Assessment of hemodialysis adequacy in patients with helicobacter pylori infection before and after eradication therapy

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ABSTRACT

Background: Helicobacter pylori has notable relationship with hemodialysis. H. pylori infection is a major risk factor for gastrointestinal troubles in dialysis patients. All hemodialysis patients should have regular assessment of dialysis adequacy. For the adequacy of hemodialysis, Urea reduction ratio (URR) and Kt/V are commonly used.

Objective: The purpose of this study was to study adequacy of hemodialysis in patients with positive H. pylori stool antigen (HpSA) before and after eradication therapy (ET).

Results: After ET, the GIT symptoms improved in 63.89% of negative HpSA patients, persisted in 16.67% and relieved in 19.44%, The mean URR before ET was 67.71 ± 2.76 and after ET was 69.25 ± 2.49, with a significant difference between before and after ET (P value = 0.002). The mean Kt/V before ET was 1.40 ± 0.08 and after ET was 1.43 ± 0.07, with a significant difference between before and after ET (P value = 0.004).

Conclusion: This study concluded that hemodialysis adequacy increased after eradication of H. pylori, thus it is recommended to eradicate H. pylori in patients on hemodialysis.

Keywords: Helicobacter pylori, Hemodialysis, Dialysis Adequacy, Urea reduction ratio, URR, Kt/V.

INTRODUCTION

Helicobacter pylori (H. pylori) has notable relationship with end stage renal disease (ESRD) and hemodialysis in several ways. First, H. pylori contribute to development of peptic ulcer disease, esophago-gastro-duodenal erosions, and anemia due to gastroduodenal blood loss that is common in hemodialysis patients. Second, H. pylori produces gastric mucosal inflammation and, may contribute to dyspepsia, anorexia, malignancies, and malnutrition in hemodialysis patients. Third, H. pylori may have an independent role in anemia in dialysis patients.(1)

Patients receiving hemodialysis often encounter gastrointestinal troubles over their long treatment period. H. pylori infection is thought to be one of the major risk factors for gastrointestinal troubles in dialysis patients.(2) Data concerning H. pylori infection frequency in hemodialysis patients are conflicting. Studies on H. pylori infections in uremic patients have rates varying from 27% to 73%.(1,4)

In most studies the prevalence of H. pylori infection in ESRD patients receiving hemodialysis was shown to be equal or lower compared to subjects with normal renal function in various different geographic populations irrespective to presence/absence of gastric symptoms.(1, 3,10) In hemodialysis patients, the frequency of gastroduodenal ulcers and gastric cancer is reported to be higher than in healthy people. Because hemodialysis patients are often receiving anticoagulant or antiplatelet drugs, bleeding from gastroduodenal ulcers may be fatal. Thus, H. pylori eradication is considered to be an important treatment for hemodialysis patients in order to prevent gastroduodenal ulcers and gastric cancer.(4)
**H. pylori** has several adaptations for the acidic environment of the stomach. One of them is production of large amounts of urease, and it has been estimated that up to 10% of the total protein content of *H. pylori* consists of urease, which converts urea into ammonia and bicarbonate. The ammonium hydroxide formed raises pH of gastric juice and enables *H. pylori* colonization of gastric mucosa. It has been debated that urease is essential for gastric colonization, although, urease negative strains have been isolated from patients. In patients with ESRD, high gastric juice urea concentrations, by providing substrate, might lead to elevated concentrations of ammonia, and ammonia has been incriminated as a main factor injuring gastric mucosa by several groups.

Invasive and noninvasive methods are available to detect *H. pylori* infections. However, dialyzed patients are often unwilling to undergo invasive procedures such as endoscopies. Because patients with ESRD receive anti-secretory drugs and require multiple antibiotic treatments for septic complications, accidental eradication of *H. pylori* infections is possible. Therefore, many *H. pylori*-negative patients with positive serology were previously infected with *H. pylori* and accidentally cured.

Wang et al proposed that stool antigen is a noninvasive and reliable tool for screening *H. pylori* infections before therapy and assessing the success of eradication therapy in patients with ESRD.

All hemodialysis patients should have regular global assessments of dialysis adequacy. This should include urea clearance, volume control, blood pressure, mineral metabolism, and clinical symptoms. Although practice guidelines have traditionally emphasized the role of urea clearance, this parameter is only one component of dialysis adequacy. Once dialysis inadequacy is confirmed, increase one or more of the following treatment parameters: blood flow rate, dialyzer coefficient of area (KoA), dialysis frequency, dialysis time, dialysate flow, needle size, and ensure adequate anticoagulation.

