Gastroesophageal Reflux Disease in Chronic Renal Failure Patients: Evaluation by Endoscopic Examination

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Background: The association between gastroesophageal reflux disease (GERD) and chronic renal failure (CRF) remains unclear. The aim of the present study is to assess the gastroendoscopic findings and the prevalence of GERD in CRF patients by endoscopic examination.
Patients and Methods: This study consisted of 156 CRF patients (97 men and 59 women, mean age: 64.2 years) whose creatinine level was more than 2 mg/dl and who underwent endoscopic examination. We checked their renal function, gastrointestinal symptoms and gastroendoscopical findings, and examined the relationship between renal function and gastroendoscopic findings, and the prevalence of GERD.
Results: In the gastroendoscopic findings of the 156 CRF patients who underwent endoscopic examination, the prevalence of GERD was 34.0%. Especially, in symptomatic cases, the prevalence of GERD was 44.0%. In hemodialysis patients, the prevalence of GERD was 50.0%. The prevalence of GERD tended to increase as renal function become worse. There were statistically significant differences between the patients on hemodialysis and pre-dialysis in the prevalence of GERD ($P < 0.01$). The severity of GERD tended to be mild.
Conclusions: Compared to the reported prevalence of GERD in 6010 Japanese adults (16.3%), the prevalence of GERD in CRF patients, especially who underwent hemodialysis (50.0%), was increased.

Key words: gastroesophageal reflux disease (GERD); chronic renal failure (CRF); hemodialysis (HD), endoscopic examination

INTRODUCTION

Gastroesophageal reflux disease (GERD) develops when acidic gastric contents reflux into the esophagus. The condition is believed mainly to be due to an increase in the number of transient LES relaxations. Other major mechanisms include decreased clearance of esophageal contents and reflux owing to impaired peristalsis, decreased gastric emptying with resultant reflux into the esophagus, and increased gastric acid production with a resultant increase in the potency of the reflux. Chronic renal failure (CRF) is associated with an increased incidence of acid-related gastrointestinal disorders [1–3]. The association between GERD and CRF remains unclear. In our study [4] by questionnaire for the diagnosis of reflux disease (QUEST) produced by Carlsson *et al*. [5], the prevalence of GERD was 24.2% in the 418 stable hemodialysis (HD) patients who did not undergo endoscopic examination. Compared to the reported prevalence of GERD in 6010 Japanese adults (16.3%) [6], the prevalence of GERD in CRF patients who underwent HD (24.2%) was increased. Although we are now aware of the increasing prevalence of symptomatic GERD in HD patients, little is known about the gastroendoscopic findings and the prevalence of endoscopical GERD in CRF patients. The aim of the present study is to assess the gastroendoscopic findings and the prevalence of endoscopical GERD in CRF patients by endoscopic examination.

PATIENTS AND METHODS

This study involved consisted of 156 CRF patients (97 men [62%] and 59 women [38%], mean age: 64.2 [range: 29–89] years) whose creatinine level was more than 2 mg/dl and who underwent endoscopy examination at our hospital between January 2001 and March 2004. This group involved 42 patients (27%) with some upper GI symptoms, 55 patients (35%) with DM and 87 patients (56%) with HT (Table 1). To investigate renal function, we classified the patients into three categories based on the creatinine level and as follows: 2 < Cr. < 5 (44 patients [28%]), Cr. 5 < and patients on pre-dialysis (53 patients [34%]), Cr. 5 < and patients on hemodialysis (59 patients [38%]) (Table 1). As we could not examine glomerular filtration rate (GFR) of all patients, we used serum creatinine level as renal function. These clinical findings were compared with the gastroendoscopic findings retrospectively.

For statistical analysis, the χ^2 test was used and *P*-values of < 0.05 were considered statistically significant.

