Close association between Helicobacter pylori infection and serum homocysteine in stable hemodialysis patients

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Hyperhomocysteinemia is a factor that is suggested to be responsible for the development of atherosclerosis in the setting of chronic H. pylori infection. In the recent years, homocysteine has been shown to be an important contributor to atherosclerosis. This study was undertaken to elucidate whether and how in patients with uremia on maintenance hemodialysis, the infection of H. pylori affects the levels of homocysteine. Study patients were 39 (F=15 M=24) stable hemodialysis (HD) (diabetic=12 non-diabetics=27) patients. Mean ages of patients were 46(±18) years. The length of the time patients had been on hemodialysis were 30± (35) months (median: 18 months). The value of serum homocysteine of all patients was 5 (±2) µmol/L (median: 4.5 µmol/L). The value of serum Helicobacter pylori (H. Pylori) specific IgG antibody titers of was 7.6 (±9.9) u/ml (median: 2 u/ml). In the present study a significant positive correlation of serum homocysteine with H. pylori infection was found. As mild-to-moderate elevations in serum homocysteine levels are also observed in the great majority (>85%) of patients with end-stage renal disease who are undergoing maintenance dialysis, further research is needed to determine the importance of this association in hemodialysis patients and whether treatment of H. pylori infection in hemodialysis patients can diminish serum homocysteine level.

Key words: Hemodialysis, end-stage renal failure, serum homocysteine, Helicobacter pylori infection


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Introduction
Helicobacter pylori (H. pylori) is a spiral-shaped bacterium that causes chronic infection in human stomachs, and often leads to gastritis and peptic ulcers. Recent data indicate a possible correlation between H. pylori infection and coronary heart disease. The connection between H. pylori infection and hyperhomocysteinemia is one way in which this organism may be linked to the development of coronary diseases. Researches have shown strong associations between hyperhomocysteinemia and inadequate vitamin intake and insufficient vitamin concentrations in plasma, particularly vitamin B6, vitamin B12 and folate levels.

Several studies have demonstrated that H. pylori infection has negative effects on serum levels of vitamin B12 and folate. Homocysteine metabolism involves a complex interaction between folate and vitamin B12. It has been well established that chronic H. pylori infection causes atrophic gastritis and decreased absorption of both vitamin B12 and folate acid has been documented in patients with this condition. This study was...
performed to elucidate whether and how in patients with uremia on maintenance hemodialysis, the infection of *H. pylori* affects the serum level of homocysteine.

**Materials and Methods**

This is a cross-sectional study that was conducted on patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. All study patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, post-prandial fullness, early satiety, bloating and belching. Exclusion criteria for patients were using of proton pump inhibitors and antibiotics or taking aluminum hydroxide jells as well as active or chronic infection before the study. Serum homocysteine (total) was measured as follows. Blood samples were drawn after an overnight fast. Each blood samples were centrifuged within 15 min of venopuncture, and were measured by enzyme-linked immunosorbent assay (ELISA) method using DRG kits (DRG Diagnostics, Berlin, Germany). Serum total Homocysteine (Hcy) have a normal range of 25-125 µmol/L. Levels of serum Leptin (normal range of values for males is 3.84 (±1.79) and for females 7.36 (±3.73) ng/ml) were also measured by ELISA method using DRG of USA. Serum helicobacter pylori specific IgG antibody titers (titer >10 U/ml was interpreted as positive according to the manufacturer’s instructions) was measured by ELISA method using Trinity Biotech Kits (USA). Intact serum PTH (iPTH) was measured by the radioimmunoassay (RIA) method using DSL-8000 kits of USA (normal range of values is 10-65 pg/ml). Also peripheral venous blood samples were collected for biochemical analysis including serum post and predialysis blood urea nitrogen (BUN), Chol, albumin (Alb), C-reactive protein (CRP) were measured using standard methods. Plasma HCO₃ was measured by arterial blood gas. Levels of serum iron, total iron binding capacity (TIBC) and serum ferritin (by RIA method) were measured using standard kits . Plasma HCO₃ was measured by arterial blood gas. Levels of serum iron, total iron binding capacity (TIBC) and serum ferritin (by RIA method) were measured using standard kits . For patients also complete blood count containing hemoglobin (Hgb) and hematocrit (Hct) were measured using Sysmex-KX-21N Cell counter (SYSMEX CORPORATION; Mundelein, Illinois, Sysmex America, Inc.). For the efficacy (adequacy) of hemodialysis the urea reduction rate (URR) was calculated from pre-and post-blood urea nitrogen (BUN) data . Body mass index (BMI) calculated using the standard formula (postdialyzed weight in kilograms/height in square meters; kg/m²). Duration and doses of hemodialysis treatment were calculated from patients' records. The duration of each hemodialysis session was four hours. For statistical analysis, the data are expressed as the Mean ± SD and median values. Statistical correlations were assessed using the partial correlation test. Comparison between the groups was done using Student's t-test. Statistical analysis was performed on all hemodialysis (HD) patients, females, males, diabetics and non diabetic groups separately. All statistical analyzes were performed using SPSS (version 11.5.00). Statistical significance was determined at a p-value lower than 0.05.

