

Original research article

**EVALUATION OF CKD PATIENTS FOR GERD AND GASTRODUODENAL ULCERATIONS AND THEIR CORRELATION WITH *H. PYLORI* STATUS**

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**Abstract**

Kidney damage for  $\geq 3$  months, as defined by structural or functional abnormalities of the kidney, with or without decreased Glomerular filtration rate (GFR). A proper GI assessment is of paramount importance either for a prospective renal transplantation candidate or those patients having even minor GI symptoms when they are on maintenance haemodialysis or conservative management of CRF. *Helicobacter Pylori* infection is accepted as an etiological factor of chronic gastritis, peptic ulcer disease, and other gastrointestinal (GI) disorders. Gastrointestinal symptoms, particularly heartburn, pyrosis, and regurgitation, are frequent findings in end-stage renal disease (ESRD) patients and in renal transplant recipients (RTRs). These complaints may be due to gastroesophageal reflux disease (GERD).

**Aims and Objectives:** Endoscopic finding in patients of CKD with special evaluation on diagnosis of *H. pylori* infection.

**Methodology:** We conducted an observational study on 50 patients, who are diagnosed to have Chronic kidney disease and being admitted to M.B hospital Udaipur in medicine department over a period of one year. All patients with chronic kidney disease underwent upper gastrointestinal endoscopy and biopsy for *H. pylori* were included in the study.

**Results:** Majority of the subjects belongs to age group of 31 to 40 years (26%) and least belongs to 70 to 80 years age group (6%). Out of the 50 subjects, males were 28 and females were 22. Majority of the cases in our study belonged to stage IV. 84% of the cases had upper gastrointestinal involvement on endoscopic examination in our study. Erosive gastritis (26%), either antral or fundal, was the predominant lesion found

on endoscopy. Majority of the subjects having erosive gastritis, had stage IV CKD (53.8%). Out of 50 cases in our study 55% of subjects had lesions of the stomach, 26% of subjects had lesions in the duodenum, 19% of subjects had lesions in oesophagus. Out of 50 subjects in our study 52% were undergoing haemodialysis and 48% of subjects were under conservative management. Majority of subjects undergoing haemodialysis were belongs to stage V. Biopsy for Pylori were done to all 50 patients out of which 22 (44%) detected positive.

**Conclusion:** Majority of the patients with chronic kidney disease have upper gastrointestinal involvement on endoscopic evaluation. Erosive gastritis is the most common upper gastrointestinal manifestation in our study. Upper gastrointestinal manifestations are predominant in stage V. Upper gastrointestinal findings are frequently observed in chronic kidney disease patients on dialysis. Early diagnosis and management can reduce mortality and morbidity and prevent fatal complication like massive upper gastrointestinal bleed.

This study showed that positive Pylori were detected in 44% of patients so upper GI endoscopy with biopsy is an acceptable procedure for these patients.

**Keywords:** Chronic kidney disease, Upper gastrointestinal manifestations, Erosive gastritis, Gerd, *H. pylori*.

## Introduction

Definition of chronic kidney disease: Kidney damage for  $\geq 3$  months, as defined by structural or functional abnormalities of the kidney, with or without decreased Glomerular filtration rate (GFR), manifest by either: Pathological abnormalities; or markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests. GFR  $< 60$  mL/min/ 1.73 sqm for  $\geq 3$  months, with or without kidney damage <sup>[1]</sup>.

Even in asymptomatic patients of chronic renal failure (CRF) on maintenance haemodialysis, investigators have shown that the GI blood loss is much more than in controls. Hence, a proper GI assessment is of paramount importance either for a prospective renal transplantation candidate or those patients having even minor GI symptoms when they are on maintenance haemodialysis or conservative management of CRF <sup>[2]</sup>.

