The study of relationship between helicobacter pylori and Iron Deficiency Anemia in patient who referred to hematological clinic in Educational Emam Khomeini hospital

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ABSTRACT

Iron deficiency is estimated to be the most common nutritional deficiency in both developed and underdeveloped nations. Despite a thorough clinical and endoscopic evaluation, large case series have shown that more than one-third of patients do not have a lesion to account for their iron deficiency. Helicobacter pylori infection could account for some of these unexplained cases of iron deficiency. This study was a case control survey. The objective was to investigate the relationship between Helicobacter pylori infection and iron-deficiency anemia (IDA). Blood sampling and a questionnaire survey were performed on 200 anemic case and 200 control samples. Hemoglobin, ferritin, and immunoglobulin G antibody to H pylori were measured to compare the prevalence of IDA and H pylori infection in the groups. Tow groups was matched with age and sex. The rate of seropositivity in case group was 69.9% and in control group was 47.2% and this difference was significant statistically. (p= 0.001) but odds ratio for seropositivity in anemic group was weak and that's amount was 0.38 with 95% confidence interval 0.22-0.68. The rate of seropositivity hadn't relationship with age. Serum IgG antibody's levels were found lower in females than males. High levels were most common among persons in 40-49 years group of age. This difference was significant. This case control survey demonstrates a high rate of past or current infection with H. pylori in the patient with anemia. The age when infection is acquired appears to be quite young. Given the relative ease and simplicity of H. pylori treatment and the encouraging results in literature, H. pylori testing and treatment for persons with unexplained IDA appears to be clinically indicated.

Key Words: Helicobacter pylori, Iron Deficiency Anemia, Ferritin, IRAN, Case Control study.
INTRODUCTION

Iron deficiency is estimated to be the most common nutritional deficiency in both developed and underdeveloped nations, the most common cause of anemia, and one of the most common organic disorders in clinical practice.[1],[2] Gastroenterologists are frequently asked to perform endoscopic evaluation of patients with iron deficiency to determine if mucosal lesions causing chronic blood loss are present, including neoplasms, ulcers, and angiodysplasias. Depending on the clinical population and setting, stool testing for ova and parasites to rule out hookworm and serology or duodenal biopsies to rule out celiac sprue may also be appropriate. Despite a thorough clinical and endoscopic evaluation, large case series have shown that more than one-third of patients do not have a lesion to account for their iron deficiency,[3],[4] raising the question as to whether there are as yet unrecognized causes of iron deficiency. 

*Helicobacter pylori* infection could account for some of these unexplained cases of iron deficiency. Accumulating evidence suggests that this is the case, i.e., that *H. pylori* gastritis, without peptic ulcer, can be associated with low iron stores and anemia. *Helicobacter pylori* is a small, curved, highly motile, Gram negative bacillus that colonises only the mucus layer of the human stomach. Since its discovery in 1984, it has been recognised as the principal cause of peptic ulcer disease and as the main risk factor for the development of gastric cancer. However, most infected people (>70%) are asymptomatic. We therefore need to discover how infection is acquired, why ulcers or cancer occur in so few of those infected, and how this subgroup can be identified and treated.

Epidemiologic studies have shown that persons seropositive for *H. pylori* infection have a significantly lower serum ferritin level. [5-9] In a population-based study (n=2794) from Denmark, *H. pylori* -seropositive persons were at 40% increased risk of having reduced serum ferritin level (<30 mg/L) compared to seronegative individuals (after adjustment for age, gender, menopausal status, socioeconomic status, blood donation, and alcohol consumption).[6] Analysis of a cross-sectional national health survey from Germany (n=1806) revealed that persons with *H. pylori* infection had 17% decrease (95% CI 9.8-23.6) in serum ferritin concentration, after adjustment for age and sex.[5] A study of Alaskan natives (n=2080) also showed an increased risk of low serum ferritin for persons seropositive for *H. pylori* infection (relative risk 1.13, p=0.013). Positive findings were also reported in a study of Korean children aged 6-12 (n=753), in whom *H. pylori* seropositivity was associated with lower mean serum ferritin level (24 ng/mL vs. 39 ng/mL, p<0.001), and a significantly increased prevalence of iron deficiency (serum ferritin <15 ng/mL).[9] Another study of Korean adolescents (n=937) confirmed a significant association between *H. pylori* seropositivity and anemia, hypoferritinemia and iron deficiency.[10] An epidemiologic study of Australian women showed significantly lower ferritin levels in women with *H. pylori* infection compared to non-infected controls despite similar dietary iron intake.[8]

While the above studies support an association between *H. pylori* infection and indices of iron stores, a few (usually smaller) epidemiologic studies have not found significant association between *H. pylori* infection and iron indices. In a study of 1060 adults from New Zealand, there was no significant differences in serum ferritin level according to *H. pylori* status,[11] and a study of 693 Korean children found no significant difference in the prevalence of *H. pylori* infection for children with and without IDA.[12]
Therefore we were designed a research to investigate the relationship between Helicobacter pylori infection and iron-deficiency anemia (IDA).

**MATERIALS AND METHODS**

This study was a case control survey. The objective was to investigate the relationship between Helicobacter pylori infection and iron-deficiency anemia (IDA). Blood sampling and a questionnaire survey were performed on 200 anaemic case and 200 control samples. Hemoglobin, ferritin, and immunoglobulin G antibody to H pylori were measured to compare the prevalence of IDA and H pylori infection in the groups.

