A Prospective study on Upper Gastrointestinal Endoscopic lesions in Chronic Kidney disease patients in a tertiary care centre in South India

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Abstract
Chronic Kidney disease (CKD) is a slow and progressive loss of kidney function over time regardless of cause. CKD virtually affect the functions of all organ system in our human body. Gastrointestinal symptoms and complications are more common in chronic kidney disease.

Aim: To study the Clinical symptoms, frequency and type of upper Gastrointestinal lesions in Chronic Kidney disease.

Materials & Methods: A total number of 80 patients diagnosed as CKD Stage (3-5) admitted in medicine ward and nephrology unit from February 2017 to January 2018 were selected for study. All patients underwent a detailed History, Clinical examination, Renal Function tests, Ultrasound Abdomen and upper GI Endoscopy.

Results: Eighty patients of CKD stage 3-5 were included in study, of which 58 were males and 22 were females. Ages of patient ranged from 11-80 years while maximum age group was from Fifth decade. Majority of patients were in CKD stage 5. The predominant symptoms were anorexia, nausea and vomiting. Endoscopically, 86% of patients had one or more upper GI mucosal lesions. Lesions were more frequent in the stomach. Inflammatory lesions were the most common upper GI lesion seen.

Conclusion: Gastrointestinal symptoms are common in CKD patients. Majority of the patients have upper GI mucosal lesions in endoscopy. Recognition of these lesions and prompt management can significantly reduce the morbidity and mortality in CKD patients.

Keywords: Chronic kidney disease, Endoscopy, Mucosal lesions, Symptoms, stages.

Introduction
Chronic kidney disease (CKD) is a progressive loss in renal function, characterized by nephron damage and depletion. CKD is associated with several diseases due to a multifactorial damage that leads to a loss in function of all systems of human body. CKD is particularly associated with several abnormalities in the gastrointestinal tract involving all its segments.

CKD results in wide range of symptoms from anorexia to nausea and electrolyte imbalance contributing to a state of malnutrition. About 80%...
of CKD patients present with some type of symptoms in the gastrointestinal tract (GIT) during the course of their disease. The cause for GIT symptoms in CKD is multifactorial in origin. The toxic products retention (endogenous and exogenous) and alteration of the homeostasis of the extracellular environment are the most proposed mechanism for GIT symptoms.

Fiber-optic endoscopes which revolutionized the examination of GI tract shows a wide range of pathological lesions in CKD. Many studies are present in literature giving an insight into prevalence of GI symptoms, endoscopic findings and documentation of different data and experiences.

Materials and Methods
A total number of 80 patients diagnosed as CKD and admitted in Medicine ward / Nephrology unit of Dhanalakshmi Srinivasan medical college and hospital, Siruvachur, Perambalur, Tamilnadu, between February 2017 and January 2018 were selected in this study.

Inclusion Criteria
1. Patients diagnosed as CKD with GFR <60ml/min/1.73m2 (Stage 3-5) (KDIGO guidelines)
2. Patients with age varying from 11 to 80 years.
3. Both male and female patients.
4. Patients on conservative treatment / Hemodialysis (HD) / Peritoneal dialysis

Exclusion Criteria
1. Patients in Stage 1 and Stage 2 CKD. (KDIGO guidelines)
2. Patients in uremic encephalopathy.
3. Patients undergone Renal transplant
4. Patients having H/o acid peptic disease
5. Drug intake like NSAIDs, steroids
6. Corrosive poisoning
7. Chronic alcoholic, Chronic smoker were excluded.

All the CKD patients satisfying the above criteria were subjected to detailed clinical history taking, thorough clinical examination and various Routine investigations like Complete Hemogram, Liver Function test, Renal Function Test, ECG, ECHO and ultrasound abdomen. Upper gastrointestinal endoscopy was performed using fiberoptic endoscope after an overnight fasting. Pre informed consent was obtained from all patients before their inclusion into the study. The oesophagus, stomach and duodenum were studied for mucosal changes.

