



## Original Research Article

## STUDY OF UPPER GASTROINTESTINAL CHANGES IN CHRONIC KIDNEY DISEASE

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**Abstract:** Chronic Kidney Disease (CKD) is defined as the presence of objective kidney damage or Glomerular Filtration Rate (GFR) of 60ml/min/1.73m<sup>2</sup> or less, for at least 3 months, irrespective of the underlying etiology of kidney damage. It results in various complications involving virtually every system of the body. Gastrointestinal (GI) complications are known to occur commonly in patients with CKD. In this study, 100 patients of CKD stage 3-5 (GFR <60 ml/min/1.73m<sup>2</sup>) were evaluated for presence of any upper GI lesions, using Upper Gastrointestinal Endoscopy (UGIE) so as to guide for early preventive and therapeutic strategies. 86% of total patients studied had one or more upper GI lesions; gastritis, esophagitis and gastric ulcer being the most prevalent lesions. These lesions are more common in advanced stages of CKD. The symptoms due to these lesions can markedly affect the quality of life and contribute to increased rates of malnutrition among CKD patients. Recognition of their presence, early diagnosis and management of these upper GI lesions can reduce morbidity and mortality in CKD patients.

**Key Words:** Chronic kidney disease, upper gastrointestinal lesions, upper gastrointestinal endoscopy, gastrointestinal complications, gastritis, oesophagitis

## INTRODUCTION

Chronic kidney disease (CKD) is a long term disorder which can arise from damage to the kidneys from variety of diseases. According to the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical practice guidelines, to diagnose CKD, there must be<sup>1</sup>

1. Kidney damage for >3months defined as either structural or functional abnormalities.
2. Glomerular Filtration Rate (GFR) <60ml / min / 1.73m<sup>2</sup> for >3 months with or without evidence of structural damage.

CKD is a silent epidemic of the 21<sup>st</sup> century. Surveys have suggested that as many as 16% of the adult population have CKD. Its occurrence is not confined to developed countries; it is universal. Every year over one lakh people in India are diagnosed with CKD necessitating a kidney transplant or continual dialysis<sup>2,3</sup>.

CKD leads to disturbances in the function of virtually every organ system. The gastrointestinal complications include anorexia, nausea and vomiting, hiccups, stomatitis, oesophagitis (with or without fungal/viral infection) and abnormalities in oesophageal motility, gastritis, duodenitis, peptic ulcer, hiatus hernia, colonic diseases in the form of angiodysplasia, colonic obstruction, pseudo obstruction and resultant bowel perforation, diverticulosis (particularly in patients with polycystic kidney disease), idiopathic ascites and peritonitis<sup>4</sup>. Patients with End stage renal disease (ESRD) also suffer from recurrent gastrointestinal bleeding episodes with superficial mucosal inflammatory lesions

as the underlying cause along with effects of uremia on the gastrointestinal mucosa and platelet adhesiveness. The role of heparinization in patients on dialysis has also been implicated in the etiology of gastrointestinal bleeding<sup>5</sup>.

Upper gastrointestinal endoscopy is not only sensitive to pick milder inflammatory changes or superficial ulcerations, but also helps in pinpointing the source of bleeding. Upper gastrointestinal bleeding is reported to be the cause of death in 3-7% patients with moderate to severe CKD<sup>5</sup>.

The etiology of upper GI disorders in ESRD is multifactorial and includes hypergastrinemia, Helicobacter pylori infection, effects of uremia on the GI mucosa, psychological stress, endocrine disturbances of CKD, gastroparesis, and miscellaneous causes like acidosis, hypo or hypercalcemia, hyperkalemia and hyperparathyroidism<sup>6,7,8</sup>.

The aim of this study was to determine the prevalence of various upper GI lesions in patients with Chronic Kidney Diseases (GFR <60 ml/min/1.73 m<sup>2</sup>) by means of Upper GI Endoscopy and to evaluate their relationship with stage of CKD or GFR.

## MATERIALS AND METHODS

This study was carried out in 100 cases diagnosed as CKD, admitted in Medical wards/Nephrology department of Guru Nanak Dev Hospital attached to Government Medical College, Amritsar, after obtaining their informed consent.

