

A COMPREHENSIVE ENDOSCOPIC ANALYSIS OF UPPER GASTROINTESTINAL DISORDERS IN CHRONIC KIDNEY DISEASE

Himanshu Devender Kumar¹, Richa Goel², P. K. Prasher³, Kartar Singh⁴

¹Consultant Associate, Aashirwad Advanced Heart Lung and Critical Care Centre, Karnal, India.

²Assistant Professor, Department of Biochemistry, Kalpana Chawla Govt Medical College, Karnal, India.

³Professor, Department of Medicine, MMIMSR, Mullana, India

⁴Professor, Department of Gastroenterology, MMIMSR, Mullana, India.

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Corresponding Author:

Dr. Richa Goel,

Email: richambbs@gmail.com

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Abstract

Background: Chronic kidney disease (CKD) is associated with various gastrointestinal (GI) manifestations, particularly in the upper GI tract. Despite increasing recognition of these issues, the endoscopic findings in CKD patients remain underexplored. Understanding the upper gastrointestinal endoscopic manifestations of CKD can aid in early diagnosis and management, potentially improving patient outcomes. This study aims to evaluate the upper gastrointestinal endoscopic findings in patients with chronic kidney disease and to assess the degree of upper GI findings and GI symptoms based on stages of CKD. **Materials and Methods:** A prospective observational study was conducted over 18 months, involving patients diagnosed with CKD who underwent upper gastrointestinal endoscopy for clinical indications. Endoscopic findings such as gastritis, peptic ulcer disease, esophagitis, gastroesophageal reflux disease (GERD), and varices were recorded. **Result:** The study included 50 patients with CKD stages 2 to 5. Endoscopic findings revealed a high prevalence of gastritis, peptic ulcer disease, and GERD in advanced CKD stages. The most common endoscopic finding was gastritis seen in 36% of the subjects. The normal endoscopic finding was seen in 32% of the subjects. 14% of the patients had duodenitis and GERD was seen in 12% of CKD patients. Stomach involvement was seen in 48% of the subjects via endoscopy. **Conclusion:** Upper gastrointestinal manifestations are common in patients with chronic kidney disease, with an increased prevalence of gastritis, peptic ulcer disease, and GERD in more advanced stages of CKD. These findings highlight the need for proactive screening and management of GI symptoms in CKD patients. Early detection and appropriate treatment strategies, including careful medication management, are essential to improving the overall health and quality of life of CKD patients.

INTRODUCTION

Chronic kidney disease (CKD) is a known disorder of the kidney resulting from progressive loss of the nephrons from a variety of diseases. In developed and many developing countries diabetes mellitus (DM) and hypertensive disorders are major causative factors for the occurrence of CKD, but in Asia and sub-Saharan Africa, glomerulonephritis and idiopathic causes are the leading ones.^[1]

Uremic gastropathy encompasses upper gastrointestinal (GI) signs and histopathological changes in a uremic patient, after the occurrence of a renal failure. In uremic patients, the clinical profile of upper GI disturbances varies widely, not only depending on the severity of renal function

impairment; it also varies with the stress level of the patients, and the provided treatment.^[2]

Gastrointestinal symptoms have a prevalence rate of 77% to 79%.^[3,4] The GI complications include anorexia, vomiting, nausea, hiccups, esophagitis, stomatitis, abnormalities in motility, gastritis, peptic ulcer, duodenitis, hiatus hernia, colonic obstruction, or pseudo-obstruction, bowel perforation, ascites, and peritonitis.^[5] Patients with end-stage renal disease (ESRD) often suffer from recurrent GI bleeding episodes and are found to have superficial mucosal lesions (inflammatory). Also, the role of heparinization in patients on dialysis in causing GI bleed cannot be ruled out. Upper GI bleeding is the most frequent cause of mortality among patients in Stage 4 and 5 CKD, almost up to 3-7%.^[6]

