

## Prevalence of Upper Gastrointestinal Lesions and *Helicobacter pylori* Infection in Upper Endoscopic Study of Renal Transplantation Candidates without GI Symptoms

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### ABSTRACT

**Background:** Renal transplantation is the most effective therapeutic strategy in ESRD patients. One of the renal transplantation complications is gastrointestinal bleeding due to peptic ulcers beside other upper gastrointestinal diseases that have a great impact on patients' morbidity and mortality.

**Objective:** The present study is designed for endoscopic assessment of the prevalence of upper gastrointestinal lesions and also *Helicobacter pylori* infection in ESRD patients waiting for renal transplantation who have no GI symptoms.

**Methods:** Our cross-sectional research was performed on 85 renal transplant candidates referred to organ transplantation center within 2016 to 2018. Patients who met inclusion criteria and didn't have exclusion criteria underwent upper endoscopy. We performed biopsies in each case and data were classified according to endoscopic results, *Helicobacter pylori* infection and pathologic findings.

**Results:** In 53 patients (62%) there were significant endoscopic findings. Erosive gastroduodenitis (32.5%) was the most prevalent finding. Abnormal histopathologic findings were found in 73% of patients and *Helicobacter pylori* infection was detected in 48.2%. We found significant correlation between H. Pylori infection and abnormal pathology ( $p=0.04$ ).

**Conclusion:** Our results showed that asymptomatic gastrointestinal lesions and *Helicobacter pylori* infection were significantly prevalent in kidney transplant candidates thus routine upper endoscopy is recommended in them. This can result in early detection and treatment of gastric lesions before transplantation to prevent serious long-term complications.

**KEYWORDS:** Renal transplantation; *Helicobacter pylori*; Gastrointestinal lesions

### INTRODUCTION

Different stages of chronic kidney disease (CKD) including end-stage renal disease (ESRD) are remarkably

prevalent all over the world. The prevalence of CKD is about 11% in developed countries and disease is usually diagnosed at stages I-II [1, 2], while in developing countries such as Iran, it's prevalence is over 15% and most patients are diagnosed at stages III-IV [3, 4]. Also, it is well known that kidney transplantation is the best treatment option for patients with ESRD [5].

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In uremic patients despite the high prevalence of gastrointestinal lesions and abnormal histopathologic findings, the rate of gastrointestinal symptoms is low due to peripheral motor and sensory nerve defects that reduce visceral sensitivity [6]. This pathophysiology may result in UGI complications, especially bleeding without any warning signs. It is reported that over 75% of patients undergoing dialysis suffer from gastrointestinal lesions and its complications which affect patient's outcome after renal transplantation [7-9]. Within the first 6 months after renal transplantation the prevalence of UGI complication is at the highest level that can significantly increase patients' mortality rate [10].

Like many other specialists, in our center we routinely perform upper gastrointestinal endoscopy in case of CKD patients with GI symptoms who are candidate for kidney transplantation [11]. But we do not have enough data about silent upper GI pathologies that probably have potential to affect such patients' survival as well as their quality of life. There is no specific study that statistically evaluated the precise endoscopic findings and association of *H. pylori* infection and histology but in GI-asymptomatic patients. As the first study in northern Iran, we planned this research to estimate the prevalence of upper GI lesions as well as *H. pylori* infection in renal transplantation candidates who did not show any GI symptoms. This can address the controversy of upper endoscopic evaluation in all transplantation candidates regardless of presence of GI symptoms and can optimistically give a clue to approach the patients better before the transplantation.

## MATERIALS AND METHODS

In this cross-sectional study 85 ESRD patients who were referred to Montaserie kidney transplant Hospital (Mashhad-Iran) were studied from 2016 to 2018.

A GI specialist performed upper GI endoscopy following 12-hour fasting period in all 85 patients at a single tertiary center. The entire

length of the esophagus, stomach and the first and second parts of duodenum were precisely observed. GI specialist performed three biopsies from stomach body, antrum and incisura. Specimens were sent to laboratory in order to histopathologic studies.

