Upper gastrointestinal (GI) symptoms are common in patients with severe chronic renal failure and they constitute an important component of the uremic syndrome. These symptoms usually improve with the institution of regular dialytic therapy in most patients. However, chronic hemodialysis (HD) patients continue to suffer from various symptoms referable to the upper GI tract. Gastric pathologic changes are common in HD patients. Possible etiologic factors in their pathogenesis may include high gastrin blood levels, delayed gastric emptying, and infection by Helicobacter pylori.

**Objective:** The purpose of this prospective study is to determine the prevalence of upper gastrointestinal (GI) abnormalities and *Helicobacter pylori* (*H. pylori*) infection among stable chronic hemodialysis (HD) patients.

**Methods:** The study was carried out at King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia during the period January 1996 to June 1997. Fifty-four chronic HD patients underwent upper GI endoscopy. Endoscopic changes were described and multiple antral gastric biopsies were taken for histological examination and detection of *H. pylori* infection. Gastric biopsy findings were compared to findings in 60 consecutive patients with normal renal function undergoing endoscopy for assessment of dyspepsia.

**Results:** Fifty-four stable chronic HD patients (32 men, mean age 42.4 ± 18 years) underwent upper GI endoscopy and multiple antral gastric biopsies for histological examination and *H. pylori* detection. The endoscopic findings were abnormal in 49 (90.7%) patients. Chronic gastritis was seen in 20 (37%) patients, acute gastritis was seen in 13 (20.1%) patients, duodenal ulcer was seen in 6 (11.1%) patients, duodenitis with or without erosions was seen in 5 (9.3%) patients, gastroduodenitis was seen in 3 (5.56%) patients, and gastroesophageal reflux disease was seen in 2 (3.7%) patients. Histological examination of multiple antral gastric biopsies documented chronic active gastritis in 28 (51.9%) patients. *Helicobacter pylori* were present in 34 (63%) patients. *Helicobacter pylori* were detected in the majority (85.7%) of patients with the histological diagnosis of chronic active gastritis. Patients harboring *H. pylori* were significantly older than negative patients (52±16.1 versus 33.9 ±17.3 years, *p*<0.018). In a group of 60 patients with normal renal function undergoing endoscopy for assessment of dyspeptic symptoms during the same period, chronic active gastritis was found in 40 (66.7%) patients and *H. pylori* was detected in 38 (63.3%) patients.

**Conclusion:** Upper GI abnormalities are common among HD patients even in the absence of symptoms. Biopsy proven chronic active gastritis is the most common histological diagnosis among these patients and is highly associated with *H. pylori* infection. Prevalence of *H. pylori* infection in HD patients is similar to those with normal renal function undergoing endoscopy for dyspepsia. *Helicobacter pylori* infected HD patients tend to be older than patients without *H. pylori* infection.
**Helicobacter pylori** (H. pylori). Helicobacter pylori infection of the gastric mucosa is implicated in the causation of several gastroduodenal lesions such as gastritis, peptic ulcer disease, mucosa associated lymphoid tissue (MALT) and gastric adenocarcinoma. It has been postulated that a high level of urea in the gastric mucus in patients with advanced renal failure might predispose to H. pylori infection. This stems from the notion that H. pylori urease converts urea to ammonia raising the local gastric pH and therefore enhancing the survival of the bacterium. The prevalence of H. pylori infection and its relationship to upper GI pathologic changes in HD patients has been studied extensively. The prevalence of H. pylori infection in HD patients was quite variable among the different studies. Some studies have reported lower rates of infection in HD patients when compared to patients with normal renal function. Most studies, however, have reported similar rates of infection. A number of these studies have used serologic or breath analysis methods that lacked consistent sensitivity and specificity.

In this prospective study, we performed upper GI endoscopy in 54 stable chronic HD patients. Most of these procedures were performed as part of pre kidney transplantation work up. The purpose of this study is to determine gastroduodenal lesions and to assess histologically the prevalence of H. pylori infection. Biopsy findings in these patients were compared to a control group of 60 consecutive patients with normal renal function undergoing upper GI endoscopy for evaluation of dyspepsia during the same study period.