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### Inclusion criteria

Adult patients diagnosed as having CKD, with GFR <60ml/min/1.73m<sup>2</sup> (stage 3-5) and aged more than 18 years were included in this study.

### Exclusion criteria

1. Patients of acid peptic disease.
2. Patients on high dose NSAIDS for a long duration.
3. Patients of cirrhosis with esophageal varices.
4. History of chronic alcoholism / chronic smoking / chronic tobacco chewing.
5. Patients of connective tissue disorders.

Diagnosis of CKD was established on the basis of clinical, biochemical and radiological (ultrasonography) findings. A detailed history of the patient with special reference to gastrointestinal symptoms like nausea, vomiting, anorexia, metallic taste, hiccups, abdominal pain, hematemesis etc. was taken followed by thorough clinical examination. Data was analysed using standard statistical methods.

1. Routine investigation like haemoglobin, total leucocyte count (TLC), differential leucocyte count (DLC), urine complete, fasting blood sugar, blood urea, serum creatinine and electrocardiogram (ECG) were done.
2. Glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault equation<sup>9</sup>.

Estimated Creatinine-clearance (ml/min) =  

$$\frac{(140 - \text{Age}) \times \text{Body Weight (Kg)}}{72 \times \text{Serum Creatinine (mg/dl)}}$$
 (Multiply by 0.85 in females)

3. Fiberoptic esophago-gastro-duodenal endoscopy was done in all the cases selected for this study. The oesophagus, stomach and proximal duodenum were examined for evidence of any inflammatory mucosal changes, erosions, ulcerations, bleed etc.

## RESULTS

Among the 100 patients studied, 46% were males and 54% were females. Mean age of subjects under study was 44 years and mean weight was 50kg. Mean blood urea and mean serum creatinine were 130 mg/dl and 7.39 mg/dl respectively. 42% of the patients under study had serum creatinine levels between 4-7 mg/dl, 12% had levels between 1-4 mg/dl, 28% had levels between 7-10 mg/dl, 14% patients had levels between 10-13 mg/dl and only 4% had levels more than 13mg/dl. It was observed that out of 100 patients, 98 had GFR less than 30ml/min/m<sup>2</sup>. 76% of these patients were found to be in Stage 5 of CKD and 22% were in Stage 4 of CKD. Only 2 patients were in Stage 3.

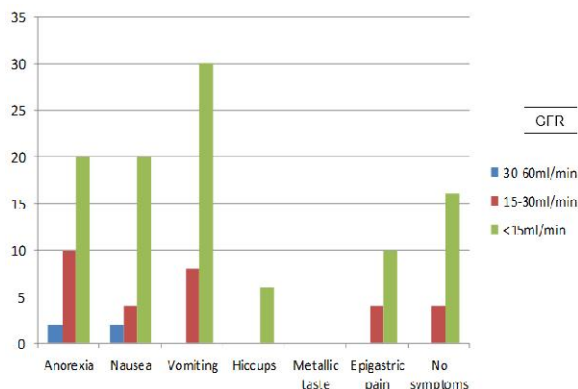
Various gastrointestinal symptoms were noted in the patients under study. It was found that 80% of the total patients had one or the other GI symptoms. There was no sex predilection for any GI symptom and all the symptoms were equally distributed in males and females. 38% of patients had vomiting, 34% had anorexia, 26% had nausea, 16% had epigastric pain and 6% had hiccups. None of the patients had upper GI bleed. 20% of the patients had no GI symptoms (Table 1).

**Table 1:** showing gastrointestinal symptoms and no. of patients

GI Symptoms	No. of Patients
Anorexia	34
Nausea	26
Vomiting	38
Hiccups	6
Epigastric Pain	16
No GI Symptoms	20

GI symptoms varied in relation to serum creatinine levels. 50% of patients having serum creatinine levels between 1-4 mg/dl had anorexia, 33% had nausea, 67% had vomiting while 17% had no GI symptoms. In patients with serum creatinine levels between 4-7 mg/dl, 29% had anorexia, 14% had nausea, 24% had vomiting, 24% had epigastric pain and 24% had no GI symptoms. In patients with serum creatinine levels between 7-10 mg/dl, 36% had anorexia, 43% had nausea, 29% had vomiting, 7% had hiccups, 21% had epigastric pain and 21% had no GI symptoms. In patients with serum creatinine levels between 10-13 mg/dl, 14% had anorexia, 29% had nausea, 71% had vomiting, 29% had hiccups and 14% had no GI symptoms. 50% of the patients with serum creatinine levels more than 13 mg/dl had vomiting and 50% had epigastric pain.