*Helicobacter Pylori* infection is accepted as an etiological factor of chronic gastritis, peptic ulcer disease, and other gastrointestinal (GI) disorders <sup>[3]</sup>. Gastrointestinal symptoms, particularly heartburn, pyrosis, and regurgitation, are frequent findings in end-stage renal disease (ESRD) patients and in renal transplant recipients (RTRs). These complaints may be due to gastroesophageal reflux disease (GERD) <sup>[4]</sup>. GERD describes the clinical manifestations of reflux of gastric contents into the oesophagus. Although the exact prevalence is difficult to determine, it seems that GERD is the most common oesophageal disease seen in primary care settings. The prevalence of GERD is now increasing; however, little is known about this condition in ESRD and RTRs. Although upper GI diseases and their complications are frequent in both patient groups, only few reports are available on the prevalence of *H. pylori* and its influence on dyspepsia and GERD in ESRD and RTRs.

Chronic renal failure (CRF) patients receiving haemodialysis treatment consist of more than 1.1 million people in the world, and the size of this population is expanding at a

rate of 7% per year according to the progress in medical and dialysis machine technique<sup>[5]</sup>. Although heart failure, angina pectoris, hypertension, parathyroid-related disease, amyloidosis, renal anaemia and infection are well known to occur by receiving haemodialysis and continuous ambulatory peritoneal dialysis (CAPD) for long periods<sup>[6]</sup>, those patients also often suffer from gastrointestinal troubles including peptic ulcer, haemorrhage, abdominal symptoms, constipation, diarrhoea, ileus, and perforation<sup>[7]</sup>.

*Helicobacter Pylori* is a spiral-shaped, microaerophilic Gram-negative flagellate bacterium that was isolated in 1983 from gastric biopsy specimens of patients with chronic gastritis<sup>[8]</sup>. The gastric mucosa of approximately 50% of the world's population is infected with *H. pylori*, and the infection levels exceed 70% in some developing areas<sup>[9]</sup>. *Helicobacter Pylori* infection plays a crucial role in the development of gastrointestinal diseases, such as peptic ulcer, gastric hyperplastic polyps, gastric adenoma, gastric cancer, and gastric mucosa associated-lymphoid tissue lymphoma, both in individuals with normal renal function and in chronic renal failure patients receiving hemodialysis and CAPD.

Patients with CKD are at increased risk for peptic ulcer disease (PUD) than the general population in long-term follow-up.

### **Aims and Objectives**

Endoscopic finding in patients of CKD with special evaluation on diagnosis of *H. pylori* infection.

### **Material and Methods**

This prospective observational study has been done on patients aged 18 years or above, who were admitted to various wards of Department of Medicine, RNT Medical College, Udaipur during Jan 2021 to Dec 2021.

### **Inclusion criteria**

1. Patients with CKD.
2. Renal transplant recipients.

A questionnaire has been used to assess renal disease (aetiology, duration, and type of treatment), symptoms of GERD, history of drug therapy, previous *H. pylori* eradication therapy, and concomitant chronic diseases.

### **Exclusion criteria**

1. Patients who have taken antibiotics within last 4 weeks.

A signed consent has been taken from every patient enrolled in this study. This prospective study has been carried out according to the guidelines of the Medical Ethical Committee of RNT Medical College, Udaipur.

All patients has been subjected to upper GI endoscopy; GERD has been diagnosed endoscopically according to the Los Angeles (LA) classification. Biopsies obtained from the lower oesophagus, the gastric antrum and the body, and from ulcer edges (if present) for histological evaluation and the presence of *H. pylori*.

## Statistical Analysis and Sample Size

Data has been described by using descriptive statistical methods, including frequency tables, statistical charts, central tendency, and dispersion indices. Proper test which ever will be required will be applied such as the chi-square test, Fisher's exact test, and Student's *t*-test, as well as ANOVA or nonparametric tests formulated by Mann–Whitney and Kruskal–Wallis. Level of significance will be checked at  $<0.05$ .

## Methodology

**Source of data:** Patients admitted to ward, department of General Medicine, RNT Medical College and MB Hospital Udaipur.