**Methods.** The study was carried out at King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia during the period January 1996 to June 1997. Fifty-four stable patients on chronic HD underwent upper GI endoscopy after obtaining an informed consent. Patients had to be on regular HD for at least 3 months before the endoscopy. Patients with history of peptic ulcer disease, or upper GI bleeding were excluded. Patients who received antibiotics or nonsteroidal anti-inflammatory drugs other than acetylsalicylic acid were deferred until 2 months after exposure to these drugs.

A single endoscopist performed the procedure on a non-dialysis day. Upper GI endoscopy was performed by an Olympus fiberoptic gastroduodenoscopy. Patients were considered endoscopically normal if no mucosal abnormalities were noted. Gastritis, duodenitis or gastroduodenitis were diagnosed if the mucosa was hyperemic, erythematous or friable. Multiple biopsies were obtained from the antrum for histology and detection of H. pylori infection. The capability of histopathologic techniques for identifying H. pylori was shown to be equivalent to that of culture in a previous study from the same institution.

Findings on antral gastric biopsies in the HD patients were compared to findings in 60 consecutive patients with normal renal function undergoing upper GI endoscopy by the same operator for dyspepsia.

Results are expressed as the mean ± SD. Comparison between groups was made using the independent t-test for numerical variables. Chi-square test was used for comparing nominal variables. Value of p<0.05 was considered statistically significant.

**Results.** A total of 54 stable patients on chronic HD for a period of at least 3 months were studied. Thirty-one were males (59.3%); age was 42.4 ± 18.8 years with a range of 16-85 years. Forty-eight patients were Saudi nationals. Duration of HD treatment prior to endoscopy was 17 ± 12.3 months with a range of 3-48 months. Etiology of end stage renal disease (ESRD) in these patients is shown in Table 1.

Elicitable symptoms in these patients at the time of endoscopy included dyspepsia in 7 patients (13%), and abdominal pain in 7 patients (13%). Forty-eight patients were asymptomatic. Physical signs included pallor in 11 patients (20.4%), abdominal tenderness in 4 patients (7.4%) and ascites in 3 patients (5.6%). Eight (14.8%) patients were taking low dose acetylsalicylic acid (81-100 mg/day) and 13 (24.1%) patients were on H2 blockers at the time of endoscopy. None were using proton pump inhibitors. The endoscopic findings were abnormal.

**Table 1 - Etiology of end stage renal disease.**

<table>
<thead>
<tr>
<th>Cause of end stage renal disease</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic glomerulonephritis</td>
<td>20</td>
<td>(37)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>13</td>
<td>(24.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4</td>
<td>(7.4)</td>
</tr>
<tr>
<td>Chronic tubulointerstitial disease</td>
<td>4</td>
<td>(7.4)</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>3</td>
<td>(5.6)</td>
</tr>
<tr>
<td>Adult polycystic kidney disease</td>
<td>2</td>
<td>(3.7)</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>2</td>
<td>(3.7)</td>
</tr>
<tr>
<td>Alport’s syndrome</td>
<td>2</td>
<td>(3.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>(7.4)</td>
</tr>
</tbody>
</table>

Total: 54 (100)
in 49 (90.8%) patients. The most commonly described endoscopic findings were chronic and acute gastritis. Together, were seen in 33 patients (61.1%). Table 2 are the lists of findings and the status of \textit{H. pylori} infection in each group. Among the 14 symptomatic HD patients, chronic gastritis was diagnosed endoscopically in 9 (64%) patients compared to 11 of 40 asymptomatic patients (27.5%). This difference was statistically significant ($p=0.01$).

