

ORIGINAL ARTICLE

Infection with Helicobacter Pylori and the Risk of Iron Deficiency AnaemiaRASHID KARIM¹, WAJID IQBAL², MAHWASH MENGAL³, MUHAMMAD ALAM MENGAL⁴, MUHAMMAD MOHSIN SIAL⁵, AHMED LATIF CHAUDHARY⁶¹Assistant Professor Gastroenterology, Department of Gastroenterology, Allama Iqbal Teaching Hospital, Ghazi Khan Medical College DG Khan²Senior Registrar Department of Gastroenterology, Timergara Teaching Hospital Dir Lower.^{3,4}Assistant Professor, Department of Physiology, Bolan Medical College Quetta, Balochistan.⁵House Officer, Department of Internal Medicine, Mayo Hospital Lahore.⁶Demonstrator, Department of Pathology, Sharif Medical and Dental College Lahore, Pakistan.Corresponding author: Wajid Iqbal, Email: drwajid1112@gmail.com**ABSTRACT****Objective:** The objective of this research is to determine the frequency of a condition known as iron deficiency anaemia (IDA) among people who have been infected with Helicobacter pylori.**Study Design:** Cross-sectional/ Prospective study**Place and Duration:** Hayatabad Medical Complex Peshawar in the duration from November, 2022 to April, 2023.**Methods:** There were a total of 116 patients with Helicobacter pylori infections, whose ages ranged from 20 to 70. After collecting demographic information from each participant (including age, sex, BMI, education level, and residence), each patient gave written informed consent. Subjects' blood was tested for iron, transferrin saturation, ferritin, which and total iron-binding capacity. Histopathology, stool antigen testing, a fast urease test, and a urea breath test can all diagnose Helicobacter pylori infection. All statistical analyses were performed in SPSS 25.0.**Results:** There were 74 (63.8%) females and 42 (36.2%) males in our study. Patients mean age was 28.13±14.68 years and had mean BMI 23.6±11.26 kg/m². The mean Hemoglobin level of the patients was 11.9±1.8 (g/dl), the iron level was 47.11±6.49 (ug/dl) and mean ferritin level was 119.6±32.68 (ng per ml). Among 116 cases, 42 (36.2%) patients had Iron Deficiency Anemia (IDA).**Conclusion:** An increased incidence of iron deficiency anaemia was seen among individuals with Helicobacter pylori infections; the majority of these patients were adult females.**Keywords:** H.pylori infection, Prevalence, Iron Deficiency Anemia (IDA),**INTRODUCTION**

Helicobacter pylori is a spiralling pathogen that is found on the mucosa of the human stomach. This bacteria can cause ulcers. The majority of cases of peptic ulcer disease and stomach cancer may be traced back to this factor [1]. Helicobacter pylori affects around 50 percent of the world's population of people. Peptic ulcer illness is a very uncommon occurrence in children, and children virtually never show any indications of having an infection [2]. Infections of the digestive tract are extremely uncommon in children [3].

H. pylori infection can lead to chronic inflammation, which in turn increases the risk of developing a number of gastrointestinal conditions, including gastric cancer, adenocarcinoma, and MALT lymphoma, as well as gastroesophageal reflux disorder and duodenal ulcers. [4] Multiple studies have shown that after the H. pylori infection has been completely cleared, MALT lymphoma in its early stage can be effectively treated.

H. pylori infection is linked to numerous extra-digestive infections and diseases, further complicating case management [5]. These diseases and infections span the autoimmune spectrum, the cardiovascular system, the pancreas, the colon, the hepatobiliary system, bronchiectasis, diabetes mellitus, the nervous system, and the blood.

Different diagnostic methods, including noninvasive and intrusive testing, can be used to draw conclusions about the underlying medical issue. Immunological procedures (serological tests, salivary and urine testing, near-patient assays), and the stool antigen test are examples of non-invasive diagnostics that are more likely to receive patient consent [6]. Patients also report a higher level of satisfaction with these treatments. However, using invasive testing or endoscopic procedures with a substantial specimen can improve the results' accuracy [7].