**Study design:** Observation study.

**Study period:** One year

**Sample size:** A total of 50 subjects diagnosed to have chronic kidney disease, presented to outpatient department or were admitted to RNT medical college, fulfilling inclusion criteria were included in this study.

## Inclusion criteria

1. Patient with CKD.
2. Renal transplant recipient.

## Exclusion criteria

1. Patients who have taken antibiotic in last 4 weeks.

## Criteria for diagnosing chronic kidney disease

1. Symptoms of uraemia for 3 months or more.
2. Elevated blood urea, serum creatinine and decreased creatinine clearance.
3. Ultrasound evidence of CKD.
  - a) Bilateral contracted kidney – size less than 8 cm in male and size less than 7 cm in female.
  - b) Poor corticomedullary differentiation.
  - c) Type 2 or 3 renal parenchyma changes.

Supportive laboratory evidence of CKD like anaemia, low specific gravity, changes in serum electrolytes etc.

Staging of chronic kidney disease is based on Glomerular filtration rate. Cockcroft Gault formula was used to calculate the glomerular filtration rate.

Cockcroft-Gault Formula for Estimating Creatinine Clearance	
$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$	

Detailed clinical history and clinical examination is under taken with preference to gastro intestinal related complaints and renal diseases. The following investigations were performed.

1. Haemoglobin, total count, ESR
2. RBS
3. Blood urea, serum creatinine
4. Serum electrolytes
5. Urine analysis
6. ECG

After selecting the patients fulfilling the above criteria, they were subject to upper gastro intestinal endoscopy at our institute, using flexible fiberoptic endoscope, manufactured by Olympus Inc. Biopsies has been obtained from the lower oesophagus, the gastric antrum and the body, and from ulcer edges (if present) for histological evaluation and the presence of *H. pylori*.

#### Estimation of sample size

Cisse Mouhamadou <sup>[68]</sup> Moustapha of Cheikh Anta Diop University Teaching Hospital, Senegal conducted a similar study to ours which estimated the prevalence of upper gastrointestinal lesions in patients with chronic kidney disease.

We have calculated our sample size for the study based on this study.

Sample size (n) is calculated from the formula:

$$= \frac{4(0.76)(0.24)}{(0.76 * 0.16)^2} = 49.3 \cong$$

Where p is prevalence, q = 1-p, L is permissible error

Prevalence of upper gastrointestinal endoscopic lesion in subjects with chronic kidney disease is 76%. p =76%=0.76 q =1-P=0.24

L =16%

**Results**

**Age distribution based on stage of CKD**

Out of 50 cases in our study 12% of subjects belongs to age group of 19 to 30 years, of which 4% subjects belongs to stage III,6% subjects belongs to stage IV, 2% subjects belongs to stage V. 26% of subjects belong to age group of 31 to 40 years, of which 4% of subjects belongs to stage II,2% of subjects belongs to stage III,18% of subjects belongs to stage IV, 25 of subjects belongs to stage V.16% of subjects belongs to age group of 41 to 50 years, of which 4% of subjects belongs to stage III, 8% of subjects belongs to stage IV, 4% of subjects belongs to stage V. 24% of subjects belongs to age group of 51 to 60 years, of which 8% of subjects belongs to stage III, 6% of subjects belongs to stage IV, 10% of subjects belongs to stage V.16% of subjects belongs to age group of 61 to 70 years, of which 2% of subjects belongs to stage III, 4% of subjects belongs to stage IV, 10% of subjects belongs to stage V. 6% of subjects belong to age group 71 to 80 years, of which 2% of subjects were there in stage III, stage IV, stage V.