Regarding the endoscopy findings, patients were divided into two groups: significant and non-significant endoscopic findings group. In significant findings group, observed lesions were classified into one of the following: esophagitis, peptic ulcer (including gastric ulcer and duodenal ulcer), erosive gastroduodenitis (presence of more than one erosion in stomach or duodenum in absence of any ulcer) and others. Non-significant finding group were divided into: completely normal and non-erosive gastritis categories.

Also, all specimens were evaluated for presence of *Helicobacter pylori* infection and tissue changes by an experienced pathologist after giemsa staining.

We analyzed extracted data by SPSS 21 statistical software and results were described by distribution tables, charts, and mean and standard deviation indicators. Chi-Square (or Fisher exact) test was applied in order to compare the distribution. The confidence interval considered 95% ( $\alpha=0.05$ ).

Inclusion criteria were ESRD patients who were candidate for renal transplantation and also were consent for involvement in the study. Exclusion criteria considered patients with clinical dyspepsia based on ROME IV criteria including: epigastric pain, heartburn, postprandial fullness and early satiety and patients with known upper gastrointestinal diseases, and those who had been using PPIs, NSAIDs, H<sub>2</sub> blockers or antibiotics over the last two weeks.

## Ethical Considerations

The study approved by Ethics Committee of Mashhad University of Medical Sciences (IR. MUMS.FM.REC.2016.244).

**Table 1:** Demographic characteristics and endoscopic findings prevalence of study groups.

Variables	Abundance	Percentage
<b>Gender</b>		
Male	45	52.9
Female	40	47.1
<b>Age</b>		
Less than 35 y/o	40	47.1
More than 35 y/o	45	52.9
<b>Cause of kidney failure</b>		
HTN	31	36.5
DM	25	29.4
Lupus nephritis	5	5.9
Nephrotic syndrome	3	3.5
Reflux nephropathy	3	3.5
ADPKD	1	1.2
Unknown	17	20
<b>Type of dialysis*</b>		
Hemodialysis	67	78.8
Peritoneal dialysis	10	11.8
<b>Endoscopic findings</b>		
<b>Significant finding</b>		
peptic ulcer	6	7
Erosive gastroduodenitis	27	31.7
Atrophic gastritis	7	8.2
Esophagitis	10	11.8
Others	3	3.5
<b>Non-significant finding</b>		
Normal	21	24.7
Nonerosive gastritis	11	12.9

\* 8 subjects were not on dialysis

## RESULTS

Out of 165 initial cases, 55 were excluded due to presence of gastric symptoms, 15 were excluded because of consuming PPI, H<sub>2</sub> blocker or antibiotics in the last two weeks and 10 were excluded due to discontent. Final 85 subjects including 45 male patients (52.9%) and 40 females (47.1%) entered the study. Other demographic characteristics are listed in Table 1.

We observed significant endoscopic abnormalities in 53 (62.4%) patients and non-significant changes in 32 cases (37.6%). We also found that gastroduodenitis was the most

common endoscopic finding (Table 1). We did not notice dialysis-associated telangiectasia in our study group.

According to statistical analysis, no correlation was found between significant endoscopic findings and variables including: age (P= 0.5), gender (P= 0.9), cause of renal failure (P= 0.9) and also dialysis modality (P= 0.08) (Table 2).

Abnormal histopathology was found in about 73% of patients. In patients with abnormal endoscopic findings, abnormal histopathologic results were significantly higher compared to those with normal endoscopic results. (83% vs. 56.2%, P= 0.03).

In addition, *H. pylori* infection was found in about 48% of all patients, which is similar to normal prevalence in asymptomatic general population. Results also showed that *H. pylori* infection was more common in patients over 35 y/o and also in male population (Table 3). However, in terms of endoscopic findings we found no significant difference between the subjects with *H. pylori* infection and non-infected individuals (P= 0.2). Also age and duration of dialysis did not have influence on *H. pylori* infection in our patients (P= 0.6, P= 0.8).

