Helicobacter pylori infection and serum magnesium in kidney disease; current concepts

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ABSTRACT

One of the problems of renal disease patients, especially patients undergoing dialysis, is gastrointestinal complications caused by *Helicobacter pylori* infection. *H. pylori* has still high prevalence in most populations. It is estimated that about half of the world population is infected with this infection and it can change levels of most micronutrients such as magnesium. Different studies demonstrate that *H. pylori* may affect the metabolism of magnesium in renal failure. The present paper investigated the association of serum magnesium level with *H. pylori* infection. Nevertheless, it should be more evaluated by researchers and still many studies are necessary to confirm this issue.

Review

Introduction

Helicobacter pylori is a spiral, highly mobile, gram-negative, and urease-positive bacterium that involves gastric mucosa. Several studies suggest that the bacterium may be one of the microorganisms that cause numerous complications and consequences. One of the most abundant infections is gastrointestinal infection in most people (more than 80%) (1,2). Considering specific morphology and very fast growth of *H. pylori*, it penetrates into the viscous mucus layer through pH-neutral conditions (Figure 1) (3). It can be inactive in difficult conditions. Various enzymes of *H. pylori* such as protease produce a high amount of osmosis that modifies the gastric mucosa and reduces the ability of acid to release more in the mucus (4). *H. pylori* infection is transmitted through various ways. Data from recent research show that transmission of infection is through consumption of contaminated water and food, interpersonal, contact with the stool or stomach secretion of infected people and

even parental. The risk of infection is higher in populated societies, poor people, and low health conditions, therefore sanitation is the effective factor in preventing the infection (1). *H. pylori* infection is a main pathogenetic factor for gastric cancer, peptic ulcer disease, chronic gastritis, and other disorders. The infection can alter the homeostasis of minerals and vitamins. It is known that *H. pylori* infection has a direct relationship with the reduction of levels of several micronutrients like cobalamin, vitamin A, C, E and B12, copper, and folic acid (4-6). In addition, the infection leads to iron-deficiency anemia through iron consumption, decreasing ascorbic acid level, and bleeding due to micro-erosions (7). Recently, multiple studies have been indicated an association between *H. pylori* infection and serum magnesium in renal disease patients that the present study addresses this issue.

Materials and Methods

In the review, we used a variety of sources including,

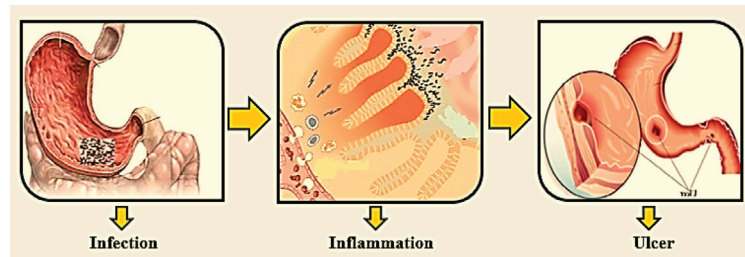*Corresponding author: Parto Nasri, Email; Parto.nasri@gmail.com

Figure 1. *Helicobacter pylori* infection.

PubMed/Medline, Google Scholar, Science Direct, Web of Science, Embase, EBSCO, Directory of Open Access Journals (DOAJ), and Scopus. The search was performed by using combinations of the keywords; Helicobacter pylori infection, serum magnesium, hypomagnesemia, renal disorders, hemodialysis, proton-pump inhibitors, nephrotoxicity, chronic kidney disease, end-stage renal disease, and renal disease patients.

