A Comprehensive Review of Chronic Kidney Disease: Pathophysiology, Diagnosis and Management

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Abstract

Chronic Kidney Disease (CKD) is a progressive and irreversible disorder characterized by a gradual decline in kidney function, leading to significant morbidity, mortality, and healthcare burden worldwide. The rising prevalence of CKD is closely associated with increasing rates of diabetes mellitus, hypertension, cardiovascular disease, and aging populations. In its early stages, CKD is often asymptomatic, resulting in delayed diagnosis and progression to advanced stages. Early identification relies on clinical evaluation, laboratory investigations such as serum creatinine, estimated GFR, urine albumin-to-creatinine ratio, and imaging studies to determine disease severity. Management of CKD focuses on slowing disease progression, preventing complications, and reducing cardiovascular risk. Key strategies include optimal control of blood pressure and blood glucose, use of renin–angiotensin–aldosterone system inhibitors, dietary modifications, and appropriate pharmacological interventions. Advanced stages require preparation for renal replacement therapy, including dialysis or kidney transplantation. This comprehensive review highlights current understanding of CKD pathophysiology, diagnostic approaches, and evidence-based management strategies, emphasizing the importance of early detection and multidisciplinary care to improve patient outcomes.

Keywords: Chronic Kidney Disease, Glomerular Filtration Rate, Renal Replacement Therapy, Kidney Transplantation.

Introduction

Chronic kidney disease (CKD) is a global public health issue, with complications including kidney failure, cardiovascular disease (CVD), and premature death. CKD is defined as renal damage or a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m² for three months. Kidney failure is a global public health issue, with rising incidence and prevalence, high expenditures, and poor results. Albuminuria, defined as an albumin-to-creatinine ratio of more than 30 mg/g in two out of three spot urine specimens, can indicate kidney impairment in several renal disorders. The CKD epidemic is global [1].

With a CKD age-standardized prevalence of 8.6% and 9.6% in men and women, respectively, in high-income countries and 10.6% and 12.5% in men and women, respectively, in low- and middle-income countries, the study found significant regional variations based on income level. In the same study, the age-standardized global prevalence of CKD stages 3–5 in persons over 20 was 5.8% in women and 4.7% in men. According to research on the incidence of CKD worldwide, there are currently an estimated 843.6 million people with CKD stages 1–5 [2].

Anatomy and Physiology of Kidney

The Normal adult kidney has a bean-like shape. Due to the liver's displacement, the right kidney is positioned slightly lower than the left. The kidneys get about 1,200 milliliters of blood every minute, making them extremely vascular organs. This is equivalent to 20% to 25% of the cardiac output of the body. Eighty percent of the renal plasma travels to the peritubular capillaries via the efferent arterioles. The remaining 20% enters Bowman's capsule after being filtered at the glomerulus. The glomerular filtration rate (GFR) is the amount of plasma that is filtered in a given amount of time [3].

One of the kidney's primary roles is to regulate the acid-base balance. Bicarbonate supplementation in CKD is reserved for patients with a bicarbonate level of 22 mEq/L. However, due to potential risk from overtreatment, supplementation should be managed to maintain a bicarbonate level of <26 mEq/L [4].

Pathophysiology

Unlike acute kidney damage (AKI), which frequently results in complete functional recovery, chronic and sustained insults from progressive nephropathies cause continuing renal fibrosis and the breakdown of normal kidney architecture. This process affects all three kidney compartments: the glomeruli, tubules, and interstitium, as well as the arteries. Histologically, it shows glomerulosclerosis, tubulointerstitial fibrosis, and vascular sclerosis. The events that cause scarring and fibrosis are complicated, overlapping, and multistage phenomena. Extrinsic inflammatory cells infiltrate the injured kidneys. Intrinsic renal cells become active, proliferate, and die. Activation and proliferation of extracellular matrix-producing cells, such as myofibroblasts and fibroblasts. Mechanisms of Rapid Progression of Chronic Kidney Disease Systemic and intraglomerular hypertension Glomerular hypertrophy. Calcium phosphate precipitation within the adrenal gland Modified prostanoid metabolism All of these pathways contribute to a histopathological condition known as glomerulosclerosis.