Multiple antral gastric biopsies were obtained for histological examination and for detection of \textit{H. pylori}. The most common pathologic abnormality is superficial chronic active gastritis seen in 28 (51.9%), followed by superficial chronic inactive gastritis in 10 (18.5%), acute gastritis in 6 (11.1%), and normal in 10 (18.5%). \textit{Helicobacter pylori} were identified to variable degrees in biopsies taken from the prepyloric mucosa in 34 patients (63%). \textit{Helicobacter pylori} positive patients were significantly older than negative patients. Mean age of positive patients was $32 \pm 16.1$ years, compared to $33.9 \pm 17.3$ in negative patients ($p=0.018$). There was no significant difference in the duration of dialytic therapy between \textit{H. pylori} positive and negative patients ($16 \pm 14.02$ and $18.6 \pm 10$ months, $p=0.668$). \textit{Helicobacter pylori} were similarly identified among the symptomatic and asymptomatic HD subgroups (57.1% and 65%, $p=0.6$). Twenty-four out of 28 (85.7%) HD patients with the histological diagnosis of superficial chronic active gastritis were positive for \textit{H. pylori} in the gastric mucosa. This prevalence is significantly higher than what is seen in patients with other histological diagnosis ($p<0.001$). These findings were compared to a control group of 60 consecutive patients with normal renal function who underwent upper GI endoscopy for evaluation of dyspeptic symptoms during the same study period. Thirty-five (58.3%) were males and 51 (85%) were Saudi nationals. The age of the control group was similar to the HD patients ($38.9 \pm 13.3$ years). Thirty-eight (63.3%) were positive for \textit{H. pylori}. There was no significant difference in the mean age of the positive and negative patients: $39.6 \pm 12.8$ and $37.5 \pm 14.4$ years.

Table 3 depicts the histological findings and the status of \textit{H. pylori} on gastric biopsy in 54 HD patients and 60 patients with normal renal function.

\textbf{Discussion.} Upper GI disorders are common among uremic patients maintained on regular HD and upper GI endoscopy is an important tool in the evaluation of such patients. Fabbian et al performed upper GI endoscopy on 57 HD patients for work up of anemia, dyspepsia or in preparation for renal transplantation. Endoscopy revealed normal mucosa in 17.5% of cases, whilst chronic gastritis was diagnosed in 30%. Chronic gastritis was also the most common microscopic abnormality diagnosed in 71.5% of biopsies. Thirteen out of 38 patients in whom multiple biopsies of gastric mucosa were performed had \textit{H. pylori} infection (34%), and none of them had normal mucosa. Our study of 54 stable chronic HD patients has demonstrated a high prevalence rate of upper GI morphologic and histologic abnormalities despite

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Endoscopic findings} & \textbf{Total patients} & \textbf{Positive of \textit{H. pylori}} \\
\textit{n} & \textbf{n} & \textbf{n} \\
\hline
Normal & 5 & 1 \\
Acute gastritis & 13 & 8 \\
Chronic gastritis & 20 & 14 \\
Gastroduodenitis & 3 & 2 \\
Erosive duodenitis & 2 & 1 \\
Duodenitis & 3 & 2 \\
Duodenal ulcer & 6 & 5 \\
Gastroesophageal reflux disease & 2 & 1 \\
\hline
\textbf{Total} & \textbf{54 (100)} & \textbf{34 (100)} \\
\hline
\end{tabular}
\caption{Endoscopic findings and \textit{Helicobacter pylori} (\textit{H. pylori}) status.}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
\textbf{Histological diagnosis} & \textbf{Hemodialysis patients} & \textbf{Normal renal function} \\
\textit{n}=54 & \textit{n}=60 & \\
\textbf{Total patients} & \textbf{Positive of \textit{H. pylori}} & \textbf{Total patients} & \textbf{Positive of \textit{H. pylori}} \\
\textit{n} & \textbf{n} & \textit{n} & \textbf{n} \\
\hline
Chronic active gastritis & 28 (51.9) & 24 (85.7) & 40 (66.7) & 32 (80) \\
Chronic inactive gastritis & 10 (18.5) & 4 (40) & 14 (23.3) & 5 (35.7) \\
Acute gastritis & 6 (11.1) & 3 (50) & 1 (1.7) & - \\
Normal & 10 (18.5) & 3 (30) & 3 (5) & 1 (33.3) \\
Others & - & - & 2 (3.3) & - \\
\hline
\textbf{Total} & \textbf{54 (100)} & \textbf{34 (63)} & \textbf{60 (100)} & \textbf{38 (63.3)} \\
\hline
\end{tabular}
\caption{Histological diagnosis and \textit{Helicobacter pylori} (\textit{H. pylori}) infection in 54 hemodialysis and 60 control patients.}
\end{table}
the absence of GI symptoms in most of these patients. The most common histological diagnosis on gastric biopsy is superficial chronic active gastritis. This high prevalence rate of chronic active gastritis was similarly found in a previous prospective study in the same hospital involving patients with normal renal function. Out of 201 patients undergoing upper GI endoscopy for the evaluation of dyspeptic symptoms in which GI biopsies were taken, 137 patients (68.2%) had a histological diagnosis of superficial chronic active gastritis. *Helicobacter pylori* were identified in 123 (76%) of these patients. The current study corroborate such findings and extend them to the HD population.

