Evaluation of hematological parameters in dyspepsia patients infected with *Helicobacter pylori*

A retrospective study from the Central Region of Saudi Arabia

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ABSTRACT

الأهداف : لتقييم المتغيرات الدموية لدى مرضى عسر الهضم المصابين بعدوى المَلْوِيّة البَوّابية في منطقة القصيم، المملكة العربية السعودية.

المنهجية : تم إجراء هذه الدراسة بأثر رجعي في مستشفى الدكتور سليمان الحبيب في القصيم، المملكة العربية السعودية. تم اشتقاق بيانات مرضى عسر الهضم من نظام التسجيل القائم في المستشفى خلال الفترة من 2020-2021م. تم استخدام نماذج الانحدار اللوجستي للتحقق من العلاقة بين بداية الإصابة بعدوى المَلْوِيّة البَوّابية وفقر الدم.

النتائج : من بين 810 مريضٍ شارك بالدراسة، كان هناك 202 (24.9%) من المرضى مصابين بعدوى المَلْوِيّة البَوّابية و144 (17.8%) مريض يعانون من فقر الدم. لم يكن حدوث فقر الدم في مجموعة المصابين بعدوى المَلْوِيّة البَوّابية أعلى إحصائيًا مما هو عليه في مجموعة الغير مصابين بعدوى المَلْوِيّة البَوّابية بعد التعديل حسب العمر، وعدد خلايا الدم، عدد الصفائح الدموية، والهيموغلوبين. كان مستوى الهيموجلوبين متطابقًا تقريبًا في المجموعتين. (p>0.05).

الخلاصة : تظهر النتائج أن الإصابة بعدوى المَلْوِيّة البَوّابية قد لا تكون مرتبطة بفقر الدم لدى مرضى عسر الهضم من المنطقة الوسطى في المملكة العربية السعودية.

Objectives: To evaluate the hematological parameters in dyspepsia patients infected with *Helicobacter pylori* (*H. pylori*) infection from Al Qassim province of Kingdom of Saudi Arabia (KSA).

Methods: This retrospective study was carried out in Dr. Sulaiman Al-Habib Hospital, Al Qassim, KSA. The data of dyspepsia and epigastric pain patients were derived from the hospital based registration system between 2020-2021. Logistic regression models were used to investigate the correlation between the onset of *H. pylori* infection and anemia.

Results: Among 810 enrolled patients, there were 202 (24.9%) patients with *H. pylori* infection and 144 (17.8%) with anemia. The prevalence of anemia in the *H. pylori* (+) group was not statistically higher than the *H. pylori* (-) group after adjusting age, red blood cell count, serum ferritin, mean corpuscular volume, platelet count, and mean corpuscular hemoglobin (*p*>0.05). The level of hemoglobin was almost identical in both the *H. pylori* (+) group and the *H. pylori* (-) group (*p*>0.05).

Conclusion: The findings show that *H. pylori* infection may not be related to anemia in dyspepsia patients from the Central region of KSA.

Keywords: hematology, anemia, dyspepsia, *Helicobacter pylori*, Saudi Arabia

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Helicobacter pylori (*H. pylori*) infection is one of the most common chronic bacteria that infect humans. Overall, approximately half of the world's population is seropositive; yet, in some developing countries, the prevalence can reach as high as 80%, while in developed countries, 40% of the population is infected.[1] *Helicobacter pylori* is a gram-negative bacteria with a spiral shape that helps to colonize the human stomach effectively.[2] *Helicobacter pylori* infections are directly associated with both benign and malignant gastric disorders. However, there are several extra-gastric manifestations involving a variety of medical subspecialties closely related to *H. pylori* infection. Hence, the involvement of *H. pylori* infection in many extra-gastric disorders remains an area of active

research.[3] Hematological consequences of *H. pylori* infection includes: iron deficiency anemia, vitamin B12 deficiency, idiopathic thrombocytopenic purpura, and gastric extranodal marginal zone lymphoma.[4]