Proteinuria, hypertension, Black race, and hyperglycemia are all clinical risk factors for rapid CKD progression. Environmental factors such as lead, smoking, metabolic syndrome, some analgesic medications, and obesity have all been associated with faster CKD progression [5].

Etiology and Risk factors

In South Asia, family history, pesticide usage, and heavy metal exposures were most commonly documented, while altitude and temperature were only mentioned in Central American studies. CKD was most commonly related to a family history of CKD, agricultural occupation, men, middle age, snake bites, and heavy metal exposure [6].

Race, gender, age, and family history are all significant factors. Low birth weight, advanced age, African-American ancestry, and a family history of renal disease are all thought to be significant risk factors for chronic kidney disease. Additionally, kidney damage can result from smoking, obesity, hypertension, and diabetes mellitus. Patients with uncontrolled diabetes and/or hypertension can easily and rapidly develop end-stage renal disease. Risks include heavy metal exposure, binge drinking, smoking, and taking analgesics. Additional risk factors include acute renal damage, a history of cardiovascular disease, hyper lipidemia, metabolic syndrome, HIV infection, hepatitis C virus, and cancer [7].

Classification and Staging of CKD

Based on stages of CKD and their classifies are Figure 1 [8] :

KDIGO: Prognosis of CKD by GFR and albuminuria categories				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Figure 1 Classification and Staging of CKD

Clinical Manifestation

Patients frequently encounter symptoms such as discomfort, exhaustion, sleep problems, itching, lethargy, appetite loss, nausea and vomiting, cognitive impairment, anxiety, and depression [9].

Anemia from decreased erythropoietin production by the kidney, iron insufficiency and decreased red blood cell survival, and mineral bone disease from disrupted calcium, phosphate, and vitamin D metabolism are among the complications [10].

Diagnostic Evaluation

Diagnostic aspect Symptoms and history Ask about symptoms and medical history (such as diabetes and high blood pressure).

Physical assessment Evaluate blood pressure, fluid levels, and kidney disease symptoms (such as pallor and edema).

Blood examinations Check the CBC, BUN, eGFR, electrolytes, and serum creatinine.

Tests on urine: To evaluate hematuria, proteinuria, and urine sediment, do a urinalysis.

Imaging research to assess kidney size, structure, and anomalies, use an MRI, CT scan, or renal ultrasound.

Biopsy (if required) For accurate CKD diagnosis and staging, think about kidney biopsy [11].

Management

Non Pharmacological

Dietary pattern, which is defined by a high intake of plant-based foods, whole grains, fish, and olive oil and a reduced intake of red and processed meats.

It is best to make sure that there is no increase in body weight when determining the daily fluid requirements, which can be accomplished by ingesting an average of 2.0–2.5 L.

A daily protein intake of 0.8 g/kg body weight slows the course of chronic kidney disease.

A daily sodium intake of no more than 2-3 g, or around 5 g of table salt, is advised [12].

Pharmacological

Reducing Risk of Cardiovascular Disease

An important component of CKD therapy is the decrease of cardiovascular risk. Patients with CKD aged 50 and older should be treated with a low- to moderate-dose statin, regardless of their low-density lipoprotein cholesterol level. Smoking cessation should also be promoted. According to professional opinion, persons with CKD should aim for systolic and diastolic blood pressures of less than 140 mm Hg and less than 90 mm Hg, respectively, according to the Eighth Joint National Committee (JNC 8) and Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The intensive therapy group had a higher probability of at least a 30% drop in eGFR to a level less than 60 mL/min/1.73 m².

