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RESEARCH ARTICLE

Gastrointestinal Disorders And Chronic Kidney Disease.

Atef Ahmed Ibrahim MD, Roshdy Mohammed KhalafallaMD, Adel Ahmed AbouElkheirMD, Amr Mostafa El-HammadyMD, GameelSaadAbdElfattahM.B.B.C
Department of Internal Medicine, Faculty of Medicine, Benha University.

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Corresponding Author
Gameel Saad Abd Elfattah

Abstract

Gastrointestinal complications are known to commonly occur in patients with renal failure. Uremia and dialysis have long been speculated to increase the risk of lesions in the gastrointestinal tract and accessory organs. In addition, gastrointestinal procedures such as gastrointestinal bypass surgery and the administration of colonoscopy preparations can lead to the development of renal complications. Results from studies that have attempted to define the association between renal dysfunction and gastrointestinal complications are, however, conflicting and limited by small and varied sample populations. No clear management guidelines currently exist for many of the gastrointestinal problems that accompany renal failure. This Review examines the existing data on gastrointestinal complications in patients with chronic kidney disease and end-stage renal disease and aims to outline the etiology and management of common gastrointestinal disorders in such patients.

Introduction:-

The prevalence of chronic kidney disease (CKD) and end stage renal disease (ESRD) has increased steadily over the past decade in the US. Studies indicate there is range wide between 4 million to 10 million of people in the US are affected by CKD, and approximately 560,000 of these patients require dialysis **[1].** The prevalence of gastro intestinal symptoms in patients with renal failure is thought to range from 70% to 79%. The prevalence of these disorders is generally similar in pre-dialysis patients, patients on hemodialysis, and patients on peritoneal dialysis, but a trend towards increasing symptoms with increasing duration of renal failure exists **[2].** The most common gastrointestinal symptoms in patients with renal failure include nausea, vomiting, abdominal pain, constipation, diarrhea and bleeding, IBS also has a high prevalence in these patients, ranging from 11% to 33%. Gastrointestinal bleeding is a known complication of renal failure. There are many gastrointestinal disorders unique to peritoneal dialysis such as peritonitis, acute mesenteric ischemia and encapsulating peritoneal sclerosis **[3].**
Gastrointestinal procedures such as gastrointestinal bypass surgery and the administration of colonoscopy preparations can lead to the development of renal complications **[4].**

Aim of the Work:-

Aim of this work is to highlight the connection between gastrointestinal disorders and chronic kidney disease.

Definition of CKD:

CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m2 for 3 months or more, irrespective of cause. Kidney damage in many kidney diseases can be ascertained by the presence of albuminuria, defined as albumin-to-creatinine ratio >30 mg/g in two of three spot urine specimens **[5].**

Gastrointestinal Symptoms:-

The most common gastrointestinal symptoms in patients with renal failure include nausea, vomiting, abdominal pain, constipation, and diarrhea.

Constipation:-
The prevalence of constipation is as high as 63% in patients on hemodialysis and 29% in patients on peritoneal dialysis, The association of constipation with renal failure is attributed to lifestyle changes that relate to renal dysfunction, including reduced levels of activity, reduced fiber intake (owing to potassium-restricted diets), use of phosphate binders, and the presence of multiple comorbidities such as diabetes and cerebrovascular disease **[6].**Treatment of constipation in these patients is similar to that used in the general population. Uremic retention molecules are a large group of molecules that accumulate in the gastrointestinal tract of patients with renal failure and are believed to contribute to the uremic syndrome. Current treatment strategies to reduce levels of uremic retention molecules include prebiotic and probiotic therapy to decrease the amount of proteolytic bacterial species in the colon**[7].**

Gastroparesis:-
Pathogenesis:-
The mechanisms underlying this association are unknown. Hyperglycemia and autonomic polyneuropathy may lead to gastroparesis and its resulting symptoms**[8].**
Treatment of gastroparesis in patients with renal failure is symptoms-based. Gastroprokinetic medications, such as metoclopramide and erythromycin can be safely used in patients on hemodialysis **[9].**

Upper Gastrointestinal Lesions:-
The pathogenesis of upper gastrointestinal lesions in patients with renal failure remains undefined**[10].** Some studies have reported that hypergastrinemia leads to hypochlorhydria rather than increased acid secretion**[11].**Helicobacter pylori infection may also contribute to the increased prevalence of upper gastrointestinal lesions in patients with renal failure. The H. pylori stool antigen test, noninvasive tests, such as serology tests and the urea breath test seem to be less sensitive and specific in patients with renal failure than in patients with normal renal function Compared with pathological diagnosis by esophagogastroduodenoscopy **[12].** Esophagogastroduodenoscopy should also be performed in any patients with evidence of 'alarm' symptoms, including weight loss, progressive dysphagia, recurrent vomiting, evidence of gastrointestinal bleeding, or family history of cancer**[13].**
Once infection with H. pylori is established in patients with renal failure, management of H. pylori should be started by 'Triple therapy', which involves the administration of a proton pump inhibitor, clarithromycin and either amoxicillin or metronidazole should be initiated**[13].**