Upper gastrointestinal endoscopy (UGIE) is a sensitive procedure for studying the upper GI tract. Mucosal lesions of the GI tract need an endoscopic examination. Not only esophagitis, gastritis and duodenitis also can be easily identified and a biopsy can be taken for histological examination.^[7] Many times patients suffer from subclinical symptoms like loss of appetite, nausea, and heartburn. These minor symptoms are frequently attributed to hyperacidity due to uremia and dealt with proton pump inhibitors (PPIs) and HD. Upper GI Endoscopy of these patients can help in localizing the lesion and provide better-targeted treatment to the patients.^[7]

The present study was planned to study the occurrence of various upper GI lesions in patients diagnosed with CKD, having some or other form of upper GI symptoms, utilizing Upper GI Endoscopy and to assess their relationship with the stages of CKD.

MATERIALS AND METHODS

The present study was conducted in the Department of General Medicine in collaboration with the Department of Gastroenterology, MMIMSR, Mullana, Ambala after obtaining the approval from institutional ethical committee. It was a cross-sectional study including fifty patients with a diagnosis of chronic kidney disease.

Inclusion criteria:

1. All patients diagnosed with CKD based on guidelines by Kidney Disease Outcomes Quality Initiative (K/DOQI)8:
 - a. Kidney damage for >3 months is defined as either structural or functional abnormalities.
 - b. Glomerular Filtration Rate (GFR) <60ml / min / 1.73m² for >3 months with or without evidence of structural damage.
2. Age more than 18 years.

Exclusion criteria:

Patients of CKD with one or more of the following

1. High-dose NSAIDS intake
2. Chronic liver disease.
3. History of alcohol intake
4. History of smoking
5. History of tobacco chewing

This study was conducted for 18 months. Patients were taken from the inpatient department (IPD) of the medicine department. We enrolled 50 patients with CKD having upper GI symptoms, fulfilling the inclusion and exclusion criteria, who agreed to enroll in the study after written and informed consent. Antacids were stopped in all the patients, one week before upper GI endoscopy.

Study tools and strategy: Data was collected using a piloted proforma meeting the objectives of the study after informed consent. Routine investigation like complete hemogram, erythrocyte sedimentation rate (ESR), urine routine examination, renal function tests (RFT), liver function tests (LFT), electrocardiogram (ECG) and ultrasonography (USG) was done in every case.

Glomerular filtration rate (GFR) using the Modification of Diet in Renal Disease (MDRD-186) equation was calculated in all the cases.

$$eGFR \text{ (mL/min/1.73 m}^2\text{)} = 186.3 \times (\text{Scr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if Black})$$

Statistical methods employed: Patients were observed based on gender, grades of anemia (NKF9 and WHO10 classification), and CKD stage. Data collected were entered into Microsoft Excel. The data was compiled and analyzed by using appropriate statistical methods using SPSS version 20.

RESULTS

In our study, the mean (\pm SD) age was 53.16 ± 12.81 years with a range from 23 years to 86 years and the majority of the subjects were in the age group 50-59 years at 32 % (16 out of 50). The majority of the subjects were females being 56 % (28 out of 50) and 44% (22 out of 50) of subjects were males. The study group showed a mean (\pm SD) eGFR of 16.52 ± 9.45 mL/min/1.73m². 54% (27 out of 50) of the subjects belonged to Stage 5 CKD with eGFR < 15 mL/min/1.73m².

In this study, the most common symptom in CKD patients was nausea in 38 % of the subjects followed by anorexia in 30 % of the subjects. The prevalence of vomiting, epigastric pain, and heartburn was 26 %, 20 %, and 18 % respectively. Only 8 % of subjects had regurgitation and 4 % had dysphagia. No case of upper GI bleed was encountered in the study [Figure 1].

