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CLINICAL STUDY

Gastric Metaplasia and *Helicobacter pylori* Infection in Hemodialysis Patients

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Abstract

Background: Upper gastrointestinal (UGI) symptoms are common in hemodialysis (HD) patients, while gastric metaplasia (GM) and *Helicobacter pylori* infections are key causes for UGI symptoms. This study is targeted to compare GM and *H. pylori* infections in patients with different durations of HD. *Methods*: A total of 406 subjects from Ningbo Urology and Nephrology Hospital were included. The mean age of subjects was 44.7 $\pm$ 13.5 years; 62.9% were male; and subjects were divided into four groups according to different HD durations. Upper endoscopy and lesion were performed in these patients and methylene blue staining was used in detecting *H. pylori* and GM. *Results*: Erosive gastritis was the most common symptom in uremic subjects. GM was found in 139 patients. The longer the dialysis duration, the higher the incidence rate of GM ($p < 0.05$). *H. pylori* infection accounted for 24.1% in HD patients. The occurrence of *H. pylori* infection decreased as dialysis periods progressed within the first 4-year follow-up after the start of HD. *Conclusions*: Almost all patients with HD experienced gastrointestinal discomfort in the current patient cohort. The most common mucosal lesion observed in our study pool was chronic erosive gastritis. The overall incidence of GM was normal at 35.0%, since quite a part of patients are the elderly group in this study. We need not worry about this too much, unless the HD patients have registered for renal transplantation or are suffering from severe gastrointestinal discomfort.

Keywords: uremia, gastrointestinal symptoms, hemodialysis, gastric metaplasia, *Helicobacter pylori*

INTRODUCTION

Gastrointestinal symptoms are common in hemodialysis (HD) patients,[1] although the type of symptoms may vary considerably in different geographical regions.[2–4] Gastric metaplasia (GM) has high risk of turning out to be a precursor of indigestive tumor. Patients with chronic renal failure (CRF) were reported to have a higher incidence rate of GM. So among the long-term HD patients the incidence of intestinal metaplasia will continue to increase regardless of the dialysis duration, which in turn will raise the incidence of digestive tumors.

Helicobacter pylori infection is the most common chronic bacterial infection in humans. It is estimated that approximately 40–60% of the world population are colonized with this agent.[5] In addition to the direct effects of *H. pylori*, complications related to infection with this bacterium are serious public health threats. *H. pylori*, a Gram-negative and spiral-shaped bacillus colonizing in the antrum of the stomach, can cause type B chronic-active antral gastritis. Research has demonstrated that a number of diseases concerning gastrointestinal system are linked with *H. pylori* infection. Specifically, this condition plays an important role in the pathogenesis of peptic ulcer disease and is also associated with gastric cancer. In anyway, regardless of the prevalence of *H. pylori* infection in China and the dialysis duration, it changes. This study focused on the incidence rates of GM and *H. pylori* in patients according to HD duration. Therefore we evaluated a local sample of 406 HD patients excluding those patients with diabetes and historical stomach and intestinal disorders with respect to endoscopic and histological findings.

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METHODS

Subjects

Patient selection and division

A total of 406 HD patients from Ningbo Urology and Nephrology Hospital were included in this study carried out between September 2006 and April 2011. There were 247 males and 159 females (1.55:1) aged between 10 and 81 years, with a mean age of 44.7 ± 13.5 years. All the dialysis patients were routinely administered HD but not peritoneal dialysis. Infection by *H. pylori* is common in diabetics, who also failed to fully control hyperglycemia. Evidence has shown that the incidence of *H. pylori* infection might be increased in patients with type 2 diabetes mellitus (T2DM) compared with the normal population.[6–8] Thus, patients with T2DM and historical gastrointestinal disorders were excluded from this study. All patients enrolled in this study were having data on endoscopy. The patients were divided into four groups according to different dialysis durations as follows:

Group 1: HD duration of less than 1 year (275 patients)
Group 2: HD duration between 1 year and 3 years (70 patients)
Group 3: HD duration between 3 and 4 years (28 patients)
Group 4: HD duration of more than 4 years (33 patients).

