Relationship of *Helicobacter Pylori* Specific IgG Antibodies with Serum Magnesium in Patients on Maintenance Hemodialysis

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**KEY WORDS**: chronic renal failure, hemodialysis, serum magnesium, *Helicobacter pylori*

**ABSTRACT**

Dyspeptic symptoms are quite common in patients on long-term hemodialysis, and *Helicobacter pylori* is thought to play an important role in the pathogenesis of active gastritis and other upper gastrointestinal mucosal lesions in these patients. This study investigated the probable association of serum magnesium (Mg$^{2+}$) with *H pylori* infection in patients on maintenance therapy.

*H pylori* specific IgG antibody titers and Mg$^{2+}$ levels were measured in 44 patients on hemodialysis (34 nondiabetic and 10 diabetic). A positive correlation was found between anti *H pylori* IgG antibody titers with Mg$^{2+}$ in all patients, as well as an association between Mg$^{2+}$ with infection of *H pylori*. This study found Mg$^{2+}$ acquisition by CorA is essential for *H pylori* in vitro and that high Mg$^{2+}$ levels, and probably its higher concentration in gastric mucosa, might facilitate the colonization of *H pylori* in the stomachs of patients on hemodialysis. Further investigation is needed to define the clinical significance of this finding.

**INTRODUCTION**

*Helicobacter pylori* has been shown to play an important role in the development of gastritis and gastric ulcer. Patients with chronic renal failure often have dyspeptic symptoms and may develop peptic disease or digestive disorders leading to severe gastrointestinal complications. Studies on the relationship between high serum urea nitrogen, creatinine, and *H pylori* infection in patients on hemodialysis still provide conflicting results. Although the precise nature of the gastroduodenal involvement in these patients remains unclear, the link between *H pylori*, chronic gastritis, and peptic ulcer disease has grown stronger. It has been reported that patients with chronic renal failure have a tendency toward increased incidences of peptic ulcer diseases; however, it is yet unclear whether the increased incidence is due to altered gastric acidity, hypersecretion of gastrin, or increased colonization of *H pylori*. Few reports are available regarding the promoting factors that affect *H pylori* infection in patients on hemodialysis. Lack of a sig-
significant relationship between parathyroid hormone (PTH) abnormalities, which are frequently seen in patients on hemodialysis, and H. pylori infection was noted in another study. Also, a study by Araki and colleagues proposed that high serum levels of pepsinogen II was an interacting factor for H. pylori infection in patients on dialysis. 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 chronic renal failure, the limited ability of the kidney to excrete an increased magnesium load may result in toxic concentrations of the ion in serum. Following the institution of long-term hemodialysis treatment, the major determinant of magnesium balance is the concentration of magnesium in the dialysate. Thus in end-stage renal failure, magnesium concentrations are increased in the serum and red cells of patients, and magnesium retention could be a problem in patients on maintenance hemodialysis. Magnesium seems to be an important factor both for acid gastric secretion regulation (together with Ca2+) and for H. pylori survival and virulence. Therefore, it is important to assess if H. pylori infection is accompanied by variations in the serum magnesium availability of patients under regular hemodialysis.

According to the previously mentioned data concerning the status of serum magnesium in patients on maintenance hemodialysis, this study investigated the probable association of serum magnesium with H. pylori infection in patients with end-stage renal failure undergoing regular hemodialysis treatment.

**PATIENTS AND METHODS**

This cross-sectional study was conducted on patients with end-stage renal disease who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. Patients who used H2 proton pump inhibitors and antibiotics as well as those who had an active or chronic infection during the last month before the study were excluded. All patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating, and belching. Magnesium was measured by a standard kit in all patients. H. pylori specific IgG antibody titer was measured by enzyme-linked immunosorbent assay (ELISA). A titer >10 U/mL was interpreted as positive according to the manufacturer’s instructions. Duration and dose of hemodialysis treatment were calculated from patients’ records. The duration of each hemodialysis session was 4 hours. For statistical analysis, descriptive data are expressed as mean ± SD. Comparison between groups was performed using Student’s t-test. For correlations, a partial correlation test was used. All statistical analyses were performed using the SPSS (version 11.5.00) (SPSS Inc, Chicago, IL). Statistical significance was inferred at *P*<0.05.

**RESULTS**

The total number of patients was 44 (17 women, 27 men), consisting of 34 nondiabetic patients on hemodialysis (13 women, 21 men) and 10 diabetic patients on hemodialysis (4 women, 6 men). Table 1 shows the patients’ data. Mean ± SD of age of the total number of patients was 43 ± 17.6 years. The length of the time patients had been on hemodialysis was 29 ± 34 months (median 17.5 months). The value of serum magnesium of total patients was 2.5 ± 0.41 mg/dL, and the value of serum H. pylori specific IgG antibody titers of the total number of patients was 7.7 ± 10.3 U/mL (median 2 U/mL). In this study population, there was no signifi-
cant difference between the *H. pylori* IgG antibody levels when broken out by gender or diabetic status, as well as no significant difference in serum magnesium levels in regard to gender or diabetic status. A significant positive correlation of anti *H. pylori* IgG antibody with serum magnesium $(r=0.31, P=0.050$; Figure 1) in the total patient population was seen (adjusted for dialysis sessions).