RESULTS

The prevalence of GERD was highest (53 patients [34.0%]) in the gastroendoscopic findings of the 156

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Table 1 Clinical characteristics of 156 CRF patients

	Patients (n = 156)
Mean age (years)	64.2 (range: 29–89)
Sex	
Male	97
Female	59
Cases with Upper GI Symptoms	42
Renal function	
2 < Cr. < 5	44
Cr. 5 <, without hemodialysis	53
Cr. 5 <, with hemodialysis	59
Complications	
Diabetes Mellitus	55
Hypertension	87

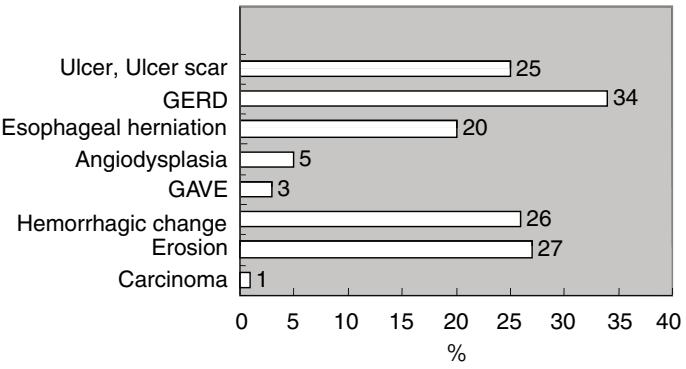

Fig. 1 The prevalence of GERD was highest (53 patients [34.0%]) in the gastroendoscopic findings of the 156 CRF patients who underwent endoscopic examination. Gastric ulcer and ulcer scar, erosion, hemorrhagic change (hematin), angiodysplasia and gastric antral vascular ectasia (GAVE) were seen in 39 patients (25%), 42 patients (27%), 41 patients (26%), 8 patients (5%) and 5 patients (3%).

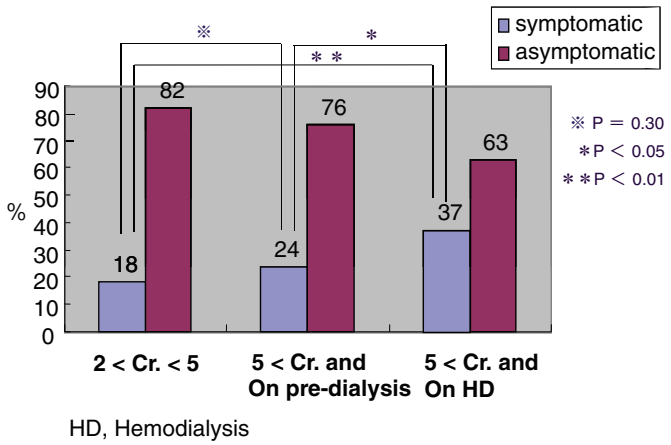

Fig. 2 In relationships between renal function and gastrointestinal symptoms, as renal function became worse, symptomatic cases tended to increase. There were statistically significant differences between the patients on hemodialysis and pre-dialysis.

CRF patients who underwent endoscopic examination (Fig. 1). Gastric ulcer and ulcer scar, erosion, hemorrhagic change (hematin), angiodysplasia and gastric antral vascular ectasia (GAVE) were seen in 39 patients (25%), 42 patients (27%), 41 patients (26%), 8 patients (5%) and 5 patients (3%), respectively (Fig. 1). In the evaluation of 42 patients (27%) with some upper GI symptoms, 22 patients (52%) underwent hemodialysis, and the prevalence of GERD was highest (18 patients [44.0%]) in the gastroendoscopic findings. And in relationships between renal function and gastrointestinal symptoms, as renal function became worse, symptomatic cases tended to increase. There were statistically significant differences between the patients on hemodialysis and pre-dialysis (Fig. 2). In relationships between renal function and gastroendoscopic findings, in the patients on hemodialysis the frequency of GERD and erosion increased, especially the prevalence of GERD was highest (50.0%). There were statistically significant differences between the patients on hemodialysis and pre-dialysis (Fig. 3). The severity of GERD tended to be mild. In the patients with GERD, 77% was grade M or A of modified Los Angels grading system. Esophageal herniation was seen in 19 patients (32%) (Fig. 4).