Magnesium level in different diseases

Magnesium, as an intracellular cation and cofactor for over 900 enzymes, involves in important cellular processes, such as energy production, DNA transcription, DNA structure maintenance, regulation of cell proliferation, differentiation, apoptosis, and bone metabolism. The ion affects the function of muscles, blood vessels, bones, nervous system, pancreas, and kidneys (8-10). The normal range of serum magnesium concentration is 1.8 to 2.4 mEq/L. Magnesium is mainly found in legumes, nuts, green vegetables, seeds, and even water. Therefore, the consumption of a diet of magnesium-rich will help to meet the daily requirement of magnesium (11). In general, the average daily intake of magnesium in a healthy person is 12 mmol/day. About 2 mmol/day of magnesium is excreted in the gastrointestinal tract, bile, pancreas and intestinal juices (12). Details of magnesium metabolism have been demonstrated in Figure 2. The different factors such as storage in skeletal muscle and bone, intestinal uptake, and renal excretion play a vital role in magnesium balance. Serum level less than 1.5 mEq/L is called hypomagnesemia. Hypomagnesemia is related to malnutrition, alcoholism, malabsorption, and renal disease (11). It may occur by numerous medications including proton-pump inhibitors (PPIs), aminoglycoside antibiotics, cisplatin, thiazide diuretics (13). The relationship between low-level of magnesium and the prevalence of diseases as atherosclerosis, insulin resistance, type 2 diabetes, high blood pressure, and cardiovascular disease has been proven. However, hypomagnesemia accelerates immune stress response in the animal model (14). Low-serum magnesium increased the mortality rate in patients with cardiovascular disease and accelerated subclinical atherosclerosis by enhancing artery intima thickness. Although this relationship requires more research in the future (15). Serum level higher than 2.5 mEq/L is called hypermagnesemia. Hypermagnesemia is less common and can be the result of the excessive intake of magnesium, renal failure, depression, milk-alkali syndrome, and Addison's disease (12). Magnesium, as a cofactor, interferes with glucose metabolism and plays a main role in phosphorylation reactions. Hypomagnesemia has no positive effect on impairing insulin-mediated glucose uptake, glucose-induced insulin secretion, and post-receptor signaling of insulin. Magnesium can regulate
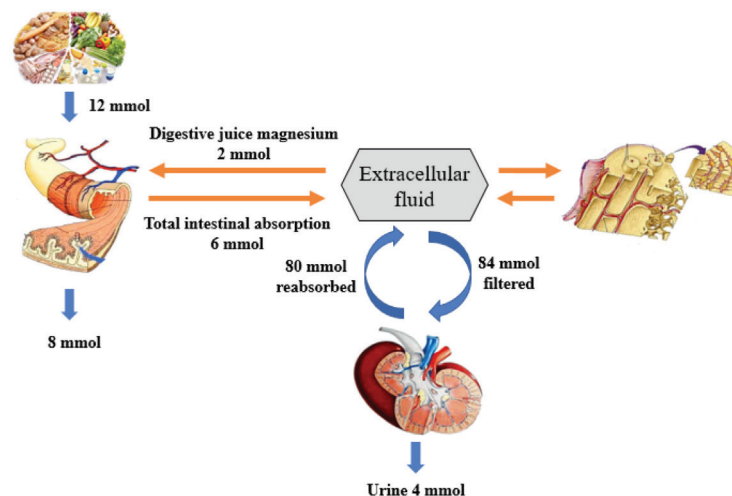

Figure 2. Magnesium distribution in the body.

lipid metabolism and affect lipid parameters like LDL-cholesterol, HDL-cholesterol, serum total cholesterol, and triglyceride. It has been suggested a kind of relationship between hypomagnesemia and lipid parameters (16). Nasri et al in a cross-sectional study evaluated serum creatinine, cholesterol, HDL-C, triglyceride, serum lipoprotein (a), glycosylated hemoglobin (HgbA1c), and serum magnesium to detect the correlation between serum magnesium and lipids profile in diabetes mellitus patients. This study was done on 122 patients with mean age 63 years. According to the results of this study, the mean serum magnesium level and creatinine clearance were 2 mg/dL and 64 cc/min, respectively. In this study, a significant reverse relationship was observed between serum magnesium level and serum LDL-C, serum cholesterol, and also with age of patients. Furthermore, a positive correlation of serum magnesium with serum creatinine was confirmed. Although, there was no significant association between serum magnesium level and HDL-cholesterol, triglyceride, serum lipoprotein (a), albumin, and serum HgbA1c (17).

One of the most effective medicines utilizable to contrast with different types of cancers, such as ovarian, bladder, head and neck cancer is cisplatin. Long-term use of this drug may lead to ototoxicity, myelosuppression, and especially nephrotoxicity. The complications of the use of this medication are renal tubule dysfunction, reduced glomerular filtration rate, and acute or chronic kidney failure. Cisplatin induces hypomagnesemia in treated head and neck cancer patients which eventually contribute to nephrotoxicity. A study was conducted to evaluate the effect of magnesium supplements on cisplatin-induced nephrotoxicity in cisplatin-treated head and neck cancer patients. The results of this study demonstrated that reduced creatinine clearance in the magnesium-supplemented and crystalloid-only (after two courses) groups was 4.9 mL/kg/min and 15.0 mL/kg/min respectively and magnesium-supplemented regimen inhibits cisplatin-induced nephrotoxicity in head and neck cancer patients (18).