Similarly, with respect to GFR, patients with GFR between 30-60 ml/min/m<sup>2</sup> were two in number and both had anorexia and nausea. Among patients with GFR between 15-30 ml/min/m<sup>2</sup>, that is, Stage 4 CKD, 45% had anorexia, 18% had nausea, 36% had vomiting, 18% had epigastric pain and 18% had no GI symptoms. In patients with GFR less than 15ml/min/m<sup>2</sup>, that is, Stage 5 of CKD, 26% had anorexia, 26% had nausea, 37% had vomiting, 8% had hiccups, 13% had epigastric pain and 21% had no GI symptoms (Table 2, Graph 1)



**Graph 1:** shows no. of patients having gastrointestinal symptoms in relation to GFR

Upper GI endoscopy of patients revealed that 86% of total patients studied had one or more upper GI lesions. 68% patients had gastritis, 42% had esophagitis, 22% had gastric ulcer, 8% had duodenitis, 6% had hiatus hernia, 2% had duodenal ulcer and 14% had no GI lesions (Table 3).

**Table 3:** showing endoscopic findings and no. of patients

Endoscopic findings	No. of Patients
Esophagitis	42
Gastritis	68
Duodenitis	8
Gastric Ulcer	22
Duodenal Ulcer	2
Hiatus Hernia	6
Normal	14

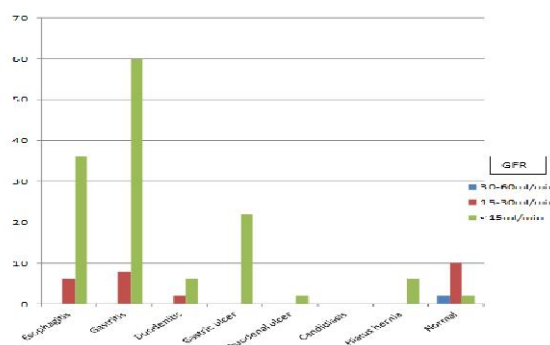
Endoscopic upper GI lesions varied in relation to serum creatinine levels. In patients with serum creatinine between 1-4 mg/dl, 17% had esophagitis, 34% had gastritis, 17% had duodenitis and 50% had no GI findings. In patients with serum creatinine between 4-7 mg/dl, 43% had esophagitis, 67% had gastritis, 9% had duodenitis, 14% had gastric ulcer, 5% had duodenal ulcer and 14% had no GI lesions. In patients with serum creatinine between 7-10mg/dl, 43% had esophagitis, 71% had gastritis, 7% had duodenitis, 36% had gastric ulcer, 21% had hiatus hernia and 7% had no GI lesions. In patients with serum creatinine between 10-13mg/dl, 57% had esophagitis, 86% had gastritis and 43% had gastric ulcer. In patients with serum creatinine levels more than 13mg/dl, 50% had esophagitis and all were having gastritis.

With respect to GFR, it was observed that both patients in Stage 3 of CKD had no endoscopic GI lesion. Among patients in Stage 4 of CKD, that is, GFR between 15-30 ml/min/m<sup>2</sup>, 27% patients had esophagitis, 36% had gastritis and 9% had duodenitis while 45% had no GI lesion. Among patients in Stage 5 of CKD, that is, GFR less than 15ml/min/m<sup>2</sup>, 47% had esophagitis, 79%

had gastritis, 8% had duodenitis, 29% had gastric ulcer, 3% had duodenal ulcer, 8% had hiatus hernia and 3% had no GI lesion (Table 4, Graph 2).

**Table 4:** showing no. of patients with endoscopic findings in relation to GFR

Endoscopic findings	15-30 ml/min	<15 ml/min
Esophagitis	6	36
Gastritis	8	60
Duodenitis	2	6
Gastric Ulcer	-	22
Duodenal Ulcer	-	2
Candidiasis	-	-
Hiatus Hernia	-	6
Normal	10	2



**Graph 2:** showing no. of patients with endoscopic findings in relation to GFR. All findings were more prevalent in stage 5 CKD.