Endoscopic Evaluation

Upper gastrointestinal (UGI) endoscopy was performed after an overnight fast by using an Olympus GIF XQ260 gastroscope (Olympus Inc., Tokyo, Japan) by the same endoscopist. Endoscopic evaluation was performed with reference to the Sydney system and the updated Sydney system.[9–11]

Histopathological Examination and *H. pylori* Identification

Two gastric biopsies were taken from intact mucosa in the antrum within 5 cm of the pylorus, were then fixed in 10% formalin and sent for histopathological examination and *H. pylori* identification. *H. pylori* were detected under microscopy on the histological sections stained with methylene blue. The extension of GM was judged by dying endoscopy with methylene blue solution. A mild degree of GM referred to the presence of a single small focus of metaplastic cells usually at the tip of a villus; a moderate degree indicated the presence of multiple small foci or a large area of metaplasia occupying less than half of the mucosal surface; and a severe degree referred to the presence of the change in more than half of the biopsy surface.

Statistical Analysis

The statistical analysis was carried out using fourfold table to obtain χ^2-value. All statistical analyses were evaluated using SPSS version 11.500 (SPSS Inc., Chicago, IL, USA). The values of p less than 0.05 were considered significant.

RESULTS

Endoscopic Findings, Histopathological Examination, and *H. pylori* Identification

The age difference was not statistically significant ($p > 0.05$). Normal gastrointestinal mucosa was observed endoscopically in only 1 patient (0.2%), while various abnormalities were seen in 405 patients (99.8%) (see Table 1). In this study, erosive gastritis (42.6%) and superficial gastritis (26.1%) were the first two most common symptoms that occur in uremic subjects, respectively, which resulting from higher serum levels of urea, anemia and fluctuations in the gastric blood supply in the HD patients. Among all the gastrointestinal disorders, the incidence rates of the top three GM were gastric cancer (100%), erosive gastritis (37.0%), and multiple ulcers (33.3%), respectively. The positive rates of *H. pylori* infection were 75% for multiple ulcers, 50% for gastric cancer, and 41.2% for duodenal ulcer. Nevertheless, the two differences were not statistically significant ($p > 0.05$).

GM was present in 142 patients (35.0%) (see Table 2). The longer the dialysis duration the higher the incidence rate of GM. But, the differences were not statistically significant ($p > 0.05$). The GM was mild in 105 (73.9%), moderate in 26 (18.3%), and extensive in 11

Table 1. Endoscopic evaluation in hemodialysis patients.

	Male ($n = 247$)	Female ($n = 159$)	Total ($n = 406$)	GM ($n = 139$)	*Helicobacter pylori* ($n = 98$)
Age (years)	44.4 ± 13.9	45.2 ± 12.9	44.7 ± 13.5		
Chronic erosive gastritis	121	72	173 (42.6%)	64	52
Chronic superficial gastritis	58	48	106 (26.1%)	31	30
Chronic bile reflux gastritis	24	23	47 (11.6%)	11	6
Chronic atrophic gastritis	1	0	1 (0.2%)	1	0
Chronic duodenitis	45	24	69 (17.0%)	13	16
Gastric ulcer	14	8	22 (5.4%)	6	5
Duodenal ulcer	12	5	17 (4.2%)	6	7
Multiple ulcers	9	3	12 (3.0%)	4	9
Gastric cancer	2	0	2 (0.5%)	2	1

Note: GM, gastric metaplasia.

Table 2. GM and *Helicobacter pylori* infection in hemodialysis patients according to hemodialysis (HD) duration.

