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CHRONIC KIDNEY DISEASE AND DAMAGE TO THE GASTROINTESTINAL TRACT

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Summary

Introduction. The work is devoted to problem of gastrointestinal tract functioning due to chronic problem in kidneys. The initial recognition of kidney disease as independent from other medical conditions is widely attributed to Richard Bright's 1827 book "Reports of Medical Cases," which detailed the features and consequences of kidney disease. The CKD influence GIT by Disruption of the colonic microbiome and its attendant as a result of which there is loss of gut barrier integrity and increased generation of uremic toxins resulting in disruption of GIT normal functioning.

Goal. To study the causes of clinical manifestations of chronic kidney disease and how it affects GIT.

Materials and Methods. Review of modern and foreign literary sources; methods – description, analysis, abstracting.

Results and discussion. CKD is common in US and in adults over 30 the reason behind that is Diabetes leading to kidney disease. Both: type 1 and type 2 diabetes. But also heart disease and obesity can contribute to the damage that causes kidneys to fail. Research suggests that gene GPX1, GSTO1, GSTO2, UMOD, and MGP genes are associated with CKD. The pathophysiology of CKD has a lot to contribute in GIT malfunctioning.

Conclusions. The link between GIT malfunctioning and kidney pathology can be explained by the pathophysiology of CKD and its outcomes affecting GIT.

Key words: chronic kidney disease, pathophysiology, uremia.

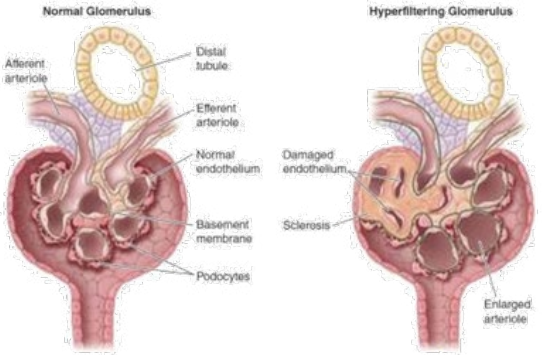
Introduction

Chronic kidney disease (CKD) is a range of pathophysiologic events associated with abnormal functioning of kidneys and a progressive decline in glomerular filtration rate. The risk of CKD progressing development is intimately connected to GFR and the amount of albuminuria. The term end-stage renal disease represents a stage of CKD due to the increase accumulation of toxins, electrolytes and fluids which is normally excreted by the kidneys leads to death unless these toxins are eliminated by renal replacement therapy (using dialysis or kidney transplantation).

Pathophysiology of CKD

The two mechanisms of damage are:

1) **initiating mechanisms specific to the underlying etiology** (e.g., toxin exposure to renal tubules and interstitium, abnormal kidney development, immune complex activation due to inflammation in certain types of glomerulonephritis);
2) **hyperfiltration and hypertrophy** of the remaining viable nephrons, there will be reduction in renal function from long-term reduction in renal mass. The reductions in nephron number are mediated by vasoactive hormones, cytokines, and growth factors. Eventually, these short-term adaptations of hyper filtration and hypertrophy to maintain GFR become maladaptive as the increased pressure and flow within the nephron predisposes to distortion glomerular architecture, abnormal podocyte function, and disruption of the filtration barrier leading to sclerosis and dropout of the remaining nephrons. Increased intrarenal activity of the renin-angiotensin system (RAS) appears to contribute both to the initial compensatory hyper filtration and to the subsequent maladaptive hypertrophy and sclerosis.



Risk factors

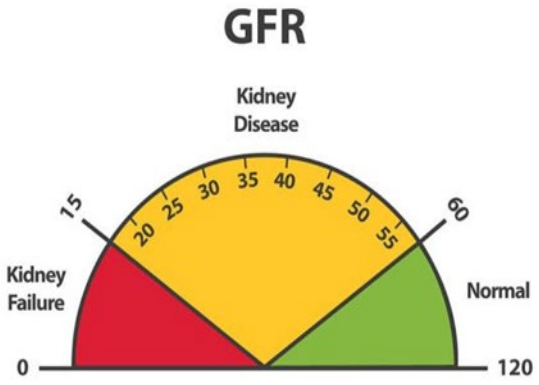
Risk factors include childhood obesity, hypertension, diabetes mellitus, autoimmune disease, and advanced age, a family history of kidney disease, a previous acute kidney injury, and the presence of proteinuria, abnormal urinary sediment or structural abnormalities of the urinary tract.

