Relationship of Helicobacter Pylori Specific IgG Antibodies with Serum Magnesium and Serum Lipid Profile in Patients on Maintenance Hemodialysis

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Abstract:

**Background:** Helicobacter pylori are thought to play an important role in the pathogenesis of active gastritis and other upper mucosal lesions in chronic hemodialysis patient which thoughtto result in dyspeptic symptoms.

**Aim:** The aim of the study is to determine the prevalence of Helicobacter pylori infection in patient on maintenance hemodialysis and to assess the probable association of serum lipid profile and serum magnesium with H. pylori infection in these patients.

**Material & Methods:** This cross-sectional study was conducted on patients with end stage renal disease who were undergoing maintenance hemodialysis treatment. were enrolled in the present studya total number of 42 hemodialysis patients (24 male and 18 female). Of the total number; 10 were diabetic and 32 were non diabetic. Demographic data including age, gender, duration of hemodialysis and clinical data including diabetes mellitus, upper gastrointestinal symptoms and laboratory measurements were obtained from related questionnaires. Venous blood samples were collected for biochemical analysis of the following markers: serum magnesium, total cholesterol, triglyceride; high density lipoprotein-cholesterol, low density lipoprotein-cholesterol and very low density lipoprotein-cholesterol.

**Result & Conclusion:** We conclude that there was no significant correlation between gender, age, duration of hemodialysis, DM, serum triglyceride, VLDL-C and magnesium and H. pylori infection in these patients.

**Key words:** Chronic renal failure, Hemodialysis, Serum magnesium, Helicobacter pylori.

Introduction:

Helicobacter pylori (H. pylori) is a gram-negative, spiral-shaped pathogenic bacterium that specifically colonizes the gastric epithelium and causes chronic gastritis, peptic ulcer disease and/or gastric malignancies (1,2). The prevalence of H. pylori infection is related to socioeconomic status and living conditions during early life (3). H. pylori infection affects more than (50%) of the world population (4,5). Patients with end-stage renal disease (ESRD) receiving hemodialysis often have various gastrointestinal troubles such as nausea, dyspepsia, appetite loss, epigastric discomfort, and heartburn (6).
These gastrointestinal complications would be directly associated with *H. pylori* infection in hemodialysis patients\(^6,7\). Infec\(\text{t}\)ion with *H. pylori* is also associated with anorexia, inflammation, and malnutrition in dialysis patients. Malnutrition is a relevant risk factor for mortality for patients on maintenance hemodialysis treatment\(^8,9\).

Magnesium (Mg) is an important intracellular cation that is distributed into three major compartments: mineral phase of bones (65%), intracellular space (34%) and extracellular fluid (1%). About one-third of circulating Mg is bound to plasma protein, with the remaining two-thirds free, and presumably biologically free\(^10\).

Renal excretion is the major route of magnesium elimination from the body and a positive magnesium balance would be expected under conditions of renal insufficiency. In end-stage renal disease, the limited ability of the kidney to excrete an increased magnesium load may result in toxic concentrations of the ion in serum\(^11\). Magnesium concentrations are increased in serum and red cells in CRF patients\(^12\). Magnesium seems to be an important factor for both gastric acid secretion regulation (together with Calcium) and for *H. pylori* survival and virulence\(^10,13,14\).

**Aim:**

The aim of the study is to determine the prevalence of *Helicobacter pylori* infection in hemodialysis patients and to assess the probable association of serum lipid profile and serum magnesium with *H. pylori* infection in these patients.