Anemia is a significant public health problem across the world. It has been attributed to increased morbidity and mortality in women, child's development delay, cognitive impairment, increased risk of infection, and reduced productivity due to declining work capacity, resulting in a significant economic burden on the family and entire population.[5] Established mechanisms for anemia includes: underproduction anemia, increased destruction, and blood loss. Once anemia has been diagnosed, a search for the underlying cause is necessary. The most common cause of anemia is an iron deficiency affecting over one billion people, majorly women, and children.[6] *Helicobacter pylori* has been implicated as a possible etiology for anemia. Several epidemiological and clinical trials demonstrated a correlation between *H. pylori* infection and anemia. Nonetheless, conflicts emerge among the findings of several trials concerning the role of *H. pylori* in inducing anemia.[7] The pathophysiologic processes by which *H. pylori* contributes to iron deficient anemia are not fully understood. It has been proposed that *H. pylori* infection stimulates the liver to produce a hormone called hepcidin. Hepcidin controls iron metabolism in enterocytes and releases stored iron from macrophages of the reticuloendothelial system, resulting in the condition termed as "anemia of inflammation".[8] Preliminary studies indicated that serum hepcidin levels were increased in patients with *H. pylori* infection and these levels returned to normal when the infection is eradicated.[9] Chronic gastritis induced bleeding, which occurs in patients infected with *H. pylori*, is another possible mechanism of iron deficiency anemia. The prevalence of anemia and *H. pylori* infection are common in developing countries. However, the related available data of Saudi Arabia's population is still limited.[10] Therefore, this study aimed at investigating the correlation between *H. pylori* infection and anemia among Saudi patients with unexplained anemia and to study the relationship between *H. pylori* infection and the hematological parameters of these patients through a case-control study.

Methods. A retrospective study was carried out on 810 Saudi patients (381 males and 429 females). The

inclusion criteria were as follow: Saudi patients who were tested for *H. pylori* infection using the *H. pylori* stool antigen test. Patients with dyspepsia and epigastric pain attending the inpatient and outpatient setting of Dr. Sulaiman Al-Habib Hospital in Al Qassim, Saudi Arabia, were enrolled between March 2020-2021. There were no gender, age, or body mass index limitations. The exclusion criteria was patients having a history of blood loss, such as gastrointestinal bleeding, were excluded as potential causes of anemia. Also, patients with incomplete hematological tests (hemoglobin and mean cell volume [MCV]) were excluded from the study.

The ethical approval was obtained from the Research Ethics Committee of Al Habib Research Centre, Al Qassim, Saudi Arabia (study no. RC 20.04.133). Written informed consents were obtain from all participated patients. All procedures carried out in this study involving the participants were in accordance with the Ethical Standards of the Institutional or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable Ethical Standards.

A medical record review of all recruited participants was carried out, and data related to demographic characteristics and the results of hematological parameters (hemoglobin, red blood cells [RBCs], platelets, MCV, and mean corpuscular hemoglobin [MCH]) were collected.

According to the World Health Organization (WHO) gender-based criteria, defined anemia as a hemoglobin level <13 g/dL for men and <12 g/dL for women. Iron-deficiency anemia is defined as serum ferritin level <21 ng/ml and the hemoglobin level is less than adjusted values for age and gender. Serum ferritin was measured using the ARCHITECT 7k59 assay, a 2-step chemiluminescent microparticle immunoassay (CMIA). The correlation between anemia and *H. pylori* infection was studied.

Patients' stools were collected and examined for *H. pylori* antigen with an onsite *H. Pylori* Ag rapid test (CTK Biotech, Inc., USA, 2017).

Statistical analysis. The Prism-version 5 software was used for the data analysis, and the data was analyzed using ANOVA. Some data was also analyzed and validated by Statistical Package for Social Sciences, version 20 (IBM Corp., Armonk, NY, USA) using the Chi-square test. A *p*-value of <0.05 was considered significant.