Staging of CKD

To stage CKD, we estimate the GFR or eGFR. These estimates are only approved if the patient is in steady state (that's the serum creatinine level should be stable.

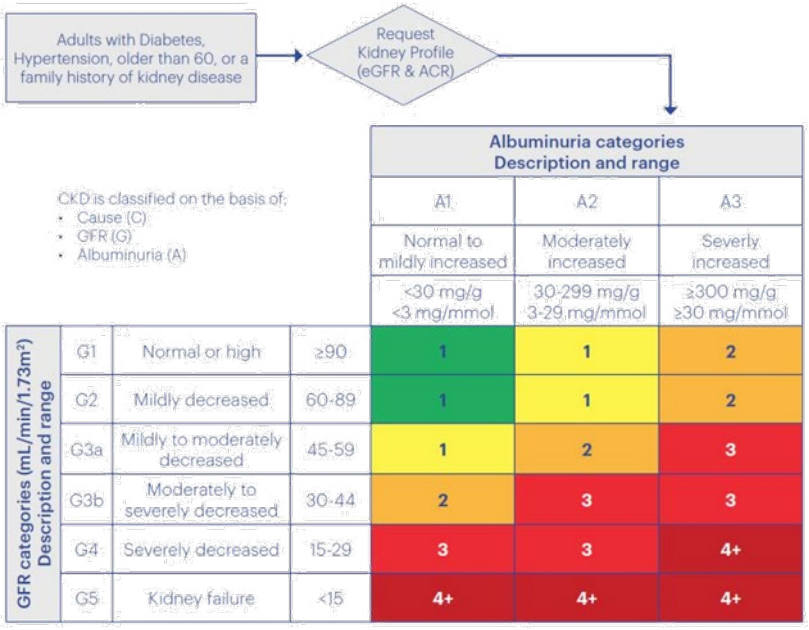
Albuminuria measurement is important in monitoring nephron injury (Albuminuria is marker for systemic vascular disease and endothelial dysfunction) and to check the therapy response of CKD, especially chronic glomerular diseases. Now the morning urine collection has been replaced by UACR.

UACR above 17 mg albumin/g creatinine in men and 25 mg albumin/g creatinine in women serves as a marker not only for early detection of primary kidney disease, but for systemic micro vascular disease as well.



A Kidney Failure Risk (KFR) equation has been devised to predict the risk of progression to stage 5 dialysis-dependent kidney disease.

Stages 1 and 2 CKD are usually asymptomatic, such CKD can only be diagnosed by laboratory testing, with progression to CKD stages 3 and 4, clinical and laboratory complications become more prominent.



GFR categories (mL/min/1.73m²) Description and range				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severly increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90	1	1	2
	G2	Mildly decreased	60-89	1	1	2
	G3a	Mildly to moderately decreased	45-59	1	2	3
	G3b	Moderately to severely decreased	30-44	2	3	3
	G4	Severely decreased	15-29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

All the organs are affected in this disease, but the most evident complications include anemia and associated easy fatigability; decreased appetite with progressive malnutrition; abnormalities in calcium, phosphorus, and mineral-regulating hormones, such as 1,25(OH)2 D3 (calcitriol), parathyroid hormone (PTH), and fibroblast growth factor 23 (FGF-23); and abnormalities in sodium, potassium, water, and acid base homeostasis. If repeat testing shows declining GFR, albuminuria, or uncontrolled hypertension, referral to a nephrologist is appropriate.

If the patient progresses to stage 5 CKD, toxins will accumulate in the patients and the patient experiences a marked disturbance in his daily life activities, well-being, nutritional status, and water and electrolyte homeostasis, eventuating in the uremic syndrome.