**Materials and methods:**

**Patients:**

This cross-sectional study was conducted on patients with end stage renal disease who were undergoing maintenance hemodialysis treatment. A total number of 42 hemodialysis patients (24 male and 18 female) with end stage renal disease were enrolled in the present study. This study was conducted from 01\01\2012 to 01\01\2013 at the dialysis unit/Kirkuk general hospital. The age distribution range from 10-80 years (y) (26.19% are less than 30 year old, (52.3%) were between 30-60 year old, and (21.4%) were above 60 years. The dose of dialysis was as the following, 25 patient (59.5%) had 3 hour twice weekly dialysis, 8 patients (19.0%) had two hour twice weekly dialysis, 3 patients (7.14%) had two hour three time weekly dialysis, 2 patient (4.7%) three hour once weekly dialysis, 1 patient (2.38%) had one and half hour twice weekly dialysis, 1 patient (2.38%) had three hour thrice weekly dialysis, 1 patient (2.38%) had three hours thrice weekly dialysis, and 1 patient (2.38%) had 2 hours once weekly dialysis. Most of the patients are adequately dialyzed. Duration of dialysis were as the following, 24 patient (57.14%) had less than 3 month dialysis duration, 12 patients (28.57%) had duration of dialysis between 3 month-12 month, 6 patients had duration of dialysis more than 12 month (14.28%). 38 patients (90.47%) they were on regular hemodialysis, but the remainder small number, 4 patients (9.52%) had irregular dialysis. Demographic data including age, gender, duration of hemodialysis and clinical data including diabetes mellitus, upper gastrointestinal symptoms and laboratory measurements were obtained from related questionnaires. All patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Patients...
on H2 blocker or antibiotic, and those with history of active or chronic infection within last one month have been excluded from the present study.

**Laboratory methods:**
Venous blood samples were collected for biochemical analysis including serum Mg⁺, total cholesterol, triglyceride; HDL-cholesterol, LDL-cholesterol and VLDL-cholesterol and were measured using standard laboratory methods and according to the manufacture instruction. The presence of Serum IgG antibody against *H. pylori* was determined by immunochromatography assay using (ACON®) kit and the result were interpreted according to the manufacturer’s instruction.

**Statistical analysis:**
Data analysis was performed by using SPSS software (statistical package for the social science, version 20.0). The results were expressed as mean±SD. The Chi-square (χ²) test and the student’s *t*-test were used where appropriate. A P-values <0.05 were considered statistically significant.

**Result:**
This study was carried out on 42 (F=18, M=24) hemodialysis (diabetic-10; non-diabetics-32) patients with upper gastrointestinal symptoms. Tables 1 and 2 summarize patient’s data. Eighteen patients (42.9%) were diagnosed with *H. pylori* infection (11 male and 11 female; mean age 49.3±31.4 years range) and 24(57.1%) (13 male and 7 female; mean age 40.7±30.06 years, range) were found uninfected. There was no difference in the gender distribution and the age between *H. pylori* positive and negative patients. The mean duration of hemodialysis for *H. pylori*-positive and -negative patients was 7.24±5.80 months and 5.35±4.26 months, respectively. This difference was not statistically significant (p=0.472).