**Table 1:** Percentage of various upper gastro intestinal findings in CKD patients

Type of Lesion	No of Patients	Percentage
Erosive Gastritis	13	26%
GERD With or without Duodenitis	10	20%
Duodenal Ulcer	4	8%
Gastric Ulcer	4	8%
Pan Gastritis	3	6%
GERD With Gastritis	2	4%
Erosive Esophagitis	2	4%
Pale Gastric Mucosa	2	4%
Angiodysplasia Of Stomach	1	2%
Hiatus Hernia	1	2%
Normal Study	8	16%

Out of 50 subjects, 42 (84%) had upper gastrointestinal involvement on endoscopic examination. Most common upper gastrointestinal lesion in our study is erosive gastritis 13(26%), followed by gastro oesophageal reflux disease with or without Duodenitis. 10 (20%), duodenal ulcer, gastric ulcer 4(8%) each, pangastritis 3(6%), GERD with gastritis, erosive esophagitis, pale gastric mucosa 2(4%) each, angiodysplasia and hiatus hernia 1(2%) each.16% Of chronic kidney disease subjects had no abnormalities in endoscopic examination. (Table 1)

**Table 2:** UGI manifestations based on CKD stage

UGI Manifestations	Stage I	Stage II	Stage III	Stage IV	Stage V
Erosive gastritis	-	-	15%	53.8%	30.7%
Gerd with or without duodenitis	-	-	10%	60%	30%
Esophagitis	-	-	-	50%	50%

Duodenal ulcer	-	-	-	50%	50%
Gastric ulcer	-	-	25%	50%	25%
Gerd with gastritis	-	-	-	50%	50%
Pan gastritis	-	-	-	66.6%	33.3%
Pale gastric mucosa	-	-	100%	-	-
Angiodysplasia	-	-	-	-	100%
Hiatus hernia	-	-	-	-	100%
Normal study	-	25%	62.5%	12.5%	-

Erosive gastritis 26%, either antral or fundal, was the predominant lesion found on endoscopy of whom 15% of subjects belong to stage III, 53.8% of subjects belongs to stage IV, 30.7% of subjects belong to stage V. GERD with or without Duodenitis 16% was next of whom 10% of subjects belongs to stage III, 60% of subjects belongs to stage IV, 30% of subjects belongs to stage V. Duodenal ulcers 8% of whom 50% each in stage IV and stage V. Gastric ulcers were seen in 8% of the subjects of whom 25% each in stage III and stage V, 50% of subjects were there in stage IV. Pan gastritis involving entire stomach is seen in 6% of whom 66.6% of subjects belong to stage IV, 33.3% of subjects belongs to stage V. 4% of subjects with Esophagitis of whom 50% each in stage IV and stage V, pale gastric mucosa each contribute to 4% of subjects belongs to stage III. Angiodysplasia and hiatus hernia were seen in very few patients 2% each belongs to stage V. (Table 2)

**Table 3:** Percentage of frequency of involvement of esophagus, duodenum, stomach in CKD patients

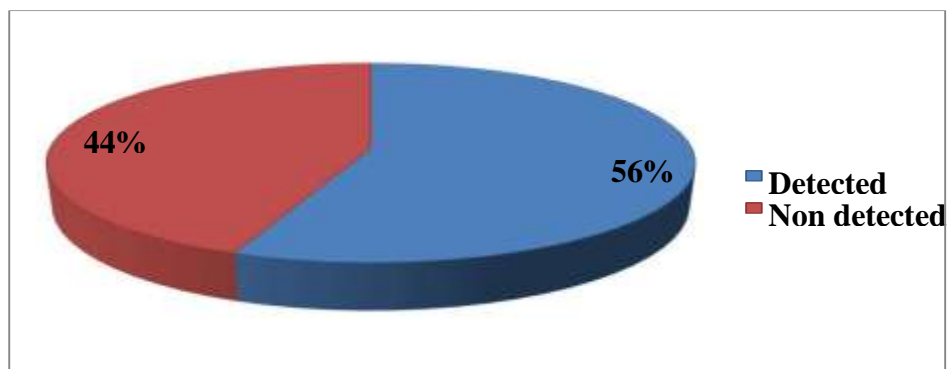
UGI Findings	No. of patients	Percentage
Stomach	23	55
Duodenum	11	26
Esophagus	8	19
Total	42	100

