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Original Research

GESDAV

Iron deficiency and *Helicobacter pylori* infection

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ABSTRACT

Background: Iron deficiency (ID) is the most common cause of anemia worldwide. Recently, there has been evidence suggest that there is an association between *Helicobacter pylori* infection and ID. **Purpose:** Based on high prevalence of ID and *H. pylori* infection in our region, we aimed in this study to examine the association between *H. pylori* infection and ID. **Subjects and Methods:** During the period of months from March 2012 to January 2013, this study was conducted in King Hussein Medical Center in Amman, Jordan. The study group consisted of 150 patients with *H. pylori* infection and 50 healthy subjects as a control group. Blood samples were collected for serum iron, total iron binding capacity (TIBC), serum ferritin, and complete blood count. **Results:** Serum iron and TIBC in *H. pylori* positive group were lower than in the healthy group (109.82 ± 34.6 vs. 117.78 ± 32.64 μg/dl, $P = 0.37$) and (326.88 ± 83.94 vs. 332.43 ± 79.34 μg/dl, $P = 0.12$), respectively. The mean of serum ferritin was significantly lower in *H. pylori* positive group (213.87 ± 137.23 ng/ml) than the control group (268.34 ± 165.45 ng/ml, $P = 0.027$). Hemoglobin levels were lower in patients group (14.3 g/dl vs. 14.9 g/dl $P = 0.44$). **Conclusion:** Our study reports that *H. pylori* infection might have a role in ID and subsequently ID anemia.

KEY WORDS: Anemia, *Helicobacter pylori*, iron deficiency, serum iron, total iron binding capacity

INTRODUCTION

Helicobacter pylori is a microareophilic, Gram-negative, spiral shaped and flagellated organism. *H. pylori* is the most common chronic bacterial infection of human, present in almost half of the word population [1]. The pathogen has been shown to be a causative agent of disease states of varying degrees of severity including chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue lymphoma [2].

Iron deficiency (ID) is the most widespread cause of anemia worldwide [3]. It is also estimated to be the most common nutritional deficiency in both developing and developed countries [4]. ID defined as reducing in the total body iron content, ID results in impairments in immune, cognitive, and reproductive functions, as well as lowered work performance. ID developed in three stages these are iron depletion, iron deficient erythropoiesis, and ID anemia (IDA) [5].

According to several studies *H. pylori* requires iron to survive and may play an important role in IDA and ID, but mechanism remain unclear [6,7]. Barabino hypothesized that gastritis increase level of neutrophil – derived lactoferrin, since *H. pylori* has a lactoferrin-binding protein receptor, the infection would result in increased iron losses related to bacterial turnover [8]. Seemingly that the pathogenesis is multifactorial; including combination of reduced iron absorption related decreased acid secretion, increased iron loss from micro-bleeding and utilization by *H. pylori*.

Because of the importance of this medical issue, this study was carried out to examine the iron status in patients with *H. pylori* infection and those without, using laboratory measurements of ID bio-indicators including serum iron, total iron capacity (TIBC), and serum ferritin.

SUBJECTS AND METHODS

Study Population

The subjects in this study were selected from patients attending the outpatient specialty clinics in King Hussein Medical Center during the period from March 15, 2012 to January 10, 2013. Two hundred subjects were selected, 150 of them have *H. pylori* infection, while 50 are healthy (113 male, 87 female) aged 23-86 years (mean 54.5 years), after the interview for 3 min all volunteers completed a written informed agreement for participation in this study, blood samples were collected from these patients for serum iron, serum ferritin, TIBC, and complete blood count (CBC) and *H. pylori* IgG antibodies. All tests were done in Medical Biochemistry Department in King Hussein Medical Center in Jordan. Our study was supported by Ethics Community in King Hussein Medical Center.

Exclusion Criteria

Patients had complaints of chronic abdominal pain, nausea, or vomiting. Patients with hematological disease other than IDA,

celiac or other chronic diseases, recent gastrointestinal bleeding or parasitic infection were excluded. All patients were without clinical signs of other infections.

Methods

CBC determination of hemoglobin and hematocrit (Hct) levels were performed using a multiparameter cell counter Sysmex k 1000 hematology analyzer (Tao electronics, Japan). This analyzer is calibrated and controlled with standard laboratory quality control methods.

Ferritin concentrations were measured using hormones Auto-analyzer Cobas e411 (Roche Diagnostics GmbH, Mannheim, Germany), and serum iron levels were measured using Hitachi 917 biochemistry automated analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Ferritin levels <15 μg/dl were defined as ID. Hemoglobin levels <14 g/dl for male and <12 g/dl were defined as anemia, IDA was diagnosed when had both ID and anemia.

TIBC concentrations were measured spectrophotometrically (Hitachi, Tokyo, Japan) using the commercial kit (RANDOX LABORRATORIES Limited, Ardmore Diamond Road Crumlin, Co, Antrim United Kingdom BT29404.