Results. A total of 810 dyspepsia patients (mean age of 37.68±18.7 years) were enrolled in this study,

including 429 (53%) females and 381 (47%) males, who were suspected of *H. pylori* infection. *Helicobacter pylori* infection was assessed using the *H. Pylori* stool antigen test. The proportion of patients with *H. pylori* (+) infection is 24.9%, while patients without *H. pylori* (-) infection is 75.1%. There was no significant difference between *H. pylori* status and age (*p*=0.388), hemoglobin (*p*=0.289), RBC count (*p*=0.292), serum ferritin (*p*=0.775), MCV (*p*=0.358), platelet (*p*=0.948), and MCH (*p*=0.296). The complete data is summarized in Table 1 and the gender based distribution among the studied patients with and without *H. pylori* infection is presented in Figure 1.

Patients were also subdivided into 2 groups according to *H. pylori* antigen status; a group of *H. pylori* Ag positive (n=202) and a group of *H. pylori* Ag negative (n=608). The group of *H. pylori* positive was further divided into 2 groups; group anemic (n=35) and

non-anemic (n=167). There was a significant difference in hemoglobin level, RBC, MCV, MCH, and serum ferritin between anemic and non-anemic patients infected with *H. pylori* (*p*<0.05).

Anemia was found in 35/202 (17.3%) patients infected by *H. pylori* and 99/608 (16.3%) patients without *H. pylori* infection. The complete results are summarized in Table 2.

Figure 2 demonstrates the prevalence pattern of anemic patients infected with or without *H. pylori*. The data pointed out that the difference between the 2 groups was not statistically significant (*p*>0.05).

Discussion. This study aims at determining the occurrence of anemia in dyspepsia patients suspected of *H. pylori* infection in Al Qassim province of Saudi Arabia. A total of 810 patients were studied first to check the prevalence of *H. pylori* infection.

Table 1 - Hematological characteristics in *H. pylori* positive and negative patients.

Parameters	*H. pylori* infection		*P*-value
	Positive (n=202)	Negative (n=608)	
	Mean±SD		
Male/female (ratio)	M=103/F=99 (1.04)	M=278/F=330 (0.84)	-
Age (years)	38.66±1.177	37.35±0.7851	0.3879
Hemoglobin	13.83±0.1376	13.67±0.07388	0.2889
RBC	4.962±0.04242	4.913±0.02315	0.2916
Serum ferritin	58.71±3.622	57.61±1.854	0.7748
MCV	86.31±0.4327	86.77±0.2483	0.3576
Platelet	275.7±5.018	276.1±3.227	0.9483
MCH	27.81±0.3460	29.39±0.8619	0.2957

H. pylori: *Helicobacter pylori*, RBC: red blood cell count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, SD: standard deviation
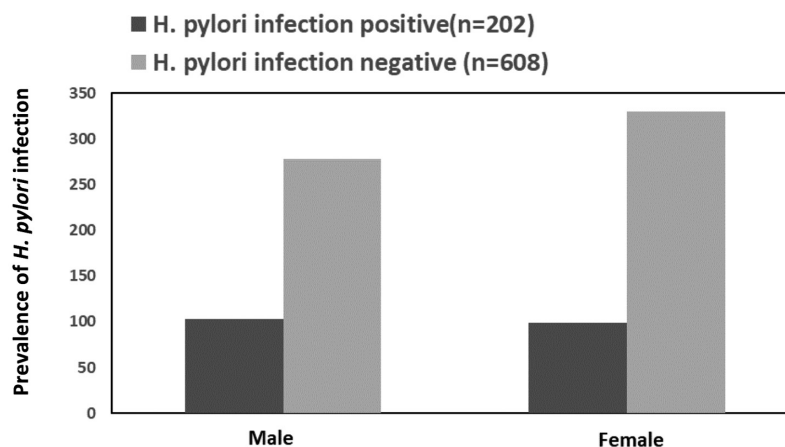

Figure 1 - Gender wise distribution of patients with and without *Helicobacter pylori (H. pylori)* infection.