### DISCUSSION

Patients with CKD often suffer from comorbidities such as diabetes and coronary artery disease; however, the most common, non-renal, chronic disorders in patients with ESRD are gastrointestinal disorders<sup>10</sup>. This highlights the need to understand the gastrointestinal disorders that accompany CKD. This study examined the most common upper GI lesions that occur in patients with CKD using upper GI endoscopy. Prevalence of GI symptoms in patients with CKD is thought to range from 70 to 79%. The prevalence of these disorders is generally similar in predialysis patients, patients on hemodialysis, and patients on peritoneal dialysis<sup>10</sup>, but a trend towards increasing symptoms with increasing duration and severity of CKD exists.

Various GI symptoms were noted in the patients under study. It was found that 80% of the patients had one or the other GI symptoms. This result was consistent with the studies conducted by Farsakh et al.,<sup>11</sup> in 1996 (prevalence of GI symptoms was 70% in CKD patients undergoing hemodialysis), and Cano<sup>10</sup> in 2007 (72% CKD patients had GI symptoms). In a prospective study of 85 patients admitted to a dialysis unit, Margolis et al.,<sup>12</sup> noticed that 59% patients had symptoms of nausea, vomiting, or epigastric pain. The clinical syndrome of uraemia is known to be associated

with prominent GI symptoms. Most common are anorexia, nausea, intermittent vomiting and hiccups. Sometimes there is a selective loss of appetite for foods high in proteins<sup>13</sup>. Some of the symptomatology is no doubt due to central effects of urea and other metabolic waste products which circulate in high concentrations in blood, but there are significant lesions in GI tract as well. These symptoms usually respond to protein restriction. When kidney disease is advanced, dialysis may be required for their control. Intractable hiccup is another problem which has been seen even in well dialysed patients.

In this study, it was observed that nausea, vomiting and hiccups were more common in patients in Stage 5 CKD than in patients in Stage 4 CKD. This shows that uraemia has some role in causing these GI symptoms.

In this study, various upper GI lesions were found in 86% of the patients; only 14% of the patients had no Upper GI lesions on endoscopy. In a similar study carried out by Nardone<sup>14</sup> in 2005 with 50 CKD patients, it was observed that 90% patients had upper GI lesions on endoscopy. Khedmat<sup>15</sup> in 2007 observed that 79% CKD patients had upper GI lesions. Al-Mueilo in his study on 54 patients on chronic hemodialysis found that endoscopic findings were abnormal in 49 (90.7%) patients<sup>16</sup>. Wee et al., (1990)<sup>17</sup> observed endoscopic signs of gastro duodenal mucosal inflammation including erythema, petechiae and erosions in approximately half of all the uraemic patients on maintenance hemodialysis.

This study revealed gastritis to be the most frequent lesion in patients of CKD. It was found in 68% patients. This result was similar to the findings of study by Nardone<sup>14</sup> who found that 56% of CKD patients had gastric erosions. In his study, only 18% of CKD patients had esophagitis, but in our study, 42% of patients had esophagitis. This finding was similar to the findings of study by Khedmat<sup>15</sup>, who found esophagitis to be present in 38% of the patients undergoing hemodialysis. Misra et al.,<sup>18</sup> found esophagitis in 47% of the CKD patients in his study. Margolis et al.,<sup>12</sup> found gastritis in 22% and esophagitis in 13% patients. Al-Mueilo<sup>16</sup> observed chronic gastritis in 20 (37%), acute gastritis in 13 (20.1%), duodenal ulcer in 6 (11.1%), duodenitis with or without erosions in 5 (9.3%), gastroduodenitis in 3 (5.56%), and gastroesophageal reflux disease in 2 (3.7%) out of the total 54 subjects that he studied.

McConnell et al., studied gastric acid secretion in uremic patients. All 15 patients on chronic hemodialysis at the time of study had high normal to increased gastric acid secretion, both basal and

stimulated<sup>19</sup>. Other authors have also demonstrated that patients with CKD who are on maintenance hemodialysis tend to be relative hyper secretors of gastric acid.

