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Association of *Helicobacter pylori* specific IgG antibody with serum magnesium levels in peritoneal dialysis patients

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ABSTRACT

Introduction: Few studies have reported the relationship between serum magnesium and *Helicobacter pylori* infection in chronic kidney disease (CKD) and patients receiving dialysis.

Objectives: In this study, we aimed to test, the relationship between serum magnesium (Mg) level and *H. pylori* infection in CKD patients receiving peritoneal dialysis.

Patients and methods: Around 40 patients were evaluated through the study. Serum magnesium levels and *H. pylori* specific IgG antibody levels were assessed.

Results: The mean serum magnesium level was 3.00 ± 0.36 mg/dL. No significant difference was seen in serum Mg level between positive and negative groups of *H. pylori*. No correlations were reported between *H. pylori* IgG titers with age, serum Mg, Ca, P, parathyroid hormone (PTH), vitamin D, albumin, urea, creatinine (Cr) and plasma hemoglobin ($P > 0.05$).

Conclusion: In this study no correlation between serum magnesium levels and *H. pylori* specific IgG antibody was detected. We believe that this is the first study evaluating the relationship between serum magnesium level and *H. pylori* infection in peritoneal dialysis patients. More and larger clinical investigations are required to consider the conflicting results of studies regarding the association of serum magnesium and *H. pylori* in patients undergoing dialysis.

Implication for health policy/practice/research/medical education:

In a study on 40 peritoneal dialysis patients, no correlation between serum magnesium levels and *Helicobacter pylori* specific IgG antibody was detected. We believe that this is the first study evaluating the association between serum magnesium level and *H. pylori* infection in peritoneal dialysis patients. More and larger clinical studies are required to consider the conflicting results of studies regarding the association of serum magnesium and *H. pylori* in patients undergoing dialysis.

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Introduction

Helicobacter pylori infection is a major worldwide health issue, more than half of the world's population are affected by *H. pylori* (1). *H. pylori* is the most common chronic bacterial infection of human gastrointestinal tract (2). It has been associated with various gastric and extra-gastric disorders. *H. pylori* infection is an important cause of gastritis, peptic ulcer and gastric cancers (3,4). *H. pylori* is also associated with various extra-gastric disorders such as iron deficiency anemia, idiopathic thrombocytopenic

purpura (ITP) and also colonic, cardiovascular, hepatobiliary and pancreatic diseases (5,6).

Hemodialysis and chronic renal failure (CRF) patients often complain of various gastrointestinal complications such as nausea, dyspepsia, appetite loss, epigastric discomfort, peptic ulcers and gastrointestinal bleeding. These symptoms decrease the quality of life. Additionally, gastrointestinal complications may alter patients' nutrition status, effecting the morbidity and mortality rate (7).

Around two million people (prevalence: 296 per million

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people) receive dialysis worldwide (8) and the proportion of the patients increase 7% annually (9). The prevalence of *H. pylori* infection in end-stage renal disease (ESRD) and dialysis patients have found conflicting results. The prevalence of *H. pylori* infection in CRF patients has been reported as high as 64% and significantly higher in dialysis patients compared to normal controls (10). However, other studies do not support the association of *H. pylori* infection with chronic kidney disease (CKD) or dialysis. Some studies have hypothesized a protective effect of long-term treatment with dialysis on infection by *H. pylori* (7,11).

Helicobacter pylori is a gram-negative bacterium which can persistently colonize the human stomach. For successful colonization, the pathogenic bacteria sense subtle changes in their environment such as the low pH characteristic of the gastric niche, alterations in nutrient availability including divalent cations, fluctuations in osmolality, and the presence of the human immune system and rapidly respond with alterations in their transcriptional profile (12,13).

Magnesium (Mg) is the fourth most abundant cation in human body. Mg is predominantly intracellular and about 1% of body Mg²⁺ presents in the extracellular fluid. The normal serum level of Mg is usually in the range of 1.7-2.2 mg/dL. Mg metabolism and excretion (which are predominantly renal) are impaired in kidney failure and dialysis patients. When glomerular filtration rate falls below 30 mL/min, Mg excretion decreases and serum Mg level increases subsequently (14). Parathyroid hormone (PTH) and vitamin D affect intestinal Mg absorption, and also its bone and renal re-absorption.

Mg is an essential cofactor for several enzymes in human body and also an essential element for pathogens such as *Helicobacter*. Some recent studies have shown an association between *H. pylori* infection and serum Mg level in ESRD patients (15).