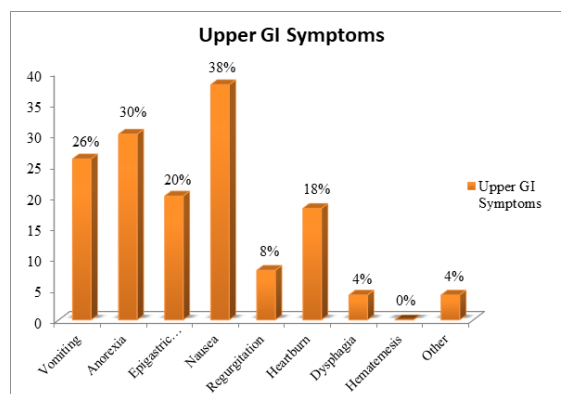


Figure 1: Histogram showing the frequency distribution of upper GI symptoms in the study

Nausea was the most common symptom encountered in Stage 3 (50%, 2 out of 4) and Stage 4 (52.63%, 10 out of 19) patients. In Stage 5, the most common symptom was anorexia, seen in 33.33% (9/27) of the patients [Figure 2].

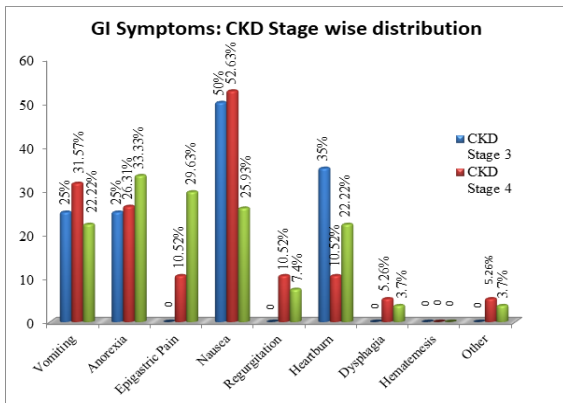


Figure 2: Histogram showing upper GI symptoms frequency based on CKD stage

In this study, the most common endoscopic finding was gastritis seen in 36% of the subjects. 14% of the patients had duodenitis and GERD was seen in 12% of CKD patients. The normal endoscopic finding was seen in 32% of the subjects [Figure 3].

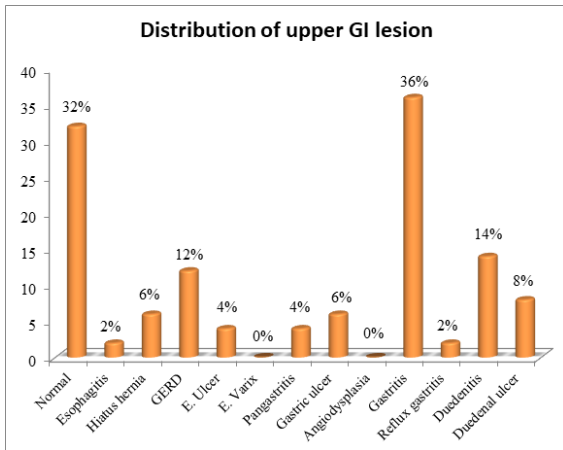


Figure 3: Histogram showing the distribution of upper GI lesions in the study

Among the genders, the most common endoscopic finding was gastritis seen in 31.82 % (7/22) of males and 39.29 % (11/28) of female subjects. The normal endoscopic finding was seen in 31.82 % (7/22) of males and 32.14 % (9/28) of female subjects [Figure 4].

