

The Correlation Between H. Pylori Infection with Serum Ferritin Concentration and Iron Deficiency Anemia

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ABSTRACT

Iron deficiency is the most common cause of anemia worldwide, however a significant number of these patients remain undiagnosed. Based on the high frequency of iron deficiency anemia and H. pylori infection in Iran, we have evaluated their correlation in this study.

184 patients mostly with GI system complaints were referred for determination of serum anti H. pylori IgG and IgA levels. In addition, we performed complete cell blood count and serum ferritin concentration tests for all the patients. Statistical analysis was performed on the results in order to determine possible correlations.

Our results showed that in 77.8% of our patients at least one of serum anti H. pylori IgG or IgA antibodies was positive. The rate of positive serology was increased in higher age groups. Patients' gender did not influence the results. Serum ferritin level did not show any correlation with H. pylori infection and the frequency of iron deficiency anemia was not higher in infected individuals.

Although many studies have shown positive correlation between H. pylori infection and iron deficiency anemia, however few studies have not confirmed these findings. Our study does not support this correlation, as well. Due to high frequency of both iron deficiency anemia and H. pylori infection in Iran, further large scale studies are recommended.

Key Words: Helicobacter pylori, Anemia, ferritin

ÖZET

Helikobakter Piloni Enfeksiyonu ile Serum Ferritin Konsantrasyonu ve Demir Eksikliği Anemisi Korelasyonu

Vakaların önemli bir kısmına tanı konulamamasına rağmen, demir eksikliği dünyada aneminin en sık nedenidir. Bu çalışmamızda, İranda Helikobakter Piloni enfeksiyonu ve demir eksikliği anemisinin yüksek oranda görülmesine dayanarak, muhtemel korelasyonunu araştırdık.

Gastrointestinal şikayetleri olan 184 hasta serumunda anti H. Piloni IgG ve IgA seviyeleri çalışıldı. Ek olarak bu hastaların tam kan sayımları ve serum ferritin konsantrasyonları çalışıldı. Muhtemel bir korelasyonu belirlemek için istatistiksel analizler yapıldı. Sonuçlarımız hastalarımızın %77.8'inde serumda anti H. Piloni IgG ve/veya IgA antikorlarının pozitif olduğunu gösterdi. Yaşlı hastalarda seroloji pozitifliği daha fazlaydı. Cinsiyetin etkisi gösterilemedi. Serum ferritin düzeyleri H. Piloni enfeksiyonu varlığı ile korelasyon göstermedi ve demir eksikliği anemisi, enfekte kişilerde yüksek oranda değildi.

Bazı çalışmalarda H. Piloni enfeksiyonu ile demir eksikliği arasında pozitif korelasyon gösterilse de bunlar azınlıkta kalmaktadır. Bizim çalışmamız bu korelasyonu desteklememektedir. Ancak İran gibi demir eksikliği anemisi ve H. Piloni enfeksiyonlarının fazla olduğu bölgelerde daha geniş çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Helikobakter Piloni, Anemi, Ferritin

INTRODUCTION

Iron deficiency is the most common cause of anemia in the world, affecting an estimated 500 to 600 million individuals (1,2). It is also estimated to be the most common nutritional deficiency in both developing and developed nations (1,3). Established causes of iron deficiency include inadequate iron intake, chronic blood loss, mal-absorption, hemolysis or a combination of these factors. Iron deficiency anemia (IDA) is often an indication to evaluate the upper and lower gastrointestinal tract to exclude chronic blood loss secondary to cancers, ulceration, angiodysplasia or mal-absorption from celiac disease. However, endoscopic studies are frequently unrevealing and the cause of IDA remains unexplained in a significant proportion of cases (1). Several reports have demonstrated that H. pylori infection could be proposed as a new cause of IDA (1,4-7). However, a few epidemiologic studies do not support an association between H. pylori infection and IDA (1,9). Since the prevalence of IDA is considerably high in Iran (10), in this study, we have evaluated its correlation with H. pylori infection. We have also evaluated the correlation between H. pylori infection with age, sex and hematologic parameters including white blood cell (WBC) and platelet counts, hemoglobin concentration and hematocrit (Hct) value.

MATERIALS AND METHODS

A total of 184 outpatients, including 83 males and 101 females with the age range from 2 to 83 years were participated in this study, in Emam Reza Teaching Hospital, Mashhad. Out of these patients, 161 were referred with complaints of dyspeptic problems and 23 had extragastric disease such as skin diseases, suspiciously related to H. pylori infection. All patients completed a written informed consent for participation in this study.

Adequate amount of blood samples were collected. Complete blood count (CBC), determination of hemoglobin and Hct levels were performed using a multi parameter cell counter (Sysmex K-21, Japan). This instrument is calibrated and controlled with standard laboratory quality control methods.

Patients sera were tested for anti H. pylori IgA and IgG levels using a commercial enzyme linked immunosorbent assay (ELISA) kit (Trinity Biotech, Ireland). Results were expressed as Immune Status Ratio (ISR) which is calculated by dividing the sample optical density value by the cutoff value determined using the recommended procedure by the manufacturer. ISR values ≤ 0.90 and ≥ 1.10 were considered negative and positive respectively. Samples with equivocal values between 0.91 and 1.09 were excluded from our analysis.

Ferritin concentrations were measured using a commercial radioimmunoassay (RIA) kit (Kavoshyar,

Table 1. Prevalence, average ages, sex, ferritin and Hemoglobin levels in H. pylori positive (HP+) and H. pylori negative (HP-) patients, Emam Reza Teaching Hospital, Mashhad, Iran.

