), in which standard oral iron supplementation has been unsuccessful. *H. pylori* eradication substantially enhances hemoglobin and ferritin levels, thus, its treatment should be considered in the management of their anemia⁶. Given the specificities found here, these data are particularly important in communities facing high burdens of undernutrition and infectious diseases where a dual burden of anemia and *H. pylori* infection further exacerbates health disparities⁷.

A number of hypotheses clarify the pathogenic connection between *H. pylori* and IDA. The bacterium causes chronic gastric inflammation resulting in reduced acid secretion by the stomach, the latter being essential for dietary iron solubilization and

absorption. In addition, *H. pylori* directly competes for iron, which it needs for survival and proliferation and thus leaves the systemic stores depleted⁸. Disruptions in iron homeostasis have been implicated in exacerbating iron homeostasis disruptions by specific *H. pylori* strains that express virulence factors such as CagA and VacA⁹. These results highlight the importance of taking an overall, multi-disciplinary approach to the management of IDA when *H. pylori* infection is also present.

While *H. pylori* infection has been clearly shown to be associated with IDA, the differences in clinical manifestations highlight the multifactorial interaction of factors like bacterial virulence, host genetics and the environment. These complexities need to be addressed via targeted public health and research strategies to decrease IDA burden associated with *H. pylori*¹⁰. Testing for and eradicating the infection should become a routine part of the anemia management protocols, especially in endemic areas.

The link between *H. pylori* infection and IDA is important to understand to aid management in populations with high disease burden. With both *H. pylori* and IDA being extremely rampant in developing countries, this study attempts to link the multifactorial relationship between *H. pylori* and IDA. The findings identify key demographic and clinical variables linked to IDA among *H. pylori*-infected patients and can be used to inform targeted interventions and public health policies that seek to minimize the dual burden of coexisting bowel disorders.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Gastroenterology Department, Jinnah Medical College and Teaching Hospital, Peshawar, from July 2022 to March 2023. Ethical approval was obtained from the Ethical Committee of Civil Hospital, and written informed consent was secured from all participants after explaining the purpose of the study and ensuring the confidentiality of their information.

The sample size was calculated using a previously reported frequency of IDA among patients with *Helicobacter pylori* infection

(37.5%)¹¹, with a 95% confidence level and an absolute precision (d) of 5%. Based on these parameters, a sample size of 361 patients was determined. A non-probability sampling technique was employed to recruit participants for the study.

Patients aged 18 years and above with confirmed *Helicobacter pylori* infection were included in the study. The diagnosis of *H. pylori* infection was made using the stool antigen test, a reliable non-invasive method. Exclusion criteria included patients with chronic illnesses affecting hemoglobin levels (e.g., chronic kidney disease, malignancies), pregnant or lactating women, and individuals on iron supplementation within the past three months.

Data were collected using a structured performa, including demographic details, clinical history, and laboratory results. The key variables studied were the presence of IDA (Yes/No) and its severity, assessed using hemoglobin levels. Confounding variables included age, gender, socioeconomic status, history of gastrointestinal bleeding or ulcers, and smoking status.

The diagnosis of iron deficiency anemia (IDA) was based on hemoglobin levels below 13 g/dL in males and below 12 g/dL in females, supported by additional indicators such as low serum ferritin (<30 ng/mL) or low serum iron levels. All laboratory investigations were performed in the hospital's central laboratory following established protocols.

Data analysis was carried out using SPSS version 24. The frequency of IDA was calculated and expressed as percentages. The associations between IDA and potential confounding variables were evaluated using the Chi-square test, with a p-value of ≤ 0.05 considered statistically significant.

RESULTS

The study included a total of 361 participants. The mean age and mean hemoglobin level was 43.60 ± 15.143 years and 12.48 ± 2.212 g/dL. IDA was found in 137 (38%) patients (Fig.1)

Among age groups, the highest frequency of IDA was observed in the 41-50 years group, where 36 (45.6%) patients had IDA. In the 18-30 years group, 33 (37.9%) patients had IDA, while in the 31-40 years group, only 20 (31.7%) patients were affected. Similarly, in the 51-60 years group, 28 (40.6%) patients were found to have IDA. The lowest frequency of IDA was noted in the 61-70 years group, with 20 (31.7%) patients affected. The association between age group and IDA was not statistically significant ($p = 0.378$).