Objectives

In this study we have assessed the association between serum Mg level and *H. pylori* infection in ESRD patients receiving peritoneal dialysis.

Patients and Methods

Study population

This cross-sectional study was conducted on a group of ESRD patients undergoing peritoneal dialysis referred to Shafa peritoneal dialysis center. Patients on peritoneal dialysis for at least 6 months were enrolled in the study. Patients receiving antibiotics for *H. pylori* treatment, antacids, proton pump inhibitors and nonsteroidal anti-inflammatory drugs (NSAIDs) during the past 2 months were excluded from the study. The results of examination drug administration and medical history of patients was recorded.

Biochemical analysis was assessed including Mg, Ca, P, albumin, PTH, 25-hydroxyvitamin D [25(OH)D], serum urea and creatinine (Cr).

Serum *H. pylori* specific IgG antibody was measured using ELISA method. A titer ≥ 5 U/mL was interpreted as positive according to the manufacturer's instructions.

Ethical issues

1) The research followed the tenets of the Declaration of Helsinki and its later amendments; 2) informed consent was obtained; and 3) This study was approved by the Ethics Committee of Shahid Beheshti University of Medical sciences.

Statistical analysis

Statistical analysis was performed by SPSS software (version 22); results were given as mean \pm standard deviation (SD). Comparison between groups were evaluated by the independent sample *t* test and Mann-Whitney U test. Statistical significance was considered as *P* value of less than 0.05.

Results

In this cross-sectional study 40 peritoneal dialysis patients were included (18 male, 22 female). Patients' ages ranged between 16–80 years with the mean (SD) of 53.3 ± 14.5 years (Table 1). Serum *H. pylori* specific IgG antibody was positive in 18 patients (45%). Serum Mg level was in the range of 2.3 to 4.1 mg/dL with the mean (SD) of 3.00 ± 0.36 mg/dL. The mean (SD) Mg level in *H. pylori* positive

Table 1. Demographic and biochemical data of patients

Parameter	Minimum	Maximum	Mean	Median
Age (y)	16	80	53.35 \pm 14.57	50
<i>H. pylori</i>	0.5	100	25.43 \pm 36.87	4
Mg (mg/dL)	2.3	4.1	3 \pm 0.36	3
Calcium(mg/dL)	6.8	11.9	9.69 \pm 0.92	9.6
Phosphorus (mg/dL)	3	8	4.91 \pm 1.05	4.85
Vit D (ng/mL)	3	50	13.44 \pm 9.88	13
Alb (g/dL)	3.4	5.2	4.16 \pm 0.51	4.1
IPTH (pg/mL)	28	1700	206 \pm 292.54	123
Hb (g/dL)	7.3	16.7	11.68 \pm 1.91	11.6
Urea (mg/dL)	39	181	107 \pm 34.51	110
Creatinine (mg/dL)	3.2	17.8	8.74 \pm 3.7	7.8

patients was 2.98 ± 0.31 mg/dL, and 3.01 ± 0.36 mg/dL in *H. pylori* negative patients. No significant difference of Mg level between *H. pylori* specific IgG antibody positive and negative groups was detected ($P=0.8$) (Table 2). There was not association of *H. pylori* specific IgG antibody titers with age, serum mg, serum Ca, P, PTH, vitamin D, Alb, urea, Cr and hemoglobin (Figure 1). A positive significant correlation of serum Mg with serum Cr levels was found ($r=0.4$, $P=0.009$).

Discussion

In this study no correlation between *H. pylori* titer and serum Mg levels was seen. This study showed no relationship between serum Mg level and *H. pylori* infection.

In a study conducted by Nasri et al, a significant positive correlation of helicobacter IgG antibody and plasma Mg in 44 ESRD patients undergoing hemodialysis was detected (15).

Likewise, Baradaran et al found a significant negative correlation between serum *H. pylori* specific IgG antibody and serum Mg and serum iPTH levels through a research on 72 kidney transplanted patients. They found a positive correlation between serum *H. pylori* IgG and Cr clearance (16). In another study, Baradaran et al investigated 94 CKD patients with type 2 diabetes mellitus. In their study, no significant association between serum *H. pylori* specific IgG antibody titers and serum Mg levels, even among individuals with Cr clearance below 40 mL/min was detected. According to their studies, they hypothesized that high levels of serum Mg, and probably the higher concentration of Mg in gastric mucosa might aggravate helicobacter colonization in the stomach of patients undergoing hemodialysis, though not in individuals with various stages of CKD who were not receiving hemodialysis (17).