Hypertension

Numerous guidelines offer algorithms that specify which medications should be used to treat hypertension in individuals with chronic kidney disease. It is important to assess the existence and severity of albuminuria. Adults with diabetes and a urine ACR of at least 30 mg per 24 hours or any adult with a urine ACR of at least 300 mg per 24 hours should block the renin-angiotensin-aldosterone system with either an angiotensin-converting enzyme inhibitor (ACE-I) (Enalapril , Captopril , Ramipril)or an angiotensin II receptor blocker (ARB)(Losartan) . Patients with decreased ejection fraction heart failure, resistant hypertension, or albuminuria may potentially be candidates for aldosterone receptor antagonists (spironolactone). Calcium channel blockers (Amlodipine, Nifedipine),Diuretics(furosemide) , Beta Blockers (propranolol) also used in management of Hypertension.

Diabetes mellitus

The majority of guidelines indicate a goal hemoglobin A1c of approximately 7.0%, which may slow the progression of CKD. Drugs that are mostly eliminated by the kidneys, like glyburide, should generally be avoided. On the other hand, medications that are metabolized by the liver and partially eliminated by the kidneys, like metformin and some dipeptidyl peptidase 4 and sodium-glucose co-transporter-2 inhibitors, may need to have their dosage reduced, especially if eGFR is less than 30 mL/min/1.73 m². In patients with type 2 diabetes and CKD stage G2-G3/A3 receiving ACE-I or ARB therapy, the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical

Evaluation trial showed that those randomized to canagliflozin had a 30% lower risk of developing the primary composite renal outcome than those randomized to placebo.

Management of CKD complications

Anemia and the Role of Erythropoietin

One of the most frequent side effects of CKD is anemia. Hemoglobin (defined as <13 g/dL in men and <12 g/dL in women) was included in a study. An evaluation of iron storage should be part of the initial workup for anemia; individuals who are iron deficient may benefit from intravenous or oral iron replacement. Patients may be referred to a nephrologist for consideration of additional medical therapy, such as erythropoietin-stimulating agents, if their hemoglobin levels are consistently below 10 g/dL despite treating reversible causes. However, these risks must be balanced against any potential benefits, as erythropoietin-stimulating agents have been linked to an increased risk of death, stroke, and venous thromboembolism.

Electrolytes, Mineral and Bone Abnormalities

Between 3% and 11% of CKD patients have abnormal electrolytes. Dietary restrictions and supplement prescriptions are common first treatment options. Oral bicarbonate supplementation should be taken into consideration for patients whose serum bicarbonate level is consistently below 22 mmol/L because research has indicated that chronic metabolic acidosis is linked to a quicker progression of chronic kidney disease. The majority of nephrologists concur that concurrent hyperphosphatemia, hypocalcemia, and vitamin D deficiency should be addressed, such as with a low-phosphate diet, phosphate binders, adequate elemental calcium intake, and vitamin D supplementation, even though the ideal intact parathyroid hormone level for CKD is still unknown [13].

Dialysis

Hemodialysis

A dialyzer (filtering machine) is used in hemodialysis to remove waste and excess fluid from your blood before returning the filtered blood to your body. Before beginning hemodialysis, a little surgery is required to construct a vascular access site (an opening into one of your blood vessels), typically in your arm. This access site is necessary to ensure that blood can be easily transferred from your body to the dialyzer and back into your body. Hemodialysis can be performed in a dialysis center or at home. Treatments typically take four hours and are scheduled three times each week. Some folks may require additional time for therapy due to their specific demands Figure 2[14].