Serological Studies

Serum levels of anti-*H. pylori* IgG were measured by the use of commercial ELISA kit (DIA, `12nostic Bioprobes, Via.G.Carduccu n 27, 20099 San Giovanni (Milano-Italy) based on a monoclonal antibody against 64-kD *H. pylori* antigen.

Statistical Analysis

All values were summarized as mean ± standard deviation. Statistical analysis were performed using SPSS for windows 15.0 (SPSS Inc. Headquarters, Chicago, III., USA) software program and Microsoft Excel 2007 program. $P < 0.05$ was considered to be statistically significant.

RESULTS

We assessed 200 subjects, 150 with *H. pylori* infection and 50 controls. The patients group (85 male and 65 female with a mean age 52.8 ± 17.98). The control group (28 male and 22 female with a mean age 48.56 ± 16.46). No significant differences were found between mean ages ($P = 0.42$) [Table 1].

The results of biochemical studies revealed that serum iron and total binding capacity in *H. pylori* infected subjects were lower than in the control group (109.82 ± 34.6 vs. 117.78 ± 32.64 μg/dl, $P = 0.37$) and (326.88 ± 83.94 vs. 332.43 ± 79.34 μg/dl, $P = 0.12$), respectively.

The mean of ferritin was significantly lower in *H. pylori* positive group (213.87 ± 137.23 ng/ml) than control group (268.34 ± 165.45 ng/ml, $P = 0.027$) [Table 2].

Table 1: Characteristics in both groups

	H. pylori seropositive	*H. pylori* seronegative	*P* value
n	150	50	
Age (mean±SD)	52.8±17.98	48.56±16.46	0.43
Male	85	19	0.52
Female	65	31	0.61

SD: Standard deviation, *H. pylori: Helicobacter pylori*

Table 2: Laboratory findings among both groups

Test	*H. pylori* seropositive	*H. pylori* seronegative	*P* value
Hemoglobin (g/dL)	14.3	14.9	0.44
Serum iron (μg/dL)	109.82±34.6	117.78±32.64	0.37
Serum ferritin (ng/ml)	213.87±137.23	268.34±165.45	0.027
TIBC (μg/dL)	332.88±83.94	326.43±79.34	0.12

TIBC: Total iron binding capacity, *H. pylori: Helicobacter pylori*

The mean hemoglobin levels were (14.3 g/dl and 14.9 g/dl $P = 0.44$) in *H. pylori* positive subjects and control subjects, respectively, these differences were not statistically significant [Table 1].

ID was found in 18% of the patients (serum ferritin levels below 15 μg/L).

White blood cell (WBC) and platelet counts and Hct levels did not show any significant differences between patients group and control group.

Among patients with *H. pylori*, 48% had anemia (low level of hemoglobin), and in control group its frequency was 25% ($P = 0.62$).

Among patients with *H. pylori*, 23% had IDA and in the control group its frequency was 15% ($P = 0.48$).

DISCUSSION

ID is the most common cause of anemia in the world [9]. Infection with *H. pylori* is recognized as a major risk factor for chronic gastritis, peptic ulcer, and gastric cancer. *H. pylori* infection more widespread in developing countries in comparison with developed countries [10-12]. Iron plays an important role in biological systems particularly in a wide range of oxidation-reduction processes, which are essential for life. It is also definitive growth factor for virtually all bacteria. During infection, the total amount of extracellular iron is reduced in the host (hypoferremia of infection) which in turn results into the release of lactoferrin from neutrophils. The released lactoferrin captures the iron from transferrin. The lactoferrin-iron complex is then picked up by fixed or circulatory macrophages, which are removed rapidly from circulation by the reticuloendothelial system [8]. Other probable mechanism of anemia is occult blood loss and decreasing of iron absorption during chronic gastritis due to *H. pylori* infection and decreased iron absorption due to chronic gastritis [4,13].

Our results support that *H. pylori* infection is associated with ID, this proposal is achieved by many studies. Baysoy *et al*. have

investigated *H. pylori* related-changes in gastric physiology and histology in children. They have reported that *H. pylori* infection is associated with low serum iron levels and with a decrease in gastric juice ascorbic acid concentration [14]. A study including 2080 adult patients in Alaska, where there is a high prevalence of *H. pylori*, have suggested a significant correlation between *H. pylori* and IgG positivity and low serum ferritin levels [15].

Moreover, Boggs reviewed that eradication of *H. pylori* with a triple therapy consisting of lansoprazole, clarithromycin, and amoxicillin for 14 days leads to serum ferritin levels elevation significantly in both IDA and ID groups without iron supplements, indicating that complete recovery of ID and IDA can be achieved with the treatment of *H. pylori* infection [16].