Results
A total number of 80 Chronic kidney disease patients were enrolled for the study from February 2017 to January 2018. The Upper GI Endoscopy was done after clinical assessment and relevant investigations.

| Age group | Male | Female |
|-----------|------|--------|
| 11-20     | 2    | 1      |
| 21-30     | 7    | 2      |
| 31-40     | 11   | 5      |
| 41-50     | 19   | 8      |
| 51-60     | 11   | 4      |
| 61-70     | 5    | 2      |
| 71-80     | 3    | 0      |
| Total     | 58   | 22     |

Table 1- Age and Sex distribution

Figure 1 – Sex Distribution
Out of 80 patients, 72.5% were males and 27.5% were females. The age group of the study population ranges from 11-80 years. The most common age group was 41-50 years.

### Table 2 Stages of CKD in Study Population

| CKD STAGES  | n (%)  |
|-------------|--------|
| CKD STAGE 3 | 18 (22.5%) |
| CKD STAGE 4 | 26 (32.5%) |
| CKD STAGE 5 | 36 (45%) |

The majority of the patients ie 45% belong to Stage V CKD. Twenty six patients were in Stage IV CKD and remaining eighteen were in CKD Stage 3. Depending on the modes of treatment, patient were divided into two groups namely conservative and dialysis treatment. 80% of patients were on conservative management and 20% were on dialysis treatment. Out of 16 patients who were on dialysis as a mode of treatment, 13 patients received Hemodialysis and 3 patients received peritoneal dialysis.

Gastrointestinal symptoms were present in 85% of patients studied. Anorexia was the most frequent symptom (83%). The second most common symptom was nausea (76%) which was followed by vomiting (64%), heart burns (38%), abdominal pain (28%) and hiccups (20%) in the decreasing order of frequency. The least common presentation was gastrointestinal bleed which occurred in 6 patients (8%).

### Table 3 Baseline Analysis of GI Symptoms

| GI SYMPTOMS  | N (%)  |
|--------------|--------|
| Anorexia     | 67 (83%) |
| Nausea       | 61 (76%) |
| Vomiting     | 51 (64%) |
| Heart burns  | 30 (38%) |
| Abdominal pain | 22 (28%) |
| Hiccups      | 16 (20%) |
| GI bleed     | 6 (8%)  |

### Table 4 Lesions in Upper GI Endoscopy

| TYPE OF LESION  | N (%)  |
|-----------------|--------|
| Esophagitis     | 26 (32%) |
| Hiatus hernia   | 6 (8%)  |
| Esophageal ulcer| 1 (1.5%) |
| Esophageal varix| 1 (1.5%) |
| Pangastritis    | 38 (48%) |
| Pale mucosa     | 12 (15%) |
| Gastric ulcer   | 4 (5%)  |
| Angiodysplasia  | 2 (2.5%) |
| Erosive gastritis| 10 (12.5%) |
| Duodenitis      | 15 (19%) |
| Duodenal ulcer  | 3 (4%)  |

The Upper GI mucosal lesions were present in 69 patients on endoscopic examination. Remaining 11 patients have normal UGI mucosa. The most
common upper GI mucosal lesion was pan gastritis which was seen in 48% of patients. Oesophagitis occupies the next in place (32%). 10% of patients had gastro esophageal reflux and 8% had hiatus hernia. Rest of the findings in oesophagus such as oesophageal ulcer and oesophageal varices was seen in 1 patient each.

Pale gastric mucosa contribute to 15% of patients. Gastric ulcer was seen in 5% of cases while duodenal ulcer in 4%. Only 2% showed angiodysplasia in stomach. In duodenum, duodenitis was seen in 19% of patients. GI bleeding was present in 6 patients (8%). On endoscopy evaluation of UGI bleed patients, 5 patients had erosive gastritis and one had angiodysplasia. Mucosal lesions were more frequent in stomach.
Table 5 – Endoscopy Lesions vs Treatment Modalities

| ENDOSCOPIC LESIONS                  | CONSERVATIVE n=64 | DIALYSIS n=16 |
|-------------------------------------|------------------|---------------|
| Normal                              | 10(16%)          | 1(6%)         |
| Inflammatory lesions                |                  |               |
| Gastritis/Duodenitis/Esophagitis     | 24(38%)          | 7(44%)        |
| Ulcers                              | 5(8%)            | 2(12%)        |
| Angiodysplasia                      | 1(1.5%)          | 1(6%)         |
| Hiatus hernia                       | 5(8%)            | 1(6%)         |
| Pale mucosa                         | 7(11%)           | 5(31%)        |