Table 2 - Hematological characteristics in anemic and non-anemic patients infected with or without *H. pylori* infection.

Parameters	*H. pylori* infection positive (n=202)			*H. pylori* infection negative (n=608)		
	Hb <12gm/dl (n=35)	Hb ≥12gm/dl (n=167)	*P*-value	Hb <12gm/dl (n=99)	Hb ≥12gm/dl (n=509)	*P*-value
	Mean±SD			Mean±SD		
Male/female (ratio)	M=5/F=30 (0.167)	M=98/F=69 (1.420)	-	M=13/F=86 (0.151)	M=265/F=244 (1.09)	-
Prevalence (%)	17.3	82.7	0.0001	16.3	83.7	0.0001
Age(years)	41.83±3.29	38.00±1.24	0.2190	36.56±2.01	37.50±0.85	0.6563
Hemoglobin	10.77±0.15	14.47±0.11	0.0001	10.90±0.10	14.21±0.062	0.0001
RBC	4.39±0.10	5.08±0.04	0.0001	4.40±0.05	5.01±0.02	0.0001
MCV	80.02±1.43	87.62±0.35	0.0001	80.81±0.73	87.92±0.23	0.0001
Serum ferritin	13.06±4.97	68.27±3.87	0.0001	14.08±1.65	66.08±1.98	0.0001
Platelet	277.8±5.4	274.3±5.071	0.6407	307.7±10.98	269.9±3.14	0.0001
MCH	24.51±0.57	28.51±0.38	0.0001	24.82±0.29	30.28±1.02	0.0192

H. pylori: *Helicobacter pylori*, Hb: Hemoglobin, RBC: red blood cell count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, SD: standard deviation
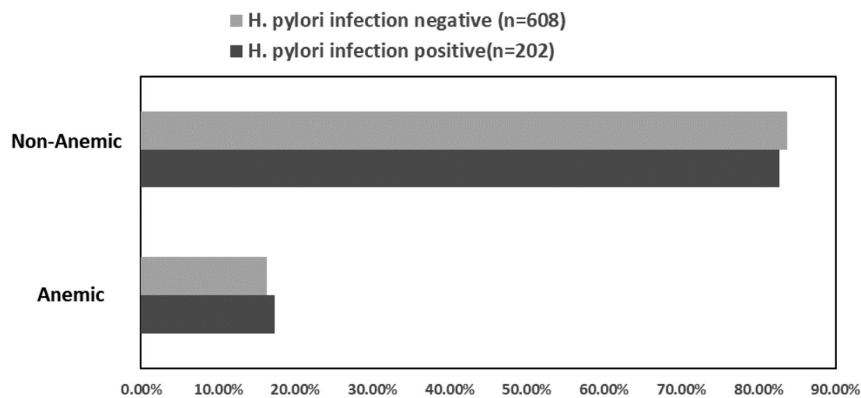
Figure 2 - Prevalence pattern of anemia in patients infected with or without *Helicobacter pylori (H. pylori)*.

Approximately 24.9% of them were found to have *H. pylori* (+) infection. The prevalence of *H. pylori* positivity varies from region to region. In 2017, Hooi et al,[11] carried out a systematic review and meta-analysis on the worldwide prevalence of *H. pylori* infection. They pointed out a wide variation in the prevalence of *H. pylori* infection between regions and countries. They reported that the prevalence was highest in Africa followed by Latin America, the Caribbean, and Asia. However, the rate of *H. pylori* infection was lowest in Northern America and Oceania.[11] In highly developed countries, such as the Western World, the prevalence of *H. pylori* infection has decreased during the previous 2 decades, while the prevalence has risen in developing and newly industrialized countries. These variations in the prevalence of *H. pylori* infection are reflected in the variation of the socioeconomic status of the nations at the level of urbanization, sanitation, and the availability to access hygienic food and clean water.[11] The variation