	Group 1 ($n = 275$)	Group 2 ($n = 70$)	Group 3 ($n = 28$)	Group 4 ($n = 33$)
Sex (male/female)	156/119	49/21	20/8	22/11
Age (years)	44.1 ± 13.4	45.7 ± 12.8	43.1 ± 15.2	43.5 ± 14.2
Age range (years)	10–81	29–78	23–77	12–74
Helicobacter pylori (positive/total)	65/275 (23.6%)	21/70 (30.0%)	12/28 (42.9%)	0/33 (0)
GM (positive/total)	84/275 (30.5%)	28/70 (40.0%)	14/28 (50.0%)	16/33 (48.5%)

Note: GM, gastric metaplasia.

Table 3. Different levels of the GM in hemodialysis patients according to hemodialysis (HD) duration.

	Group 1 ($n = 84$)	Group 2 ($n = 28$)	Group 3 ($n = 14$)	Group 4 ($n = 16$)	Total ($n = 142$)
Mild (positive)	66	19	10	10	105
Moderate (positive)	14	4	4	4	26
Extensive (positive)	4	5	0	2	11

Note: GM, gastric metaplasia.

(7.8%) (see Table 3). Of 406 cases, the positive rate of *H. pylori* was 24.1%. The prevalence of *H. pylori* infection decreased as dialysis periods progressed within the first 4-year follow-up after the start of HD ($p < 0.05$).

DISCUSSION

The results of this study confirm the high incidence of chronic erosive gastritis in HD patients, which is consistent with the previous reports.[4] The high occurrence of this type of lesion may be partly due to the cure of *H. pylori* infection during the clinical course of maintenance HD.[12] Also it was secondary to an abnormal gastrointestinal hormone excretion and drug-induced disorders.[13] From the observation of gastrointestinal disorders in HD patients, the GM was mainly seen among gastric cancer, erosive gastritis, and multiple ulcers (100%, 37.0%, and 33.3%, respectively), although the difference was not statistically significant ($p > 0.05$). *H. pylori* infection was more common in patients with gastric ulcer and gastric cancer, respectively. Therefore, we assume that *H. pylori* infection was still a risk factor for peptic ulcers among the HD patients, which was the same with the general population. However, there are also some studies that suggest that the risk factors for peptic ulcer had some differences between the HD patients and general population,[14] assuming that the incidence rate of atrophic gastritis is comparatively lower although the reason is unknown. The possible reason for the difference might be due to limited subjects.

In this study, the overall incidence rate of GM is at 35.0%, which is slightly lower than the 39% incidence rate seen in a previous study of 120 patients with nonulcer dyspepsia and unknown renal disease.[15] There are also some other sources that reported 30–65% incidence of GM in HD patients. Our study shows that the male patients were leading to the gradually increased incidence rate of GM according to the dialysis duration, although the difference was not statistically significant ($p > 0.05$). This may be explained by the low estrogen concentrations commonly seen in women with CRF, which tend to persist even after starting HD. Most were mild intestinal metaplasia in our study. Moderate and severe metaplasia remained at 26.06%. There is less than 38% incidence reported by Wyatt et al.[16] in biopsy specimens from patients with dyspepsia showing comparable degrees of metaplasia (more than 5% of the epithelial surface). Age was a second factor closely involved in the proportion of GM considering that our study included a big part of elderly patients. Although the pH of the gastric juice was not measured in our research, the previous studies have suggested that some patients with CRF have increased gastric acidity. Maybe this is another important factor connected with the presence of a mild incidence of GM in these patients, as the association between high gastric acidity and duodenal GM had been previously noted clinically and experimentally.

H. pylori is a Gram-negative bacterium closely associated with type B gastritis and peptic ulcer disease and its infection has been linked to mucosa-associated lymphoid tissue lymphoma and gastric adenocarcinoma.[17] Various studies have reported a prevalence of *H. pylori* infection of 34–75% in HD patients on HD similar to that in the general population.[18,19] Khedmat et al.[4] reported that *H. pylori* infection was found to be higher in HD patients (CRF: 66.2%; HD: 63%) than in renal transplantation (RT) recipients (40%) and controls (34.8%) ($p < 0.01$); Schoonjans et al.[20] reported that a positive *Helicobacter* status based on serology was not related to the presence of whether on dialysis therapy or not. Recent consensus showed that the prevalence of *H. pylori* infection in HD patients was significantly lower than in subjects with normal renal function.[21] Other investigators found a lower prevalence of *H. pylori* among dialysis patients than in individuals with normal renal functions and concluded that patients with renal dysfunction appear to be partially protected against *H. pylori*.[22] Possible postulated protective mechanisms might include antibiotic use or use of aluminum-containing antacids prescribed for HD

