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Relationship of Helicobacter Pylori Infection and Serum Ferritin Level

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ABSTRACT

Background: *Helicobacter pylorus* colonizes the stomachs of half of the world's population and usually persists in the gastric mucosa of human hosts for decades of life. Although most *H. pylori*-positive people are asymptomatic, the presence of *H. pylori* is associated with increased risk for the development of peptic ulcer disease, gastric adenocarcinoma and gastric lymphoma and iron deficiency anemia.

Aim of the study: The aim of this study is to evaluate the association between *H. pylori* infection and low serum ferritin levels.

Methods: 115 serum samples were subjected to test for *H. pylori* infection and serum ferritin level. Age group ranges between 5-55 years with mean of 30 years old, all were subjected to be tested by rapid and ELISA test for *H. pylori* and assessment of serum ferritin level.

Results: The prevalence rate of infection is 60% in which most of the infected had low serum ferritin level.

Conclusion: This study provides further evidence that any H. pylori infection is associated with higher prevalence of anemia and low serum ferritin level.

KEYWORDS: ELISA, Ferritin, *Helicobacter pylori*.

INTRODUCTION

Helicobacter pylori are a helix shaped microaerophilic, Gram-negative, bacteria. This bacterium is one of the most important human pathogens, infecting more than 50% of the human population and survives intragastric acidity long enough to colonize the stomach.[1] The infection is acquired by oral ingestion of the bacterium and is mainly transmitted within families. The main source of transmission is the mother within families, and is usually acquired in early childhood and persists for life.[2] Over 80% of infected individuals are asymptomatic and the remaining causes chronic and active gastritis, peptic ulcer disease which is associated with increased risk of developing gastric cancer.[3] The gastric pH in the mucus layer is thought to vary between 4 and 6.5, with occasional acid alterations to less than pH 2.1-3. Resistance of *H. pylori* to acid alterations requires production of ammonia by large amount of urease enzyme that account for up to 10% of its total protein content.[4]

The majority of colonizing *H. pylori* resides within the gastric mucus and do not directly interacts with host cells. Although *H. pylori* was long considered to be an extracellular

bacterium, recent studies have provided evidence that *H. pylori* occasionally enters epithelial cells via a zipper-like mechanism.[5] Despite causing numerous gastric environmental changes and eliciting a host immune response, *H. pylori* can persistently colonize the human stomach for long periods.[6]

H. pylori bacteria can create an autoimmune response against the parietal cells of the stomach, these cells are responsible for the production of the hydrochloric acid that helps to break down food and damage to these parietal cells can cause a drop in your stomach acid levels. When this happens, food may not be broken-down properly. In particular, you may have a hard time breaking down proteins and releasing minerals such as iron from the food. As a consequence, the iron may not be absorbed effectively from the gut into your body.[7]

Earlier studies suggest an association between *H. pylori* induced gastritis and iron deficiency anemia and several Epidemiologic studies have shown that persons seropositive for *H. pylori* infections have a significant lower serum ferritin level[8] and eradication of *H. pylori* infection in iron-deficient anemic patients was found to reverse the iron deficiency status in both children and adults.[9]

The mechanisms by which H. pylori infection can cause iron deficiency anaemia are still unclear, One hypothesis that chronic *H. pylori* infection leads to atrophy of the gastric glands and reduction of gastric hydrochloric and ascorbic acid secretion.[10] This in turn leads to increases

in intragastric pH, which may impair iron absorption, other possible mechanisms are expression of iron transport regulators and uptake of iron by *H. pylori* bacteria in the gastric mucosa.[11] It appears that *H. pylori* absorbs iron from lactoferrin via a specific lactoferrin-binding protein that is expressed by *H. pylori*, and lactoferrin levels in the gastric mucosa have been shown to be significantly higher in *H. pylori*-positive patients with iron deficiency anemia.[12] Ferritin mop up free intracellular iron and in so doing provide two advantages to the bacteria; which enable them to store iron as essential micronutrient and protect them against oxidative stress by host cell.[13]

MATERIALS AND METHODS

This cross sectional study carried out on 115 patients attending primary health care canter of Shahid baxtyar clinic in Suleimani (Iraq) for 2 months starting from June to august 2014.

Ethical consideration had been taken from the directory of health care center. Study participants complaining about epigastric and abdominal pain belongs to all age group.

All other possible causes of acute and chronic abdominal pain were excluded from study by doing abdominal ultra sound and full investigations by receiving five milliliters (5 ml) of venous blood after a 12 hour fasting period, 2 ml of this blood was transferred to EDTA tube for estimation of complete blood count and the remaining 3 ml of blood were centrifuged at 3000 rpm (round per minute) for 5 minute to obtain serum which were used for estimation of serum ferritin and *H.pylori* test.

H. pylori status was analyzed by rapid immuno chromatography test rapid (Plasmatic chromatography product, UK) and ELISA test for IgG, IgA and IgM antibodies in the serum by using Monobind Inc USA Accu Bind ELISA test at the same time and level of <20 U/ml regarded as normal for IgG, IgA and <40 U/ml for IgM.