**Aim of the work**

The aim of the work was to study gastric symptoms and adequacy of hemodialysis in ESRD patients on regular hemodialysis with positive *H. pylori* antigen before and after eradication therapy.

**Material and Methods**

**Patients and Methods:**

This study included 40 patients with ESRD undergoing maintenance hemodialysis treatment 3 times weekly; the duration of each hemodialysis session was 4 hours, with bicarbonate basis dialysate and polysulfone membranes. All the patients were older than 18 years old and had gastric symptoms like stomach pains, nausea, bloating, belching, vomiting or melena. All the patients had positive stool for *H. pylori* antigen.

Eradication therapy was given; triple therapy with a proton pump inhibitor (pantoprazole 40 mg twice daily), amoxicillin (1 g twice daily), and clarithromycin (500 mg twice daily) for 14 days, then proton pump only for 14 days. Patients were encouraged to increase dietary intake of yogurt with probiotics. Then, after one month of the end of therapy, changes in gastric symptoms were detected along with *H. pylori* stool antigen (HpSA). For the adequacy of hemodialysis, URR and SpKt/V were calculated and compared before and after eradication therapy.

**Urea Reduction Ratio (URR):**

It is described by the following equation: \( \text{URR} = \frac{[1-(\text{Urea post-dialysis}/\text{Urea pre-dialysis})] \times 100}{t} \)

**Single-pool Kt/V (spKt/V):**

One commonly used estimating equation for spKt/V (\( K \) is dialyzer clearance of urea, \( t \) is dialysis time, \( V \) is volume of distribution of urea about equal to patient’s total body water) was developed by Daugirdas. SpKt/V is calculated monthly via urea kinetic modeling or Daugirdas second generation natural logarithm formula and used for patients receiving thrice-weekly hemodialysis.

\[ \text{SpKt/V} = -\ln (R-0.008 \times t)+(4-5.5 \times R) \times UF/W \]

\( R, UF, W \) are the post dialysis BUN, pre dialysis BUN, and UF/W volume in liters, respectively.

**Results**

The age of patients in the present study ranged from 19 to 75 years with mean age of 51.43 ± 13.5 years and median 53.5 years. Males (65%) outnumbered females (35%), with a sex ratio of 1.86. The dry weight of patients in the present study ranged from 47.5 to 103.5 Kg with mean dry weight of 66.91 ± 10.37 Kg and median 66.25 Kg. The duration of dialysis ranged from 6 months to 9 years, with a mean of 3.41 ± 2.08 years and a median of 3 years. The cause of renal failure was diabetic nephropathy in 22.5% of the studied patients, hypertension in 20%, combined hypertension/diabetes in 15%, and chronic glomerulonephritis in 10%. Arteriovenous fistula (AVF) was used as an access for hemodialysis in 92.5% and dialysis catheter in 7.5%.
Nausea was the GIT symptom in 87.50% of the studied patients, followed by epigastric pain in 70%, and then bloating in 45%. One month after the end of eradication therapy 90% of the studied patients were converted from positive H. pylori antigen in stool to negative, while 10% were persistent positive H. pylori. The GIT symptoms improved in 63.89% of negative HpSA test patients, persisted in 16.67% and relieved in 19.44%, whereas, they persisted in 75% of persistent positive H. pylori patients and improved in only 25%.

Before eradication therapy the mean Hemoglobin level in the studied patients was 8.81 ± 0.96 and after eradication therapy it was 9.20 ± 1.27. There was a significant difference in Hb level between the patients before and after the eradication therapy (P value = 0.03). Before eradication therapy the mean WBC’s count in the studied patients was 6.89 ± 2.23 and after eradication therapy it was 6.73 ± 2.17. There was a significant difference in WBC’s count between the patients before and after the eradication therapy (P value = 0.048).

Before eradication therapy the mean urea level pre-dialysis in all studied patients was 198.78 ± 44.14 and after eradication therapy it was 203.83 ± 39.00. There was no significant difference in urea level Pre-dialysis between the patients before and after the eradication therapy (P value = 0.50).

Before eradication therapy the mean URR in patients who converted to HpSA negative was 67.71 ± 2.76 and after eradication therapy it was 69.14 ± 2.49. There was a significant difference between the two results (P value = 0.002). While in persistent positive H. pylori patients the mean URR before the eradication therapy was 66.13 ± 4.76 and after eradication therapy was 67.00 ± 2.49.