Out of 50 cases in our study 55% of subjects had lesions in stomach, 26% of subjects had lesions in duodenum, 19% of subjects had lesions in oesophagus. (Table 3)

**Table 4:** Distribution of stage of CKD based on mode of treatment

CKD	Type of treatment					
	HD		Conservative		Total	
	No	%	No	%	No	%
I	0	0	0	0	0	0
II	0	0	2	4	2	4
III A	0	0	6	12	6	12
III B	0	0	5	10	5	10
IV	11	22	11	22	22	44
V	15	30	0	0	15	30
Total	26	52	24	48	50	100

Out of 26 subjects undergoing haemodialysis of whom 22% of subjects were stage IV, 30% of subjects were stage V. Out of 24 subjects under conservative management 4% of subjects were in stage II, 22% of subjects were in stage III and stage IV. All subjects in stage V are undergoing haemodialysis in our study. (Table 4)



**Graph 1:** Distribution of patients based on *h. pylori* infection detected or non-detected

### Discussion

Our study includes 50 study subjects who were diagnosed to have chronic kidney disease and fulfilled inclusion criteria. Various parameters assessed in this study were: upper gastrointestinal endoscopic findings, blood urea, serum creatinine, serum electrolytes, urine examination, ultrasonography of the abdomen and pelvis.

Our study highlights the high prevalence of upper gastrointestinal endoscopic lesions in patients with chronic kidney disease [84%]. Similar study conducted by other workers in chronic kidney disease patients also shows high prevalence of upper gastrointestinal endoscopic lesions. A study done by Mohit Goyal <sup>[10]</sup> *et al.* in 2014 observed that 86% subjects have upper gastrointestinal lesions. A similar study done by Sreelatha <sup>[2]</sup> *et al.* in 2015 has prevalence of 68%. A study done by Khedmat <sup>[11]</sup> in 2007 has prevalence of 79% subjects with upper gastrointestinal lesion. A similar study done by Nardone <sup>[12]</sup> *et al.* in 2005 has prevalence of 90%. A study done by Al-Mueilo <sup>[13]</sup> has prevalence of 90.7%. A similar study done by Agarwal <sup>[14]</sup> observed 95.7% prevalence. A similar study done by Varma <sup>[15]</sup> *et al.* has prevalence of 72% subjects with upper gastrointestinal manifestations.

Of the 50 patients in our study, 84% had upper gastrointestinal involvement on endoscopic examination. Remaining 16% had a normal endoscopic study. Erosive gastritis 26%, either antral or fundal, was the predominant lesion found on endoscopy. GERD with or without duodenitis (16%) was next. Duodenal ulcers and gastric ulcers were seen in 8% of the subjects. Pan gastritis involving entire stomach is seen in 6%. Esophagitis, pale gastric mucosa each contribute to 4%. Angiodysplasia and hiatus hernia were seen in very few patients (2% each). Upper gastrointestinal lesions in our study had a predominant localization to the gastric and duodenal level.

In a study conducted by Varma <sup>[15]</sup> *et al.* gastritis was the major lesion 27%; other lesions seen were duodenitis 14%, gastro duodenitis 20% and peptic ulcer 6.5%. In a study conducted by Sreelatha <sup>[2]</sup> *et al.*, erosive gastritis was the major lesion 16%. Stomach was involved in 48%, followed by oesophagus (29%) and duodenum (23%).