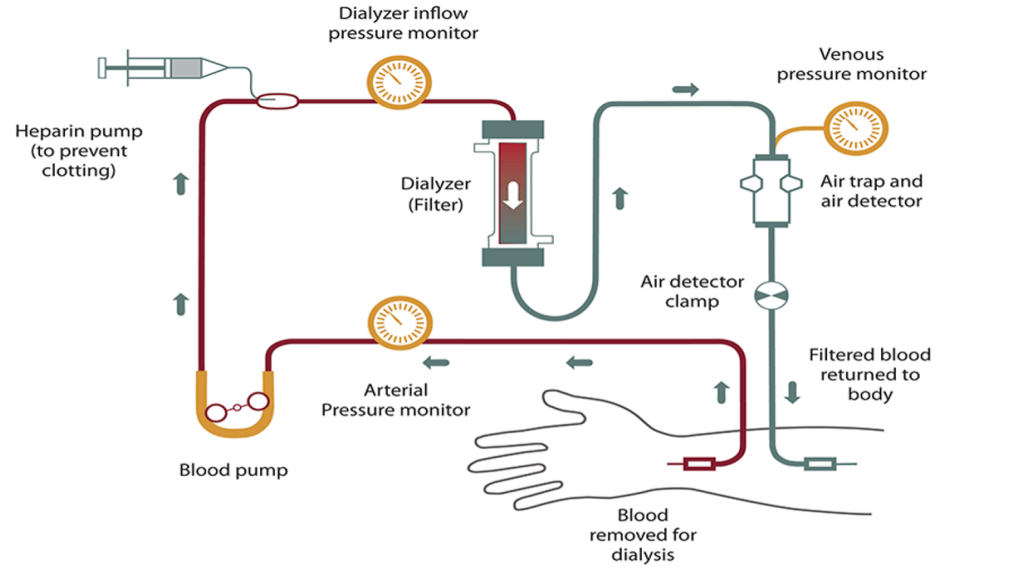

Figure 2 Hemodialysis

Peritoneal dialysis

Peritoneal dialysis involves filtering your blood inside your own body rather than using a dialyzer machine. In this method of dialysis, the abdominal lining acts as a filter. To begin peritoneal dialysis, a little procedure is required to insert a catheter in your belly. During each treatment, your stomach is gradually filled with dialysate via the catheter.

As your blood flows normally through the area, the dialysate draws surplus fluid and waste items out of the blood vessels and into the stomach area. After a few hours, the fluid combination is drained from your belly with the same catheter and bag that were used at the start of the procedure.

Continuous Ambulatory Peritoneal Dialysis (CAPD) and Automated Peritoneal Dialysis (APD) are two of the most popular forms of peritoneal dialysis. The type of PD you are using and your medical condition will determine the supplies and equipment required, the length of each treatment (also called an exchange), and the number of treatments per day Figure 3 [14].