patients during the course of their illness. In addition, uremia could change the bacterial colonization of the UGI tract, thus reducing *H. pylori* infection. In our study the *H. pylori* prevalence was 24.1%, which was less than in the general population. The higher incidence of hypochlorhydria could contribute to decreased frequency of *H. pylori*. Long-term dialysis decreased the prevalence of *H. pylori*.[23] The reduction of gastric acid secretion related to chronic gastritis may be involved.[24] In our study, we found that during the first 4 years of dialysis, both the dialysis time and the incidence rate of *H. pylori* infection increased, showing some differences compared with other post-report.[25,26] Smoking and psychological factors may be reasons in our study. In this study, the main patients were male[27] and most of them had a smoking history. At the beginning of the first 4 years of HD, most patients did not fully quit smoking while smoking could cause an increase in the *H. pylori* infection rate.

CONCLUSIONS

In this study, we found that almost all HD patients experienced gastrointestinal discomfort. The overall incidence of *H. pylori* infection was low at 24.1%, although there had been a general uptrend in the first 4 years of dialysis. Long-term HD might decrease the prevalence of *H. pylori* infection as a whole. The overall incidence of GM was normal at 35.0%, since most of the elderly dialysis patients were included in this study. We need not worry about this too much, unless the HD patients have registered for renal transplantation or are suffering from severe gastrointestinal discomfort. More extensive and multicenter trials are needed to address the various aspects of these results for a final conclusion.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

[1] Shirazian S, Radhakrishnan J. Gastrointestinal disorders and renal failure: Exploring the connection. *Nat Rev Nephrol*. 2010;6(8):480–492.

[2] Asl MK, Nasri H. Prevalence of *Helicobacter pylori* infection in maintenance hemodialysis patients with non-ulcer dyspepsia. *Saudi J Kidney Dis Transplant*. 2009;20(2):223–226.

[3] Abdulrahman IS, Al-Quorain AA. Prevalence of gastroesophageal reflux disease and its association with *Helicobacter pylori* infection in chronic renal failure patients and in renal transplant recipients. *Saudi J Gastroenterol*. 2008;14(4):183–186.

[4] Khedmat H, Ahmadzad-Asl M, Amini M, et al. Gastroduodenal lesions and *Helicobacter pylori* infection in uremic patients and renal transplant recipients. *Transplant Proc*. 2007;39(4):1003–1007.

[5] Bener A, Uduman SA, Ameen A, et al. Prevalence of *Helicobacter pylori* infection among low socio-economic workers. *J Commun Dis*. 2002;34(3):179–184.

[6] Talley NJ, Howell S, Jones MP, Horowitz M. Predictors of turnover of lower gastrointestinal symptoms in diabetes mellitus. *Am J Gastroenterol*. 2002;97(12):3087–3094.

[7] Bytzer P, Talley NJ, Hammer J, Young LJ, Jones MP, Horowitz M. GI symptoms in diabetes mellitus are associated with both poor glycemic control and diabetic complications. *Am J Gastroenterol*. 2002;97(3):604–611.

[8] Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: A population-based survey of 15,000 adults. *Arch Intern Med*. 2001;161(16):1989–1996.

[9] Tytgat GN. The Sydney System: Endoscopic division. Endoscopic appearances in gastritis/duodenitis. *J Gastroenterol Hepatol*. 1991;6(3):223–234.

[10] Sipponen P, Price AB. The Sydney system for classification of gastritis 20 years ago. *J Gastroenterol Hepatol*. 2011;26(Suppl. 1):S31–S34.