In the study done by Esfahani <sup>[16]</sup> gastritis was predominant (60.8%), followed by duodenitis at 13% and gsatoduodenitis at 7.2%. In a study conducted by Agarwal <sup>[14]</sup> *et al.* uremic gastropathy was found in 91.4%, oesophageal involvement was 63%. In Moustafa *et al.* <sup>[17]</sup> gastritis at 49% was the most common lesion, hiatus hernia 20%, peptic esophagitis 16%, duodenal bulbitis 14% were also reported. In Burkinia Faso study gastric lesions were most common with 68.7%, followed by duodenal 32%. In a study conducted by Nardone <sup>[12]</sup> *et al.* 56% of patients has gastric lesions, 18% of the subjects has esophagitis and 36% had duodenitis. In a study conducted by Mohit Goyal <sup>[10]</sup> gastritis is most frequent lesion in patients with CKD (68%), followed by esophagitis 42% and duodenitis 8%. In a study done by Al Mueilo <sup>[13]</sup> 57% of the subjects had gastritis, 9.3% had duodenitis. In a study conducted by Margolis *et al.* <sup>[18]</sup> duodenitis is most frequent lesion at 60%, followed by gastric 22%. Erosive gastritis (32%) was the most common gastrointestinal lesion in a study done by Nand <sup>[19]</sup> *et al.* Elevated gastrin levels, *Helicobacter Pylori* infection, toxic effects of urea and other toxic molecules on gastric mucosa are thought to be responsible for erosive gastritis.

Majority of the subjects in our study 22 out of 50 belong to stage IV 44% of which 95% have upper gastrointestinal involvement; followed by stage V 30% of which 100% have upper gastrointestinal involvement, followed by stage III 22% of which 54.5% have upper gastrointestinal involvement. 4% of subjects belong to stage II, the upper gastrointestinal endoscopy examination reveals no abnormality. The study does not include subject belong to stage I.

A study done by sreelatha <sup>[2]</sup> *et al.* has majority of the patients 30 out of 50, belong to stage V chronic kidney disease of which 21 subjects (70%) showed upper gastrointestinal involvement. subjects belong to stage IV of whom 8 subjects (57%) have upper gastrointestinal manifestations. 6 subjects belong to stage III of which 5 subjects (83.3%) have upper gastrointestinal involvement.

A similar study done by Mohit Goyal <sup>[10]</sup> *et al.* observed that endoscopic lesions were common in Stage V than in stage IV of chronic kidney disease. 88% of subjects having gastritis were in stage V, whereas only 12% of the subjects with gastritis were in stage IV. Among subjects with stage IV, chronic kidney disease; 45% had no gastrointestinal lesions whereas only 3% of the patients in Stage V of Chronic Kidney Disease had no endoscopic evidence of gastrointestinal lesions.

Among 50 patients 24 (48%) were on conservative treatment and 26 (52%) were undergoing haemodialysis. Out of 26 patients on haemodialysis 25 (96.1%) had upper gastrointestinal lesion. Out of 24 patients on conservative treatment 17 (70.8%) had upper gastrointestinal lesions. A similar study done by Sreelatha <sup>[2]</sup> *et al.* of 50 subjects 26 (52%) were undergoing haemodialysis, 18 (36%) subjects underwent conservative management and 6 (12%) subjects underwent CAPD. Out of 26 HD subjects 18 (69.2%) had upper gastrointestinal involvement and 18 patients who were put on conservative management, 11 (61.1%) patients had positive endoscopic Finding.

In our study biopsy performed to all 50 patients out of which 22 (44%) were detected positive for *H Pylori*. 1 patient belong to stage 2, 1 patient belong to stage 3A, 4 patients belong to stage 3B, 12 patients belong to stage 4 and 4 patients belong to stage 5.

## Conclusion

Majority of the patients with chronic kidney disease have upper gastrointestinal involvement on endoscopic evaluation.

Erosive gastritis is the most common upper gastrointestinal manifestation in our study.

Upper gastrointestinal manifestations are predominant in stage V.

Upper gastrointestinal findings are frequently observed in chronic kidney disease patients on dialysis.

Early diagnosis and management can reduce mortality and morbidity and prevent fatal complication like massive upper gastrointestinal bleed.

This study that abnormal endoscopic and histologic findings as well as positive *H. pylori* infection were observed in a large number of CKD patients, so upper GI endoscopy and biopsy is an acceptable procedure for these patients.

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