Magnesium level in renal disease patients

Kidney disorders are recognized as one of the prevalent diseases in the general population, thus the treatment and prevention of them have significant clinical importance. Several factors are involved in causing renal failure including side effects of some medications (19). The kidneys have an essential role in maintaining magnesium balance (12). Magnesium homeostasis can change in renal disease especially chronic kidney disease (CKD) and end-stage renal disease (ESRD) (13). Additionally, it is identified that serum magnesium level alters in patients with ESRD undergoing dialysis, acute renal failure, continuous ambulatory peripheral dialysis, and rhabdomyolysis. Some studies suggested that urinary excretion of magnesium may reduce in stone formers

which can help to the pathogenesis of renal calculi (12).

It is reported that low-serum magnesium leads to high cardiovascular mortality and increases the progression of kidney disorders in 191 diabetics with CKD (20). In addition to the mentioned studies, Parvizi et al demonstrated that magnesium has a protective effect on renal function in diabetic rats. Magnesium sulfate administration decreased creatinine, serum BUN, and blood glucose and also improved oxidative damages and renal disorder (21).

Lipid disorders are one of the serious problems of population since kidney dysfunction is a known factor in the occurrence of this disorder. Dyslipidemia is recognized as a major cause of atherosclerosis progression in hemodialysis patients. A study was carried out on 36 hemodialysis patients to show the correlation of serum magnesium with factors involved in the progression of dyslipidemia in hemodialysis patients including triglyceride, HDL-C, LDL-C, cholesterol, serum lipoprotein (a), intact parathyroid hormone (PTH), magnesium, phosphorus, and calcium. At the end of the study, there was no relationship between intact PTH, serum calcium, and Ca×P product with lipids levels. However, a positive relation was identified between serum magnesium with triglyceride level and lipoprotein (a). Additionally, magnesium could modify enzymes involved in lipoprotein synthesis and triglyceride metabolism (22).

Proton- pump inhibitors (PPIs) are one of the most common treatments for all diseases associated with gastric acid. Recently, there are reports of hypomagnesemia caused by the consumption of PPIs, which are often due to reduced magnesium gastrointestinal reabsorption. Although, the prevalence of hypomagnesemia following PPIs intake is still unclear. PPIs may alter serum magnesium level in hemodialysis patients that many studies should be conducted to clarify the association between PPIs and magnesium levels in these patients. About this issue, Nakashima et al conducted a study on 1189 hemodialysis patients. Biochemical factors such as albumin, creatinine, alkaline phosphatase, potassium, magnesium, calcium, phosphorus, blood urea nitrogen, hemoglobin, C-reactive protein, and intact PTH were measured. The results showed that 104 of the 1189 HD patients have hypomagnesemia. The mean serum magnesium levels were significantly less in PPI consumers group than H2 receptor antagonists consumers group or patients receiving no anti-acid drugs (23).

Erectile dysfunction is the prevalence among elderly patients. It has been suggested that hypomagnesemia affects erectile dysfunction in the elderly with CKD. Toprak et al evaluated the relationship between erectile dysfunction and hypomagnesemia in a cross-sectional study on of 372 patients with CKD aged 65–85 years and reported that erectile dysfunction causes hypomagnesemia in elderly patients with reduced kidney function (24).

A different study on gene mutations effect and

magnesium level identified that mutations in tight-junction gene claudin 19 (CLDN19) affected magnesium homeostasis and high expression of CLDN19 induces excretion of renal magnesium in patients with renal failure (25).