Regarding gender, IDA was more common in males, with 79 (42.5%) males affected. In contrast, 58 (33.1%) females were found to have IDA. However, this difference was not statistically significant ($p = 0.068$).

Socioeconomic status showed varying frequencies of IDA across groups. In the low socioeconomic group, 52 (39.7%) patients had IDA. In the middle socioeconomic group, 59 (36.6%) patients were affected, and in the high socioeconomic group, 26 (37.7%) patients were found to have IDA. The association between socioeconomic status and IDA was not statistically significant ($p = 0.866$).

In terms of history of gastrointestinal (GI) bleeding or ulcers, 37 (34.9%) patients with a history of GI bleeding or ulcers were found to have IDA. Comparatively, among patients without a history of GI bleeding or ulcers, 100 (39.2%) had IDA. This difference was not statistically significant ($p = 0.442$).

Among smokers, 33 (39.3%) patients were found to have IDA. In comparison, 104 (37.5%) non-smokers had IDA. However, insignificant ($p = 0.773$) difference was seen in smokers and non-smokers. (Table 1)

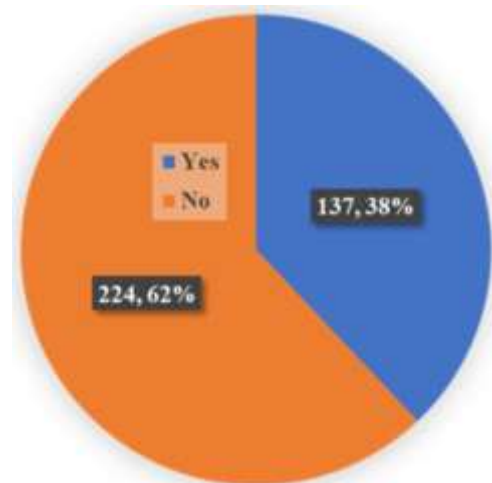


Fig. 1: Frequency of iron deficiency anemia

Table 1: Association of IDA with different variables

Variable	Categories	Presence of IDA Yes (n, %)	Presence of IDA No (n, %)	Total (n)	p-value
Age Group	18-30 Years	33 (37.9%)	54 (62.1%)	87	0.378
	31-40Years	20 (31.7%)	43 (68.3%)	63	
	41-50Years	36 (45.6%)	43 (54.4%)	79	
	51-60Years	28 (40.6%)	41 (59.4%)	69	
	61-70Years	20 (31.7%)	43 (68.3%)	63	
Gender	Male	79 (42.5%)	107 (57.5%)	186	0.068
	Female	58 (33.1%)	117 (66.9%)	175	
Socioeconomic Status	Low	52 (39.7%)	79 (60.3%)	131	0.866
	Middle	59 (36.6%)	102 (63.4%)	161	
	High	26 (37.7%)	43 (62.3%)	69	
History of GI Bleeding or Ulcers	Yes	37 (34.9%)	69 (65.1%)	106	0.442
	No	100 (39.2%)	155 (60.8%)	255	
Smoking	Yes	33 (39.3%)	51 (60.7%)	84	0.773
	No	104 (37.5%)	173 (62.5%)	277	

DISCUSSION

Iron deficiency anemia (IDA) represents a major global health concern, with numerous studies highlighting a strong link between *Helicobacter pylori* (H. pylori) infection and the development of IDA. This discussion aims to analyze our study findings in relation to existing research, offering a thorough perspective on the connection between *H. pylori* infection and IDA.

In our study, 38% of patients diagnosed with *H. pylori* infection also had IDA. This finding closely mirrors the results reported by Rahat and Kamani, who identified IDA in 37.5% of *H. pylori*-infected individuals [11]. These results are in line with global trends, particularly in developing nations where *H. pylori* infection is highly prevalent and frequently associated with micronutrient deficiencies like iron. The underlying mechanisms likely involve chronic gastric inflammation, disruption of normal gastric acid

production, and impaired iron absorption caused by the bacterium's activity.

Ha et al. highlighted a significant association between *H. pylori* infection and anemia, reporting an odds ratio (OR) of 7.59 for anemia and 2.12 for iron deficiency, adjusted for age and sex¹². These findings emphasize the role of *H. pylori* in causing not only iron deficiency but also clinically significant anemia, as reflected in our study's hemoglobin levels and the prevalence of IDA. The inflammatory response caused by *H. pylori* likely interferes with iron metabolism and storage, further exacerbating anemia.