In this study, inclusion Criteria were age > 18 years, iron deficiency anemia (IDA) defined as: Hgb < 14 g/L for men and 12 g/L for women, and a serum ferritin level less than 45 ug/L and exclusion Criteria were obvious non-GI cause of blood loss, Chronic renal failure (BUN>60, Creatinine > 4), Hemolytic anemia, thalassemia, aplastic anemia, Known alcoholism or cirrhosis of the liver, Regular use (>3x weekly) of NSAIDS, Prior gastric resection, Celiac disease, Known GI or hematologic malignancy, Known inflammatory bowel disease.

A group of 200 patients referred to a university hospital hematology department at 2006 and who met a history of iron deficiency anemia (defined as hemoglobin concentration less than 14 g/L for men and less than 12 g/L for women and 200 control group that matched with case group with age and sex. Immediately after blood collection, a drop of blood was drawn into a microcuvette for hemoglobin measurement. Serum samples then were frozen at –30°C until processed for testing. Serum ferritin concentrations were determined by using a radioimmunometric assay. Iron deficiency was defined as a serum ferritin concentration of <10 µg/L and iron deficiency anemia (IDA) defined as: Hgb < 14 g/L for men and 12 g/L for women, and a serum ferritin level less than 10 ug/L. We conducted serologic testing for H pylori-specific antibodies using the HM-CAP enzyme immunoassay (E-Z-EM, Lake Success, NY) to detect immunoglobulin G antibodies against high molecular weight cell-associated proteins of H pylori.

As most of the study questions concerned differences between groups, the main analytic strategy used was analysis of variance (ANOVA), but univariate and multivariate logistic regression analyses with odds ratios and 95% confidence limits as well as linear regression analyses were also used. For relationship between IDA and H.pylori MACNEMAR test were used. The data were analyzed with SPSS Statistical Software. Rates of H. pylori infection were calculated for samples, including age-, sex. For the purposes of analysis sera with H. pylori-specific IgG values within the indeterminate range were considered positive. For comparisons of the presence of H. pylori-specific IgG and low serum ferritin level prevalence and for correlation of these two factors, chi-square, Fisher's exact, and Mantel-Haenszel (MH) tests were used for trend as appropriate. The procedures and protocols of the studies were approved by the Joint Ethics Committee of the oromieh medical University. Participation was based on verbal consent by which subjects gave permission to use their medical records.

**RESULTS**

Mean of case group age's was 42.78 and for control group was 43.166 and this differences was not significant statistically.(T.test; p=0.88) therefore tow groups was matched with age. In case group (anemic) 64.1% of person's were female and in
control groupes 64.8% were female. This difference was not significant statistically (p=0.51). A total of 400 serum samples were tested for IgG antibody to H. pylori; 58.3% were positive, for an overall seropositivity rate of 74.8%. The rate of seropositivity in case group was 69.9% and in control group was 47.2% and this difference was significant statistically. (p=0.001) but odds ratio for seropositivity in anemic group was weak and that's amount was 0.38 with 95% confidence interval 0.22-0.68.

Thirty-two percent of individuals were in age 18 to 29 years. Fifty percent of individuals were under 40 years and fifty percent were up to 40 years. Mean of individual age was 42.98 with std. deviation of 18.69. Range of individual age was 18 to 85 years, by age 18 to 29 years, the rate of H. pylori seropositivity was 30.9%.

There was a higher rate of seropositivity among females 60.2%, than among males, 39.8%. This difference was not significant ($\chi^2 = 2.37; P = 0.081$).

Serum ferritin levels were found lower in males than females. Low levels were most common among persons in 40-49 years group of age.

Serum IgG antibody's levels were found lower in females than males. High levels were most common among persons in 40-49 years group of age. This difference was significant (Fisher Exact test; $P = 0.012$). This case control survey demonstrates a high rate of past or current infection with H. pylori in the patient with anemia. The age when infection is acquired appears to be quite young.

**DISCUSSION**

The association of low serum ferritin levels, a marker of iron deficiency, with the presence of H. pylori-specific IgG supports the earlier endoscopic findings of H. pylori-associated gastritis as a cause of elevated stool heme levels (13). This
association appeared to be particularly strongest for those Alaska Natives <20 years of age, regardless of whether the analysis either included or excluded sera with indeterminate results. We have since found a similar association between both anemia and iron deficiency and *H. pylori* seropositivity among anemic patients. Our findings are also supported by another large serosurvey for *H. pylori* in adults in Denmark in which serum ferritin levels were found to be significantly lower in adult men and postmenopausal women who were *H. pylori* IgG positive than in noninfected persons (14). A smaller study in Australia also showed that serum ferritin levels were significantly lower in women who were *H. pylori* IgG positive than in women who were *H. pylori* negative (15).

The evidence to support a causal association between *H. pylori* gastritis and decreased iron stores comes from case reports, epidemiologic studies and small clinical trials. The initial case report describing a possible causal association between *H. pylori* gastritis and iron deficiency anemia (IDA) was published by Dufour *et al* , in which a seven year-old boy with refractory unexplained IDA had resolution of anemia following treatment of *H. pylori* -related pangastritis.[16] This case report was followed by several other similar case reports that describe IDA with no apparent cause other than *H. pylori* -associated gastritis, with normalization of hemoglobin and iron indices after successful *H. pylori* treatment (without need for continuing iron supplementation).[17-31]

**CONCLUSION**

In summary, a growing body of evidence supports a clinically significant influence of *H. pylori* infection on body iron stores. The report by Valiyaveettil *et al* provides further data that patients with unexplained IDA benefit from testing and treatment for *H. pylori* infection. Epidemiologic studies also support an association between *H. pylori* infection and low iron stores, and several reports have shown resolution of refractory cases of anemia after *H. pylori* treatment. Given the relative ease and simplicity of *H. pylori* treatment and the encouraging results in literature, *H. pylori* testing and treatment for persons with unexplained IDA appears to be clinically indicated.

**REFERENCES**