### Table-1. Comparison between pre and post-ET regarding URR in negative and persistent positive HpSA

<table>
<thead>
<tr>
<th>URR</th>
<th>Negative H. pylori (n=36)</th>
<th>Persistent positive H. pylori (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-therapy</td>
<td>post-therapy</td>
</tr>
<tr>
<td>Min</td>
<td>57.45</td>
<td>60.42</td>
</tr>
<tr>
<td>Max</td>
<td>71.98</td>
<td>72.50</td>
</tr>
<tr>
<td>Mean</td>
<td>67.71</td>
<td>69.25</td>
</tr>
<tr>
<td>SD</td>
<td>2.76</td>
<td>2.49</td>
</tr>
<tr>
<td>Median</td>
<td>67.97</td>
<td>70.09</td>
</tr>
</tbody>
</table>

P values* 0.002* 0.58

*Significantly different at P ≤ 0.05

### Table-2. Comparison between pre and post-ET regarding Kt/V in negative and persistent positive HpSA

<table>
<thead>
<tr>
<th>Kt/V</th>
<th>Negative H. pylori (n=36)</th>
<th>Persistent positive H. pylori (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-therapy</td>
<td>post-therapy</td>
</tr>
<tr>
<td>Min</td>
<td>1.10</td>
<td>1.18</td>
</tr>
<tr>
<td>Max</td>
<td>1.50</td>
<td>1.50</td>
</tr>
<tr>
<td>Mean</td>
<td>1.40</td>
<td>1.43</td>
</tr>
<tr>
<td>SD</td>
<td>0.08</td>
<td>0.07</td>
</tr>
<tr>
<td>Median</td>
<td>1.42</td>
<td>1.45</td>
</tr>
</tbody>
</table>

P values* 0.004* 0.56

*Significantly different at P ≤ 0.05

### Urea reduction ratio (URR): Table 1 shows that before eradication therapy the mean URR in patients who converted to HpSA negative was 67.71 ± 2.76 and after eradication therapy it was 69.14 ± 2.49. There was a significant difference between the two results (P value = 0.002). While in persistent positive H. pylori patients the mean URR before the eradication therapy was 66.13 ± 4.76 and after eradication therapy was 67.00 ± 2.49.
3.45. There was no significant difference between the two results (P value = 0.58).

The phytochemical study of 8 medicinal plants and 6 families has been studied. In this study we found that *Echinops echinatus Roxb.*, *Ricinus communis L* and *Abutilon Indicum* plants contain high flavonoids than other plant studied plants. Information has been given in table 1. The each species provided Ethnobotanical information: taxon name, family, vernacular name, plant parts their use in the treatment of jaundice diseases. In this study, plants were dominant for jaundice because of majority of flavonoids present in leaf extract. Comparison of the plant parts used as a medicinal source indicates that the leaf predominates followed by root, bark.

**Kt/V (Daugirdas II)**

Table 2 shows that before eradication therapy the mean Kt/V in patients who converted to HpSA negative was 1.40 ± 0.08 and after eradication therapy it was 1.43 ± 0.07. There was a significant difference between the two results (P value = 0.004). While in patients who remained HpSA positive the mean Kt/V before the eradication therapy was 1.35 ± 0.12 and after eradication therapy was 1.38 ± 0.08. There was no significant difference between the two results (P value = 0.56).

**Discussion**

Sufferers from ESRD need dialysis therapy to remove the fluid and waste products built up during interdialytic period.\(^{[43]}\)

In this study the age of patients ranged from 19 to 75 years with mean age of 51.43 ± 13.5 years. Approximate results were shown in the study by Jalalzadeh et al (2012),\(^{[43]}\) in which the mean age of patients infected by *H. pylori* and on Hemodialysis was 59.0 ± 16.2.

In the present study, in 87.5% of the studied patients nausea was the main GIT symptom, followed by epigastric pain in 70%, and then bloating in 45%. While, in the study by Hauser et al (2015),\(^{[39]}\) epigastric pain was the main symptom of *H. pylori* infection representing 93.38% of symptoms followed by bloating.

In the present study, one month after the end of eradication therapy 90% of the studied patients were converted from positive *H. pylori* antigen in stool to negative, while 10% remained positive. This was similar to the study by Hauser et al (2015),\(^{[39]}\) in which, the percentage of cure after eradication therapy was 87.38% in probiotics receiving patients and 72.55% in the group receiving the eradication therapy only. According to Ierardi et al,\(^{[41]}\) no therapy regimen can cure *H. pylori* infections in all treated patients, and some patients remain infected despite several consecutive standard therapies.