**Results**

The study was carried on 39 (F=15 M=24) stable hemodialysis (HD) (diabetic=12 non-diabetics=27) patients. Table 1 summerise patients' data. Mean ages of patients were 46 (±18) years. The length of the time patients had been on hemodialysis was 30±(35) months (median: 18 months). The value of serum homocysteine of all patients was 5 (±2) µmol/L (median: 4.9 µmol/L). The value of serum homocysteine in the female and male groups were 5 (±3) µmol/L (median:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Means±SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age years</td>
<td>1846 ± 18</td>
<td>42</td>
</tr>
<tr>
<td>DHy months</td>
<td>3530 ± 18</td>
<td>18</td>
</tr>
<tr>
<td>Dialysis dose sessions</td>
<td>381279 ± 156</td>
<td></td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>21.6±4.3</td>
<td>21</td>
</tr>
<tr>
<td>H. pylori-IgG u/ml</td>
<td>7.6±9.9</td>
<td></td>
</tr>
<tr>
<td>Leptin ng/ml</td>
<td>10±14</td>
<td>6.8</td>
</tr>
<tr>
<td>Chol mg/dl</td>
<td>38116 ± 110</td>
<td>110</td>
</tr>
<tr>
<td>Hgb g/dl</td>
<td>28.9 ± 9</td>
<td>4</td>
</tr>
<tr>
<td>Alb g/l</td>
<td>0.5 3.8 ± 4</td>
<td>4</td>
</tr>
<tr>
<td>Homocysteine µmol/L</td>
<td>5±2</td>
<td>4.3</td>
</tr>
<tr>
<td>URR %</td>
<td>8.58 ± 58</td>
<td>58</td>
</tr>
<tr>
<td>CRP mg/L</td>
<td>6.78 6</td>
<td>6</td>
</tr>
<tr>
<td>Hct %</td>
<td>6.28 ± 29</td>
<td></td>
</tr>
<tr>
<td>HCO₃ mEq/L</td>
<td>20±2.3</td>
<td>20</td>
</tr>
<tr>
<td>iPTH Pg/ml</td>
<td>434±455</td>
<td>309</td>
</tr>
<tr>
<td>Ca mg/dl</td>
<td>7.7±1</td>
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</tr>
<tr>
<td>P mg/dl</td>
<td>6.4±1.9</td>
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</tr>
<tr>
<td>Ferritin ng/dl</td>
<td>519±299</td>
<td>426</td>
</tr>
<tr>
<td>Iron µg/dl</td>
<td>350±454</td>
<td>69</td>
</tr>
<tr>
<td>TIBC µg/dl</td>
<td>968±562</td>
<td>1059</td>
</tr>
</tbody>
</table>

*duration of hemodialysis
3.7 µmol/L and 5(±2) µmol/L (median: 4.9 µmol/L) respectively. Mean±SD of hemoglobin and hematocrit level of all patients were 9±2 g/dl (median: 9 g/dl), and 28±6% (median: 29%) respectively. The value of serum Helicobacter pylori (H. pylori) specific IgG antibody titers of all patients was 7.6 (±9.9) u/ml (median: 2 u/ml). The value of serum helicobacter pylori (H. pylori) specific IgG antibody titers in the female and male groups were 5.9 (±8) u/ml (median: 2 u/ml) and 8.7 (±10.9) u/ml (median: 2 u/ml) respectively. In this study no significant difference of serum homocysteine and H. pylori - IgG antibody level between males and females or diabetic and non-diabetic hemodialysis patients were found (p N.S.).

In this study in non diabetic group a significant positive correlation of serum homocysteine with H. pylori - IgG antibody level (r= 0.77, p=0.016). In male group also in male group and a significant positive correlation of serum homocysteine with H. pylori - IgG antibody level (r= 0.56, p =0.028; Figure 1) (adjusted for age, duration and doses of dialysis, serum iPTH, serum leptin, CRP, albumin and serum ferritin for two above correlations) were seen. No significant correlation of serum homocysteine with H. pylori - IgG antibody level all patients, female and diabetic HD groups was seen (p N.S.).

