Journal of Nephropathology

Evaluation of noninvasive tests for diagnosis of *Helicobacter pylori* infection in hemodialysis patients

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Original Article

ARTICLE INFO

ABSTRACT

Background: Hemodialysis is the most common method of renal replacement therapy for treatment of acute and chronic kidney failure. *Helicobacter* pylori (*H. pylori*) plays a major role in development of peptic ulcer, gastric neoplasms, and lymphoma as well as increased risk of cardiovascular disorders in hemodialysis patients.
Objectives: In this study the diagnostic values of noninvasive tests [i.e. urea breath test (UBT), *helicobacter pylori* stool antigen test (HPSA) and serology] in diagnosis of H. pylori infection in hemodialysis patients have been studied.
Patients and Methods: All patients undergoing hemodialysis in Fatemieh Hospital, Semnan, Iran, were enrolled in the study, and their *H. pylori* status were assessed by using non-invasive tests including UBT, HPSA and serology. Patients with at least two out of 3 positive tests were considered infected with *H. pylori*.
Results: The sensitivity, specificity, and positive and negative predictive values of the tests used in diagnosing *H. pylori* infection were 62.5%, 65.4%, 62.5% and 65.4% for UBT, 100%, 72.2%, 58.3% and 100% for serology, and 100%, 75%, 60.9% and 100% for fecal antigen test, respectively.
Conclusions: This study showed that *H. pylori* serology and stool antigen tests have higher diagnostic values than UBT, and they are more reliable than UBT in diagnosis of *H. pylori* infection in hemodialysis patients.

Implication for health policy/practice/research/medical education:
Helicobacter pylori in hemodialysis patients play a major role in occurrence of peptic ulcer, gastric neoplasms, lymphoma as well as increased risk of cardiovascular disorders.

Please cite this paper as: Tamadon MR, Saberi Far M, Soleimani A, Ghorbani R, Semnani V, Malek F, Malek M. Evaluation of noninvasive tests for diagnosis of *Helicobacter pylori* infection in hemodialysis patients. J Nephropathology. 2013; 2(4): 249-253, DOI: 10.12860/JNP.2013.39

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1. Background

Chronic renal failure refers to a process with significant and irreversible loss in number of nephrons. Hemodialysis is the most common method of renal replacement therapy which removes the toxins, fluids and electrolytes (1). Direct effects of *Helicobacter pylori* and its related complications are the major health problems in hemodialysis patients (2). Helicobacter pylori (*H. pylori*) plays a major role in occurrence of peptic ulcer, gastric neoplasms, lymphoma and mucosa-associated lymphoid tissue (MALT). It may also lead to increased risk of cardiovascular disorders, the main causes of death in this population (4).

Prevalence of *H. pylori* varies in different geographic areas, and it is closely related to the socioeconomic status of the patients (2, 3). In the United States and other developed countries the prevalence of *H. pylori* infection is 30%, and in developing countries it is more than eighty percent (2). There are heterogeneous data about the prevalence of *H. pylori* infection in hemodialysis patients. Prevalence of *H. pylori* infection in different studies varies from 34% to 75% (5).

Diagnostic tests for *H. pylori* are divided into two categories; invasive and noninvasive. Invasive tests, including histology, urease, and culture tests, need upper GI endoscopy to obtain specimens for diagnostic evaluations. Hemodialysis patients usually undergo several therapeutic/diagnostics procedures, and they are often reluctant to invasive procedures such as endoscopy. This matter determines the necessity of reliable noninvasive diagnostic tests for these patients (4).

H. pylori stool antigen test (HPSA), serology and urea breath test (UBT) are noninvasive tests for detection of *H. pylori*, and they decrease the necessity of invasive procedures such as endoscopy. HPSA is the latest non-invasive diagnostic tests (6). There is little information about the usefulness of noninvasive diagnostic tests for detection of *H. pylori* infection in hemodialysis patients. Among the noninvasive methods, serology and UBT are common and widely used tests (4).

Few studies have determined the diagnostic value of these tests in hemodialysis patients (8). The recent consensus has suggested that the prevalence of *H. pylori* infection in hemodialysis patients has been markedly lower than others (9).

2. Objectives

In this study the diagnostic value of noninvasive tests (UBT, HPSA and serology) in the diagnosing *H. pylori* infection in hemodialysis patients has been investigated.

3. Patients and Methods

In this study, all hemodialysis patients in Fatemiyeh Hospital, Semnan, Iran, were included to the study. All patients were enrolled in study after written consent and description of the project for them.

Patients who received proton pump inhibitors (PPIs), those who were not able to discontinue the treatment at least two weeks before the study, and patients receiving antibiotics for 4 weeks and bismuth for 2 weeks before beginning of the study were excluded. All patients completed a questionnaire and underwent the following tests: 1) UBT with IsoMax (Isodiagnostika company, Inc, Canada); all values more than +10 were considered positive; 2) IgA and IgG antibodies levels of *H. pylori* with the IBL kit (Germany) according to the manufacturer's instructions by ELISA; all values more than 10u/ml were considered positive; 3) *H. pylori* Stool Antigen test.

For stool antigen test, 10 grams stool specimens were obtained after at least 12-hours fasting state, and the amount of *H. pylori* antibodies were

measured with IBL kit (Germany) by ELISA and values more than 0.1 were considered positive.

In this study we used a combination of three tests (UBT, HPSA and serology) as the gold standard; if two out of them were positive, they were considered infected with *H. pylori* and if two out of three tests were negative, they were considered uninfected.

The sensitivity, specificity, positive and negative predictive values of each noninvasive test were compared to the gold standard test. In statistical analysis, ROC curve was used for quantitative responses. Sensitivity, specificity, positive and negative predictive values were calculated for the qualitative responses.