The mean serum Mg⁺, triglyceride and VLDL-C levels in *H pylori*-positive and *H pylori*-negative patients were not significantly different (P values >0.05). However, the mean serum cholesterol level was significantly lower in seropositive patients than in seronegative (P=0.000). Also, there was significant decreases in the mean serum HDL-c (P=0.017) and LDL-c (P=0.004) in *H pylori*-positive patients. The most often reported upper gastrointestinal symptoms were: epigastric pain 6(14.3%), epigastric burning 10(23.8%), postprandial fullness 8(19.0%), early satiety 24(57.1%), bloating 15(35.7%) and belching 13(31.0%). There was no significant differences in the reported symptoms between *H pylori*-positive and *H pylori*-negative patients (P values >0.05).
Table (1): Demographic and laboratory parameters between H. pylori positive and negative HD patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>H. pylori positive n= 18</th>
<th>H. pylori negative n= 24</th>
<th>p-value</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>11/11</td>
<td>7/13</td>
<td>0.327</td>
<td>0.962</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.36±31.4</td>
<td>40.7±30.06</td>
<td>0.089</td>
<td>1.743</td>
</tr>
<tr>
<td>Duration of HD (months)</td>
<td>7.24±5.80</td>
<td>5.35±4.26</td>
<td>0.472</td>
<td>0.726</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Mg</td>
<td>2.0227±1.956</td>
<td>1.9910±1.623</td>
<td>0.547</td>
<td>0.608</td>
</tr>
<tr>
<td>Serum total cholesterol</td>
<td>113.6364±92.54</td>
<td>152.30±121.564</td>
<td>0.000</td>
<td>4.017</td>
</tr>
<tr>
<td>Serum triglyceride</td>
<td>149.5045±121.98</td>
<td>127.69±108.35</td>
<td>0.328</td>
<td>0.99</td>
</tr>
<tr>
<td>Serum HDL-cholesterol</td>
<td>31.8955±26.406</td>
<td>39.645±33.582</td>
<td>0.017</td>
<td>2.496</td>
</tr>
<tr>
<td>Serum LDL-cholesterol</td>
<td>59.174±46.08</td>
<td>87.11±61.35</td>
<td>0.004</td>
<td>3.043</td>
</tr>
<tr>
<td>Serum VLDL-cholesterol</td>
<td>27.255±23.0861</td>
<td>25.5150±20.461</td>
<td>0.545</td>
<td>0.611</td>
</tr>
</tbody>
</table>

Table (2): Comparison of upper gastrointestinal symptoms between H. pylori positive and H. pylori negative patients.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>total</th>
<th>H. pylori- positive</th>
<th>H. pylori- negative</th>
<th>p-value</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epigastric pain</td>
<td>6(14.3%)</td>
<td>3</td>
<td>3</td>
<td>0.9</td>
<td>0.016</td>
</tr>
<tr>
<td>Epigastric burning</td>
<td>10(23.8%)</td>
<td>5</td>
<td>5</td>
<td>0.863</td>
<td>0.300</td>
</tr>
<tr>
<td>Postprandial fullness</td>
<td>8(19.0%)</td>
<td>3</td>
<td>5</td>
<td>0.524</td>
<td>0.406</td>
</tr>
<tr>
<td>Early satiety</td>
<td>24(57.1%)</td>
<td>13</td>
<td>11</td>
<td>0.327</td>
<td>0.963</td>
</tr>
<tr>
<td>Bloching</td>
<td>15(35.7%)</td>
<td>5</td>
<td>10</td>
<td>0.167</td>
<td>1.909</td>
</tr>
<tr>
<td>Belching</td>
<td>13(31.0%)</td>
<td>4</td>
<td>9</td>
<td>0.143</td>
<td>2.143</td>
</tr>
</tbody>
</table>

Discussion:

H. pylori is considered to be the cause of gastritis and gastric ulcer. It is also closely associated with some other gastrointestinal diseases, such as gastric hyperplastic polyps, gastric adenoma, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma (15-16). With regard to H. pylori infection in patients with ESRD, many issues remain to be clarified. We investigated the prevalence of H. pylori infection in our HD patients. The results of our study found out that the prevalence of H. pylori infection was (42.9%) which needs to be treated. Patients receiving dialysis had significantly lower prevalence of H. pylori infection according to, Hopkins R.J et al, Jaspersen D et al, Nakajima F et al, Misra F et al, Khedmathas indicated that the prevalence of H. pylori infection is higher in dialysis patients. In our study patient receiving hemodialysis had an significant lower prevalence of H pylori infection comparing to other study (17-20). This can be explained in three ways: first blood urea levels as well as urea nitrogen levels in gastric secretions are higher in dialysis patients than in patients with normal renal function, and high urea levels inhibit H. pylori growth in the stomach (21) this higher urea level in our patient due to under-dialysis in Iraq; second H. pylori might be eradicated upon antibiotic
treatment, both because antibiotics are commonly used during the initial treatment periods, and because antibiotic concentrations are higher in patients with renal failure; third patients receiving dialysis have higher levels of pro-inflammatory cytokines, including interleukins 1b, 6 and 8, and tumor necrosis factor, from activated inflammatory cells infiltrating the gastric mucosa \(^{(22)}\). As a result, the gastric atrophy progresses, accompanied by increased pH, and finally *H. pylori* are not able to live in gastric mucosa \(^{(23)}\).