Groups	Prevalence (%)	Age (years)	Sex	Hemoglobin(gr/dl)	Ferritin ($\mu\text{g/L}$)
HP+	77.8	43.3	M= F	14.7 \pm 1.5	49 \pm 38
HP-	22.2	28.3	M= F	14.6 \pm 1.4	54 \pm 47

Iran). Ferritin levels $<15 \mu\text{g/L}$ were defined as iron deficiency. Hemoglobin levels $<14 \text{ g/dL}$ for male and $<12.5 \text{ g/dL}$ for female were defined as anemia. Iron deficiency anemia (IDA) was diagnosed when had both iron deficiency and anemia (14).

Statistical analysis was carried out using SPSS statistical software. Comparison between variables was performed using student t-test and chi square. P value <0.05 was considered significant.

RESULTS

Anti H. pylori IgG/IgA antibodies were positive in 77.8% of the patients (Table 1). Most individuals (97.8%) infected with H. pylori had elevated levels of specific IgG antibodies, however, only in 30.7% of the cases the IgA levels exceeded the cutoff levels. 78.8% of the patients with gastrointestinal (GI) symptoms and 70% of patients with extragastric symptoms were determined seropositive. Epigastric pain was the most prevalent symptom (69.7%) among patients referred with GI complains. Mean age in seropositive patients was 43.3 years ranging from 4 to 83 years (Table 1). An age dependent progression pattern was detected in H. pylori seropositivity in participants. Gender had no significant effect on the prevalence of anti H. pylori antibodies (Table 1). Mean hemoglobin levels were 14.7 g/dL and 14.6 g/dL in seropositive and seronegative patients, respectively. Mean hemoglobin levels of seropositive and seronegative individuals were 13.86 g/dL and 13.83 g/dL in females and 15.69 g/dL and 15.86 g/dL in males, respectively. These differences were not statistically significant (Table 1).

Serum ferritin concentrations in seropositive and seronegative patients were 49 (± 38) $\mu\text{g/L}$ and 54

(± 47) $\mu\text{g/L}$, respectively which were not significantly different ($p=0.58$), (Table 1).

17.6% of the patients had iron deficiency with serum ferritin levels below 15 $\mu\text{g/L}$. 79.8% of them were seropositive for H. pylori infection. On the other hand, 81.6% of the patients with serum ferritin levels $\geq 15 \mu\text{g/L}$ were seropositive for this infection. Statistical analysis did not reveal any significant difference between these two groups.

Of all participants, only four (one male and three females) were diagnosed with IDA. Three of these individuals were seropositive for H. pylori infection. We did not observe significant difference in H. pylori infection, between patients with IDA and without IDA.

WBC and platelet counts and Hct levels did not show any significant differences between seropositive and seronegative patients for H. pylori.

DISCUSSION

Iron deficiency is the most common cause of anemia in the world (1,2). Iron deficiency and IDA both are prevalent in Iran (10). Infection with H. pylori is recognized as a major risk factor for chronic gastritis, peptic ulcer and gastric cancer. H. pylori infection is more prevalent in developing countries in comparison to developed countries (11, 12). Several clinical reports have demonstrated that H. pylori gastritis has emerged as a new cause of refractory IDA unresponsiveness to iron therapy and not attributable to usual causes such as intestinal losses or poor intake (1,4-7,15,16). Iron occupies a unique position in biological systems participating in a wide range of oxidation-reduction processes which are essential for life. It is also a

crucial growth factor for virtually all bacteria. During infection, the total amount of extracellular iron is reduced in the host (hypoferrinemia 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 reticuloendothelial system (4). Other possible pathogenic mechanism of anemia are occult blood loss secondary to chronic erosive gastritis and decreased iron absorption secondary to chronic gastritis and hypochlorhydra (1,5,6,17).

Serological methods can be employed as noninvasive reliable tools for diagnosis of *H. pylori* infection (18). Our study shows *H. pylori* IgG and IgA seropositivity in 97.8% and 30.7%, respectively. *H. pylori* IgG yields sensitivity and specificity of 96.8% and 73.1%, respectively (18). Most individuals infected with *H. pylori* have elevated levels of IgG antibodies but only in about two third of the cases the IgA titer exceed the cutoff level (19). Some infected subjects with elevated IgG levels subsequently produce IgA antibodies and their IgA levels will increase during infection (11, 19, 20).

The rate of *H. pylori* infection increases with age (11, 20). In this study we have also found a similar pattern of age-dependent progression to other studies. We did not observe any significant difference in relation to gender. Some authors believe this infection is more common in male (11), but others did not find any significant difference between two genders in *H. pylori* infection (18,20).

According to some reports, *H. pylori* seropositive subjects had lower serum ferritin concentrations in comparison to seronegative individuals (5,13). However, we did not find any association between *H. pylori* infection and serum ferritin levels. Indeed there was no significant correlation between *H. pylori* infection and patients with iron deficiency (serum ferritin <15 µg/L) or patients with IDA. It is noteworthy to mention that some other studies have reported the same observations (9, 21).

As with other study (22) we did not found any correlation between *H. pylori* infection and WBC and platelet counts, hemoglobin and hematocrit levels.

CONCLUSIONS

Since the prevalence of both *H. pylori* infection and iron deficiency are high in our region, we designed this study to look into the correlation between these two. Although many studies have shown an association between *H. pylori* infection and iron deficiency, however, few other studies as well as this study have not reported such an association.

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