In a study by Hafizi et al, a group of stable kidney transplanted patients were assessed. Serum Mg level in the *H. pylori* positive group was significantly higher than patients negative for *H. pylori* ($P=0.005$), suggesting a positive relationship between serum Mg and *H. pylori* infection in this study too (18).

Assessing some serum trace element levels in otherwise healthy children with *H. pylori* infection, Öztürk et al found significant lower serum Mg levels in *H. pylori* positive children compared to healthy controls (19). Mg is an important cofactor for many enzymes and has an important role in principle biochemical pathways essential for bacterial growth and survival. Pathogenic bacteria express various uptake systems to overcome the lack of mg in the environment. The transmembrane protein CorA is essential for Mg^{2+} acquisition required for *H. pylori* survival in low-Mg environment, while *CorA* mutants did not grow in media without Mg^{2+} supplementation (20). It seems that *H. pylori* may alter the host electrolyte (Ca^{2+} and Mg^{2+}) concentration, by increasing cytosolic free Ca^{2+} concentration and activation of parietal cell protein kinase

Table 2. Demographic and biochemical data of patients infected with *Helicobacter pylori* and patients negative for *Helicobacter pylori*

Parameter	Mean value (<i>H-pylori</i> positive)	Mean value (<i>H-pylori</i> negative)	P
Age (y)	55 ± 12.9	52 ± 16	0.524
Serum magnesium (mg/dL)	2.98 ± 0.31	3.01 ± 0.36	0.797
Serum creatinine (mg/dL)	8.31 ± 3.79	9.09 ± 3.79	0.522
Serum urea (mg/dL)	110.33 ± 34.07	104.41 ± 35.437	0.596
Serum phosphorus (mg/dL)	5.09 ± 0.83	4.76 ± 1.21	0.324
Calcium (mg/dL)	9.5±0.44	9.8±1.8	0.45
Vitamin D (ng/mL)	10.9±8	15.4±10.8	0.13
Alb (g/dL)	4.2±0.53	4.1±0.49	0.65
iPTH (pg/mL)	161±156	243±368	0.38
Plasma hemoglobin (g/dL)	12.03 ± 2.41	11.40 ± 1.39	0.309

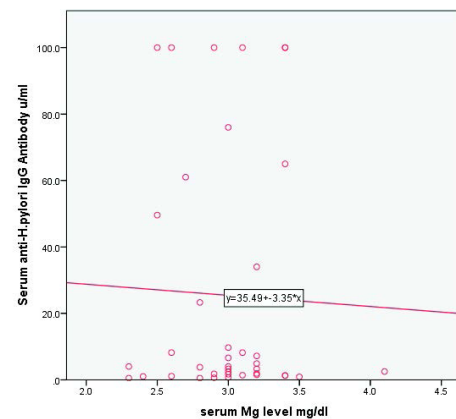


Figure 1. No significant correlation was found between serum *H. pylori* IgG and serum magnesium level.

(PKC), through the bacterial synthesis of the fatty acid MOA (21).

Mg is also essential for eukaryotic cells. It is vital for numerous physiological functions. Particular Mg concentrations can modulate signaling processes and acid secretion function in parietal gastric cells (presumably by influencing the cellular calcium homeostasis) (22).

Conclusion

In the current study no association of serum Mg levels with *H. pylori* infection was detected. Serum Mg level reflects the circulating level of Mg^{2+} and it is a poor indicator of the intracellular Mg availability (23,24). It is possible that Mg exchange rate between serum and cellular compartments does not allow reaching the steady state in a short period (21). Hence, more studies are recommended to assess the effect of serum Mg on *H. pylori* infection in renal failure patients receiving dialysis in order to offer a hypothesis for *H. pylori* eradication.

Limitations of the study

The major limitation of this study is small proportion of patients participating in the study. Larger studies are required to assess the effect of serum Mg on *H. pylori* infection in renal failure patients receiving peritoneal dialysis.

Authors' contribution

AA and RT conceived the study and contributed to reagents and tools. AA and SMK conducted the research. AA and MB analyzed the data and drafted the final manuscript. All authors read, revised, and approved the final manuscript.

Conflicts of interest

There were no points of conflicts.

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