Gastrointestinal Bleeding:-
Gastrointestinal bleeding is a known complication of renal failure however, its pathogenesis remains uncertain. Some have attributed gastrointestinal bleeding to the effects of uremia on the gastrointestinal mucosa; others have suggested that uremia may affect platelet adhesiveness, which may explain the prolonged gastrointestinal bleeding seen in patients with renal failure. In addition, the role of heparinization and the widespread use of antiplatelet agents in patients on dialysis have been implicated in the etiology of gastrointestinal bleeding**[14].** All of the above explanations probably contribute in some way to the higher incidence of acute, chronic, upper, and lower gastrointestinal bleeding that is seen in patients with renal failure compared with that seen in the general population. Angiodysplasia of both the upper and lower gastrointestinal tract seems to be more common in patients with renal failure than in the general population **[15]** and causing gastrointestinal hemorrhage and recurrent bleeding in patients with renal failure**[16]** The effect is probably caused by a need for thrice weekly anticoagulation treatment in patients on dialysis and the association of anticoagulants with an increased risk of bleeding in patients with angiodysplasia**[17].**

Initial treatment of angiodysplasia includes local ablation with argon plasma coagulation, laser coagulation, or heat coagulation. If these methods fail, surgical resection is often considered**[18].** Acute upper gastrointestinal bleeding occurs more commonly in patients with renal failure because of an increased risk of gastrointestinal bleeding, such as use of NSAIDS, aspirin, or anticoagulants **[19].**

Acute Pancreatitis:-
The reason for the higher prevalence of pancreatic abnormalities in patients with renal failure related to increases in the concentration of gastrointestinal hormones, such as cholecystokinin, serum gastric inhibitory peptide, and glucagon cause a hypersecretion of pancreatic enzymes and subsequent damage**[20].** The most common symptom in patients presenting with pancreatitis is severe abdominal pain, other common symptoms include nausea and vomiting, and abdominal tenderness, levels of amylase and lipase may be useful in the diagnosis of pancreatitis in

patients with renal failure **[21].**Imaging as abdominal ultrasonography and abdominal CT scans is often considered for individuals in the general population or with renal failure who present with prolonged fever, marked epigastric tenderness, or hemodynamic instability. Most cases of pancreatitis in patients with renal failure can be managed conservatively, that is, with bowel rest or nasogastric suction. As in the general population, drainage and debridement should be reserved for patients with pseudocysts or necrosis **[22].**

Acute Mesenteric Ischemia:-
The most common symptoms were abdominal pain, fever, guarding, and leukocytosis. Diagnosis was confirmed by colonoscopy or CT scanning with an opaque enema**[23].** Cardiovascular pathology and atherosclerosis are thought to be the main risk factors for the development of acute mesenteric ischemia in patients on hemodialysis**[24].** The majority of patients with acute mesenteric ischemia, however, do not respond to fluids and the preferred treatment is laparotomy and surgical resection of the infarcted bowel**[25].**

Problems Unique to Peritoneal Dialysis:-
Peritonitis caused by gram-negative, polymicrobial, fungal organisms,diverticulosis and encapsulating peritoneal sclerosisare the most common problems related to peritoneal dialysis and diagnosed by clinical, laboratory and radiological findings **[26].** Suspicious clinical signs and symptoms include early satiety, abdominal fullness, anorexia, nausea, vomiting, constipation, diarrhea, weight loss, and a loss of ultrafiltration capacity.Diagnosis is often confirmed through abdominal ultra-sonography and CT scanning. Treatment strategies in encapsulating peritoneal sclerosis include tamoxifen, immunosuppressive medications, and surgical enterolysis or adhesiolysis**[27].**

Drugs And Gastrointestinal Disease In Chronic Kidney Disease:-
*Calcium carbonate*is used to treat hyperphosphatemia in patients with advanced renal insufficiency by combining with dietary phosphate to form insoluble calcium phosphate, which is excreted in feces. Gastrointestinal side effects of Calcium carbonate: Constipation, laxative effect, acid rebound, nausea, vomiting, anorexia, abdominal pain, xerostomia, flatulence **[28].**

Statins are used in treatment of dyslipidemias or primary prevention of cardiovascular disease. Gastrointestinal side effects of statins:Flatulence, constipation, abdominal pain , diarrhea, nausea, dyspepsia **[29].**