In the present study, one month after the end of eradication therapy, the GIT symptoms improved in 63.89% of negative HpSA test patients, persisted in 16.67% and relieved in 19.44%. While, they persisted in 75% of positive HpSA test patients and improved in only 25%. In the study by Utia et al (2010),\(^{[42]}\) the symptoms relieved after eradication therapy in 76.4% of negative *H. pylori* patients, and persisted in 32.6%, surprisingly, all the symptoms of the patients in the positive group were relieved.

In the present study results showed that before eradication therapy the mean creatinine level in the studied patients was 9.60 ± 2.33 and after eradication therapy it was 9.05 ± 2.14. There was a significant difference in creatinine level between the patients before and after the eradication therapy (P value <0.001). This is similar to Jalalzadeh et al (2012),\(^{[43]}\) who found after eradication of *H. pylori* in patients on hemodialysis that the mean creatinine level decreased from 9.0 to 8.6 after one line of therapy and from 10.59 to 10.4 after another line of therapy.

Although the same researcher, Jalalzadeh et al (2010),\(^{[43]}\) showed that there was no significant difference in creatinine level, where mean creatinine level changed from 9.8 before eradication to 9.4 after eradication by 8 weeks and 10.1 after eradication by 6 months (P value = 0.4 after 8 weeks and 0.4 after 6 months) in patients on hemodialysis.

In the present study results showed that before eradication therapy the mean URR in patients who converted to HpSA negative was 67.71 ± 2.76 and after eradication therapy it was 69.25 ± 2.49. There was a significant difference between the two results (P value = 0.002). This was similar to the study by Nomer et al,\(^{[40]}\) that showed a significant difference (P value = 0.001), in which before eradication therapy the mean URR in patients who converted to HpSA negative was 46.93 ± 8.02 and after eradication therapy it was 51.96 ± 4.75.

In the present study, in patients who persisted HpSA positive the mean URR before the eradication therapy was 66.13 ± 4.76 and after eradication therapy was 67.00 ± 3.45. There was no significant difference between the two results (P value = 0.819).

In the present study results showed that, before eradication therapy the mean Kt/V in patients who converted to HpSA negative was 1.40 ± 0.08 and after eradication therapy it was 1.43 ± 0.07. There was a significant difference between the two results (P value = 0.004). While in patients who persisted HpSA positive the mean Kt/V before the eradication therapy was 1.35 ± 0.12 and after eradication therapy was 1.38 ± 0.08. There was no significant difference between the two results (P value = 0.56).

In the present study results showed that, before eradication therapy the mean Kt/V in patients who converted to HpSA negative was 1.40 ± 0.08 and after eradication therapy it was 1.43 ± 0.07. There was a significant difference between the two results (P value = 0.004). While in patients who persisted HpSA positive the mean Kt/V before the eradication therapy was 1.35 ± 0.12 and after eradication therapy was 1.38 ± 0.08. There was no significant difference between the two results (P value = 0.56).

In the study by Jalalzadeh et al,\(^{[43]}\) 2012 he stated that, after eradication of *H. pylori* in patients on
hemodialysis, the mean Kt/V increased from 1.25 to 1.29 in the group who received a regimen containing 20 mg omeprazole, 500 mg amoxicillin, and 250 mg azithromycin, administered twice a day for 14 days, with continued administration of omeprazole for two additional weeks, on the contrary it decreased from 1.06 to 1.03 in the group who received a regimen containing 20 mg omeprazole, 500 mg amoxicillin, and 250 mg clarithromycin twice a day for 14 days, also with continued administration of omeprazole for two additional weeks.

**Conclusion**

1. Hemodialysis adequacy increased after eradication of Helicobacter pylori.
2. Triple therapy is effective for eradication of *H. pylori* infection in hemodialysis patients, and probiotics improve eradication rates.
3. Most of GIT symptoms were improved after eradication of Helicobacter pylori.
4. Hemoglobin level increased post eradication of Helicobacter pylori.
5. WBC’s count decreased post eradication of Helicobacter pylori.
6. It is essential to eradicate Helicobacter pylori in patients on hemodialysis.

**Recommendations**

1. Dyspeptic symptoms should not be ignored among patients treated by hemodialysis, and should be investigated.
2. All dyspeptic patients on hemodialysis should be screened for *H. pylori* infection.
3. It is recommended to eradicate *H. pylori* in patients on hemodialysis.
4. Patients on hemodialysis should be encouraged to increase dietary intake of yogurt with probiotics.
5. Hemodialysis centers should have a continuous quality improvement/patient review system in place that recognizes patients who are receiving suboptimal dialysis adequacy, identifies the cause, and corrects it.
6. Further studies, with large sample population (patients), should be conducted.

**Conflict of Interests**

Authors declare that there is no conflict of interests regarding the publication of this paper.

**References**


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