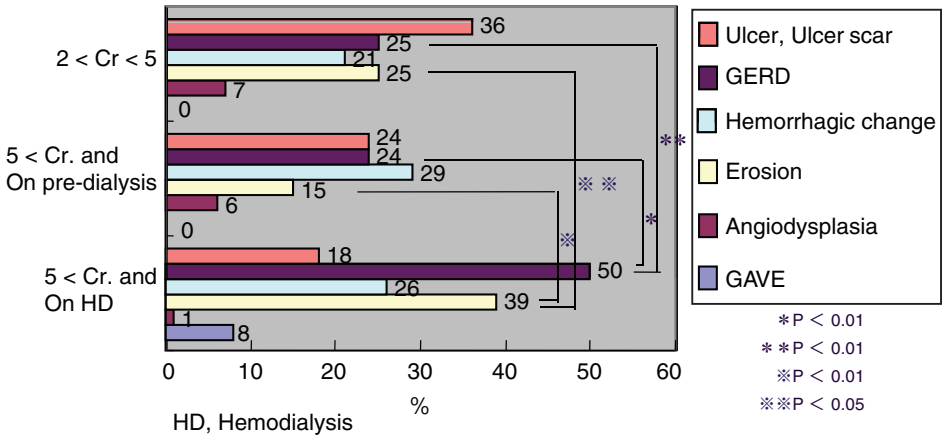

Fig. 3 In relationships between renal function and gastroendoscopic findings, in the patients on hemodialysis the frequency of GERD and erosion increased, especially the prevalence of GERD was highest (50.0%). There were statistically significant differences between the patients on hemodialysis and pre-dialysis.

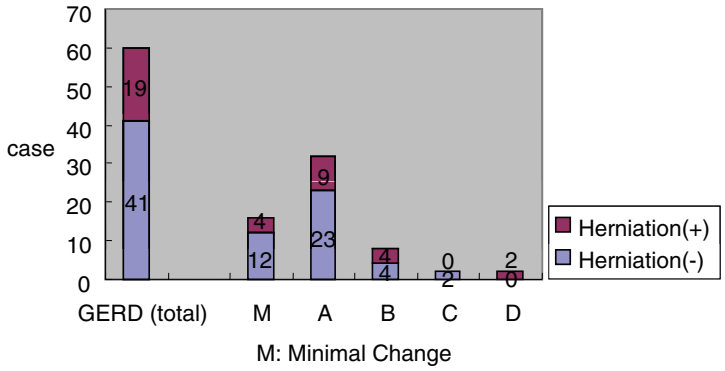

Fig. 4 The severity of GERD tended to be mild. In the patients with GERD, 77% was grade M or A of modified Los Angels grading system. Esophageal herniation was seen in 19 patients (32%).

DISCUSSION

GERD is one of acid-related gastrointestinal disorders, because GERD develops when excessively acidic gastric contents reflux into the esophagus. CRF is associated with an increased incidence of acid-related gastrointestinal disorders [3–5]. Therefore we can predict high morbidity of GERD in CRF patients, but the association between GERD and CRF remains unclear.

In our study [4] by questionnaire for the diagnosis of reflux disease (QUEST) produced by Carlsson *et al.* [5], the prevalence of GERD was 24.2% in the 418 stable hemodialysis (HD) patients who did not undergo endoscopy examination. Compared to the reported prevalence of GERD in 6010 Japanese adults (16.3%) [6], the prevalence of GERD in CRF patients who underwent HD (24.2%) was increased. In this QUEST study [4] we could suggest the increasing prevalence of symptomatic GERD in HD patients. Further we would to know about the gastroendoscopic findings and the prevalence of endoscopical GERD in CRF patients.