Angiotensin converting enzyme (ACE) inhibitors are widely used in the treatment of hypertension, chronic kidney disease, and heart failure. (ACE) gastrointestinal side effects include Pancreatitis, glossitis, dyspepsia, abnormal taste, abdominal pain, vomiting, nausea, diarrhea, anorexia, constipation **[30].**

Iron supplements may be given orally or intravenously totreat and prevent development of iron deficiency. Gastrointestinal tract symptoms and limited efficacy so intravenous ironis preferred rather than oral iron in most patients on PD and home HD.Iron is best absorbed as the ferrous(Fe2+) salt in a mildly acidic medium. Gastrointestinal tractsymptoms as (abdominal discomfort, nausea/vomiting, diarrhea/constipation) suffered by some patients seem to be directly related tothe amount of elemental iron ingested **[31].**

Bisphosphonates can be given to patients with any conditioncharacterized by excessive bone resorption, such as osteoporosis,hypercalcemia of any cause, metastatic bone disease, and Pagetdisease. The bisphosphonates are non-hydrolyzable analogs ofinorganic pyrophosphate that adsorb to the surface of bonehydroxyapatite and inhibit calcium release by interfering withosteoclast-mediated bone resorption. The bisphosphonatesgastrointestinal side effects include abdominal pain , acid reflux , dyspepsia, nausea, flatulence ,diarrhea, gastroesophageal reflux disease, constipation , esophageal ulcer, abdominal, distension, gastritis, vomiting,dysphagia, gastric ulcer , melena .

Calcium channel blockers are widely used in the treatment ofhypertension, angina pectoris, cardiac arrhythmias, and otherdisorders, and the longer-acting preparations have beenprescribed with increasing frequency. Calcium channel blockers gastrointestinal side effects are dyspepsia, constipation, vomiting, diarrhea**[32].**

Proton pump inhibitors (PPIs) should beadministered before the first meal of the day. In most individuals,once-daily dosing is sufficient to produce the desired level of acidinhibition, and a second dose, which is occasionally necessary,should be administered before the evening meal. PPIs should notbe given concomitantly with H2-antagonists, prostaglandins, or otherantisecretory agents because of the marked reduction in their

acidinhibitoryeffects when administered simultaneously. (PPIs) gastrointestinal side effects include abdominal pain, diarrhea, nausea, vomiting, flatulence, acid regurgitation, constipation**[33].**

Conclusions:-

Gastrointestinal symptoms and gastrointestinal disease are common in patients with renal failure. The prevalence of upper gastrointestinal lesions, acute and chronic episodes of gastrointestinal bleeding, pancreatitis, and ischemic colitis seems to be higher in patients with renal failure than in the general population. An increase in the number of patients undergoing gastrointestinal bypass surgery or receiving colonoscopy preparations also seems to have led to the development of previously unrecognized renal complications. Unfortunately, the lack of well-designed studies means that ambiguity still surrounds the pathogenesis, diagnosis, and treatment of gastrointestinal diseases in patients with renal failure. More research is needed to formulate appropriate screening and treatment plans for these patients.