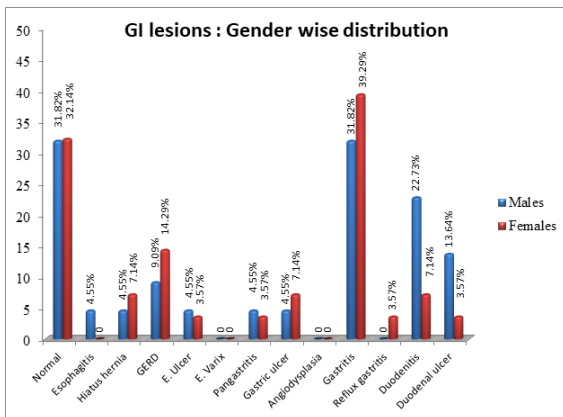


Figure 4: Endoscopic GI lesions distribution among both gender

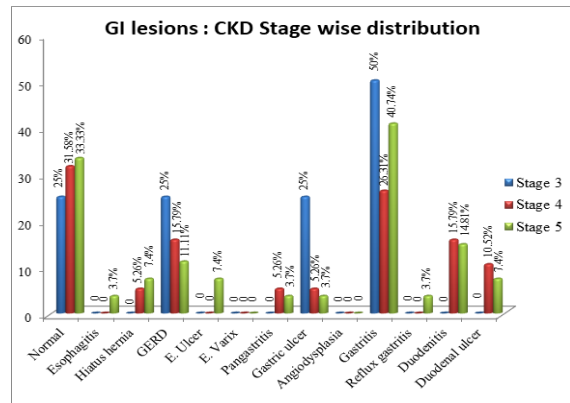


Figure 5: Endoscopic GI lesions distribution among different stages of CKD.

Among the CKD stages, gastritis was the most common finding in Stage 3 (50%) while 25% of Stage 3 CKD patients had normal UGIE. In Stage 4, 31.58% of patients had normal endoscopy while 26.31% had gastritis, 15.79% had duodenitis and 10.52% had a duodenal ulcer. In Stage 5 CKD, 33.33% had normal UGIE while 40.74% had gastritis, 14.81% had a duodenitis, and hiatus hernia was observed in 7.4% of Stage 5 CKD patients [Figure 5]

DISCUSSION

More than 1.1 million CKD patients are on maintenance HD treatment and their number is increasing at the rate of 7% per year. Despite the progress and development of newer treatment modalities and advancements in the dialysis machine,^[11] upper GI symptoms frequently occur in these patients. Not only uremia but dialysis also precipitates GI symptoms in these patients.^[12]

Upper Gastrointestinal Symptoms in CKD

Renal dysfunction leads to perturbation in acid-base homeostasis, deranged hormonal synthesis, and excretion, fluid and electrolyte disturbances, and disturbed waste excretion.^[13] Patients of ESRD often have malnutrition which has been related to anorexia and resultant decreased oral intake in the patients. However, only a few authors have studied these symptoms in the early stages of non-dialysed CKD patients. One MDRD study has reported that GI symptoms such as anorexia and nausea appear in the early stages of CKD patients, contrary to the belief of the emergence of uremic symptoms in the ESRD stage.^[14]

Although, in our study, we included patients with dyspeptic symptoms only, studies by Farsakh et al,^[3] observed about 70% of patients having GI symptoms and Cano et al found 72% of CKD patients with GI symptoms.^[15] In our study, the most common symptom experienced by patients was Nausea (38%), followed by anorexia in 30% of the subjects. Most of these patients belonged to Stages 4 and 5 of CKD. We didn't encounter any patients with upper GI bleed. In our study, the prevalence of vomiting, epigastric pain, and heartburn was 26 %, 20 %, and

18 % respectively. Only 8 % of subjects had regurgitation and 4 % had dysphagia. In an Indian study in 2017, 100% of the patients had anorexia. Nausea (94%) and vomiting (72%) were also a frequent finding. GI bleeding was present in 8% of the subjects.^[16] In a study by Shabka et al, upper GI bleeding was observed in 80% (24) of the subjects while epigastric pain was seen in 13.3% of the subjects, and 3.3% had complaints of vomiting.^[17] Similar findings of nausea and vomiting being the commonest symptoms were reported by Goyal M et al,^[18] Moustapha et al,^[19] Bansal et al,^[20] and Margolis et al.^[21]

We observed nausea as the most common symptom in Stage 3 (50%, 2 out of 4) and Stage 4 (52.63%, 10 out of 19) CKD patients. In Stage 5 CKD, the most common symptom was anorexia, seen in 33.33% (9/27) of the patients. It can only be speculated that the high occurrence of these GI symptoms is due to increasing uremia among these patients. Epigastric pain in 29.63%, nausea in 25.93%, and vomiting was seen in 22.22% of the ESRD patients. Nausea, anorexia, and vomiting were frequent findings in all the stages of CKD. Similar was the observation of Thomas et al.^[12]