in the prevalence of *H. pylori* infection was not only reported among different countries but these variations have also been reported significantly even within the same country.[12] Importantly, the variation in the prevalence of *H. pylori* infection has been reported in different regions of Saudi Arabia.[13,14] Few studies on *H. pylori* in the country have shown a high prevalence in various age groups of patients.[13] Recently, variation in *H. pylori* infection among Saudi children was also seen in metropolitan cities such as Jeddah and Riyadh.[13,15] It is also important to point out that the variation in the prevalence of *H. pylori* infection from region to region has important implications on the global future prevalence of sequelae associated with *H. pylori*, as this infection has been found to be associated with other chronic disorders including gastric cancer and disorders associated with anemia.[16,17] The current study aims at analyzing the association of *H. pylori* infection with age, hemoglobin, RBC count, serum levels of ferritin,

MCV, platelet count, and MCH. In order to determine these factors, the levels of these factors were analyzed in patients with confirmed *H. pylori* (+) cases and the levels were compared with *H. pylori* (-) cases. The data point out no significant association of *H. pylori* infection with the patients' age, hemoglobin levels, RBC count, serum ferritin, MCV, and platelet count with MCH levels ($p>0.05$). These findings have been supported by a number of previously studied reports carried out among different populations.[18,19] However, several findings were also reported.[20,21] These variations may be due to the differences in the social and economic status of different populations.

Anemia has now been considered as a major public health issue worldwide and its prevalence is often associated with numerous disorders including: chronic disorders associated with kidney dysfunctions, malaria, schistosomiasis, and so on.[22] Several studies explored an association of *H. pylori* infection with anemia in different regions of the world, but controversies are all around.[7] Some of them considered that anemia is a complication of *H. pylori* infection, whereas others have reported no correlation between them.[7] In order to determine an association of *H. pylori* infection with anemia in Saudi patients, they were subdivided into 2 groups according to *H. pylori* antigen status, namely, a group of *H. pylori* (+) and a group of *H. pylori* (+). The group of *H. pylori* (+) was further divided into 2 groups; group anemic and nonanemic. The data showed a significant difference in hemoglobin level, RBC, MCV, MCH, and serum ferritin between anemic and non-anemic patients infected with *H. pylori* ($p<0.05$). Moreover, the data also determined that anemia was found in 17.3% *H. pylori* (+) cases and 16.3% anemia in *H. pylori* (-) cases. In general, the data showed no association of anemia with *H. pylori* infection. These findings were consistent with a number of studies.[23] However, different observations were also reported by others as well.[24,25] This may be due to the variations in the characteristics of the patients from different populations. The underlying reasons for these variations among different populations still requires further research. The implications of the findings in this study provided an understanding of the relationship between anemia and patients infected with *H. pylori*. These findings support the controversy of previous studies regarding the role of *H. pylori* in causing anemia.

Study limitations. Despite its attempt to study the correlation between *H. pylori* infection and anemia in the Saudi population, this study has not confirmed the actual causality between *H. pylori* infection and anemia, as the study was an observational study, which might not be the optimal design for establishing a causal association between *H. pylori* infection and anemia. Besides, the study was carried out on dyspeptic patients who might have many underlying conditions as confounding factors that could not be fully controlled, impacting the statistical correlations between *H. pylori* infection and anemia. In addition, the study has been carried out only on patients from a single hospital (Dr. Sulaiman Al-Habib Hospital, Al Qassim, Saudi Arabia), which has made it impossible to generalize the findings to all of Saudi Arabia.

In conclusion, this study has indicated that *H. pylori* infection may not be related to anemia in dyspepsia patients.

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