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Prevalence of Helicobacter Pylori in Long-Term Dialysis Patients

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Abstract

Background and Aims: Helicobacter pylori (H. pylori) has been reported to play an important role in the development of gastritis and gastric ulcer. Here we report the prevalence of H. pylori infection in 87 hemodialysis (HD) patients.

Methods: In the present study we investigated the prevalence of H. pylori infection in 87 HD patients by three methods: serum anti-H. pylori IgG, H. pylori stool antigen (HpSAg) and Urease Breath Test (UBT). All the three methods confirmed each other and when 2 out of the 3 methods showed positive findings, patients were regarded as H. pylori -positive. We also assessed the relationship between clinical factors, serum urea nitrogen, creatinine levels, and duration of dialysis, age and gender with the prevalence H. pylori in these patients.

Results: Eighty seven HD patients (48 male and 39 female) with the mean age of 54.4±16.7 years old and mean dialysis duration of 36.2±33.5 months were assessed. Fifty five (63.2%) of them had dyspepsia. The prevalence of H. pylori infection was 44.8%. Multivariate logistic regression analysis revealed the serum urea nitrogen level was significantly associated with H. pylori prevalence (P=0.03, 95% CI: 1.4-35.8). High serum urea nitrogen seems to correlate with a high prevalence of H. pylori infection. The prevalence of H. pylori infection was low in young patients, but high in elderly patients (P=0.04, 95%CI: 0.97-10.3). There was no significant correlation between gender, duration of dialysis, serum Cholesterol, Triglyceride, creatinine, Hemoglobin, albumin, calcium and phosphor and H. pylori infection in these patients.

Conclusions: Among dialysis patients, the proportion of H. pylori-positive patients was not low. Dialysis treatment may influence H. pylori infection.

Keywords: Hemodialysis, End-Stage Renal Disease, Helicobacter Pylori, Prevalence.

Introduction

Patients with chronic renal failure (CRF) present with various clinical symptoms, including nausea, dyspepsia, loss of appetite, epigastric discomfort, and heartburn, as well as histological, physiological, and functional disorders of the gastrointestinal system (1, 2). These symptoms not only decrease the quality of life, but also may affect their nutrition status, thus contributing to the development of malnutrition, which is a potent predictor of morbidity and mortality in patients with CRF. About 25–75% of patients with CRF undergoing dialysis suffer from a number of gastrointestinal lesions and complications such as: gastric erosions, Peptic ulcer disease, angiodysplasia, and gastrointestinal bleeding (3-10).

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Dialysis patients may have a higher risk of gastric mucosal damages compared with individuals with normal renal function (11, 12) by hypergastrinemia (13) high ammonia levels (14) and enhanced inflammation. It is generally known that Helicobacter pylori (H. pylori) plays an important role in the pathogenesis of gastritis or gastric ulcer (15). H. pylori has high urease activity, and produces ammonia in the presence of urea. In patients with end-stage renal disease (ESRD), blood urea levels are high, and gastric juice urea nitrogen levels are also high (16). H. pylori infection promotes the production of a high level of ammonia (17). Ammonia is considered to be an etiological factor involved in gastric mucosal disorders (18). Then, gastrointestinal symptoms in dialysis patients might be caused not only by H. pylori infection, but also by high urea levels, decline of gastrointestinal motility, and amyloid protein deposition. Several studies have investigated H. pylori; however, many aspects remain to be clarified with regard to H. pylori infection in patients with ESRD, especially in patients receiving long-term dialysis. In dialyzed patients, the incidence of ulcer is similar to that in patients who do not receive dialysis (5, 6). Also has been reported that the prevalence of H. pylori infection is lower in dialyzed patients (19-20).

In this study, we investigated the relationship between the incidence of H. pylori infection by measuring H. pylori antibody levels and H. pylori stool antigen (HpSAg) and Urease Breath Test (UBT) in patients with ESRD who had dyspepsia.

Materials and Methods

The present study included 87 patients with end-stage of renal disease (ESRD) who had been dialyzed in two HD centers (Valiasr & Beheshti hospitals) in Zanjan, one of provinces of Iran, between 2008 and 2009. Out of eighty-seven ESRD patients, 55 patients had dyspepsia (27 females and 28 males, mean age: 54.4±16.7 years). And among 87 ESRD patients, 39 patients (44.8%) were proved to be infected with H. pylori (21 male and 18 female; mean age 59±16.2 years) and 48 patients (55.2%) were uninfected (27 male, 21 female; mean age 51±17.3 years). To confirm H. pylori infection three types of tests were used: Anti H. pylori serology, H. pylori stool Ag (HpSAg) and urease breath test (UBT). If two tests out of these three tests came out positive, the patients were considered infected.