Etiologies of CKD

- Diabetic nephropathy
- Glomerulonephritis
- Hypertension associated CKD
- Autosomal dominant polycystic kidney disease
- Other cystic and tubulointestinal nephropathy

Epidemiology

The population data states that at least 6% of the adult population in the United States has CKD at stages 1 and 2. An additional 4.5% of the U.S. population is estimated to have stages 3 and 4 CKD. The relative contribution of each category varies among different geographic regions, the most frequent cause of CKD in North America and Europe is diabetic nephropathy, most often secondary to type 2 diabetes mellitus. Patients with newly diagnosed CKD often have hypertension. However, it is now appreciated that such individuals can be considered in two categories. The first includes patients with a subclinical primary glomerulopathy, such as focal segmental or global glomerulosclerosis. The second includes patients in whom progressive nephrosclerosis and hypertension is the renal correlate of a systemic vascular disease. Nevertheless, it should be appreciated that the majority of patients with early stages of CKD succumb to cardiovascular and cerebrovascular complications before they progress to the more advanced stages of CKD.

Uremia and CKD

The pathophysiology of uremic syndrome is divided into three manifestations of dysfunction: (1) those consequent to the accumulation of toxins that normally undergo renal excretion; (2) those consequent to the loss of other kidney functions, such as fluid and electrolyte homeostasis and hormone regulation; and (3) progressive systemic inflammation and its vascular and nutritional consequences.

Uremia causes disturbances in every organ system. Chronic dialysis can reduce severe manifestations especially florid. However, even optimal dialysis therapy is not completely effective as renal replacement therapy. Renal replacement therapy is only done when dialysis does not help.

Fluid, electrolyte, and acid base disorders

1) **Sodium and water homeostasis**

Hyponatremia is not common in CKD patients. Thiazide diuretics have limited utility in stages 3-5 CKD, such that administration of loop diuretics, like furosemide, bumetanide, or torsemid. The combination of loop diuretics with metolazone may be helpful. Diuretic resistance with intractable edema and hypertension in advanced CKD may serve as an indication to initiate dialysis.

In addition to problems with salt and water excretion, some patients with CKD may instead have impaired renal conservation of sodium and water. When an extra renal cause for fluid loss, such as gastrointestinal (GI) loss, is present, these patients may be prone to ECFV depletion because of the inability of the failing kidney to reclaim filtered sodium adequately. Furthermore, depletion of ECFV, whether due to GI losses or overzealous diuretic therapy, can further compromise kidney function through under perfusion, or a “prerenal” state, leading to acute-on-chronic kidney failure.

2) **Potassium homeostasis**

In CKD, the decrease in the GFR does not necessarily mean decrease in potassium, which is predominantly mediated by aldosterone-dependent secretion in the distal nephron. Another defense against potassium retention in these patients is augmented potassium excretion in the GI tract. Notwithstanding these two homeostatic responses, hyperkalemia may be precipitated in certain settings. These include increased dietary potassium intake, hemolysis, hemorrhage, transfusion of stored red blood cells, and metabolic acidosis.

Certain causes of CKD can be associated with earlier and more severe disruption of potassium-secretory mechanisms in the distal nephron, out of proportion to the decline in GFR. These include conditions associated with hyporeninemic hypoaldosteronism, such as diabetes, and renal diseases that preferentially affect the distal nephron, such as obstructive uropathy and sickle cell nephropathy.

Hypokalemia is not common in CKD which is usually due to decreased dietary potassium intake.

3) **Metabolic acidosis**

Metabolic acidosis is a common disturbance in advanced CKD. Hyperkalemia, if present, further depresses ammonia production. The combination of hyperkalemia and hyperchloremic metabolic acidosis is often present, even at earlier stages of CKD (stages 1-3), in patients with diabetic nephropathy or in those with predominant tubulointerstitial disease or obstructive uropathy.

Treatment of Fluid, electrolyte, and acid base disorders

Dietary salt restriction and the use of loop diuretics, occasionally in combination with metolazone, may be needed to maintain euvolemia. Water restriction is indicated only if there is a problem with Hyponatremia.

