Effect of Helicobacter Pylori Eradication on Hemodialysis Efficacy in Egyptian Patients

Abdel-Naser Abdel-Atty Gad-Allah[1], Ashraf Ghareib Dala[2] Amany Mohamed Abdel-Fatah[3], Safwa Toulan[4]

Internal Medicine department, Faculty of Medicine, Menofia University, Shebin Elkom, Menofia, Egypt

2 Internal Medicine department, Faculty of Medicine, Menofia University, Shebin Elkom, Menofia, Egypt

3Dialysis unit, Shebin Elkom Fever Hospital, Shebin Elkom, Menofia, Egypt

4Internal Medicine department, Faculty of Medicine, Menofia University, Shebin Elkom, Menofia, Egypt.

Email: amany.mohamed654@yahoo.com

Abstract

Background: Helicobacter pylori (H. pylori) is the most commonly identified cause of gastrointestinal (GI) infections, leading to disorders such as gastritis, ulcerative disorders, and gastric cancer. End-stage renal disease (ESRD) patients often experience GI symptoms as a characteristic of the uremic syndrome. H. pylori eradication therapy (ET) has been found to effectively relieve GI symptoms and prevent clinical complications in ESRD patients.

Methods: We conducted a prospective cohort analytic hospital-based study on various Egyptian populations from November 2021 to December 2022. The study population comprised 80 ESRD patients who tested positive for H. pylori stool antigen (HpAS). The patients were divided into four equal groups, with each group receiving a different treatment regimen. The eradication of H. pylori was evaluated by HpSA one month after the end of ET. To evaluate the adequacy of hemodialysis (HD), we calculated and compared the Urea reduction ratio (URR) and Single-pool Kt/V (spKt/V) before and after ET.

Results: The rate of improvement in GI symptoms after H. pylori eradication was 40%, 25%, 60%, and 55% in the four groups, respectively. The mean URR in the studied patients before ET was 65.13±2.46 and increased to 68.05±2.16 after ET (P value = 0.046). The mean Kt/V in the studied patients before ET was 1.32±0.08 and increased to 1.50±0.08 after ET (P value = 0.004).

Conclusion: Eradication of H. pylori using quadruple and sequential treatment regimens can improve most GI symptoms. Our study concludes that H. pylori eradication significantly improves the efficacy of HD in ESRD patients.

Keywords: Helicobacter pylori, end-stage renal disease, hemodialysis

INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative bacterium that commonly colonizes the stomach and affects nearly half of the world's population. It is known to cause various gastrointestinal (GI) disorders such as gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma. The urease enzyme produced by H. pylori facilitates its colonization in the stomach by neutralizing the acidic environment [1,2].

End-stage renal disease (ESRD) patients undergoing hemodialysis (HD) often experience gastrointestinal symptoms due to uremic syndrome. H. pylori infection is a significant contributor to the pathologic changes observed in the stomach of ESRD patients undergoing HD. This relationship can be attributed to elevated serum gastrin levels, delayed gastric emptying, or the presence of H. pylori infection [3].

The link between H. pylori infection and ESRD is multifaceted. H. pylori can cause anemia in ESRD

patients by inducing gastrointestinal bleeding, peptic ulcer disease, and esophageal-gastro-duodenal erosions. H. pylori infection also induces gastrointestinal mucosal inflammation, which can lead to malnutrition, anorexia, dyspepsia, and cancer. In addition, H. pylori may play a role in HD patients' anemia by altering the composition of gastric juice and impairing iron absorption [4].

Erythropoietin-stimulating agents (ESAs) are used to manage anemia in ESRD patients, but they are expensive and associated with adverse events. H. pylori infection can potentially exacerbate anemia by impairing iron absorption. The effect of H. pylori eradication therapy (ET) on dialysis efficacy and anemia in ESRD patients is uncertain, with some studies suggesting a benefit of H. pylori eradication while others have not shown a significant effect [5-8].

This prospective cohort study aims to evaluate the impact of H. pylori eradication on HD efficacy in ESRD patients and investigate the effect of different eradication regimens on GI symptoms and anemia. The findings of this study may provide valuable insights into the management of ESRD patients undergoing HD and shed light on the role of H. pylori infection in the uremic syndrome.

SUBJECTS AND METHODS

This study is a prospective cohort analytical hospital-based study on a variety of Egyptian populations conducted from November 2021 to December 2022.