References:-

1- CoreshJ,SelvinE,StevensAetal:Prevalenceofchronickidneydiseaseinthe Unitedstates.JournalofAm.Med. Ass.298:2038-2047, 2007.
2- Strid H, Simren M, Johanasson A. et al., The prevalence of gastrointestinal symptoms in patients with chronic renal failure is increased and associated with impaired psychological general well being . Nephrology. Dialysis. Transplant. 17:1434-1439, 2002.
3- Shirazian S. and Radhakrishnan J. Gastrointestinal disorders and renal failure exploring the connection. Nat. Rev. Nephrology 6: 480-492, 2010.
4- Nelson W.K., Houghton S.G., Milliner D.S. et al: enteric hyperoxaluria, nephrolithiasis, and oxalate nephropathy. Obesity Related Diseases. 1:481-485, 2005.
5- Astor BC, Matsushita K, Gansevoort RT, et al: Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int; 79: 1331, 2011.
6- Evenepoel, P, Meijers, B. K., Bammens, B. R. &Verbeke, K. Uremic toxins originating from colonic microbial metabolism. *Kidney Int. Suppl.* **76,** S12-S19 (2009).
7- Wu, M. J. *et al*. Colonic transit time in long-term dialysis patients. *Am. J. Kidney Dis.* **44,** 322-327 (2004).
8- Drossman, D. A. *et al*. U. S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. *Dig. Dis. Sci.* **38,** 1569-1580 (1993).
9- Wysowski, D. K. &Bacsanyi, J. Cisapride and fatal arrhythmia. *N. Engl. J. Med.* **335,** 290-291 (1996).
10- Franklin, G., Musola, R. &Mencarelli, R. Morphological changes of the gastroduodenal mucosa in regular dialysis uraemic patients. *Histopathology* **6,** 429-437 (1982).
11- Muto, S., Murayama, N., Asano, Y., Hosoda, S. & Miyata, M. Hypergastrinemia and achlorhydria in chronic renal failure. *Nephron* **40,** 143-148 (1985).
12- Wang, Y. L., Sheu, B. S., Huang, J. J. & Yang, H. B. Noninvasive stool antigen assay can effectively screen Helicobacter pylori Infection and assess success of eradication therapy in hemodialysis patients. *Am. J. Kidney Dis.* **38,** 98-103 (2001).
13- Talley, N. J. American Gastroenterological Association medical position statement: evaluation of dyspepsia. *Gastroenterology* **129,** 1753-1755 (2005).
14- Ramamirtham, P. &Savides, T. J. In *Complications of Dialysis* 1stedn (ed. Lamiere, N.) 605-606 (Marcel Dekker Inc., New York, 2000).
15- Chalasani, N., Cotsonis, G. & Wilcox, C. M. Upper gastrointestinal bleeding in patients with chronic renal failure: role of vascular ectasia. *Am. J. Gastroenterol.* **91,** 2329-2332 (1996).
16- Alvarez, L., Puleo, J. &Balint, J. A. Investigation of gastrointestinal bleeding in patients with end stage renal disease. *Am. J. Gastroenterol.* **88,** 30-33 (1993).
17- Gupta, N., Longo, W. E. &Vernava, A. M. III. Angiodysplasia of the lower gastrointestinal tract: an entity readily diagnosed by colonoscopy and primarily managed nonoperatively. *Dis. ColonRectum***38,** 979-982 (1995).
18- Tomori, K. *et al*. Gastric angiodysplasia in patients undergoing maintenance dialysis. *Adv.Perit. Dial.* **19,** 136-142 (2003).
19- Tsai, C. J. & Hwang, J. C. Investigation of upper gastrointestinal hemorrhage in chronic renal failure. *J. Clin. Gastroenterol.* **22,** 2-5 (1996).

20- Bruno, M. J. *et al*. Acute pancreatitis in peritoneal dialysis and haemodialysis: risk, clinical course, outcome, and possible aetiology. *Gut* **46,** 385-389 (2000).
21- Rutsky, E. A., Robards, M., Van Dyke, J. A. & Rostand, S. G. Acute pancreatitis in patients with end-stage renal disease without transplantation. *Arch. Intern. Med.* **146,** 1741-1745 (1986).
22- Lankisch, P. G., Weber-Dany, B., Maisonneuve, P. &Lowenfels, A. B. Frequency and severity of acute pancreatitis in chronic dialysis patients. *Nephrol. Dial. Transplant.* **23,** 1401-1405 (2008).
23- Flobert, C. *et al*. Right colonic involvement is associated with severe forms of ischemic colitis and occurs frequently in patients with chronic renal failure requiring hemodialysis. *Am. J.Gastroenterol.* **95,** 195-198 (2000).
24- Ori, Y. *et al*. Non-occlusive mesenteric ischemia in chronically dialyzed patients: a disease with multiple risk factors. *Nephron Clin. Pract.* **101,** c87-;93 (2005).
25- Archodovassilis, F. *et al*. Nonocclusive mesenteric ischemia: a lethal complication in peritoneal dialysis patients. *Perit. Dial. Int.* **27,** 136-141 (2007).
26- Jain, A. K. & Blake, P. G. Non-*Pseudomonas* gram negative peritonitis. *Kidney Int.* **69,** 1107-1109 (2006).
27- Augustine, T., Brown, P W., Davies, S. D., Summers, A. M. &Wilkie, M. E. Encapsulating peritoneal sclerosis: clinical significance and implications. *Nephron Clin. Pract.* **111,** c149-c154 (2009).
28- Emmett M. A comparison of clinically useful phosphorus binders for patient. with chronic kidney failure. Kidney IntSuppl S25, 2004.
29- Gotto AM Jr. Safety and statin therapy: reconsidering the risks and benefits. Arch Intern Med 163:657, 2003.
30- Stirling C, Houston J, Robertson S, et al: Diarrhoea, vomiting and A. inhibitors:--an important cause of acute renal failure. J Hu. Hypertens 17:419, 2003.
31- Rimon E, Kagansky N, Kagansky M, et al: Are we giving too much iron. Low-dose iron therapy is effective in octogenarians. Am J Me. 118:1142, 2005.
32- KizerJR, and Kimmel SE. Epidemiologic review of the calcium channel blocker drugs. An up-to-date perspective on the proposed hazards. Arch Intern Med 161:1145, 2001.
33- Wolfe MM and Lowe RC. Investing in the future of GERD. J Clin. Gastroenterol 41:S209, 2007.