Patients on conservative treatment had higher frequency of normal endoscopy as compared to those on dialysis (16% vs 6%). The frequency of upper GI mucosal lesions were more common in dialysis group when compared to conservative management group. However Hiatus hernia was common in patients who were on conservative management.

Table 6 – Association between Endoscopic finding and CKD stage in study

| TYPE OF LESION          | CKD STAGE 3 n=18 | CKD STAGE 4 n=26 | CKD STAGE 5 n=36 |
|-------------------------|------------------|------------------|------------------|
| Normal                  | 5(28%)           | 4(15%)           | 2(5.5%)          |
| Esophagitis             | 3(17%)           | 8(31%)           | 15(42%)          |
| Hiatus hernia           | 1(6%)            | 2(8%)            | 3(8%)            |
| GER                     | 1(6%)            | 3(12%)           | 4(11%)           |
| Esophageal ulcer        | 0                | 0                | 1(3%)            |
| Esophageal varix        | 0                | 1(4%)            | 0                |
| Pangastritis            | 5(28%)           | 11(42%)          | 22(61%)          |
| Pale mucosa             | 0                | 4(15%)           | 8(22%)           |
| Gastric ulcer           | 1(6%)            | 1(4%)            | 2(5.5%)          |
| Angiodysplasia          | 0                | 0                | 2(5.5%)          |
| Erosive gastritis       | 0                | 3(12%)           | 7(20%)           |
| Duodenitis              | 2(11%)           | 4(15%)           | 9(25%)           |
| Duodenal ulcer          | 1(6%)            | 1(4%)            | 1(3%)            |

Inflammatory mucosal lesions like Pangastritis, Esophagitis and Duodenitis was higher in Stage 5 CKD when compared to Stage 3 CKD and Stage 4 CKD. Hiatus hernia, gastro esophageal reflux lesions were equal in CKD Stage 4 and CKD Stage 5. Angiodysplasia was seen only in Stage 5 CKD while no such lesion were present in CKD Stage 3 or CKD Stage 4. Pale mucosa was predominantly seen in higher Stages of kidney disease. Duodenal ulcer was similar in all Stages of kidney disease. In CKD Stage 5, 20% had erosive gastritis while in CKD Stage 4 it was only 12%.

Discussion

The digestive pathologies are more frequent in patients with chronic kidney disease (CKD). There is a clear under reporting of the disease, resulting in the lack of knowledge of the mechanisms that lead to a wide range of symptoms. In this study, the age of patients ranged from 11 to 80 years, and the majority in the age group varied from 30 to 60 years. In a study conducted by Varma et al., the age of the patients ranged from 17 to 70 years. Various GI symptoms were noted in the patients under study. It was found that 85% of the patients had one or the other GI symptoms. This result was consistent with the studies conducted by Farsakh et al., and Cano where prevalence of GI symptoms in CKD was 70% and 72% respectively. In a prospective study by Margolis et al., 59% patients had symptoms.
In this study nausea, vomiting and anorexia were the most common symptoms in both dialysed and non-dialysed patients of CKD. Similar observations have been reported by Farasakh et al\textsuperscript{2} and Sivinovic et al\textsuperscript{3}. In the Indian study by Kochar R\textsuperscript{6} and Goenka M, anorexia, nausea and vomiting were the predominant symptoms. The gastrointestinal symptoms are due to central effects of urea and other metabolic waste products which circulate in high concentrations in blood, dialysis disequilibrium syndrome or as a manifestation of volume depletion.