Study population

The study enrolled patients with ESRD undergoing HD treatment. Patients who had already eradicated H. pylori, were taking aspirin, non-steroidal anti-inflammatory medications, warfarin, bismuth preparations, proton pump inhibitors, or antibiotics within the previous eight weeks were excluded. The study recruited a total of 200 patients, of whom only 87 were positive for H. pylori stool antigen test (HpAS). Three of the positive patients died during the study, and four were lost to follow-up. The final number of participants was 80.

Ethical Considerations

All procedures in this study adhered to the guidelines established by the Menoufia University Ethical Committee, and patient consent was obtained from every subject. After being informed of the study's purpose, all enrolled patients gave their signed consent. Any unforeseen dangers were promptly disclosed to the Ethics Committee and patients.

Method

The study included 80 participants who were divided into four equally-sized groups. Group I received LCA triple therapy, which consisted of Lansoprazole 30 mg twice daily (b.i.d), Clarithromycin 500 mg b.i.d, and Amoxicillin 1 g b.i.d for 2 weeks. Group II received LCM triple therapy, which included Lansoprazole 30 mg b.i.d, Clarithromycin 500 mg b.i.d, and Metronidazole 500 mg b.i.d for 2 weeks. Group III received LCAM quadruple therapy, which consisted of Lansoprazole 30 mg b.i.d, Clarithromycin 500 mg b.i.d, Amoxicillin 1g b.i.d, and Metronidazole 500 mg b.i.d for 2 weeks. Group IV received sequential treatment, which involved taking Lansoprazole 30 mg b.i.d for two weeks; during the first week, patients took Amoxicillin 1g b.i.d, and during the second week, they took Clarithromycin 500 mg b.i.d and Metronidazole 500 mg b.i.d.

After one month following the completion of ET, changes in gastric symptoms were assessed in addition to measuring HpSA levels. To evaluate the adequacy of HD, the Urea Reduction Ratio (URR) and Single-Pool Kt/V (spKt/V) were calculated and compared before and after the ET.

Statistical analysis:

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 20. Quantitative variables were presented using means and standard deviations, while categorical variables were described using absolute frequencies. The Chi-square test and Fisher exact test were used to compare categorical variables, and the Kolmogorov-Smirnov and Levene tests were used for parametric testing. The level of significance was set at $P<0.05$.

Results

The mean total age of the studied groups was 51.12 ± 14.87 years, with 46 (57.5%) males and 34 (42.5%) females, and a mean body mass index (BMI) of 25.35 ± 4.53. No statistically significant difference was found among the groups regarding gender, age, and BMI.

Regarding GI symptoms before treatment, a comparison was made between the four groups, which revealed that epigastric pain was the most prevalent symptom in group I (25%), heartburn in group II (30%), epigastric pain in group III (20%), and nausea in group IV (25%). However, there was no statistically significant difference in the prevalence of GI symptoms among the studied groups.

After treatment, 59 (73.75%) of the total cases studied were negative for HpSA, while only 21 (26.25%) were positive for HpSA. There was no statistically significant difference among the four groups in terms of HpSA positivity (P=0.578) (Table 1).

After treatment, the response of gastrointestinal symptoms in the four groups was assessed. In group I, 40% of the negative patients (8 out of 20) showed improvement, while 10% had persistent symptoms and 5% experienced relief. Among positive patients in group I, 25% (5 out of 20) had persistent symptoms and 10% showed improvement. In group II, 25% of the negative patients (5 out of 20) showed improvement, while 35% had persistent symptoms. Among positive patients in group II, 25% had persistent symptoms and 15% showed improvement. In group III, 60% of negative patients (12 out of 20) showed improvement, while 10% had persistent symptoms and 20% experienced relief. Among positive patients in group III, only 5% (1 out of 20) had persistent symptoms and 5% showed improvement. In group IV, 55% of negative patients (11 out of 20) showed improvement, while 10% had persistent symptoms and 15% experienced relief. Among positive patients in group IV, 15% had persistent symptoms and 5% showed improvement (Table 2).

The mean hemoglobin (Hb) levels of the four groups before and after treatment were compared. In group I, the mean Hb was 8.25±1.13 before treatment and 8.87±1.32 after treatment, with no significant difference. In group II, the mean Hb was 8.84±1.56 before treatment and 8.96±1.73 after treatment, with no significant difference. In group III, the mean Hb was 8.7±3.34 before treatment and 10.5±1.34 after treatment, with a significant difference. In group IV, the mean Hb was 8.25±1.64 before treatment and 9.4±1.35 after treatment, with a significant difference (Table 3).