**Discussion**

Homocysteine (Hcy) is a sulphur amino acid formed from methionine during transmethylation, and is either salvaged to methionine by a folate- and cobalamin-dependent re-methylation reaction or directed toward degradation by the vitamin B6-dependent enzyme cystathionine β-synthase.11

Large studies have demonstrated that moderate hyperhomocysteinaemia is an independent risk factor for premature atherosclerosis and cardiovascular disease.12,13

Mild-to-moderate elevations in serum homocysteine levels are observed in the great majority (>85%) of patients with end-stage renal disease who are undergoing maintenance dialysis.12-14 Deficiency of vitamin B12 raises the serum and tissue levels of homocysteine. Atrophic corpus gastritis results in impaired secretion of intrinsic factor and may lead to malabsorption of vitamin B12 in the intestine.15 In a study conducted by Aguiler et al. on 1313 peritoneal dialysis patients showed that Infection with H. pylori is associated with anorexia, Inflammation, and malnutrition in their patients. Eradication of H. pylori significantly improves this syndrome.16 In our previous studies association of H. pylori infection with serum albumin and other nutritional parameters were shown.17-19 To test the hypothe-

![Figure 1](https://example.com/figure1.png)

*Significant positive correlation of serum homocysteine with H.Pylori-IgG antibody level*
sis that chronic atrophic gastritis induced by *Helicobacter pylori* (*H. pylori*) causes malabsorption of vitamin B12 and folate in food, leading ultimately to an increase in circulating homocysteine levels, Tamura et al conducted a study on 93 patients who underwent diagnostic coronary arteriography. The patients were divided into two groups according to the presence (n = 57) or absence (n = 36) of *H. pylori* infection. The study suggests that *H. pylori* - induced chronic atrophic gastritis decreases plasma vitamin B12 and folic acid levels, thereby increasing homocysteine levels. In the study carried-out by Sipponen et al. on population-based sample of 12,252 men (age 51-65 years) from two cities in Finland, that 2.5% of men in the age group 51-65 years in the present study population had a low serum levels of vitamin B12 level that associated with atrophic corpus gastritis. Of these men, 72% (128 of 179 tested) had an elevated Helicobacter pylori antibodies level. They concluded that low serum levels of vitamin B12 related to atrophic corpus gastritis is relatively common (prevalence 2.5%) among elderly males in the general population. An ongoing *H. pylori* infection occurs in three-fourths of these cases. To determine whether serum vitamin B12 levels in non-vitamin B12 deficient healthy adults correlate with serological evidence of *H. pylori* infection, Shuval-Sudai et al. studied 135 adults with a history of *H. pylori* eradication and found that the higher prevalence of *H. pylori* infection among subjects with serum vitamin B12 levels that are within the lower end of the normal range suggests a causal relationship between *H. pylori* infection and vitamin B12 levels in healthy adults. Hence, an association between Helicobacter pylori infection, reduced cobalamin absorption and cobalamin status and, consequently, elevated homocysteine levels, could offer an explanation why *H. pylori* infection is associated with coronary heart disease.

To determine whether *Helicobacter pylori* (*H. pylori*) infection caused hyperhomocysteinemia by altering serum vitamin B12, serum folate and erythrocyte folate levels and whether eradication of this organism decreased serum homocysteine level, Ozer et al. also studied 73 dyspeptic *H. pylori* - positive patients, they showed that eradication of *H. pylori* decreases serum homocysteine even in patients who do not exhibit gastric mucosal atrophy. They concluded that the level of homocysteine in serum is related to a complex interaction among serum vitamin B12, serum folate and erythrocyte folate levels.

One meta-analysis involving 10,000 patients revealed no meaningful correlations between *H. pylori* and vascular risk factors. Research has shown that homocysteine can directly cause endothelial damage, affect platelet function and coagulation factors, and increase the oxidation of low-density lipoproteins. Indeed in the light of these findings, a number of investigators have focused on *H. pylori* infection as a possible cause of hyperhomocysteinemia in the general population. However, in hemodialysis patients other factors are also responsible for high serum levels of homocysteine. As noted above, in the present study we found a significant positive correlation of serum homocysteine with *H. pylori* infection.

It has been well established that chronic *H. pylori* infection causes atrophic gastritis, and decreased absorption of both vitamin B12 and folic acid has been documented in patients with this condition. Patients with chronic *H. pylori* infection exhibited decreased secretion of ascorbic acid by the gastric mucosa and elevated gastric pH. It has been demonstrated that low levels of ascorbic acid in gastric juice or high pH of gastric juice could cause less folate absorption from the diet. Even in dyspeptic *H. pylori* - positive patients who do not exhibit gastric mucosal atrophy, complete eradication of *H. pylori* is associated with a significant drop in serum homocysteine. Taken together, hyperhomocysteinemia is a factor that is suggested to be responsible for the development of atherosclerosis in the setting of chronic *H. pylori* infection. Homocysteine has been shown to be an important contributor to atherosclerosis as mentioned. While in hemodialysis patients we also have hyperhomocysteinemia, further research is needed to determine the importance of this association in hemodialysis patients and whether treatment of *H. pylori* infection in hemodialysis patients can diminish serum homocysteine level.

References


Bu sayfa montajda boş bırakılacak.