The most frequent uremic symptoms are loss of appetite, vomiting, nausea, and hiccups. Patients often have selective anorexia for high protein-containing food. Sometimes there is a selective loss of appetite for foods high in proteins.^[22] Some of the symptoms appear due to high urea concentration leading to central effect and another waste metabolite in the blood. Some authors have suggested that these symptoms can be relieved with regular dialysis and a protein-restricted diet. Refractory hiccup is one serious condition that is encountered in regularly dialyzed patients.^[22]

Upper Gastrointestinal Lesions in CKD

Diabetes and cardiovascular comorbidities are frequently encountered in CKD patients; however, the most common non-renal underrated condition is upper GI lesions in ESRD patients.^[15] Authors have tried to establish a relation between the progression of CKD and these lesions but the results are inconsistent. This study aimed to see the prevalence of these lesions in CKD patients using upper GI endoscopy. Authors have observed the prevalence of upper GI lesions in 70 to 79% of CKD patients.^[18]

Our study evaluated 50 patients with CKD (Stage 3 to 5) and 68% of these patients showed an upper GI lesion on endoscopic examination, while 32% of patients had normal endoscopic findings. Similarly, in a study of 50 CKD patients, Nardone et al,^[23] found the prevalence of upper GI lesions in 90% of the CKD patients. In 2007, Khedmat et al,^[24] observed GI lesions in 79% of CKD patients. Seventy-six percent (76%) of CKD patients had abnormal upper GI endoscopic findings in a study by Moustapha et al.^[19] Similarly, Bansal et al found an abnormal finding in 87.5% of the CKD subjects.^[20] In 2014, a study of 100 patients of advanced-stage CKD patients showed abnormal endoscopy in 48% of the haemodialysed

patients, while 32% of CKD patients were on PPIs and 28% of CKD patients were on yoga therapy.^[25]

The present study observed Gastritis as the most common lesion among CKD patients. 36% of the patients had gastritis. Our finding is similar to the finding of Goyal et al,^[18] and Nardone et al,^[23] who found gastric erosions in 68% and 56% of the patients, respectively. In 2014, Nand et al,^[25] observed gastritis in 32% of the subjects who were on regular HD, which was the most common upper GI lesion in their study. Similarly, gastritis was observed as the most frequently seen lesion in upper GI endoscopy in the study of Moustapha et al,^[19] (34%) and Gupta M et al (28%).^[16] Although the study of Bansal et al,^[20] (30%) and Shabka et al,^[17] (36.7%) reported a high incidence of gastritis, it was not the most common lesion in their study.

In our study duodenitis was seen in 14 % of the subjects followed by GERD in 12 % of the subjects. Similarly, Moustapha et al,^[19] found duodenitis in 14% of the CKD patients, Bansal et al,^[20] in 35%, Gupta M et al,^[16] in 12%, Nardone et al,^[23] in 36%, Khedmat et al,^[24] in 26% and Shabka et al,^[17] in 43.3% of the subjects, while some authors observed only 8% duodenitis (Goyal et al),^[18] and Nand et al,^[25] reported none. Y Kawaguchi et al reported GERD in 34% of the 156 CKD patients.^[26]

Our study reported a very low number of esophagitis (2%). Contrary to this, Goyal et al,^[18] reported esophagitis in 18% of the patients. His findings were inconsistent with the study of Khedmat et al,^[24] who reported 38% of esophagitis also Margolis et al,^[21] observed esophagitis in 13% of CKD patients.