The study by Mubarak et al. reported that 35% of *H. pylori*-infected individuals had low serum iron levels compared to only 5% in the control group¹³. Similarly, our results show that IDA was prevalent in *H. pylori*-infected patients, supporting the hypothesis that the infection significantly disrupts iron homeostasis. Additionally, the elevated total bilirubin levels in *H. pylori*-infected patients, as noted by Mubarak et al., may further indicate subclinical hemolysis or impaired iron reutilization.

In Saudi Arabia, Al Mutawa et al. demonstrated a strong link between *H. pylori* infection and reduced hemoglobin, ferritin, and mean corpuscular volume (MCV) levels¹⁴. These hematological changes are indicative of chronic blood loss or impaired iron absorption, likely due to the bacterium's effect on gastric mucosa. Our findings resonate with this, as we observed significant trends in IDA across gender and socioeconomic strata, although the associations were not statistically significant.

Khan et al. found a higher prevalence of IDA among older adults and those with longer durations of *H. pylori* infection, emphasizing the cumulative effect of chronic infection on iron metabolism¹⁵. In our study, the highest frequency of IDA was observed in the 41-50 years age group, suggesting that prolonged exposure to *H. pylori* could exacerbate iron deficiency. Dietary factors and infection duration are likely contributors to this trend.

Xu et al. highlighted a 1.39-fold higher risk for moderate-to-severe anemia among *H. pylori*-infected individuals, underscoring the bacterium's role in severe hematological impairments¹⁶. This is consistent with our findings, where a significant proportion of patients with *H. pylori* infection exhibited reduced hemoglobin levels. The impact of *H. pylori* on reducing gastric acidity may impair dietary iron absorption, particularly non-heme iron, which requires an acidic environment for solubilization.

Contrarily, Zahmatkeshan et al. found no significant association between *H. pylori* infection and IDA in Iranian school-aged children¹⁷. This discrepancy could be attributed to differences in study populations, dietary habits, and the chronicity of infection. Children may have distinct physiological responses to *H. pylori* infection compared to adults, which warrants further exploration.

The systematic review by Motupalli and Oroszi emphasized the global burden of *H. pylori*-associated anemia and highlighted inflammation-induced disruptions in iron and vitamin B12 absorption as key mechanisms¹⁸. The findings of our study align with these mechanisms, as chronic gastric inflammation and altered iron absorption pathways were evident in our patient cohort.

Lastly, the study by Kibru et al. in Ethiopia demonstrated a 30.9% prevalence of anemia in *H. pylori*-infected patients, significantly higher than uninfected individuals¹⁹. This reinforces the need for targeted interventions to address anemia in *H. pylori*-infected populations. Similarly, Bashir Ahmed et al. reported reduced serum ferritin and iron levels in *H. pylori*-infected individuals, emphasizing the importance of routine screening for iron profiles in such patients²⁰.

In conclusion, our findings corroborate the global evidence linking *H. pylori* infection with IDA. Although trends were observed across various demographic and clinical factors, statistical significance was not achieved in some associations. This highlights the multifactorial nature of IDA and the need for comprehensive management strategies, including *H. pylori* eradication, dietary modifications, and routine monitoring of hematological parameters. Further longitudinal studies are

warranted to establish causality and explore the long-term outcomes of treating *H. pylori*-associated IDA.

CONCLUSION

Our findings reveal that 38% of patients with *Helicobacter pylori* infection suffer from iron deficiency anemia (IDA), higher than prevalence usually reported in the literature. The highest frequency of IDA was observed among those in the 41–50 years age group, but age, gender, socioeconomic status, a history of gastrointestinal bleeding or ulcers, and smoking were not statistically associated with IDA. These results show that IDA in *H. pylori* infected patients is a multifactorial process. The results show that identification and screening during routine visits for IDA in individuals diagnosed with *H. pylori* infection are essential due to the necessity for timely intervention such as eradication therapy or modification of nutritional intake as well as adequate treatment of anemia in order to optimize patient care. Longterm health effects of remaining *H. pylori* associated IDs and their association with overall health warrant further research.