As well as gastritis, H. pylori infection in children has been related to peptic ulcer disease (duodenal ulcers more so than stomach ulcers) and, in exceedingly rare cases, mucosal-associated lymphoid-type tissue lymphoma. Idiopathic thrombocytopenic purpura (ITP) and iron deficiency/anemia (IDA) are two such conditions. However, the great majority of children who contract H. pylori do not develop any symptoms and show no signs of developing serious clinical abnormalities. In youngsters

infected with H. pylori, atrophy, intestinal metaplasia, and gastric cancer are extremely rare [6,7]. A down-regulation of host immune response may start early in the natural history of infection, since it has been found that many H. pylori-infected infants had less severe gastritis and the resulting outcome of severe clinical illnesses compared to adults [7]. [7] The fact that most children born with H. pylori infection have been examined lends credence to this theory. This initial or early infection attenuation following gastric mucosal colonisation makes biological sense to permit immune evasion and establish permanent infection in a specific biological niche. According to the available data, H. pylori is a "old" pathogen in terms of human evolution. If you want to learn the ins and outs of H. pylori infection in humans, you need to know that the clinical spectrum of H. pylori-associated illness, particularly H. pylori-associated IDA, varies greatly between paediatric and adult populations.

We just concluded a randomised, placebo-controlled trial with adolescents who were suffering from iron deficiency anaemia and H pylori. We found that H pylori infection is linked to iron deficient anaemia and that investigating infection is warranted when the anaemia does not improve with iron therapy. In addition, we proposed using H pylori eradication as part of the treatment for iron deficient anaemia in those who were also infected with H pylori. Because their bodies are still expanding, adolescents require a great deal of iron to fuel their rapid pace of growth. [9] Iron deficiency now hinders both weight increase and lengthening of life span. [10]

The neurologic, behavioural, and hematologic ramifications of this prevalent co-morbidity in humans can be better understood with the help of Burns et al.'s (2017) IDA/H. pylori mice model. [11]

Vitamin B12 deficiency has been linked to gastrointestinal infections including Helicobacter pylori and idiopathic scurvy (IDA) (Kadhim et al., 2018). Even though Helicobacter pylori infection is a separate risk factor for low blood bilirubin levels, few studies have looked at the link between H. pylori and serum bilirubin (Mwafy and Afana, 2018; Zhao et al., 2019). [12-15]

This study aims to contrast iron levels in those with IDA and those without in order to further describe the connection between the two conditions.

MATERIAL AND METHODS

This prospective/cross-sectional study was conducted in Hayatabad Medical Complex Peshawar in the duration from November, 2022 to April, 2023 and comprised of 116 patients. Patients were excluded if they had gastrointestinal cancer, hematologic abnormalities, iron supplementation for at least 30 days, erythropoietin injection, overt or covert gastrointestinal haemorrhage, malnutrition, a history of gastrectomy, or had recently been hospitalised for acute illnesses. All patients provided written informed consent that included demographic information.

Patients who presented to the GI clinic complaining of dyspepsia and who ultimately needed an upper GI endoscopy. The standard data sheet included their medical background and physical examination results. Endoscopies were recommended for patients who had just stopped taking bismuth compounds, antibiotics, or proton pump inhibitors. Patients who were chosen for upper gastrointestinal endoscopy and biopsy submitted informed permission forms after obtaining detailed explanations of the procedures. Patients at the BSMMU Gastroenterology Department were given topical lignocaine anaesthetic before an experienced endoscopist examined their digestive tracts with an Olympus forward-looking video endoscope. The study population included both patients diagnosed with endoscopic atrophic or erosive gastritis and healthy controls. The endoscopy yielded two biopsy samples, one from the body and one from the stomach antrum. The fast urease test (CLO) used to detect H. pylori resulted in a pinkish or reddish coloration of the test medium when applied to biopsy samples. This new hue could last around for as long as a day.