On the other hand, we found a significant direct correlation between *H. Pylori* infection and abnormal pathology (P=0.04). (Table 4).

In addition, the mean duration of dialysis in patients with normal and abnormal pathology was  $21.57 \pm 16.16$  and  $20.68 \pm 16.17$  months respectively (P= 0.8). The average dialysis duration in patients with normal and abnormal endoscopy was not statistically different thus we found that the duration of dialysis probably dose not affect the endoscopic results ( $22.56 \pm 16.71$  and  $19.89 \pm 15.74$  months, respectively, P= 0.4).

## DISCUSSION

It is well known that kidney transplantation is the best treatment option for patients with

**Table 2:** Relationship between endoscopic findings and variables of patients (gender, age, ESRD cause, and dialysis type).

Variables	Endoscopic finding		Result
	Significant	Non-significant	
<b>Gender</b>			
Male	17(53.1)	28(52.08)	X <sup>2</sup> = 0.01, P= 0.9
Female	15(46.9)	25(47.2)	
<b>Age</b>			
Less than 35 y/o	17(53.1)	23(43.4)	X <sup>2</sup> = 0.7, P= 0.5
More than 35 y/o	15(46.9)	30(56.6)	
<b>Cause of kidney failure</b>			
HTN	12(37.5)	19(35.8)	P= 0.9
DM	10(31.3)	15(28.3)	
Lupus nephritis	3(9.4)	2(3.8)	
Nephrotic syndrome	1(3.1)	2(3.8)	
Reflux nephropathy	1(3.1)	2(3.8)	
ADPKD	0(0)	1(1.9)	
Unknown	5(15.6)	13(22.6)	
<b>Undergoing dialysis</b>			
Yes	30(93.8)	47(88.7)	X <sup>2</sup> = 0.6, P= 0.04
No	2(6.3)	6(11.3)	
<b>Type of dialysis*</b>			
Hemodialysis	28(32.9)	37(43.5)	P= 0.08
Peritoneal dialysis	2(2.3)	10(11.8)	

Data present as Abundance (Percentage)

ESRD. Despite the high prevalence of gastrointestinal lesions in uremic patients the rate of GI symptoms in them is relatively low due to peripheral motor and sensory nerve defects that reduce visceral sensitivity. This pathophysiology may result in UGI complications especially GI bleeding without any warning signs. It is reported that over 75% of patients undergoing dialysis suffer from gastrointestinal lesions and its complications which affect patients' health status after renal transplantation. Early treatment of patients GI abnormalities including ulcerative and non-ulcerative gastric lesions and also *H. pylori* infection can improve patients nutritional status and also to prevent GI malignancies as well as other comorbidities. This undoubtedly leads to better quality of life and longer survival of patients after renal transplantation.

Several mechanisms seem to increase the risk

of upper gastrointestinal diseases in ESRD patients, including pathophysiologic changes such as: hypergastrinemia, hyperammonemia, secondary hyperparathyroidism, comorbidities associated with hemodialysis and related medications [12]. Accordingly, similar studies have reported the high prevalence of gastrointestinal diseases in ESRD patients, which is also proved in our research but our main focus in this study was to give a clue about upper GI abnormalities in patients without GI symptoms that could be easily neglected [13, 14].

Patients who undergo dialysis have a higher level of inflammatory cytokines that activate the inflammatory cells in mucous membrane of the stomach. This pathophysiologic process results in gastric atrophy that leads to inappropriate environment for *H. pylori*. Besides, urea inhibits *H. Pylori* growth in mucosal layer of stomach. Also, *H. pylori* infection may be

**Table 3:** Relationship between *H. pylori* infection and patients' variables (gender, age, ESRD cause, and dialysis type).