The relationship between (DM) and *H pylori* infection is controversial. According to some studies there is a high prevalence of *H pylori* infection in patients with either type I\(^{(24)}\) or type II DM\(^{(25, 26)}\). This could be related to a reduced gastric motility and peristaltic activity \(^{(25)}\) various chemical changes in gastric mucosa following non-enzymatic glycosylation processes \(^{(25)}\) and an impaired non-specific immunity observed in diabetic patients \(^{(26)}\). In contrast, other studies showed that *H pylori* infection is not associated with DM, as there is no difference in the prevalence of *H pylori* infection between diabetics and non-diabetics \(^{(27)}\). Our study showed that *H. pylori* infection is not associated with DM in our HD patients.

Some studies shows that *H. pylori* infection may cause dyslipidemia, as it leads to elevated levels of total cholesterol\(^{(28, 29)}\), low-density lipoprotein cholesterol (LDL-c)\(^{(29, 30)}\), triglyceride concentrations\(^{(30, 31)}\) and decreased levels of high-density lipoprotein cholesterol (HDL-c)\(^{(31)}\) in the blood. According to other studies, *H. pylori* infection did not cause any significant changes in plasma levels of total cholesterol, triglycerides, LDL-c\(^{(32)}\). According to our study, the mean total cholesterol, HDL-c and LDL-c concentrations were significantly lower in *H. pylori*-positive than *H. pylori*-negative patients. In contrast, there was no association in the mean serum triglycerides and VLDL-c between our *H. pylori*-positive and-negative HD patients.

The cation metabolism of the gastric pathogen *H pylori* \(^{(33)}\) is of substantial importance for survival in the hostile and changing environment of the gastric mucosa \(^{(34) (35)}\). Mechanisms involved in maintaining cation homeostasis were shown to be required for effective gastric colonization in animal model. Although the essential biological functions of serum magnesium point toward relevance of serum magnesium acquisition in the adaptation to the gastric environment, proteins involved in *H pylori* serum magnesium uptake and metabolism have not been studied in detail \(^{(36)}\). The complete growth deficiency in media without serum magnesium supplementation and the drastic serum magnesium requirement in the range of 20 mM displayed by cor A mutant showed that *H pylori* cor A is essential for serum magnesium acquisition required for survival in low–serum magnesium environment. These finding underscore the role of *H pylori* cation metabolism in maintaining metabolic function and highlight a substantial importance of serum magnesium acquisition in gastric adaptation. The role of cor A-mediated serum Magnesium uptake in *H pylori* colonization and/or survival in gastric mucosa is supported by the serum magnesium concentration in human gastric juice which at 0.7 mM is far below the valuerquired for growth of cor A mutants. Thus, it seems very
unlikely that H pylori cor A mutants can persist in the gastric mucosa for extended time period .these observations indicate that serum magnesium is the dominant cor A substrate. This study shows no association of serum magnesium with infection of H pylori. As serum magnesium is a cofactor of many enzymes involved in central biochemical pathways within the human host, pathogenic bacteria express specific serum magnesium uptake systems, which are essential for bacterial viability. Patients on hemodialysis are more prone to have high magnesium levels. Magnesium also seems to be an important factor both for acid gastric secretion regulation (together with Ca2+) and for H pylori survival and virulence.

Conclusion:
We indicated that there was no significant correlation between gender, age, duration of hemodialysis, DM, serum triglyceride, VLDL-c and magnesium and H. pylori infection in these patients.

Acknowledgement:
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References:


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