Ferritin, serum iron, total iron-binding capacity, transferrin saturation, and ferritin levels were measured in the subjects' blood samples. Histopathology, stool antigen testing, urea breath testing, and fast urease tests can all detect H. pylori infection. SPSS 25.0 was used to conduct the comprehensive analysis. Laboratory data was analysed using mean standard deviation.

RESULTS

There were 74 (63.8%) females and 42 (36.2%) males in our study. Patients mean age was 28.13±14.68 years and had mean BMI 23.6±11.26 kg/m². The mean Hemoglobin level of the patients was 11.9±1.8 (g/dl), the iron level was 47.11±6.49 (ug/dl) and mean ferritin level was 119.6±32.68 (ng per ml). Majority of the cases were poor and were non-educated. (table 1)

Table 1: Characteristics demographics of enrolled cases

Characteristics	Frequency (116)	Percentage
Gender		
Females	74	63.8
Males	42	36.2
Mean age (years)	28.13±14.68	
Mean BMI (kg/m ²)	23.6±11.26	
mean Hemoglobin level (g/dl)	11.9±1.8	
Mean iron level (ug/dl)	47.11±6.49	
Mean ferritin level (ng/ml)	119.6±32.68	
Poor-socioeconomic status		
Yes	71	61.2
No	45	38.8
Literacy		
Yes	36	31.04
No	80	68.96

Among 116 cases, 42 (36.2%) patients had Iron Deficiency Anemia (IDA).(figure 1)

Among 42 cases of IDA, 20 patient were aged >40 years followed by 15 cases age between 31-40 years and 7 cases were aged between 20-30 years.(figure 2)