[11] Stolte M, Meining A. The updated Sydney system: Classification and grading of gastritis as the basis of diagnosis and treatment. *Can J Gastroenterol*. 2001;15(9):591–598.

[12] Moriyama T, Matsumoto T, Hirakawa K, et al. *Helicobacter pylori* status and esophagogastroduodenal mucosal lesions in patients with end-stage renal failure on maintenance hemodialysis. *J Gastroenterol*. 2010;45(5):515–522.

[13] Rey JF, Lombart J, Bournerie A, Salvadori JM. [Importance of gastroscopy in chronic uremic patients (author's transl)]. *Sem Hop*. 1982;58(13):788–792.

[14] Chen YT, Yang WC, Lin CC, Ng YY, Chen JY, Li SY. Comparison of peptic ulcer disease risk between peritoneal and hemodialysis patients. *Am J Nephrol*. 2010;32(3):212–218.

[15] Shousha S, Barrison IG, El-Sayeed W, Khan S, Parkins RA. A study of incidence and relationship of intestinal metaplasia of gastric antrum and gastric metaplasia of duodenum in patients with nonulcer dyspepsia. *Dig Dis Sci*. 1984;29(4):311–316.

[16] Wyatt JI, Rathbone BJ, Dixon MF, Heatley RV. Campylobacter pyloridis and acid induced gastric metaplasia in the pathogenesis of duodenitis. *J Clin Pathol*. 1987;40(8):841–848.

[17] Abdulrahman IS, Al-Mueilo SH, Ismail MH, Yasawy MI, Al-Qahtani FN, Al-Qorain AA. Does *Helicobacter pylori* infection in chronic renal failure increase the risk of gastroduodenal lesions? A prospective study. *Saudi J Gastroenterol*. 2004;10(2):78–85.

[18] de Bustillo EM, Sanchez TJA, Sanz JC, et al. Eradication and follow-up of *Helicobacter pylori* infection in hemodialysis patients. *Nephron* 1998;79(1):55–60.

[19] Wang YL, Sheu BS, Huang JJ, Yang HB. Noninvasive stool antigen assay can effectively screen *Helicobacter pylori* infection and assess success of eradication therapy in hemodialysis patients. *Am J Kidney Dis*. 2001;38(1):98–103.

[20] Schoonjans R, Van VB, Vandamme W, et al. Dyspepsia and gastroparesis in chronic renal failure: The role of *Helicobacter pylori*. *Clin Nephrol*. 2002;57(3):201–207.

[21] Yildiz A, Besisik F, Akkaya V, et al. *Helicobacter pylori* antibodies in hemodialysis patients and renal transplant recipients. *Clin Transplant*. 1999;13(1 Pt 1):13–16.

[22] Jaspersen D, Fassbinder W, Heinkele P, et al. Significantly lower prevalence of *Helicobacter pylori* in uremic patients than in patients with normal renal function. *J Gastroenterol*. 1995;30(5):585–588.

[23] Lopez T, Almirall J, Calvet X, et al. [*Helicobacter pylori* does not contribute to iron deficiency in hemodialysis patients]. *Nefrologia* 2006;26(6):673–678.

[24] Nakajima F, Sakaguchi M, Amemoto K, et al. *Helicobacter pylori* in patients receiving long-term dialysis. *Am J Nephrol*. 2002;22(5–6):468–472.

[25] Sugimoto M, Sakai K, Kita M, Imanishi J, Yamaoka Y. Prevalence of *Helicobacter pylori* infection in long-term hemodialysis patients. *Kidney Int*. 2009;75(1):96–103.

[26] Sugimoto M, Yamaoka Y. Review of *Helicobacter pylori* infection and chronic renal failure. *Ther Apher Dial*. 2011;15(1):1–9.

[27] Al-Mueilo SH. Gastroduodenal lesions and *Helicobacter pylori* infection in hemodialysis patients. *Saudi Med J*. 2004;25(8):1010–1014.