Variables	<i>H. pylori</i> infection		Result
	Negative	Positive	
<b>Gender</b>			
Male	19(46.3)	26(59.1)	X <sup>2</sup> = 1.4, P= 0.2
Female	22(53.7)	18(40.9)	
<b>Age</b>			
Less than 35 y/o	22(50)	18(43.9)	X <sup>2</sup> = 0.3, P= 0.6
More than 35 y/o	22(50)	23(56.1)	
<b>Cause of kidney failure</b>			
HTN	14(31.8)	17(41.5)	P= 0.4
DM	11(25)	14(34.1)	
Lupus nephritis	4(9.1)	1(2.4)	
Nephrotic syndrome	2(4.5)	1(2.4)	
Reflux nephropathy	2(4.5)	1(2.4)	
ADPKD	0(0)	1(2.4)	
Unknown	11(25)	6(14.6)	
<b>Undergoing dialysis</b>			
Yes	40(90.9)	37(90.2)	X <sup>2</sup> = 0.01, P= 0.9
No	4(9.1)	4(9.8)	
<b>Type of dialysis*</b>			
Hemodialysis	35(87.5)	30(81.1)	X <sup>2</sup> = 0.6, P= 0.5
Peritoneal dialysis	5(12.5)	7(18.9)	

Data present as Abundance (Percentage)

eliminated by antibiotics that are prescribed for other purposes during the illness. It is reported that more than 30% of patients with *H. pylori* infection who had been dialyzed for 4 years were spontaneously cured during the period [9].

In a study by Ponticelli *et al.*, the most frequent gastrointestinal complications in kidney transplant recipients found to be upper gastrointestinal including oral, esophageal and gastric lesions [15]. Similarly we found a significant percentage of Upper GI complications even in patients who do not have any GI compliant and this emphasizes the importance of gastrointestinal follow up in ESRD patients. Gu *et al.*, showed that the incidence of ulcerative diseases in dialysis patients was 13.7% and in control group was 24.9% [16].

In our study we observed a slightly lower

prevalence of gastric ulcerative lesions in the study population (7%).

Several related studies have been carried out in different countries and most of them have reported similar findings. In one research, 46% of patients had endoscopic findings other than peptic ulcer and erosive gastroduodenitis while *H. pylori* infection was reported in about one-third of total patients [17]. In our study, we detected *H. pylori* infection in 48.2% of 85 renal transplant patients who did not represent gastrointestinal symptoms and the most common endoscopic finding was erosive gastroduodenitis.

A study described that more than half of ESRD patients show at least one upper GI involvement while the frequency of ulcerative lesions was lower than nonulcerative ones. This corresponds with our results in asymptomatic

**Table 4:** Relationship between histopathology results and patients' variables (gender, age, ESRD cause, and dialysis type).

Variables	Histopathology		Result
	Abnormal histopathology	Normal histopathology	
<b>Gender</b>			
Male	32(51.6)	13(56.6)	X <sup>2</sup> = 0.1
Female	30(48.4)	10(43.5)	P= 0.8
<b>Age</b>			
Less than 35 y/o	28(45.2)	12(52.2)	X <sup>2</sup> = 0.3
More than 35 y/o	34(54.8)	11(47.8)	P= 0.6
<b>Cause of kidney failure</b>			
HTN	24(38.7)	7(30.4)	P= 0.6
DM	20(32.3)	5(21.7)	
Lupus nephritis	3(4.8)	2(8.7)	
Nephrotic syndrome	2(3.2)	1(4.3)	
Reflux nephropathy	2(3.2)	1(4.3)	
ADPKD	1(1.6)	0(0)	
Unknown	10(16.1)	7(30.4)	
<b>Undergoing dialysis</b>			
Yes	56(90.3)	21(91.3)	X <sup>2</sup> = 0.01
No	6(9.7)	2(8.7)	P= 0.8
<b>Type of dialysis*</b>			
Hemodialysis	44(78.6)	21(100)	X <sup>2</sup> = 4.3
Peritoneal dialysis	12(21.4)	0(0)	P= 0.06

Data present as Abundance (Percentage)

ESRD patients [18].