We utilized histological examination and staining for *H. pylori* as a mean of detecting the infection in our patients. This method along with tissue culture is considered the gold standard for the diagnosis of *H. pylori* infection. Several non-invasive tools to detect *H. pylori* infection in patients with normal renal function are widely utilized. These include serological immunoglobulin G, urea breath test, and *H. pylori* stool antigen assay. The accuracy of these methods in patients with ESRD is uncertain. Huang et al performed Carbon 13 (13C) urea breath testing in 70 patients with ESRD undergoing HD and 70 dyspeptic controls without renal impairment. Urea breath test was found to be only 93.8% sensitive and 85.3% specific. *Helicobacter pylori* infection in this study was defined as a positive result on either histological examination or culture of gastric biopsy. Recent study from the same group is promising. Non-invasive stool antigen assay for the detection of *H. pylori* infection in HD patients was found to be reliable with a sensitivity and specificity of 97.5% each. It also proved to be reliable in follow up of response to *H. pylori* eradication therapy.

Prevalence of *H. pylori* infection among our HD patients is high at 63% and gets much higher among patients with chronic active gastritis (85.7%). This rate is similar to that seen in patients with normal renal function evaluated in this study. Several other investigators have reported equivalent rates of *H. pylori* infections between the HD and normal populations. On the other hand, lower rates of *H. pylori* infection in HD patients have been reported by others. Such conflicting results may be related to various factors such as the method of detection, age of the patients, prior antibacterial and proton pump inhibitor use and local prevalence of *H. pylori* infection in the general population. Well-developed countries with high socio-economic level have reported lower prevalence rate of *H. pylori* infection in the general population than developing countries.

Most of the patients included in this study were a group of HD patients undergoing multidisciplinary work up in anticipation of receiving a kidney graft. The necessity to identify and eradicate *H. pylori* infection in such patients is a matter of controversy. It is reasonable to assume that eradicating *H. pylori* infection prior to kidney transplantation would result in reduction of upper GI complications after the transplantation procedure. Upper GI ulceration was common in post kidney transplant patients before the wide spread availability of effective anti-ulcer therapy. Such complications were largely attributed to steroidal and non-steroidal anti-inflammatory drugs. Most recent studies, however, revealed a dramatic drop in the rate of GI complications with a mortality rate of only 1%. This change has coincided with the wide spread use of effective H2 blockers and proton pump inhibitors.

A recent retrospective study looked at 500 renal transplant patients in whom 31% were seropositive for *H. pylori* antibodies in blood samples taken just prior to kidney transplantation. There was no difference in patient or graft survival between the seronegative and seropositive patients. Three months after kidney transplantation, there were more ulcers in the seropositive group (6% versus 3%) and more esophagitis in the seronegative group (9% versus 7%). Moreover, during the 6-year of follow-up, 2 cases of gastroduodenal malignancies were diagnosed in the *H. pylori* positive group and none in the seronegative group. These findings provide support for the strategy of eradicating *H. pylori* infection prior to undergoing kidney transplantation. Proton pump inhibitor based triple eradication therapy was shown to be equally effective in HD patients.

In conclusion, upper GI abnormalities are common among HD patients even in the absence of symptoms referable to upper GI tract. Biopsy proven chronic active gastritis is the most common histological diagnosis and is highly associated with *H. pylori* infection. *Helicobacter pylori* infection is as prevalent in HD patients as in patients with dyspepsia and normal renal function. *Helicobacter pylori* infected HD patients tend to be older than patients without *H. pylori* infection. Duration of chronic HD therapy prior to endoscopy and the presence of symptoms do not seem to have an influence on the prevalence of *H. pylori* infection.

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Gastroduodenal lesions and *H. pylori* infection in HD patients... Al-Mueilo

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