According to some studies, *H. pylori* seropositive subjects had lower serum ferritin concentration in comparison to seronegative individuals [17,18]; our data are in parallel with these results. It is noteworthy to mention that some other studies have reported inverse observations [10,19].

H. pylori infection rate increases with age [19]. In the present study, we found a similar result, we did not found any significant difference relation to gender, this finding is consistent with that reported by Jais and Barua and Mitchell and Mégraud [19,20], on the other hand, Hveem *et al*. found that *H. pylori* is more common in male [10].

As with other study, [21] we did not find any correlation between *H. pylori* infection and WBC and platelet count.

CONCLUSION

Our results support the proposal that there is an association between *H. pylori* infection and ID and further studies focusing on the post treatment measurements of serum iron and serum ferritin are required to show whether or not iron status differs with the disappearance of *H. pylori* infection.

REFERENCES

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984;1:1311-5.
2. Frenck RW Jr, Clemens J. *Helicobacter* in the developing world. Microbes Infect 2003;5:705-13.
3. DeMaeyer E, Adiels-Tegman M. The prevalence of anaemia in the world. World Health Stat Q 1985;38:302-16.
4. Annibale B, Capurso G, Martino G, Grossi C, Delle Fave G. Iron deficiency anaemia and *Helicobacter pylori* infection. Int J Antimicrob Agents 2000;16:515-9.
5. Dallman PR. Iron deficiency: Does it matter? J Intern Med 1989;226:367-72.
6. DuBois S, Kearney DJ. Iron-deficiency anemia and *Helicobacter pylori* infection: A review of the evidence. Am J Gastroenterol 2005;100:453-9.
7. Yip R, Limburg PJ, Ahlquist DA, Carpenter HA, O'Neill A, Kruse D, *et al*. Pervasive occult gastrointestinal bleeding in an Alaska native population with prevalent iron deficiency. Role of *Helicobacter pylori* gastritis. JAMA 1997;277:1135-9.
8. Barabino A. *Helicobacter pylori*-related iron deficiency anemia: A review. *Helicobacter* 2002;7:71-5.
9. DuBois S, Kearney DJ. Iron-deficiency anemia and *Helicobacter pylori* infection: A review of the evidence. Am J Gastroenterol 2005;100:453-9.
10. Hveem K, Kruger O. Epidemiology and transmission. *Helicobacter* 2003;8:385-97.
11. Veijola L, Myllyluoma E. Diagnosis. *Helicobacter* 2004;9:557-67.
12. Seo JK, Ko JS, Choi KD. Serum ferritin and *Helicobacter pylori* infection in children: A sero-epidemiologic study in Korea. J Gastroenterol Hepatol 2002;17:754-7.
13. Sarker SA, Davidsson L, Mahmud H, Walczyk T, Hurrell RF, Gyr N, *et al*. *Helicobacter pylori* infection, iron absorption, and gastric acid secretion in Bangladeshi children. Am J Clin Nutr 2004;80:149-53.
14. Baysoy G, Ertem D, Ademoglu E, Kotiloglu E, Keskin S, Pehlivanoglu E. Gastric histopathology, iron status and iron deficiency anemia in children with *Helicobacter pylori* infection. J Pediatr Gastroenterol Nutr 2004;38:146-51.
15. Yip R, Limburg PJ, Ahlquist DA, Carpenter HA, O'Neill A, Kruse D, *et al*. Pervasive occult gastrointestinal bleeding in an Alaska native population with prevalent iron deficiency. Role of *Helicobacter pylori* gastritis. JAMA 1997;277:1135-9.
16. Fagan RP, Dunaway CE, Bruden DL, Parkinson AJ, Gessner BD. Controlled, household-randomized, open-label trial of the effect of treatment of *Helicobacter pylori* infection on iron deficiency among children in rural Alaska: Results at 40 months. J Infect Dis 2009;199:652-60.
17. Ciacci C, Sabbatini F, Cavallaro R, Castiglione F, Di Bella S, Iovino P, *et al*. *Helicobacter pylori* impairs iron absorption in infected individuals. Dig Liver Dis 2004;36:455-60.
18. Seo JK, Ko JS, Choi KD. Serum ferritin and *Helicobacter pylori* infection in children: A sero-epidemiologic study in Korea. J Gastroenterol Hepatol 2002;17:754-7.
19. Jais M, Barua S. Seroprevalence of anti *Helicobacter pylori* IgG/IgA in asymptomatic population from Delhi. J Commun Dis 2004;36:132-5.
20. Mitchell H, Mégraud F. Epidemiology and diagnosis of *Helicobacter pylori* infection. *Helicobacter* 2002;7 Suppl 1:8-16.
21. Lip GY, Blann AD, Beevers DG. *Helicobacter pylori* seropositivity, lipid concentrations and haemostatic factors. J Intern Med 2000;248:354-6.

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