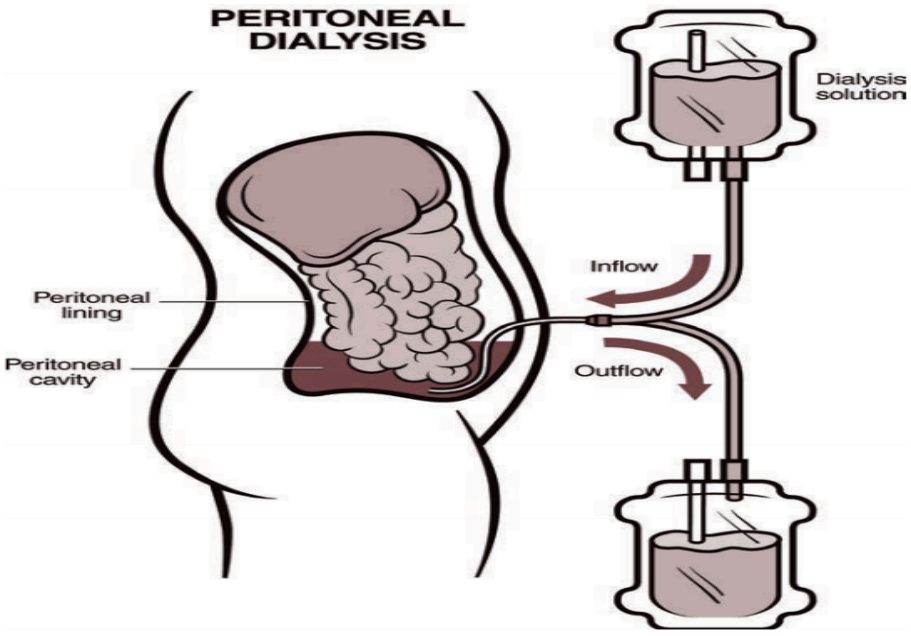

Figure 3 Peritoneal dialysis

Renal Replacement Therapy

According to KDIGO guidelines, patients with chronic kidney disease (CKD) should be referred to a nephrologist when eGFR falls below 30 mL/min/1.73 m² or when urine albumin–creatinine ratio exceeds 300 mg per 24 hours. Urgent referral is required when albuminuria is above 2200 mg per 24 hours, suggesting nephrotic-range proteinuria and possible nephrotic syndrome. Patients with polycystic kidney disease, nephrotic-range albuminuria, and certain glomerulonephritides have a higher risk of progressing to end-stage kidney disease (ESKD).The decision to initiate dialysis depends on symptoms rather than GFR alone. Dialysis is indicated in patients with uremic symptoms, refractory hyperkalemia, metabolic acidosis, or fluid overload not responding to medical therapy. Kidney transplantation is the preferred treatment for ESKD, with best outcomes from living donor transplants. Early transplant evaluation is recommended when eGFR is below 30 mL/min/1.73 m². Dialysis modality should be individualized based on patient preference and clinical suitability [13].

Prevention Strategies

Traditional preventive strategies play a key role in slowing the progression of chronic kidney disease (CKD) and reducing cardiovascular risk.

Blood pressure control is crucial, as hypertension and CKD are closely linked through mechanisms such as endothelial dysfunction, salt retention, sympathetic over activity, and activation of the renin–angiotensin–aldosterone system. Evidence from the SPRINT trial showed that targeting lower systolic blood pressure reduces cardiovascular events and mortality. Current guidelines recommend a blood pressure target of <130/80 mmHg, with recent KDOQI guidelines suggesting a systolic target of <120 mmHg for most CKD patients. Home and ambulatory blood pressure monitoring are now emphasized for accurate assessment.

Glycemic control is equally important in diabetic CKD. Maintaining HbA1c <7% helps reduce microvascular complications and slows diabetic nephropathy progression.

Lifestyle modification, including regular physical activity and smoking cessation, significantly improves outcomes. Structured exercise programs enhance physical fitness and reduce CKD progression risk.

Recent Advances and Future Perspectives

Recent advances have significantly improved chronic kidney disease (CKD) management. Sodium–glucose cotransporter-2 inhibitors (SGLT2i) represent a major breakthrough. By inhibiting glucose reabsorption in the proximal tubule, these agents provide strong renoprotective and cardiovascular benefits beyond glycemic control. Landmark trials such as CREDENCE, DAPA-CKD, and EMPA-KIDNEY showed reduced CKD progression, end-stage kidney disease, and cardiovascular events in both diabetic and non-diabetic patients, even at low eGFR levels.

Another important development is finerenone, a non-steroidal mineralocorticoid receptor antagonist. Unlike traditional agents, finerenone effectively reduces inflammation and fibrosis with a lower risk of Hyperkalemia. Phase III trials (FIDELIO-DKD and FIGARO-DKD) demonstrated significant kidney and cardiovascular protection, particularly in patients with severe albuminuria.

Future CKD management is moving toward personalized medicine, integrating genetics, biomarkers, and molecular insights to identify high-risk patients and tailor early, targeted interventions [15].

Conclusion

Chronic kidney disease (CKD) is a major global public health problem, contributing significantly to morbidity, mortality, and healthcare costs, particularly in low- and middle-income countries. It is strongly associated with diabetes, hypertension, obesity, aging, and environmental factors, and its progression leads to serious complications such as cardiovascular disease and end-stage kidney disease (ESKD). Early detection using eGFR and albuminuria, along with KDIGO-based staging, allows timely intervention. Conventional measures including blood pressure and glycemic control, dietary modification, and avoidance of nephrotoxins remain essential in slowing disease progression. Multidisciplinary care improves treatment outcomes and safety. Recent advances such as SGLT2 inhibitors and finerenone provide substantial renal and cardiovascular protection. Future CKD management will increasingly rely on personalized medicine integrating genetic, molecular, and lifestyle-based strategies to reduce disease burden and improve patient outcomes.

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