Hyperkalemia often responds to dietary restriction of potassium, the use of kaliuretic diuretics, and avoidance of both potassium supplements (including occult sources, such as dietary salt substitutes) and dose reduction or avoidance of potassium-retaining medications (especially angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs]). Kaliuretic diuretics promote urinary potassium excretion, whereas potassium-binding resins, such as calcium resonium, sodium polystyrene or patiromer can promote potassium loss through the GI tract and may reduce the incidence of hyperkalemia. Intractable hyperkalemia is an indication (although uncommon) to consider institution of dialysis in a CKD patient. The renal tubular acidosis and subsequent anion-gap metabolic acidosis in progressive CKD will respond

to alkali supplementation, typically with sodium bicarbonate. Recent studies suggest that this replacement should be considered when the serum bicarbonate concentration falls below 20-23 mmol/L to avoid the protein catabolic state seen with even mild degrees of metabolic acidosis and to slow the progression of CKD.

GASTROINTESTINAL AND NUTRITIONAL ABNORMALITIES

Uremic fetor, a urine-like odor on the breath, derives from the breakdown of urea to ammonia in saliva and is often associated with an unpleasant metallic taste (dysgeusia). Gastritis, peptic disease, and mucosal ulcerations at any level of the GI tract occur in uremic patients and can lead to abdominal pain, nausea, vomiting, and GI bleeding. These patients are also prone to constipation, which can be worsened by the administration of calcium and iron supplements. The retention of uremic toxins also leads to anorexia, nausea, and vomiting.

Protein restriction may be useful to decrease nausea and vomiting; however, it may put the patient at risk for malnutrition and should be carried out, if possible, in consultation with a registered dietitian specializing in the management of CKD patients. Weight loss and protein-energy malnutrition, a consequence of low protein and caloric intake, is common in advanced CKD and is often an indication for initiation of renal replacement therapy. Metabolic acidosis and the activation of inflammatory cytokines can promote protein catabolism. A number of indices are useful in nutritional assessment and include dietary history, including food diary and subjective global assessment; edema-free body weight; and measurement of urinary protein nitrogen appearance. Dual-energy x-ray absorptiometry is now widely used to estimate lean body mass versus fluid weight. Nutritional guidelines for patients with CKD are summarized in the “Treatment” section.

Patients with chronic kidney disease (CKD) frequently experience upper gastrointestinal (GI) symptoms including dysgeusia, anorexia, hiccups, stomatitis, nausea, vomiting, and gastro paresis. Constipation and diarrhea represent the main lower GI tract symptoms associated with CKD.

High levels of urea in the blood may cause gastrointestinal issues such as nausea, poor appetite (including an inability to consume the necessary amounts of minerals and vitamins), bad taste in the mouth, peptic ulcers, gastrointestinal bleeds, diarrhea, vomiting and more.

Tests and investigation for CKD

1# LABORATORY INVESTIGATION

Serum and urine protein electrophoresis, looking for multiple myeloma, should be obtained in all patients >35 years with unexplained CKD, especially if there is associated anemia and elevated, or even inappropriately normal, serum calcium concentration in the face of renal insufficiency. In the presence of glomerulonephritis, autoimmune diseases such as lupus and underlying infectious etiologies such as hepatitis B and C and HIV should be tested. Serial measurements of renal function should be obtained to determine the pace of renal deterioration and ensure that the disease is truly chronic rather than acute or subacute and hence potentially reversible. Serum concentrations of calcium, phosphorus, vitamin D, and PTH should be measured to evaluate metabolic bone disease. Hemoglobin concentration, iron, vitamin B12, and folate should also be evaluated. A 24-h urine collection may be helpful, because protein excretion >300 mg may be an indication for therapy with ACE inhibitors or ARBs.