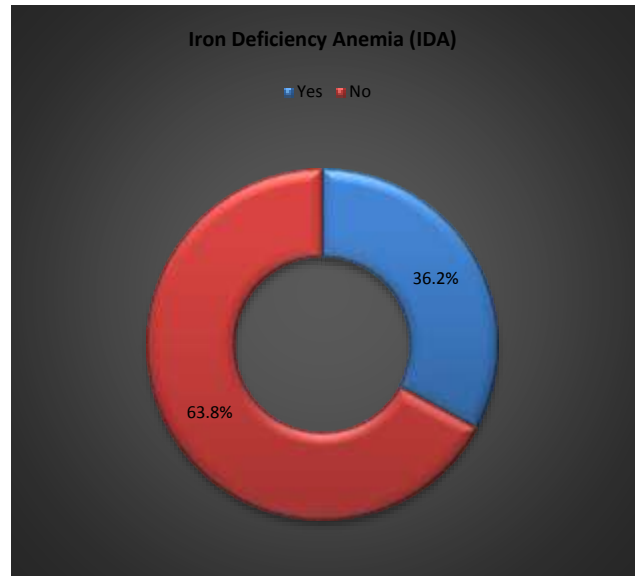


Figure-1: The overall incidence rate of IDA

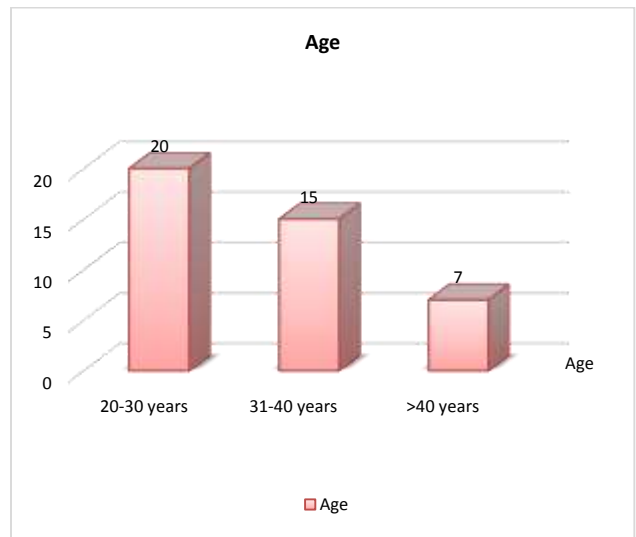


Figure-2: Age distribution of IDA patients

DISCUSSION

The findings of this study suggest that an infection with H. pylori is a prevalent cause of iron deficiency anaemia (IDA) in people with iron refractoriness or iron dependence when the traditional diagnostic work-up is ambiguous. Following the elimination of H. pylori, IDA improved in 38 percent of patients without the need for extra iron supplements, and the condition did not return at any point over the mean follow-up period of roughly two years. These data lend support to the hypothesis that an infection with H. pylori is the underlying cause. Recovery from IDA following eradication of H. pylori was also investigated in males and postmenopausal women, as well as in premenopausal women and other premenopausal women.

Our study was carried out in a region of Pakistan's province where we identified the highest rates of rural poverty. A recent study found that the regions of Eastern and Southern Europe had the greatest prevalence of H. pylori infection. These same regions also have the highest occurrences of stomach cancer in the European Union [16]. A rise in the prevalence of H. pylori infections was shown to be much higher in senior people by our research team, and similar patterns have been seen for

impovertised countries [17]. This may be due to cumulative exposure over time. It has also been noted that *H. pylori* infection is more common in women; one possible explanation is that women naturally have lower gastric acidity. Among 116 cases, 42 (36.2%) patients had Iron Deficiency Anemia (IDA). 20 patients were aged >40 years followed by 15 cases age between 31-40 years and 7 cases were aged between 20-30 years. These results are consistent with those of a recently published research [18] by Bille et al. in Cameroon, which also found a high frequency of IDA with micro cells and anaemia in the juvenile population examined.

Kishore et al. found, after analysing data from 300 patients in Pakistan, that individuals with *H. pylori* infection had significantly lower mean blood iron levels than those without the illness (110.72 28.38 g/dL versus 162.5 21.18 g/dL; $p < 0.0001$). [19]. Infection with *Helicobacter pylori* has been associated to conditions unrelated to the digestive system, such as iron deficiency anaemia (IDA) [20]. There is evidence that *H. pylori* has an effect on iron metabolism, since multiple studies have found that patients with anaemia that did not respond to iron therapy recovered when the bacteria was eradicated. [21]

Premenopausal women make up the vast majority of patients who experience a full recovery from anaemia 12 months following *H. pylori* eradication, as shown in previous research by Annibale et al [22]. However, these conclusions are at odds with the results of the present investigation. The root of the problem is the many interpretations of the word "response." The response to *H. pylori* was defined as a return to pre-anaemia values of serum ferritin. *pylori* eradication criteria in our study. Only 17 percent of patients in Annibale's trial had normal ferritin levels return after recovery from anaemia, a number that is comparable to the 23 percent we found. Infections with *H. pylori* may also contribute to IDA in premenopausal women, and eradicating *H. pylori* is advised to increase iron absorption, as shown by the results of the current investigation in males and postmenopausal women and the meta-analysis data given in the introduction [23,24].

There is evidence that treating an *H. pylori* infection can alleviate LD [25]. However, it is not known if *H. pylori*-infected individuals with LD have an increased chance of developing IDA. The current study found that IDA was ultimately diagnosed as *H. pylori* infection in individuals with and without coexisting enteropathy. This suggests that the relevance of this mild enteropathy in the aetiology of IDA in *H. pylori*-infected individuals is improbable. [26]

Anaemia risk can be affected by demographics and social conditions. Anaemia was found to have a strong correlation with living in the country. This confirms the results of the research conducted in India [27,28]. This could be associated with insufficient knowledge about healthy diets and the inaccessibility of medical facilities. As a result, they are clueless about the variables that put them at risk for anaemia and how to protect themselves from them.