In our study, the prevalence of endoscopic abnormalities was 86%. In similar studies conducted separately by Nardone\textsuperscript{7} and Khedmat\textsuperscript{8} it was observed upper GI lesions on endoscopy was 74% and 79% CKD respectively. In a similar study of UGI endoscopic evaluation in CRF by Agrawal\textsuperscript{9} et al., 85.7% patients showed UGI involvement. The Upper gastrointestinal lesions in our study had a predominant localization in stomach. In study by Serme at al\textsuperscript{10}, gastric lesions (68.7%) were at the forefront followed by duodenal lesions (32%).

Of the various types of lesions seen, inflammatory changes were the most common (42%). Prakash\textsuperscript{11} J and Agrawal BK and Tani N et al\textsuperscript{12} observed that patients with CRF had a high prevalence of inflammatory mucosal changes. In our study gastritis (60%) was the most common lesion followed in frequency by esophagitis (32%) and duodenitis (19%). This result was similar to the findings of study by Nardone\textsuperscript{7} where 56% of CKD patients had gastric erosions. In study conducted by Esfahani\textsuperscript{13}, gastritis was the predominant lesion accounting for 60.8% and other lesions like duodenitis and gastro duodenitis was 13% and 7.2% respectively. Patients of uraemia had improved capacity to secrete acid due to certain factors leading to gastritis. Haemodialysis by removing these factors allow the manifestation of undergoing hypersecretory state.

In our study, gastric ulcer (5%) and duodenal ulcer (4%) incidence was low. It was similar to Sunder et al\textsuperscript{14} who also reported low incidence of peptic ulcer. and Nardone\textsuperscript{7} in his study noticed duodenal ulcer in 6% patients. According to Andriulli\textsuperscript{15}, et al, Patients with chronic renal failure are not at a risk of developing chronic peptic ulcer. In an Indian study by Prakash et al\textsuperscript{16} also noted that risk of developing peptic ulcer is not high in patients with chronic renal failure.

Gastrointestinal bleeding is known to occur in CKD patients. Gastritis occurring in uremic patients were frequently reported to cause bleeding but according to Zukerman et al\textsuperscript{17} angiodysplastic lesions were the leading cause. Goldstein\textsuperscript{18} also reported a higher frequency of angiodysplasia lesions in severe uremia. In the present study, GI bleeding was present in 6 patients (8%). On endoscopy evaluation of these UGI bleed patients, 5 patients had erosive gastritis and one had angiodysplasia. Boyal\textsuperscript{19} et al also reported that gastric bleeding sites rather than duodenal ulceration were the most common source of bleeding. As in our study, the prevalence of angiodysplasia is relatively rare. Hiatus hernia was found in 8% patients in this study. Our study was consistent with study done by Khedmat\textsuperscript{8} et al, who noticed hiatus hernia in 9% patients. According to the study conducted by Farsakh\textsuperscript{2} et al., hiatus hernia was more frequent in hemodialysis patients. But in our study, hiatus hernia was more in conservative management patients.

Most of the patients in our study belong to Stage V CKD (45%). The majority of the patients (80%) in the study were on conservative treatment rather than dialysis. Patients on conservative treatment had higher frequency of normal endoscopy when compared to those on dialysis (16% vs 6%). In our study there was no significant difference in the incidence of abnormal findings in dialysis group on comparison to non-dialysis group. Margolis et al\textsuperscript{4} and Andrivilli et al\textsuperscript{15} also found no relationship between duration of dialysis with the presence or absence of gastrointestinal lesion. According to our study, the more is the stages of renal
impairment, the more is the chance of getting upper gastro-intestinal lesions.

**Conclusion**
The most common, non-renal, chronic disorders in patients with CKD are GI disorders. CKD is associated with several abnormalities of all the segments in the GI tract. The genesis of GI symptoms in CKD is multifactorial. Upper gastrointestinal lesions often overlooked can lead to major complications in CKD. Thus recognition of these lesions and early management can significantly reduce the morbidity and mortality in CKD patients.

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