Serum feritin were tested by using Immulite kit (chemiluminescent immunoassay system, UK) and level of 28-365 ng/ml was regarded normal for males and 5-148 ng/ml for females according to manufacturer recommendation.

Serum C. Reactive Protein (CRP) were also tested using latex agglutination test (Plasmatic UK); semi-quantitative measurement. Levels of CRP were analyzed in all the patients and grouped categorically as normal CRP < 6mg/L; 12,24,48,96 mg/L, according to manufacturer recommendation.

Table No 1: Age group distribution

Age	Female	Male	Total
5-15	6	1	7
16-25	32	4	36
26-35	40	4	44
36-45	20	1	21
46-55	6	1	7
Total	104	11	115

T-test-2.707, *p value* is: 0.0133

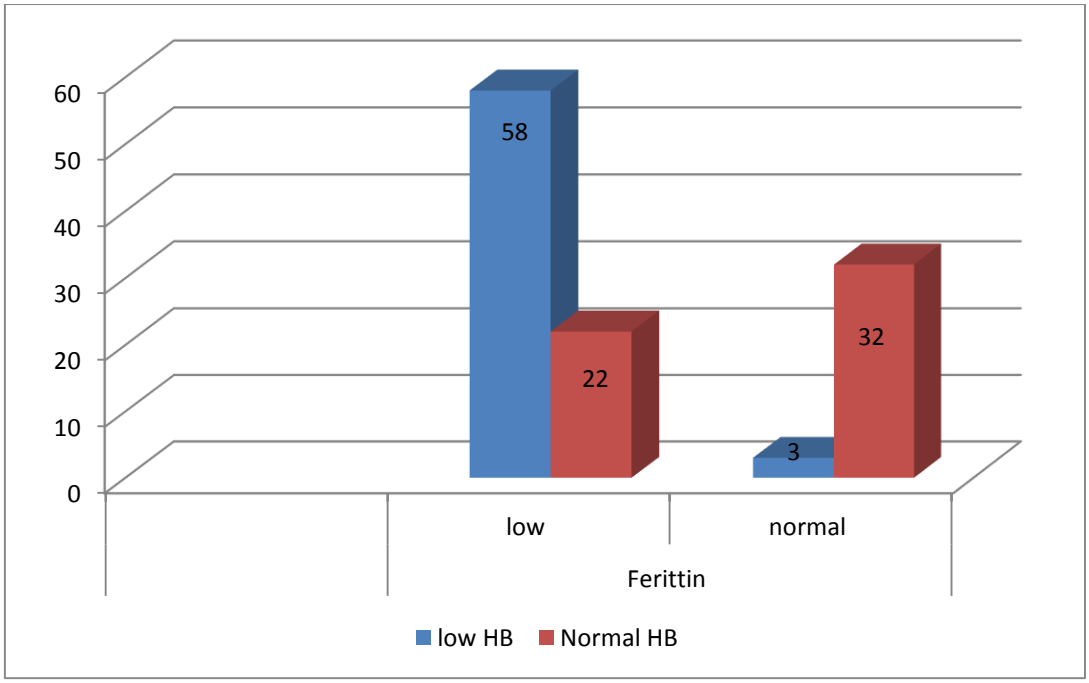

Figure 1: Relation of serum ferritin to hemoglobin level

Table 2: Relation of serum ferritin level with rapid *H. pylori* test

Serum ferritin level	H. pylori rapid test		Total
	Positive	Negative	
Low serum ferritin	49	31	80
Normal serum ferritin	20	15	35
Total	69	46	115

Table 3: comparison of rapid *H.pylori* test with Elisa test

Rapid *H.pylori* test	ELISA test for *H.pylori* test								
	IgM	IgA	IgG	IgM, IgG	IgA, IgM	IgG, IgA	ALL +	ALL -	Total
Positive	7	3	10	14	5	10	15	5	69
negative	9	4	5	6	3	5	3	11	46
Total	16	7	15	20	8	15	18	16	115

T -test is: 1.55521 *p value*: 0.711

Table 4: Relation of serum ferritin level to ELISA test for *H.phlori*

Serum ferritin level	H.pylori ELISA test		
	IgM	IgA	IgG
Low serum ferritin	49	30	48
Normal serum ferritin	20	15	20
Total	62	48	68

T- Test is 3.16; *p value*: 0.017

Table 5: Relation of CRP to the ELISA test for *H. pylori* test.

CRP	*H.Pylori* (IgM)		Total
	Positive	Negative	
Positive	28	3	31
negative	34	50	84
Total	62	53	115

chi square test is: 22.6 , *p value* : 0.0000

RESULTS

The study group consist of 115 patients with abdominal and epigastric pain; 104 female and 11 male. Age group ranges between 5-55 years with mean of 30 years old as illustrated in table1.