CONCLUSION

An increased incidence of iron deficiency anaemia was seen among individuals with *Helicobacter pylori* infections; the majority of these patients were adult females.

REFERENCES

- Marshall, B.J.; Warren, J.R. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984, 1, 1311–1315.
- Suerbaum, S.; Michetti, P. *Helicobacter pylori* infection. *N. Engl. J. Med.* 2002, 347, 1175–1186.
- Torres, J.; Perez-Perez, G.; Goodman, K.J.; Atherton, J.C.; Gold, B.D.; Harris, P.R.; Madrazo-de la Garza, A.; Guarner, J.; Muñoz, O. A comprehensive review of the natural history of *Helicobacter pylori* infection in children. *Arch. Med. Res.* 2000, 31, 431–469.
- Dincă, A.L.; Meliț, L.E.; Mărginean, C.O. Old and New Aspects of *H. pylori*-Associated Inflammation and Gastric Cancer. *Children* 2022, 9, 1083.
- Ranjbar, R.; Behzadi, P.; Farshad, S. Advances in diagnosis and treatment of *Helicobacter pylori* infection. *Acta Microbiol. Immunol. Hung.* 2017, 64, 273–292.

- Ricci, C.; Holton, J.; Vaira, D. Diagnosis of *Helicobacter pylori*: Invasive and noninvasive tests. *Best Pract. Res. Clin. Gastroenterol.* 2007, 21, 299–313.
- Islam, M.; Rahman, S.; Shamsuzzaman, S.; Muazzam, N.; Kibria, S.; Hossain, M.; Ahmed, N.; Sarkar, A.; Nahar, S. A comparative study among different invasive methods for the diagnosis of *Helicobacter pylori*. *Faridpur Med. Coll J.* 2010, 5, 21–24.
- Choe YH, Kim SK, Son BK, Lee DH, Hong YC, Pai SH (1999) Randomized placebo-controlled trial of *Helicobacter pylori* eradication for iron-deficiency anemia in preadolescent children and adolescents. *Helicobacter* 4:135–139.
- Hallberg L, Hulten L, Lindstedt G, et al. (1993) Prevalence of iron deficiency in Swedish adolescents. *Pediatr Res* 34:680–687.
- Sanstead HH, Carter JR, House FR, McConnell F, Horton KB, Vander Zwag R (1971) Nutritional deficiencies in disadvantaged preschool children. Their relationship to mental development. *Am J Dis Child* 121:455–463
- M. Burns, A. Amaya, C. Bodi, Z. Ge, V. Bakthavatchalu, K. Ennis, T.C. Wang, M. Georgieff, J.G. Fox, J.R. Connor. Non-*Helicobacter pylori* infection and low dietary iron alter behavior, induce iron deficiency anemia, and modulate hippocampal gene expression in female C57BL/6 mice. *PLoS ONE*, 12 (3) (2017), p. e0173108
- G. Kadhim, M. Shikh, H. Omar, A. Ismail. Vitamin B12 deficiency in *Helicobacter pylori* infected patients. *OALib*, 5 (03) (2018), pp. 1-4
- Mwafy and Afana, 2018 S.N. Mwafy, W.M. Afana. Hematological parameters, serum iron and vitamin B₁₂ levels in hospitalized Palestinian adult patients infected with *Helicobacter pylori*: a case-control study. *Hematol. Transfus Cell Ther.*, 40 (2) (2018), pp. 160-165
- Zhao et al., 2019 M.M. Zhao, J. Krebs, X. Cao, J. Cui, D.N. Chen, Y. Li, L. Hua, J. Mann, J.K. Yang. *Helicobacter pylori* infection as a risk factor for serum bilirubin change and less favourable lipid profiles: a hospital-based health examination survey. *BMC Inf. Dis.*, 19 (1) (2019), p. 157