Exclusion criteria included a history of previous treatment for H. pylori, use of any of the proposed antibiotics in the previous six months as well as non-cooperation for doing UBT. All of the patients gave informed consent before their initial evaluation for upper GI tract symptoms. Standard dialysis was performed for 4 hours, three times a week. The mean duration of dialysis was 36.2± 35.6 months (range: 1-192 months).

A blood extraction was performed during the dialysis and patients were asked to take a stool sample for the study. Both serum and feces were immediately frozen at -70ºC until analysis.

Sera were tested for H. pylori antibodies by a commercial ELISA test in accordance with the manufacturer's instructions. Patients with an antibody titer of 1.8 or more were regarded as positive for H. pylori.

An enzyme-linked immunosorbent assay (ELISA) using polyclonal antibodies Premier Platinum HpSAg was also performed in accordance with the manufacturer's specifications.

UBT was also performed using the modified European protocol.

Statistics

For statistical analysis SPSS software version 17 was used. The Chi-square test and the student's t-test were used where appropriate. Parametric data are presented as mean±s.d. and nonparametric data as median (25–75% quartiles). All P-values were two sided, and P-values <0.05 were considered statistically significant.

Results

Eighty seven HD patients, including 48 male and 39 female with mean age of 54.6±16.7 years on dialysis for 36.2 months were selected. Thirty nine patients were diagnosed with H. pylori infection (21 male and 18 female; mean age 59±16.2 years range) and 48 (27 male, 21 female; mean age 51±17.3 years, range) were found uninfected according to the serology, stool antigen test or 13 C-urea breath test.

With respect to age, 34.2 % of HD patients were less than 50 years old had H. pylori. The percentage in the patients at the range of 50 to 79 years was 50% and, 75 percent of the patients older than 80 years of age were positive for H. pylori.

The prevalence of H. pylori infection was low in young patients, but high in elderly patients (P= 0.04, 95%CI: 0.97-4.3).

With respect to serum urea nitrogen, results indicate that high serum urea nitrogen seems to correlate with a high prevalence of H. pylori infection. Multivariate logistic regression analysis revealed that the serum urea nitrogen level was significantly associated with H. pylori prevalence (P = 0.03, 95%CI: 1.4-35.8).

There was no significant correlation between gender, duration of dialysis, serum cholesterol, triglyceride, creatinine, hemoglobin, albumin, calcium and phosphorus and H. pylori infection in these patients (Table 1).

Discussion

Helicobacter 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 (21-23).

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 not low in these group patients.

H. pylori infection between patients with renal failure and patients without chronic renal failure

In Japan, Tokushima performed biopsies, and reported that there was no significant difference in the proportion of H. pylori –positive patients between

Table 1. Demographic and laboratory parameters between H. pylori positive and negative HD patients

Variables	H. pylori positive N=39 (44.8%)	H. pylori negative N=48 (55.2%)	P value
Gender (F/M)	18/21	21/27	0.83
Age (years)	59±16.2	51±17.3	0.04
Duration of dialysis (months)	43.1±35.4	30.6±28.9	0.1
Dyspepsia	25	30	0.52
Serum albumin	4.1±0.5	4.2±0.6	0.5
Triglyceride	158±76	166±83	0.7
Cholesterol	175±102	179±98	0.6
BUN	94±47	75±32	0.03
Creatinine	10±2.9	9.9±3.5	0.9
Hemoglobin	10.4±2.1	10.3±1.9	0.8
Calcium	9.5±1	9.5±1.1	0.8
KT/V	1.15±0.3	1.29±0.2	0.1

patients with renal failure and patients without chronic renal failure (24). Recently, associations between patients with CRF and the prevalence of H. pylori infection have been reported (17, 19, 25-27).

Association H. pylori with progression of renal dysfunction

Although there is no significant evidence that H. pylori infection is directly associated with progression of renal dysfunction, patients receiving chronic HD and continuous ambulatory peritoneal dialysis (CAPD) often incur gastrointestinal troubles over their long treatment period (3-9).

Dialysis patients frequently develop gastric/duodenal ulcers (8). If H. pylori is involved in the development of ulcers in patients with renal failure, as is frequently reported, eradication therapy should be aggressively performed (22, 28). However, few studies have reported H. pylori infection in long-term dialysis patients. The relationship between H. pylori and ulcers in patients with renal failure is unclear.