The pathophysiology of GERD is multifactorial and depends on interaction between aggressive factors and defensive factors. It is believed mainly that the aggressive factor is an increased gastric acid production and the defensive factor is a decreased gastric emptying.

First we have to consider the association of CRF with an increased gastric acid production as an aggressive factor. Although we cannot say that increased acid production occurs in all CRF patients, some patients certainly have increase acid production. Hypergastrinemia is in fact present [7, 8] in CRF patients, and higher acid production can occur secondary to hypergastrinemia, which can be a consequence of decreased clearance of gastrin owing to a reduced GFR. And Straathof *et al.* reported that postprandial plasma concentrations of gastrin decrease lower esophageal sphincter pressure and increase the transient lower esophageal sphincter relaxations associated with reflux [9]. We could not examine serum gastrin in this study, the prevalence of GERD tended to increase as renal function become worse. Serum gastrin may be an important factor as both an aggressive and a defensive factor. On the other hand several studies have shown that rates of *H. pylori* infection in CRF are lower than expected [10–13]. Shousha *et al.* found that the prevalence of antral *H. pylori* was significantly less in patients with renal disease (24%) than in a control group (42%) [12]. These lower rates of *H. pylori*, which lead to hyperacidity state in stomach, may potentially

be a mechanism by which CRF can be associated with GERD. Although we could not examine the rate of *H. pylori* infection in this study, this also may be an important factor.

Then we also have to consider the association of CRF with a decreased gastric emptying as a defensive factor. Although this study did not involve the patients on peritoneal dialysis, a patient on peritoneal dialysis would be expected to have delayed gastric emptying simply due to the physical impairment caused by the peritoneal fluid. A lot of CRF patients have DM and HT as complications. We can also predict decreased gastric emptying by DM neuropathy and LES relaxations by Ca-antagonists and nitrites. CRF patients in this study also involved 55 patients (35%) with DM and 87 patients (56%) with HT. However we could not show the association of GERD with DM or HT. Three studies demonstrated delayed gastric emptying in uremic predialysis patients [14–16]. The researchers have also documented delayed gastric emptying in hemodialysis patients [17, 18]. The situation is meddled by other studies that have not demonstrated decreased gastric emptying in hemodialysis patients [16, 19–21].

In this study the prevalence of GERD was highest (34.0%) in the gastroendoscopic findings of the 156 CRF patients who underwent endoscopical examination (Fig. 1). In relationships between renal function and gastroendoscopic findings, in the patients on hemodialysis the frequency of GERD and erosion increase, especially the prevalence of GERD was highest (50.0%). There were statistically significant differences between the patients on hemodialysis and pre-dialysis (Fig. 3). These results suggest to us that CRF patients, especially on hemodialysis, might have specific risk factors that make them susceptible to GERD.

In the gastroendoscopic findings of 156 CRF patients who underwent endoscopy examination, the prevalence of GERD was highest. The overall proportion of reflux esophagitis in 6010 Japanese adults was 16.3% in prospective evaluation by gastroendoscopy [6]. Several studies using endoscopic examination suggested that the overall prevalence of reflux esophagitis in Western countries was around 10%–20% [22, 23]. Compared to this reported prevalence of GERD in 6010 Japanese adults (16.3%) [6] the prevalence of GERD in CRF patients, especially who underwent hemodialysis (50.0%), was increased. Probably contained patients with unstable or severe CRF might cause this high prevalence. In an endoscopic surveillance study in adults, no difference was seen in the incidence of esophagitis between patients with CRF and healthy controls [24]. On the other hand, in an uncontrolled study using 24 hour pH-metry, Ruley et al found that 73% (16 of 22) of children with CRF had significant GERD. Although some mechanisms potentially lead to an increase of GERD in CRF, it would be insufficient to suggest that the incidence of GERD is increased in CRF patients without further study.

CONCLUSION

Compared to the reported prevalence of GERD in 6010 Japanese adults (16.3%), the prevalence of GERD in CRF patients, especially who underwent hemodialysis (50.0%), was increased.

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