Comparison of the studied groups before and after treatment with regard to URR is presented in Table 4. No significant difference was found in groups I and II before and after treatment, for both negative and positive HpSA. However, in groups III and IV, a significant difference was found in negative HpSA before and after treatment, regarding URR, with P values of 0.040 and 0.029, respectively. Overall, the mean URR in the studied patients before the end of ET was 65.13±2.46, and after ET it was 68.05±2.16, with a P value of 0.046.

There was no significant difference in spKt/V between negative and positive HpSA before and after treatment in groups I and II. However, in groups III and IV, there was a statistically significant difference in negative HpSA before and after treatment with P=0.030 and 0.019, respectively (Table 5). The mean Kt/V in the studied patients before ET was 1.32±0.08, and after ET, it was 1.50±0.08, showing a significant difference (P value = 0.004).

Finally, a significant positive correlation was observed between response to treatment and the efficacy of HD, with P-values of 0.002 and 0.003, respectively (Table 6).

Table 1 Comparison between the studied groups according to the presence of HpSA after treatment

HpSA (after)	Total (n= 80)		Group I (n= 20)		Group II (n= 20)		Group III (n= 20)		Group IV (n= 20)		χ^2	^{MC}p
	No.	%	No.	%	No.	%	No.	%	No.	%		
Negative	59	73.75	13	65.0	12	60.0	18	90.0	16	80.0	2.411	0.578
Positive	21	26.25	7	35.0	8	40.0	2	10.0	4	20.0		

χ^2: Chi-square test MC: Monte Carlo P: P value for comparing the studied groups

Table 2 Comparison between studied groups according to GI symptoms after treatment

GI symptoms (after)	Group I (n=20) No (%)		Group II (n=20) No (%)		Group III (n=20) No (%)		Group IV (n=20) No (%)	
	-ve	+ve	-ve	+ve	-ve	+ve	-ve	+ve
Improved	8(40)	2(10)	5(25)	3(15)	12(60)	1(5)	11(55)	1(5)
Persisted	4(10)	5(25)	7(35)	5(25)	2(10)	1(5)	2(10)	3(15)
Relieved	1(5)	0(0)	0	0(0)	4(20)	0	3(15)	0

Table (3): Comparison between studied groups before and after treatment as regarding to hemoglobin level.

Mean Hb % (g/dl)	**Group I (n=20)**	**Group II (n=20)**	**Group III (n=20)**	**Group IV (n=20)**	**p-value**
Before treatment Mean ± SD.	8.25±1.13	8.84±1.56	8.7±3.34	8.25±1.64	0.9171
After treatment Mean ± SD.	8.87±1.32	8.96±1.73	10.5±1.34	9.4±1.35	0.764
P value	0.652	0.356	0.033*	0.042*	

Group I: patients under triple therapy (LCA) **Group II:** patients under triple therapy (LCM)
Group III: patients under quadruple therapy (LCAM) **Group IV:** patients under sequential treatment
SD: Standard deviation P: P value for comparing between the studied groups

Table 4 Comparison between studied groups before and after regarding URR in each group

URR (%)	N	Before	After	t	p
Group I					
Negative HpSA	13	60.15± 4.72	61.01± 3.29	0.016	0.897
Positive HpSA	7	61.03± 3.76	61.99± 2.45	0.014	0.902
Total	20	60.23± 4.24	61.24± 2.96	0.016	0.896
Group II					
Negative HpSA	12	65.61± 3.1	66.72± 3.2	0.018	0.891
Positive HpSA	8	64.52± 2.9	65.01± 3.01	0.003	0.951
Total	20	65.15± 3.2	66.02± 3.1	0.017	0.895
Group III					
Negative HpSA	18	64.71± 2.76	69.41± 2.47	4.78	0.026*
Positive HpSA	2	65.12± 4.75	66.01± 3.35	0.058	0.808
Total	20	65.84± 2.34	69.62± 2.34	4.203	0.040*
Group IV					
Negative HpSA	16	65.58± 2.12	69.14± 2.64	4.795	0.028*
Positive HpSA	4	65.22± 3.22	66.01± 3.13	0.003	0.952
Total	20	65.52± 2.14	68.05± 2.53	4.828	0.029*
Total patients					
Negative HpSA	59	64.34± 2.24	68.13± 2.31	3.902	0.048*
Positive HpSA	21	66.02± 3.8	66.47± 2.49	0.052	0.818
Total	80	65.13± 2.46	68.05± 2.16	3.685	0.046*

t: Paired t-test P: P value for comparing before and after *: Statistically significant at $P \leq 0.05$