2# IMAGING STUDIES

The most useful imaging study is a renal ultrasound, which can verify the presence of two kidneys, determine if they are symmetric, provide an estimate of kidney size, and rule out renal masses and evidence of obstruction. Because it takes time for kidneys to shrink as a result of chronic disease, the finding of bilaterally small kidneys supports the diagnosis of CKD of long-standing duration. If the kidney size is normal, it is possible that the renal disease is acute or subacute. The exceptions are diabetic nephropathy (where kidney size is increased at the onset of diabetic nephropathy before CKD supervenes), amyloidosis, and HIV nephropathy, where kidney size may be normal in the face of CKD. Polycystic kidney disease that has reached some degree of renal failure will almost always present with enlarged kidneys with multiple cysts (Chap. 309). A discrepancy >1 cm in kidney length suggests either a unilateral developmental abnormality or disease process or Reno vascular disease with arterial insufficiency affecting one kidney more than the other. The diagnosis of Reno vascular disease can be undertaken with different techniques, including Doppler sonography, nuclear medicine studies, or CT or magnetic resonance imaging (MRI) studies. If there is a suspicion of reflux nephropathy (recurrent childhood urinary tract infection, asymmetric renal size with scars on the renal poles), a voiding cystogram may be indicated. However, in most cases, by the time the patient has CKD, the reflux has resolved, and even if still present, repair does not improve renal function. Radiographic contrast imaging studies are not particularly helpful in the investigation of CKD. Intravenous or intra-arterial dye should be avoided where possible in the CKD patient, especially with diabetic nephropathy, because of the risk of radiographic contrast dye-induced renal failure. When unavoidable, appropriate precautionary measures include avoidance of hypovolemia

at the time of contrast exposure, minimization of the dye load, and choice of radiographic contrast preparations with the least nephrotoxic potential. Additional measures thought to attenuate contrast-induced worsening of renal function include judicious administration of sodium bicarbonate–containing solutions and N-acetyl cysteine.

3# KIDNEY BIOPSY

In the patient with bilaterally small kidneys, renal biopsy is not advised because (1) it is technically difficult and has a greater likelihood of causing bleeding and other adverse consequences, (2) there is usually so much scarring that the underlying disease may not be apparent, and (3) the window of opportunity to render disease-specific therapy has passed. Other contraindications to renal biopsy include uncontrolled hypertension, active urinary tract infection, bleeding diathesis (including ongoing anticoagulation), and severe obesity. Ultrasound-guided percutaneous biopsy is the favored approach, but a surgical or laparoscopic approach can be considered, especially in the patient with a single kidney where direct visualization and control of bleeding are crucial. In the CKD patient in whom a kidney biopsy is indicated (e.g., suspicion of a concomitant or superimposed active process such as interstitial nephritis or in the face of accelerated loss of GFR), the bleeding time should be measured, and if increased, desmopressin should be administered immediately prior to the procedure. A brief run of hemodialysis (without heparin) may also be considered prior to renal biopsy to normalize the bleeding time.

ESTABLISHING THE DIAGNOSIS AND ETIOLOGY OF CKD

The most important initial diagnostic step is to distinguish newly diagnosed CKD from acute or subacute renal failure, because the latter two conditions may respond to targeted therapy. Previous measurements of serum creatinine concentration are particularly helpful in this regard. Normal values from recent months or even years suggest that the current extent of renal dysfunction could be more acute, and hence reversible, than might otherwise be appreciated. In contrast, elevated serum creatinine concentration in the past suggests that the renal disease represents a chronic process. Even if there is evidence of chronicity, there is the possibility of a superimposed acute process (e.g., ECFV depletion, urinary infection or obstruction, or nephrotoxin exposure) supervening on the chronic condition. If the history suggests multiple systemic manifestations of recent onset (e.g., fever, polyarthritis, rash), it should be assumed that renal insufficiency is part of an acute systemic illness. Although kidney biopsy can usually be performed in early CKD (stages 1-3), it is not always indicated. For example, in a patient with a history of type 1 diabetes mellitus for 15-20 years with retinopathy, nephrotic-range proteinuria, and absence of hematuria, the diagnosis of diabetic nephropathy is very likely and biopsy is usually not necessary. However, if there were some other finding not typical of diabetic nephropathy, such as hematuria or white blood cell casts, or absence of diabetic retinopathy, some other disease may be present and a biopsy may be indicated. In the absence of a clinical diagnosis, kidney biopsy may be the only recourse to establish an etiology in early-stage CKD. However, as noted above, once the CKD is advanced and the kidneys are small and scarred, there is little utility and significant risk in attempting to arrive at a specific diagnosis. Genetic testing is increasingly entering the repertoire of diagnostic tests, since the patterns of injury and kidney morphologic abnormalities often reflect overlapping causal mechanisms, whose origins can sometimes be attributed to a genetic predisposition or cause.