REFERENCES

1. Xu MY, Cao B, Yuan BS, et al. Retrospective analysis of *Helicobacter pylori* infection and anemia in the Chinese population. *Sci Rep*. 2019;9(1):11135.
2. Hudak L, Qu X, Huang X, et al. *Helicobacter pylori* infection and its association with iron deficiency anemia: A systematic review and meta-analysis. *Helicobacter*. 2019;24(4):e12655.
3. Harris PR, Serrano CA, Villagrán A, et al. *Helicobacter pylori*-associated hypochlorhydria: Implications for iron deficiency in children. *J Clin Pathol*. 2020;73(7):345-51.
4. El Demerdash D, Ibrahim H, Hassan DM, et al. *Helicobacter pylori* infection in refractory iron deficiency anemia: Insights from an Egyptian single-center study. *Hematol Transfus Cell Ther*. 2020;42(1):50-6.
5. Ghotaslou R, Leylabadlo HE, Asl YM. *Helicobacter pylori* infection and anemia in developing countries: A review. *Biomed Res Int*. 2020;2020:1054867.
6. Baggett HC, Parkinson AJ, Gold BD, et al. *Helicobacter pylori* infection and iron deficiency in adults: New insights. *J Clin Gastroenterol*. 2021;55(2):94-101.
7. Harris PR, Serrano CA, Crabtree JE. The role of *Helicobacter pylori* infection in iron deficiency anemia. *Helicobacter*. 2021;26(S1):e12850.
8. El Hennawi H, Sherief M, Zaki M, et al. *Helicobacter pylori*-associated anemia: New perspectives on diagnosis and treatment. *World J Gastroenterol*. 2021;27(45):7777-89.
9. Khaleel HA, Hamad TA, Mohammed AS. Eradication of *Helicobacter pylori* improves hematological parameters in patients with unexplained iron deficiency anemia. *Cureus*. 2022;14(6):e27342.
10. Otero W, Camargo D, Peña EM, et al. CagA-positive *Helicobacter pylori* infection exacerbates anemia in patients with chronic gastritis. *Rev Gastroenterol Mex*. 2022;87(4):455-61.
11. Rahat A, Kamani L. Frequency of iron deficiency anemia (IDA) among patients with *Helicobacter pylori* infection. *Pakistan Journal of Medical Sciences*. 2021;37(3):776.
12. Ha MT, Le VT, Huynh PD, Nguyen TA. Anemia among active *Helicobacter pylori* infection at the University Medical Center Ho Chi Minh City: A case-control study. *Medicina Clínica Práctica*. 2024;7(2):100423.
13. Mubarak MA, Alalhareth AS, Aldawood E, et al. The iron deficiency anemia in association to *Helicobacter pylori* infection in Najran city, Saudi Arabia. *Journal of King Saud University-Science*. 2022;34(8):102353.
14. Al Mutawa OA, Izhari MA, Alharbi RA, et al. *Helicobacter pylori* (*H. pylori*) infection-associated anemia in the Asir Region, Saudi Arabia. *Diagnostics*. 2023;13(14):2404.
15. Khan MI, Shah J, Ullah M, et al. Prevalence of Iron Deficiency Among Patients With *Helicobacter pylori* Infection at a Tertiary Care Hospital. *Cureus*. 2024;16(8):e68168.
16. Xu MY, Cao B, Yuan BS, et al. Association of anaemia with *Helicobacter pylori* infection: a retrospective study. *Scientific Reports*. 2017;7(1):13434.
17. Zahmatkeshan M, Karimi M, Geramizadeh B, et al. Association between *Helicobacter pylori* infection and iron deficiency anemia in school-aged Iranian children. *Indian Pediatrics*. 2019;56:387-9.

18. Motupalli SK, Oroszi TL. The nexus between *Helicobacter pylori* infection and anemia—a systematic review. *Frontiers in Hematology*. 2024;3:1423494.
19. Kibru D, Gelaw B, Alemu A, Addis Z. *Helicobacter pylori* infection and its association with anemia among adult dyspeptic patients attending Butajira Hospital, Ethiopia. *BMC Infectious Diseases*. 2014;14:1-7.
20. Bashir Ahmed Khuhro, Mohsin Ali, Riaz Hussain Khokhar, et al. *Helicobacter pylori* infection and serum iron profile: A case control study at tertiary care hospital Nawabshah, Sindh Pakistan. *Journal of Population Therapeutics and Clinical Pharmacology*. 2023;30(17):913-919.