In 2000, Van Vlem prospectively assessed gastric emptying in 53 non-diabetic patients (26 on hemodialysis and 27 healthy controls)<sup>20</sup>. Gastric emptying was significantly longer in dyspeptic patients on hemodialysis than in healthy controls and in dyspeptic patients on hemodialysis than in non-dyspeptic patients on hemodialysis. Delayed gastric emptying may explain gastritis, gastric erosions and ulceration observed in CKD patients.

*Helicobacter pylori* infection may also contribute to the increased prevalence of upper GI lesions in CKD patients. Although some studies have shown that the prevalence of *H. pylori* infection is higher in patients with CKD than in the general population<sup>14,15</sup>, other studies have not<sup>13,21,22</sup>. The reported prevalence of *H. pylori* infection varies greatly - ranging from 49% to 66% in patients with CKD and from 35% to 75% in control groups<sup>14,15</sup>. Al-Mueilo<sup>16</sup> in his prospective study on 54 chronic hemodialysis patients, performed upper GI endoscopy and multiple antral gastric biopsies for histological examination and *H. pylori* detection. Histological examination of biopsies documented chronic active gastritis in 28 (51.9%) patients. *Helicobacter pylori* were present in 34 (63%) patients. Misra et al., in a similar study observed that prevalence of *H. pylori* was less in patients as controls (35.2% Vs 54%) and concluded that upper GI tract abnormalities in CKD mainly occur due to metabolic changes in response to high urea concentration in gastric juice and are not related to *H. pylori* infection<sup>18</sup>.

In this study, duodenitis and duodenal ulcer were found in 8% and 2% of total patients respectively. Some studies conducted earlier found higher number of patients having duodenitis and duodenal ulcer. Margolis et al.,<sup>12</sup> found duodenitis in 60% of the CKD patients. Nardone<sup>14</sup> in his study noticed duodenal erosions in 36% and duodenal ulcer in 6% patients. Khedmat<sup>15</sup> observed erosive duodenitis in 26% patients. Al-Mueilo<sup>16</sup> found duodenitis in only 9.3% patients in his study.

Hiatus hernia was found in 6% patients in this study. According to the study conducted by Farsakh et al.,<sup>11</sup> hiatus hernia was more frequent in hemodialysis patients. Khedmat<sup>15</sup> noticed hiatus hernia in 9% patients. Potential causes include protein malnutrition with defective collagen synthesis, or altered muscle tone.

Y. Kawaguchi *et al.*, (2009)<sup>23</sup> in his study on 156 CKD patients observed that overall prevalence of GERD was 34.0%. In patients on hemodialysis, the prevalence of GERD was 50%, thus concluding that the prevalence of GERD tends to increase as renal function worsens.

The endoscopic lesions were more common in patients in stage 5 CKD than in patients in stage 4 CKD. 86% of the patients having esophagitis were in stage 5 CKD whereas only 14% of the patients having esophagitis were in stage 4 CKD. Similarly, 88% of the patients having gastritis were in stage 5 of CKD whereas only 12% of the gastritis patients were in stage 4 CKD. None of the patients in stage 4 or less had gastric ulcer whereas 22 patients in stage 5 CKD had gastric ulcers. Among patients with CKD stage 4, 45% had no GI lesion whereas among stage 5 CKD patients, only 3% had no lesions.

In both the general population and in patients with CKD, GI symptoms can markedly affect quality of life and psychological well-being. In general, patients who experience GI symptoms have higher rates of health-care use and health-care expenditure than patients without these symptoms. GI symptoms have also been linked to increased rates of malnutrition, and malnutrition has been independently associated with increased morbidity and mortality in patients with ESRD<sup>24,25</sup>. Recognition of their presence, early diagnosis and management of these upper GI lesions can reduce morbidity and mortality in CKD patients.

### CONCLUSIONS

Gastrointestinal symptoms are common in CKD patients and constitute an important cause of seeking medical care in these patients. Upper GI symptoms like nausea, vomiting and hiccups tend to worsen with increasing uremia. Gastritis is the most prevalent upper GI lesion in CKD patients followed by esophagitis, gastric ulcer, duodenitis, hiatus hernia and duodenal ulcer. The upper GI lesions are more common in stage 5 CKD patients than in stage 4 CKD patients. Early diagnosis and management of these upper GI lesions in CKD can reduce morbidity and prevent fatal complications like massive upper GI bleed.

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