**DISCUSSION**

This study found no significant difference of anti *H. pylori* IgG antibody levels between diabetic and nondiabetic patients on hemodialysis, no significant difference of anti *H. pylori* IgG antibody levels between male and female patients on hemodialysis, as well as no significant difference of serum magnesium between diabetic and nondiabetic patients on hemodialysis, and also between male and female patients on hemodialysis. A significant positive correlation of anti *H. pylori* IgG antibody with serum magnesium in the total patient population was found.

The cation metabolism of the gastric pathogen *H. pylori* is of substantial importance for survival in the hostile and changing environment of the gastric mucosa. Mechanisms involved in maintaining cation homeostasis were shown to be required for effective gastric colonization in animal models. Although the essential biological functions of serum magnesium point toward a 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. The complete growth deficiency in media without serum magnesium supplementation and the drastic serum magnesium requirement in the range of 20 mM displayed by CorA mutants shows that *H. pylori* CorA is essential for serum magnesium acquisition required for survival in low-serum magnesium environments.

These findings underscore the role of *H. pylori* cation metabolism in maintaining metabolic functions and highlight a substantial importance of serum
magnesium acquisition in gastric adaptation. The role of CorA-mediated serum magnesium uptake in *H. pylori* colonization and/or survival in the gastric mucosa is supported by the serum magnesium concentration in human gastric juice, which at 0.7 mM is far below the values required for growth of CorA mutants. Thus, it seems very unlikely that *H. pylori* CorA mutants can persist in the gastric mucosa for extended time periods. These observations indicate that serum magnesium is the dominant CorA substrate.

This study shows the association of serum magnesium with infection of *H. pylori*. As mentioned previously, serum magnesium acquisition by CorA is essential for *H. pylori* in vitro. Because CorA mutants did not grow in media without serum magnesium supplementation, and as serum magnesium is a

### Table 1. Mean ± SD of Patients’ Data

<table>
<thead>
<tr>
<th>Total patients n=44</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>11</td>
<td>80</td>
<td>43 ± 17.6</td>
<td>40.5</td>
</tr>
<tr>
<td>DH* (months)</td>
<td>2</td>
<td>156</td>
<td>29 ± 34</td>
<td>17.5</td>
</tr>
<tr>
<td>Dialysis dose (sessions)</td>
<td>18</td>
<td>1584</td>
<td>300 ± 367</td>
<td>212</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>1.6</td>
<td>3.5</td>
<td>2.5 ± 0.41</td>
<td>2.4</td>
</tr>
<tr>
<td>AntiHP IgG (U/ml)</td>
<td>0.5</td>
<td>34</td>
<td>7.7 ± 10.3</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non diabetics n=34</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>11</td>
<td>80</td>
<td>40.6 ± 17</td>
<td>40</td>
</tr>
<tr>
<td>DH* (months)</td>
<td>2</td>
<td>156</td>
<td>33 ± 37.4</td>
<td>20</td>
</tr>
<tr>
<td>Dialysis dose (sessions)</td>
<td>18</td>
<td>1584</td>
<td>300 ± 408</td>
<td>135</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>1.6</td>
<td>3.3</td>
<td>2.45 ± 0.41</td>
<td>2.4</td>
</tr>
<tr>
<td>AntiHP IgG (U/ml)</td>
<td>0.5</td>
<td>34</td>
<td>7.6 ± 10</td>
<td>2</td>
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<table>
<thead>
<tr>
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<th>Minimum</th>
<th>Maximum</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
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<td>Age (years)</td>
<td>27</td>
<td>79</td>
<td>52 ± 16.6</td>
<td>55</td>
</tr>
<tr>
<td>DH* (months)</td>
<td>6</td>
<td>24</td>
<td>14.4 ± 6.7</td>
<td>12</td>
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<tr>
<td>Dialysis dose (sessions)</td>
<td>54</td>
<td>216</td>
<td>120.5 ± 57</td>
<td>99</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>2</td>
<td>3.5</td>
<td>2.46 ± 0.48</td>
<td>2.3</td>
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<tr>
<td>AntiHP IgG (U/ml)</td>
<td>0.5</td>
<td>33</td>
<td>8.2 ± 11.7</td>
<td>1.5</td>
</tr>
</tbody>
</table>

DH=duration of hemodialysis treatment
AntiHP=anti *Helicobacter pylori*
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.\(^{21,22}\) Patients on hemodialysis are more prone to have a high magnesium levels, which is noted in this study as well as a previous one.\(^{13}\) Magnesium also seems to be an important factor both for acid gastric secretion regulation (together with Ca\(^{2+}\)) and for \textit{H pylori} survival and virulence.\(^{14}\)

In this regard, Koga conducted a study to determine whether the magnesium ion in water could influence the colonization of \textit{H pylori} in 2-week-old miniature pigs. Koga found that magnesium ion in drinking water is essential for the colonization of \textit{H pylori} in the pig stomach.\(^{23}\) It is believed that \textit{H pylori} CorA transports nickel and cobalt in addition to serum magnesium, and that serum magnesium is the dominant CorA substrate because the CorA mutation affected neither cobalt and nickel resistance nor nickel induction of urease in \textit{H pylori}.\(^{14,19}\)

In conclusion, high serum magnesium levels, and probably its higher concentration in the gastric mucosa, might facilitate the colonization of \textit{H pylori} in the stomachs of patients on hemodialysis. Further investigation is needed to define the clinical significance of this finding.

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**REFERENCES**