In our study, hiatus hernia was observed in 6% of CKD patients. Farsakh et al³ also observed a hiatus hernia in their study. 9% of patients had a hiatus hernia in the study of Khedmat et al.^[24] Protein malnutrition has been hypothesized as the main mechanism behind a hiatus hernia in CKD patients. It may lead to defective collagen synthesis and altered muscle tone.^[18]

We observed the stomach as the most common site involved with GI lesions. It was involved in 48% of the patients, and gastritis was the most common lesion followed by a gastric ulcer in 6% and pan gastritis in 4% of the subjects. Gastritis was seen more commonly among females (39.29%) when compared with males (31.82%) (Table 26). Overall, in our study, 18 patients had complaints of gastritis, out of whom 11 (61%) belonged to Stage 5 CKD. Gastritis was observed in a high number of Stage 5 CKD patients (40.74%), followed by duodenitis in 14.81%, hiatus hernia, GERD, and duodenal ulcers were seen in 7.4 % of the Stage 5 CKD patients. A similar finding of the high occurrence of gastritis in stage 5 CKD was observed by Goyal et al, who observed it in 88% of the patients having gastritis (Including Stage 3 and 4 CKD)18. In our study, none of the patients in Stage 3 and Stage 4 CKD had esophageal ulcers, while 2 patients of Stage 5 CKD patient had ulcers. In contrast to our observation of 33.33% normal endoscopic examination in Stage 5

CKD, Goyal et al observed 45% of subjects in Stage 4 of CKD with normal endoscopic findings while in Stage 5 CKD, only 3% of patients had normal findings.^[18]

These findings emphasize some association between uremia and the pathogenesis of these upper GI lesions. Important lesions detected in this study show no relation to gender or laboratory results. Gastric lesions have shown female preponderance but that could be due to more number of female subjects in the study. Various mechanisms have been postulated behind the etiology of uremic gastropathy. Histological examination of uremic gastropathy patients has shown atrophy of the gland, infiltration of mast cells, edema of lamina propria, submucosal arteritis, and mineralization.^[27] In fact, raised gastrin levels are noted in cases of spontaneous CKD also. Although, in theory, hypergastrinemia should be correlated with the severity of CKD in studies, invariable results have been noted suggesting some other factors are also involved in the metabolism of gastrin.^[28]

McConnell et al,^[29] found hypergastrinemia in 15 patients who were on regular HD patients. Similarly, other authors have also shown high gastrin levels in patients with CKD.^[30] Gastrin-induced hypersecretion of gastric acid is responsible for gastritis, gastric ulcer, GI bleeding, and symptoms of uremia (nausea and vomiting). Reflux in patients leads to frequent episodes of inflammation, hemorrhage, and secretion of histamine from gastric mast cells.

So, a vicious cycle is created where histamine further stimulates parietal cells for H⁺ secretion. However gastric acid hypersecretion is not found in all CKD patients, some have hypochlorhydria also. Other factors playing a role in uremic gastropathy are psychological stress, H⁺ secretion due to high urea levels, erosion by NH₄⁺ liberated by bacterial activity on urea, ischemia due to vascular lesions, reduction in gastric mucosa, and biliary reflux.^[28]

Upper GI symptoms can markedly affect a person's quality of life, both physically and psychologically, not only in CKD but in a healthy individual also. Patients tend to spend more who are suffering from GI symptoms and in patients with CKD, it further aggravates the financial problems and burden on the health care system. GI symptoms also aggravate malnutrition in CKD patients, which acts as an independent risk factor for mortality and morbidity in CKD patients. Early recognition, diagnosis, and treatment can reduce morbidity and mortality in CKD patients and upper GI endoscopy is the perfect tool for the early detection of these lesions.^[31,32]

CONCLUSION

The above observations conclude that patients with CKD often experience GI symptoms like nausea, vomiting, and anorexia. Sometimes, GI bleeding is also seen in these patients. These symptoms seem to

increase with the advancement of the CKD stage and hence it can be inferred that uremia has a direct or indirect role in the causation of these symptoms. Frequent findings of gastritis, duodenitis, and duodenal ulcers in this study suggest the importance of endoscopy in symptomatic patients for early detection of GI lesions.

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