- Monzón H, Forné M, Esteve M, Rosinach M, Loras C, Espinós JC, Viver JM, Salas A, Fernández-Bañares F. *Helicobacter pylori* infection as a cause of iron deficiency anaemia of unknown origin. *World J Gastroenterol.* 2013 Jul 14;19(26):4166-71. doi: 10.3748/wjg.v19.i26.4166. PMID: 23864779; PMCID: PMC3710418.
- Venneman, K.; Huybrechts, I.; Gunter, M.J.; Vandendaele, L.; Herrero, R.; Van Herck, K. The epidemiology of *Helicobacter pylori* infection in Europe and the impact of lifestyle on its natural evolution toward stomach cancer after infection: A systematic review. *Helicobacter* 2018, 23, e12483.
- Torres, J.; Leal-Herrera, Y.; Perez-Perez, G.; Gomez, A.; Camorlinga-Ponce, M.; Cedillo-Rivera, R.; Tapia-Conyer, R.; Muñoz, O. A community-based seroepidemiologic study of *Helicobacter pylori* infection in Mexico. *J. Infect. Dis.* 1998, 178, 1089–1094.
- Bille, B.B.E.; Mabeku, L.B.K. Relationship between active *Helicobacter pylori* infection and anemia, iron deficiency, iron deficiency anemia: A cross-sectional study in a sub-Saharan setting. *JGH Open* 2022, 6, 554–568.
- Kishore, G.; Ejaz, M.; Kumar, J.; Lal, A.; Tahir, H.; Anjum, Z.; Naz, S.; Maher, W.; Khan, S.; Rizwan, A. Association Between *Helicobacter pylori* Infection and Serum Iron Profile. *Cureus* 2021, 13, e17925
- Duclaux-Loras, R.; Lachaux, A. *Helicobacter pylori* infection, a classic but often unrecognized cause of iron deficiency anemia in teenagers. *Arch. Pediatr.* 2013, 20, 395–397.
- Gheibi, S.; Farrokh-Eslamlou, H.R.; Noroozi, M.; Pakniyat, A. Refractory iron deficiency anemia and *Helicobacter Pylori* Infection in pediatrics: A review. *Iran. J. Ped. Hematol. Oncol.* 2015, 5, 50–64.
- Annibale B, Marignani M, Monarca B, Antonelli G, Marcheggiano A, Martino G, Mandelli F, Caprilli R, Delle Fave G. Reversal of iron deficiency anemia after *Helicobacter pylori* eradication in patients with asymptomatic gastritis. *Ann Intern Med.* 1999;131:668–672.
- Qu XH, Huang XL, Xiong P, Zhu CY, Huang YL, Lu LG, Sun X, Rong L, Zhong L, Sun DY, et al. Does *Helicobacter pylori* infection play a role in iron deficiency anemia? A meta-analysis. *World J Gastroenterol.* 2010;16:886–896.
- Yuan W, Li Yumin D, Yang L. Iron deficiency anemia in *Helicobacter pylori* infection: meta-analysis of randomized controlled trials. *Scand J Gastroenterol.* 2010;45:665–676
- Nahon S, Patey-Mariaud De Serre N, Lejeune O, Huchet FX, Lahmek P, Lesgourgues B, Traissac L, Bodiguel V, Adotti F, Tuszynski T, et al. Duodenal intraepithelial lymphocytosis during *Helicobacter pylori* infection is reduced by antibiotic treatment. *Histopathology.* 2006;48:417–423.
- Walker MM, Murray JA. An update in the diagnosis of coeliac disease. *Histopathology.* 2011;59:166–179.
- Bashir F, Nageen A, Kidwai SS, Zulfikar S, Shiraz S, Ara J. Anemia in Hospitalized Patient: Prevalence, Etiology and Risk Factors. *J Liaquat Uni Med Heal Sci.* 2017;16(2):80–5
- Imaad MI, Azeez K, Alwin A S V. Role of socio-demographic and cultural factors on anemia in a tribal population of North Kerala, India. *Int J Community Med Public Heal.* 2016;3(5):1183–8.