The relation of *Helicobacter pylori* infection with serum magnesium level in renal disease patients

Helicobacter pylori infection can alter the metabolism of some mineral and trace elements including magnesium in children and the lack of micronutrients induces the progression of many diseases (5). One of the causes of the presence of gastrointestinal complications in patients on hemodialysis is *H. pylori* infection. However, more the occurrence of the infection in these people is still unclear and it may be interpreted as being a result of urea concentration in gastric secretion or uremia which facilitates incidence of infection (26). Magnesium is an important mineral that participates in the reaction and process of the human body. Different evidence suggests that *H. pylori* infection can alter the level of magnesium in renal disease patients. For example, a survey of 44 hemodialysis patients, including 34 nondiabetics and 10 diabetics with ESRD illustrated a significant relationship between magnesium level and *H. pylori*. It has been exhibited that, high plasma level of magnesium leading to increased *H. pylori* activity in hemodialysis patients (27). Additionally, a study in 2005 reported the correlation between *H. pylori*-specific IgG antibody titers and magnesium levels in the stomachs of 44 hemodialysis patients (10 diabetics and 34 nondiabetics). The result of this study was revealed that colonization of *H pylori* may result from the higher concentration of magnesium in the gastric mucosa (28*)*. Hafizi et al evaluated the association between serum magnesium and *H. pylori* infection in 50 patients with kidney transplant and reported that serum magnesium was more in positive *H. pylori* patients than negative *H. pylori* patients. No significant difference observed in serum alkaline phosphatase, intact PTH, calcium, albumin, and even body mass index (BMI) between men and women (29). The findings of another study in 94 patients with type-2 diabetes mellitus with different glomerular function rates (GFRs) was in contrast with previous evidence. In this study, no significant difference detected between serum magnesium and *H. pylori* infection among T2DM patients with GFR below 40 mL/min (30). The results of study conducted by Baradaran et al on the relationship between different demographic and biochemical parameters and serum *H. pylori* IgG antibody titers in 72 renal transplants patients, (consisted of 47 males and 25 females) showed no significant association between *H. pylori* IgG antibody titers and magnesium, calcium, intact PTH, albumin, alkaline phosphatase levels, phosphorus, serum leptin, BMI, and age in women and men. In addition, a significant negative correlation was reported between serum *H. pylori* IgG Ab titer and magnesium and intact PTH while the correlation between *H. pylori* IgG Ab titer and creatinine clearance was significantly positive (31). Hyperhomocysteinemia is a main risk factor for atherosclerosis and related to changes in vascular morphology, loss of vessels endothelial function that activates the pathway of coagulation and formation of thrombosis (32). A study carried out on 39 patients under hemodialysis revealed that *H. pylori* infection can affect serum homocysteine in hemodialysis patients, although is suggested more research on this association (33). A recent study of the literature on this matter in an animal model found that the combination of bismuth and magnesium granules can clear *H. pylori* infection in KM mice by inhibition of associated inflammation factors such as IL-8 and TNF-α. on the other hand, *H. pylori* clearance rates in compound bismuth and magnesium granules group was 60.0%. Additionally, the compound improved gastric mucosal injury due to *H. pylori* infection (34). Savas et al conducted a study on 64 endoscopic findings of renal transplanted patients and investigated the prevalence of *H. pylori* infection was less in chronic renal failure patients than in the normal people since agents other than *H. pylori* involved in the occurrence of esophagogastroduedenal mucosal lesions (35). Rasmi et al surveyed the role of duration HD on the prevalence of *H. pylori* infection and concluded that the prevalence of the infection is higher in patients on long-term HD duration (26). A cross-sectional study conducted on 40 ESRD undergoing peritoneal dialysis patients including 18 males and 22 females with a range of age 16-80. Patients were dialyzed for at least 6 months and then analyzed for biochemical factors such as albumin, creatinine, serum urea, calcium, phosphorus, magnesium, 25-hydroxyvitamin D, PTH, and serum *H. pylori* specific IgG antibody. Antibody titer was positive in 45% of patients. No significant difference appeared between magnesium level and *H. pylori* specific IgG antibody. Although the positive relationship serum magnesium with serum creatinine levels was quite evident, there was no association between *H. pylori* specific IgG Ab titer and albumin, creatinine, serum urea, calcium, phosphorus, magnesium, 25-hydroxyvitamin D, PTH, and age (36).

Conclusion

Recent studies suggest that the prevalence of H. pylori is still evident in most countries and many people are affected by this infection. The result of the review revealed the association between serum magnesium level and H. pylori infection in renal disease patients. However, it should be more analyzed by researchers and many studies are necessary to confirm this issue.

Authors' contribution

BY prepared the primary draft and conducted search

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strategy. PN edited the paper. All authors read and signed the final paper.

Conflicts of interest
The authors declare that they have no competing interest.

Ethical considerations
Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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