4. Results

Overall, 50 hemodialysis patients were taken into the survey in which 60% (30 cases) were male. The patients' mean age (±SD) was 70 (±15.8) years ranging from 20 to 105 years (Table

1). Mean hemodialysis duration (±SD) was 32.3 (±28.3) months, ranging from 3 to 132 months. Twenty two patients (44%) had diabetes and 11 patients (22%) had hypertension.

Regarding to positive results for at least two of three tests and as gold standard for *H. pylori* infection, the diagnostic values of each test were determined as follow:
- Sensitivity, specificity, positive and negative predictive values for UBT in diagnosing of *H. pylori* in hemodialysis patients were 62.5%, 65.4%, 62.5% and 65.4%, respectively (Table 2).
- Sensitivity, specificity, positive and negative predictive values for serology in diagnosing of *H. pylori* in hemodialysis patients were 100%, 100%, 100% and 100%, respectively.
- Sensitivity, specificity, positive and negative predictive values for stool antigen test in diagnosing of *H. pylori* in hemodialysis patients became 95.8%, 100%, 100% and 96.3%, respectively.

5. Discussion

Table 1. Age distribution, duration of dialysis and predisposing disease in hemodialysis patients

Parameter			
Age distribution	<50	11	22
	50-59	9	18
	60-69	11	22
	70-79	15	30
	>80	4	8
	Total	50	100
Dialysis duration (year)	<1	11	22
	1	-	-
	2	13	26
	3	9	18
	4	5	10
	5	4	8
	>6	8	16
	Total	50	100
Predisposing Disease	Diabetes	22	44
	Hypertension	11	22
	Lupus	2	4
	Glomerulonephritis	1	2
	Nephrotic syndrome	2	4
	Congenital	1	2
	Unknown	11	22
	Total	50	100

Table 2. Diagnostic value of UBT, Serology and fecal antigen test in diagnosing of *H pylori*

Golden Score Test		H. pylori (Golden Score)		
		Positive	Negative	Total
UBT	Positive	15	9	24
	Negative	9	17	26
	Total	24	26	50
Serology	Positive	24	0	23
	Negative	0	26	27
	Total	24	26	50
Fecal antigen test	Positive	23	0	23
	Negative	1	26	27
	Total	24	26	5

In this study, serology test with high sensitivity and specificity (100% and 100%, respectively), was found a reliable non-invasive test. In a study by Lopez et al., specificity of serology test was very low since a lot of non infected patients had positive results. Usually immunoglobulin titers after eradication of *H. pylori* are decreased but not eliminated. Low specificity of this test is due to the fact that many hemodialysis patients are previously infected by *H. pylori*, which then is inadvertently eradicated. A cause of this inadvertent eradication is the use of anti- secretory drugs as well as various antibiotics for treatment of infectious complications. Similarly, low gastric acid output in these patients is common which creates improper environment for *H. pylori*. Also, chronic dialysis would lead to higher false positive results (4). In another study conducted by Bustillo et al., low specificity of this test was related to antibiotic therapy for infectious complications (5).

In a study in Turkey, Yildiz et al. found that positive results among the older population were higher than that of others and were related to poor health status in previous years which could result in more infections. In developing countries, however, positive cases are higher due to poor health status. Also there is a reverse correlation between duration of dialysis and positive serology results, which may be due to uremia in these patients as a cause of impairment of humeral immunity and reduced antibody responses (10).

The stool antigen test is a test with high sensitivity and specificity (95.8% and 100%, respectively). We used the IBL kit (Germany) in our study. However, other kits have been used in other studies with different results. In a study by Lopez et al. this test was done by these three Kits: Femto lab HP (Germany), PREMIER PALATINUM (USA) and SIMPLE HP (Spain). Sensitivity and specificity in each of the above kits have obvious differences. For example, sensitivity and specificity in FEMTO LAB kit were 86% and 100% in PREMIER PALATINUM kit 58% and 96% and in SIMPLE HP kit 61% and 78%, respectively. Results of Stool antigen test may differ from a kit to another and from one population to another. In another study by Nardon and colleagues in 2005, effectiveness of HPSA in hemodialysis patients was low, which might be due to chronic consumption of phosphate binding compounds in these patients (11).

UBT was not shown to be a reliable test in this study; its sensitivity and specificity are 62.5% and 65.4%, respectively. However, various studies have controversial results. In our study ISO DIAGNOSE KA kit (Canada) was used, in which at the first phase the patients exhaled 10 cc of expiratory air into the test bag after an overnight fasting. Lo-

pez et al., used ISOMED MADRID kit (Spain), in which at the first phase (according to European modified protocol) the patient ate 200 cc citric acid plus 25 mg saccharin, and test was done after 10 minutes. In this study HPSA was most reliable non-invasive test (95% sensitivity and specificity).

This study suggests that the bacterial urease activity in patients with renal failure may be increased due to higher level gastric aspirated urea and presence of other urease-producing organisms such as Proteus. In these patients, false positive results of UBT may be higher. On the other hand, hemodialysis decreases the levels of urease in the gastric contents which can lead to a reduction in false positive results thus increasing the specificity (4). Nardon et al. in a study suggested that in hemodialysis patients, false positive results of UBT may decrease. In this study specialty of the test was 100% (11).

6. Conclusions

Based on our data, it seems that *H. pylori* serology and stool antigen tests have higher diagnostic values than UBT, and they are more reliable than UBT in diagnosis of *H. pylori* infection in hemodialysis patients.

Authors' contributions

MRT, MSF and MM designed and performed the research. RG analyzed data and wrote some parts of paper. FM and VS also provided extensive intellectual contribution. MRT reviewed the draft too. MM prepared the final draft.

Conflict of interest

The authors declared no competing interests.

Financial Disclosure

Acknowledgments

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