Chronic kidney disease (CKD) can be diagnosed with blood and urine tests. In many cases, CKD is only found when a routine blood or urine test you have for another problem shows that your kidneys may not be working normally.

Misdiagnosis of ‘CKD’

Of particular concern were the high prevalence estimates of between 30 and 40% seen in the elderly.

Signs and symptoms of CKD

Early in chronic kidney disease, you might have no signs or symptoms. As chronic kidney disease progresses to end-stage renal disease, signs and symptoms might include:

- Nausea
- Vomiting
- Loss of appetite
- Fatigue and weakness
- Changes in how much you urinate
- Chest pain, if fluid builds up around the lining of the heart
- Shortness of breath, if fluid builds up in the lungs
- Swelling of feet and ankles
- High blood pressure (hypertension) that’s difficult to control
- Headaches
- Difficulty sleeping
- Decreased mental sharpness
- Muscle twitches and cramps
- Persistent itching
- Metallic taste

Signs and symptoms of kidney disease are often nonspecific, meaning they can also be caused by other illnesses. Because your kidneys can make up for lost function, signs and symptoms might not appear until irreversible damage has occurred.

Complications of CKD

Potential complications include: Fluid retention, which could lead to swelling in your arms and legs, high blood pressure, or fluid in your lungs (pulmonary edema) a sudden rise in potassium levels in your blood (hyperkalemia), which could impair your heart's function and can be life-threatening. Anemia.

Patients with chronic kidney disease (CKD) frequently experience upper gastrointestinal (GI) symptoms including dysgeusia, anorexia, hiccups, stomatitis, nausea, vomiting, and gastro paresis. Constipation and diarrhea represent the main lower GI tract symptoms associated with CKD.

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РЕЗЮМЕ

ХРОНІЧНА ХВОРОБА НИРОК ТА УРАЖЕННЯ ШЛУНКОВО-КИШКОВОГО ТРАКТУ

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Вступ. Робота присвячена проблемі функціонування шлунково-кишкового тракту за рахунок хронічної проблеми нирок. Початкове визнання хвороби нирок як незалежної від інших захворювань широко пояснюється книгою Річарда Брайта 1827 року «Звіти про Медичні випадки», де детально описані особливості та наслідки захворювань нирок.

ХХН впливає на ШКТ шляхом порушення мікробіома товстої кишки та, як наслідок, супроводжуючих його речовин, з яких відбувається втрата цілісності кишкового бар'єру та посилене утворення уремічних токсинів, що призводить до порушення нормальної роботи ШКТ.

Мета. Вивчити причини та особливості клінічних проявів хронічної хвороби нирок, що впливають на ШКТ.

Матеріали та методи. Огляд сучасних та зарубіжних літературних джерел; методи – опис, аналіз, реферування.

Результати і обговорення. ХХН є поширеним явищем у США, а у дорослих старше 30 років причиною цього є діабет, що призводить до захворювання нирок. Обидва: цукровий діабет 1 і 2 типу, але також серцеві захворювання та ожиріння, можуть сприяти пошкодженню, яке спричиняє відмову нирок. Дослідження показують, що гени GPX1, GSTO1, GSTO2, UMOD і MGP пов'язані з ХХН. Патофізіологія ХХН має великий внесок у порушення роботи ШКТ.

Висновки. Зв'язок між порушенням роботи ШКТ і патологією нирок можна пояснити патофізіологією ХХН та її наслідками, що впливають на ШКТ.

Ключові слова: хронічна хвороба нирок, патофізіологія, уремія.

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