H. pylori infection between the dialysis patients and healthy adults

Many studies have found no difference in the prevalence of H. pylori infection between dialysis patients and healthy adults. The prevalence of H. pylori infection was 70% or more in Japanese adults (29). The prevalence has decreased annually to levels similar to those reported in Europe and the United States (30). Patients receiving dialysis had significantly lower prevalence of H. pylori infection in five studies (19, 25, 31).

Jaspersen et al (19) reported that 37.0% of adults with normal renal function were positive for H. pylori, while 20.6% of patients receiving dialysis were positive for H. pylori.

Yildiz et al (3) indicated that the incidences of H. pylori infection were 72.5% and 65.9% in normal controls and patients receiving dialysis, respectively.

The prevalence of H. pylori infection in patients receiving CAPD, chronic dialysis, or kidney transplant was reported to be equal or lower when compared to the subjects with normal renal function in various populations (4-6).

Sugimoto et al (32) investigated the largest number of dialysis patients with a variety of treatment periods, and found that the prevalence of H. pylori infection in dialysis patients was significantly lower than in patients with normal renal function. In this study, there was no significant difference in the prevalence of H. pylori infection between patients with normal renal function and patients receiving less than 1 year of dialysis. Therefore, his conclusion was that the urea concentration and the antibiotic usage are unlikely contributors to decrease the prevalence of infection.

Only a few studies have indicated that the prevalence of H. pylori infection is higher in dialysis patients (7). Khedmat et al reported a total of 474 subjects (71 CRF, 73 HD, 25 transplanted, and 305 controls), that were evaluated for dyspepsia, excluding those receiving any H. pylori eradication therapy. All subjects were examined for esophagus, stomach and duodenum mucosa, and infection with HP on 2 distinct tissue samples of the antral region. H. pylori infection was found to be higher in the uremic patients (CRF, 66.2%; HD, 63%) than in the renal transplant recipients (40%) and controls (34.8%); $P < 0.001$.

Fabrizi et al reported H. pylori antibody levels in 228 dialysis patients, and reported that 56% of dialysis patients and 53% of non-dialysis patients were positive for H. pylori (33). In Japan, Tokushima indicated that the proportion of H. pylori-positive patients increased after dialysis was introduced (24).

There are at least three explanations as to why dialysis patients have low prevalence of H. pylori infection: 1) 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 (34); 2) 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; 3) 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 (35). As a result, the gastric atrophy progresses, accompanied by increased pH, and finally H. pylori are not able to live in gastric mucosa (36).

High serum urea nitrogen correlates with prevalence of Helicobacter pylori infection

Some investigators focused on the higher concentration of urea in the gastric juice of renal failure patients raising the local gastric pH and providing abundant substrate for H. pylori (7, 34). On the other hand, other investigators concluded that the higher levels of urea in the mucus of stomach in renal failure patients may result in a lower prevalence of H. pylori colonization in these patients (32). Results of the study Tsukada et al indicate that high serum urea nitrogen seems to correlate with a low prevalence of H. pylori infection. And hemodialysis patients with high serum urea nitrogen may be protected against H. pylori infection1%) and 81 HD (-) patients (69%) (40).

Gladziwa and Loffeld et al (19) reported that the higher urea levels in the blood and gastric juice of patients with renal failure do not seem to be a risk factor for infection with H. pylori (34).

Relationship of H.pylori with age

Age is a factor closely related to the proportion of H. pylori-positive patients. Fumitaka et al. showed that among dialysis patients, the prevalence of H. pylori infection was low in all the age groups over 50 years old (41). However, another study in patients on dialysis and without dialysis, it found that there was no relation between age and the incidence of H. pylori infection (25).

In this study, we investigated the prevalence of H. pylori infection in our HD patients. The main drawback of this study was the sample size which is small. The results of the present study found that the prevalence of H. pylori infection was not low in HD patients, similar to the results of other Iranian population study, which has been done by Khedmat (7).

We indicated that high serum urea nitrogen seems to correlate with a high prevalence of Helicobacter pylori infection. The prevalence of H. pylori infection was lower in young patients compared with the elderly patients. There was no significant correlation between gender, duration of dialysis, serum cholesterol, triglyceride, creatinine, hemoglobin, albumin, calcium and phosphorus and H. pylori infection in these patients.

We conclude that in order to extend the results of this study to Iranian population; studies with larger sample size are required.

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Conflict of Interest

None declared.

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