Table 5 Comparison between studied groups before and after according to spKt/V in each group

Single-pool Kt/V(spKt/V)	**N**	**Before**	**After**	**t**	**p**
Group I					
Negative HpSA	13	1.21± 0.12	1.23± 0.07	0.074	0.675
Positive HpSA	7	1.23 ± 0.08	1.24± 0.06	0.082	0.864
Total	20	1.22± 0.11	1.24± 0.06	0.003	0.985
Group II					
Negative HpSA	12	1.32± 0.08	1.36 ± 0.08	0.001	0.972
Positive HpSA	8	1.30± 0.03	1.31± 0.04	0.000	0.993
Total	20	1.31± 0.09	1.34± 0.09	0.000 6	0.979
Group III					
Negative HpSA	18	1.35± 0.09	1.51± 0.07	5.953	0.014*
Positive HpSA	2	1.34± 0.11	1.35± 0.08	0.028	0.864
Total	20	1.35± 0.09	1.49± 0.08	4.666	0.030*
Group IV					
Negative HpSA	16	1.34± 0.08	1.50 ± 0.06	6.095	0.013*
Positive HpSA	4	1.31± 0.09	1.35 ± 0.07	0.484	0.486
Total	20	1.34± 0.08	1.49± 0.07	5.421	0.019*
Total patients					
Negative HpSA	59	1.31± 0.07	1.50± 0.08	8.913	0.002*
Positive HpSA	21	1.33± 0.09	1.34 ± 0.09	0.029	0.862
Total	80	1.32± 0.08	1.50± 0.08	7.902	0.004*

t: Paired t-test P: P value for comparing before and after *: Statistically significant at $P \leq 0.05$

Table 6 Correlation between h. pylori eradication and efficacy of HD

Efficacy of HD	Response to treatment	
	r	p
URR (%)	0.790	0.002*
spKt/V	0.251	0.003*

DISCUSSION

Our study revealed that there were no significant differences in gender, age, and BMI among the analyzed groups, which is consistent with the findings of Majidi et al. After therapy, only 26.25% of the total

investigated cases had positive HpSA, consistent with the results of Majidi et al.'s study which found no differences between the four H. pylori eradication regimens used to treat ESRD patients[9].

Epigastric pain, heartburn, epigastric pain, and nausea were the most common GI symptoms in each group, respectively. The rate of GI symptom improvement after H. pylori eradication in the four groups was 40%, 25%, 60%, and 55%, respectively. *Itatsu et al* also found that patients with uremic symptoms frequently experience nausea, pain, and abdominal discomfort, and many ESRD patients also experience upper GIT problems [10]. In Bakr et al.'s study, the main GI symptom reported by 87.5% of patients was nausea, followed by epigastric pain in 70% and bloating in 45% 10 [11].

Our study has shown that treating H. pylori infection in ESRD patients undergoing HD with two specific regimens (group III and group IV) has led to a significant increase in their Hb levels. This finding suggests that chronic gastritis, impaired iron absorption, or increased blood loss resulting from H. pylori infection could contribute to anemia in this population. Additionally, our study demonstrated the safety and efficacy of H. pylori eradication with these two regimens, as evidenced by negative HPSA tests and the absence of serious adverse events. On the other hand, the two regimens that failed to eradicate H. pylori and improve Hb levels were (group I and group II). The lack of amoxicillin in these regimens may have contributed to their poor performance.

Overall, our findings suggest that H. pylori eradication with specific treatment regimens can improve Hb levels in ESRD patients undergoing HD and that failure to eradicate H. pylori may be responsible for the persistence of anemia in these patients.

The study's findings support prior research indicating a significant enhancement of Hb levels after eradicating H. pylori in ESRD patients undergoing HD. For example, Liang et al observed that administering standard triple therapy for a duration of 7 days increased Hb levels from 9.6 g/dL to 10.4 g/dL after 12 weeks of treatment among 14 HD patients[13].

The findings indicate that H. pylori eradication can lead to a significant increase in URR. This is in line with the results of Bakr et al, who reported a mean URR of 67.71 ± 2.76 before ET, which rose to 69.25 ± 2.49 after treatment. The difference between the two outcomes was statistically significant with a P value of 0.002 [11].

Our findings suggest that patients who converted to HpSA negative experienced a significant increase in Kt/V after ET. Conversely, patients who remained HpSA positive did not exhibit any significant change in Kt/V before and after ET. These results are in line with Bakr et al's study, where they reported a significant difference in the mean Kt/V before and after ET in patients who converted to HpSA negative (1.40 ± 0.08 vs 1.43 ± 0.07, P value = 0.004).