In another study, high rates of peptic ulcer and mild symptoms were observed in uremic patients despite the *H. pylori* infection [19]. Also, in the other study, the percentage of erosive gastritis lesions in patients with renal insufficiency and those on Hemodialysis was 23.9% and 30.1%, respectively, which was significantly higher than those following renal transplant as well as healthy subjects. In mentioned study, the *H. pylori* infection rate in renal failure and hemodialysis group was considerably higher than the group after renal transplant and also healthy subjects (66.2 and 63% versus 40% and 34% respectively) [20]. In another study by Cocchiara *et al.*, in which 61 patients with chronic renal failure were evaluated for *H. pylori* half of the patients were reported to be infected via endoscopic biopsies [21]. In the other research 50.2% of patients

were positive and the others were *H. pylori* negative [14]. Our results are more in concordance with the latter.

Usta *et al.*, described that *H. pylori* was more prevalent in their peritoneal dialysis patients compared to hemodialysis patients (38.7% vs. 13.6%, P=0.046). They also described that the most prevalent non-ulcerous GI lesions in their endoscopic evaluations were gastritis (62.3%), erosive gastritis (38.7%), duodenitis (18.9%), and esophagitis (13.2%) [22].

Chang *et al.*, described that among patients with peptic ulcer disease, *H. pylori* infection prevalence in the CKD (58.5%) and ESRD (56.2%) patients was lower than in non-CKD patients (70.3%) [23]. But in our study population with no GL complaint endoscopic findings in *H. pylori* positive patients did not significantly differ from non-infected individuals.

Niknam *et al.*, reported that the vast majority of their study population showed different abnormalities in their upper endoscopy, including GERD, gastric lesions, and duodenal lesions that in their study. In the stomach, 90 (30.7%) of the patients with *H. pylori* infection had abnormal non-ulcerative lesions, while only 17 (5.5%) of them had gastric ulcer and 40 (13.6%) were normal. With the ratio the same as the stomach, duodenal abnormal non-ulcerative findings (12.6%) were greater than duodenal ulcers (7.1%) in patients with *H. pylori* infection [14].

It is notable that we did not notice telangiectasia in endoscopic investigation of patients' gastric mucosa; However some previous studies and case reports found that lesion in dialysis patients presented with GI bleeding [24, 25].

The ambiguity in results of different studies can be due to differences in influencing factors such as geographical location, complications of renal failure resulting in more or less symptoms or less understanding of it, duration of dialysis, presence of any associated disorder in patients, and *H. pylori* evaluation method.

Up to our knowledge this is the first study in Iran that studies upper GI lesions in asymptomatic renal transplantation candidates.

In this prospective study, all endoscopic procedures were performed by one gastroenterologist and in all cases three biopsies were done from different points (Sydney protocol) in order to evaluate *H. pylori* and precancerous lesions.

Limitation of the study was absence of a control group to compare with normal population; however performing upper endoscopy in asymptomatic general population was not moral. Another limitation of this research was inability to evaluate inflammatory cytokines to discover their possible effects on gastrointestinal lesions as well as infection with *H. pylori*.

In conclusion, in the present study gastroin-

testinal lesions as well as *H. pylori* infection were observed in a large number of kidney transplant candidates without any GI symptom. Endoscopy could be considered as a safe and accurate method for diagnosing upper GI disorders as a part of the pre-transplantation evaluation in all candidates regardless of presence of GI symptoms. However, further studies are recommended to determine the efficacy of *H. pylori* eradication in order to improve abnormal GI findings and decrease post-transplant gastrointestinal complications such as GI bleeding and GI cancers.

**CONFLICTS OF INTEREST:** None declared.

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