The most attending group in this study is adult female with age group 26-35 years old and small attendance was recorded among 5-15 and 46-55 years, male was the less complainer , statically this age distribution is significant ($p<0.05$). Complete blood count and blood film were done for all the participants and it was found that 61(53.04%) patients had iron deficiency anemia with low hemoglobin level and 58 patients (95.05%) of them had low serum ferritin level while the remaining 3 samples showed normal ferritin level (Figure 1). All the blood samples tested for serum ferritin level, low serum ferritin were recorded among 80 (69.56%) patients and 35 (30.43%) were recorded to have normal ferritin level.

All serum specimens were examined for *H. pylori* status, rapid *H.pylori* positive were recorded among 69 (60%) patients (table 2); in which 49 (71%) of them had low serum ferritin level and 20 (28.98%) found to be normal serum ferritin (table 2). Statistically this relation was not significant ($p> 0.05$).

ELISA test were done at the same time for detection of immunity against this bacterium, by measuring serum IgM, IgA and IgG level which were observed in table 3 and it was clear that one patient may yield positive result for one or more than one test for *H. pylori* infection. Serum IgM were recorded among 62(53.91%) patients, serum IgA 48 (41.73%), and IgG were observed mostly among 68 (59.13%). Statistically this distribution is not significant ($p>0.05$).

In relation to serum ferritin level (table 4), it is clear that most patients with one positive immunoglobulin antibody; IgM, IgA and IgG had low serum ferritin level, but low serum ferritin had been also recorded among *H.pylori* negative patients. Statistically this positive relation is significant ($p <0.05$).

One of the inflammatory marker Serum C reactive protein was also investigated among all patients that attend the study. 31 samples out of all the tested samples positive for CRP in which 28 of them were positive for IgM, but 34 samples with IgM positive were negative for CRP among 62 IgM positive patients. Statistically this relation was significant (p *value* < 0.05), as 50 negative IgM samples were negative also for CRP. (Table 5)

DISCUSSION

H. pylori is one of the factors affecting iron deficiency anemia and hypo ferritinaemia, which has a higher prevalence in developing than developed countries.[14] At least half the world's population are infected by *Helicobacter pylori* which is the most widespread infection in the world, there are significant differences in the prevalence of infection both within and between countries and the overall prevalence of *H. pylori* infection in developed countries is lower than that in developing countries , this has been attributed to the poor socioeconomic status and overcrowded conditions.[15]

Earlier studies suggest an association between *H. pylori* induced gastritis and iron deficiency anemia and several epidemiologic studies have shown that persons seropositive for *H. pylori* infections have a significant lower serum ferritin level and eradication of *H. pylori* infection in iron-deficient anemic patients was found to reverse the iron deficiency status in both children and adult.[16,17]

Serology is one of the noninvasive methods for diagnosis of *H. pylori* infection. In this study IgM, IgG, IgA were planned to be examined; the prevalence of 68 (59.13%) was recorded by IgG Elisa test and 69(60%) by rapid test. It was clear that rapid test mostly reflecting previous infection as there is proximity in the prevalence of *H .pylori* infection by rapid test and IgG test while lower percentage of patients (41.73%) showed positivity to IgA in comparisons of other tests; as IgA is the weaker immunological response to infection.[18] IgM also recorded among 62(53.91%) patients, so the value of both tests somewhat similar to each other. Same prevalence was recorded in study done in same province sulaimani by Mohammed OM[19] and high level of infection were recorded in Basrrah and India.[20,21] Possibly due to life habits and improper sanitary condition in these areas. There was a study reviewing several researchers done in Iran, 5 from the Kingdom of Saudi Arabia, 4 studies from Egypt, 2 from the United Arab Emirates and one study from Libya, Oman, Tunisia, and Lebanon; all recording high prevalence rate of *H. pylori* infection by different laboratory tests , indicating high prevalence of this bacteria in developing countries.[22]

Serum ferritin is the major storage protein in the body for iron and the most powerful parameter for diagnosis of iron deficiency, anemia without inflammation.[23] Concomitant inflammation can greatly affect the level of serum ferritin, as the level of ferritin for iron-deficiency without concomitant inflammation varies from 12–15 ng/ml and with concomitant inflammation to more than 50 ng/mL.[24]

Blood loss due to gastric lesions and reduced iron absorption due to an elevated pH of gastric juice have been attributed to causes anemia in *H. pylori* infection; as there is transient hypochlorhydria of variable duration in the early phase of infection and gastric atrophic changes in the late stages of infection.[25]

Serum ferritin levels were found to be significantly lower in adult men and postmenopausal women who were *H. pylori* IgG positive than in no infected persons, this finding were supported by other research done in past.[26-28] While there are studies which failed to show the association between the lower level of serum ferritin and chronic *H.pylori* infection.[29-32] Also lower ferritin values were observed in the infected children with *H.pylori* infection.[33,34]

CONCLUSION

From the results of this study, it is concluded that a significantly low level of ferritin and hemoglobin level are present in patients with *H.pylori* infection.

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