The results of this study showed a positive correlation (P = 0.002 and 0.003, respectively) between the efficacy of HD and the eradication of H. pylori.

Conclusion

H. pylori infection testing should be performed on all dyspeptic patients on HD. Eradication of H. pylori using quadrable and sequential treatment improved most GI symptoms and is crucial to avoid complications. The results of this study concluded that H. pylori eradication in ESRD patients significantly improves HD efficacy. Further randomized controlled studies, with large sample patients, should be conducted.

Acknowledgment

I want to express my deepest appreciation to all my supervisors: Prof. Dr. Ashraf Ghareib Dala and Dr. Abdel-Nasr Abdel-Atty Gad Allah, as well as Dr. Safwa Toulan. I'm also grateful for all participants in this research. I had the pleasure of collaborating with my colleagues on the results of my research.

References

1. *Gupta N, Maurya S, Verma H, Verma VK. Unraveling the factors and mechanism involved in persistence: Host-pathogen interactions in Helicobacter pylori. Journal of Cellular Biochemistry. 2019;120:18572-87. doi.*
2. *Guevara B, Cogdill AG. Helicobacter pylori: A Review of Current Diagnostic and Management Strategies. Dig Dis Sci. 2020;65:1917-31. https://doi.org/10.1007/s10620-020-06193-7.*
3. *Seyyed Majidi M, Sanjari Pirayvatlou P, Rajabikashani M, Firoozabadi M, Seyed Majidi SA, Vafaeimanesh J. Comparison of Helicobacter pylori eradication regimens in patients with end stage renal disease. Gastroenterol Hepatol Bed Bench. 2018;11:15-19. doi.*
4. *Costa-Moreira P, Vilas-Boas F, Teixeira Fraga A, Macedo G. Particular aspects of gastroenterological disorders in chronic kidney disease and end-stage renal disease patients: a clinically focused review. Scandinavian Journal of Gastroenterology. 2020;55:129-38. doi.*
5. *Collister D, Komenda P, Hiebert B, Gunasekara R, Xu Y, Eng F, et al. The effect of erythropoietin-stimulating agents on health-related quality of life in anemia of chronic kidney disease: a systematic review and meta-analysis. Annals of internal medicine. 2016;164:472-78. doi.*
6. *Ferguson T, Xu Y, Gunasekara R, Lerner B, Macdonald K, Rigatto C, et al. The cost effectiveness of erythropoietin-stimulating agents for treating anemia in patients on dialysis: a systematic review. American Journal of Nephrology. 2015;41:89-97. doi.*
7. *Monzón H, Forné M, Esteve M, Rosinach M, Loras C, Espinós JC, et al. Helicobacter pylori infection as a cause of iron deficiency anaemia of unknown origin. World J Gastroenterol. 2013;19:4166-71. https://doi.org/10.3748/wjg.v19.i26.4166.*
8. *El-Said H, Attallah AHB, Ali-Eldin ZA. Does Helicobacter pylori infection play a role in iron deficiency anemia in hemodialysis patients? Clinical Nephrology. 2017;88:177. doi.*
9. *Majidi MS, Pirayvatlou PS, Rajabikashani M, Firoozabadi M, Vafaeimanesh J. Comparison of Helicobacter pylori eradication regimens in patients with end stage renal disease. Gastroenterology and Hepatology from Bed to Bench. 2018;11:15. doi.*
10. *Itatsu T, Miwa H, Nagahara A, Kubota M, Miyazaki A, Sato N, et al. Eradication of Helicobacter pylori in hemodialysis patients. Renal failure. 2007;29:97-102. doi.*
11. *Bakr NS, Gad MS, El-Gohary EE, El-Gaiar NH. Assessment of hemodialysis adequacy in patients with helicobacter pylori infection before and after eradication therapy. biolifejournal. 2016;4:100-06. doi.*
12. *Hauser G, Salkic N, Vukelic K, Jajacknez A, Stimac D. Probiotics for standard triple Helicobacter pylori eradication: a randomized, double-blind, placebo-controlled trial. Medicine. 2015;94. doi.*
13. *Liang C-M, Chiu C-H, Wang H-M, Tai W-C, Yao C-C, Tsai C-E, et al. First-Line Helicobacter pylori Eradication in Patients with Chronic Kidney Diseases in Taiwan. BioMed Research International. 2017;2017:3762194. https://doi.org/10.1155/2017/3762194.*