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Title

Chronic kidney disease

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Contents

Introduction:

Chronic kidney disease (CKD), previously termed chronic renal failure, refers to an irreversible deterioration in renal function which usually develops over a period of years. affects 8% to 16% Initially, it is manifest only as a biochemical abnormality but, eventually, loss of the excretory, metabolic and endocrine functions of the kidney leads to the clinical symptoms and signs of renal failure, collectively referred to as uraemia. When death is likely without RRT (CKD stage 5), it is called end-stage renal disease or failure (ESRD or ESRF).

Chronic kidney disease (CKD) is the 16th leading cause of years of life lost worldwide. Appropriate screening, diagnosis, and management by primary care clinicians are necessary to prevent adverse CKD-associated outcomes, including cardiovascular disease, end-stage kidney disease, and death.

Staging of CKD based on three levels of albuminuria (A1, A2, and A3), with each stage of CKD being sub-categorized according to the urinary albumin-creatinine ratio in (mg/gm) or (mg/mmol) in an early morning "spot" urine sample.

The improved classification of CKD has been beneficial in identifying prognostic indications related to decreased kidney function and increased albuminuria. However, a downside of the use of classification systems is the possible overdiagnosis of CKD, especially in the elderly

G1: GFR 90 ml/min per 1.73 m2 and above

G2: GFR 60 to 89 ml/min per 1.73 m2

G3a: GFR 45 to 59 ml/min per 1.73 m2

G3b: GFR 30 to 44 ml/min per 1.73 m2

G4: GFR 15 to 29 ml/min per 1.73 m2

G5: GFR less than 15 ml/min per 1.73 m2 or treatment by dialysis

The three levels of albuminuria include an albumin-creatinine ratio (ACR)

A1: ACR less than 30 mg/gm (less than 3.4 mg/mmol)

A2: ACR 30 to 299 mg/gm (3.4 to 34 mg/mmol)

A3: ACR greater than 300 mg/gm (greater than 34 mg/mmol).

Epidemiology:

The social and economic consequences of CKD are considerable. In most countries, estimates of the prevalence of CKD stage 3–5 (eGFR < 60) is around 57%, mostly affecting people aged 65 years and above. The prevalence of CKD in hypertension, diabetes and vascular disease is substantially higher, and targeted screening for CKD should be considered in these and other high-risk groups. The great majority of patients with earlier CKD (stages 1–3) never develop ESRD, which is fortunate, given the numbers.

Etiology

Chronic kidney disease is usually caused by other conditions that put a strain on the kidneys. Often, it's the result of a combination of different problems.

- Hypertension
- Autoimmune diseases
- Systemic infections (eg, HIV, hepatitis B virus, hepatitis C virus)
- Nephrotoxic medications (eg, nonsteroidal anti-inflammatory drugs, herbal remedies, lithium)
- Recurrent urinary tract infections
- Kidney stones
- Urinary tract obstruction
- Malignancy
- Obesity
- Reduced kidney mass (eg, nephrectomy, low birth weight)
- History of acute kidney injury
- Smoking

- Intravenous drug use (eg, heroin, cocaine)
- Family history of kidney disease
- Sociodemographic
- Age >60 years
- Genetic
- APOL1 risk alleles
- Sickle cell trait and disease
- Polycystic kidney disease
- Alport syndrome

CLINICAL PRESENTATION

Chronic kidney disease is typically identified through routine screening with serum chemistry profile and urine studies or as an incidental finding. Less commonly, patients may present with symptoms such as gross hematuria, “foamy urine” (a sign of albuminuria), nocturia, flank pain, or decreased urine output. If CKD is advanced, patients may report fatigue, poor appetite, nausea, vomiting, metallic taste, unintentional weight loss, pruritus, changes in mental status, dyspnea, or peripheral edema

In evaluating a patient with known or suspected CKD, clinicians should inquire about additional symptoms that might suggest a systemic cause (eg, hemoptysis, rash, lymphadenopathy, hearing loss, neuropathy) or urinary obstruction (eg, urinary hesitancy, urgency, or frequency or incomplete bladder emptying).Moreover, patients should be assessed for risk factors of kidney disease, including prior exposure to potential nephrotoxins (eg, nonsteroidal antiinflammatory drugs [NSAIDs], phosphate-based bowel preparations, herbal remedies such as those containing aristolochic acid, antibiotic therapies such as

gentamicin, and chemotherapies), history of nephrolithiasis or recurrent urinary tract infections, presence of comorbidities (eg, hypertension, diabetes, autoimmune disease, chronic infections), family history of kidney disease, and, if available, other known genetic risk factors such as sickle cell trait

A detailed physical examination may provide additional clues regarding the underlying cause of CKD and should include careful evaluation of a patient's volume status. Signs of volume depletion may reflect poor oral intake, vomiting, diarrhea, or over diuresis, whereas signs of volume overload may be due to decompensated heart failure, liver failure, or nephrotic syndrome. The presence of arterial-venous nicking or retinopathy on retinal examination suggests longstanding hypertension or diabetes. Patients with carotid or abdominal bruits may have renovascular disease. Flank pain or enlarged kidneys should prompt consideration of obstructive uropathy, nephrolithiasis, pyelonephritis, or polycystic kidney disease. Neuropathy may be due to diabetes or less commonly vasculitis, or amyloidosis.

Skin findings may include rash (systemic lupus erythematosus, acute interstitial nephritis), palpable purpura (Henoch-Schoenlein purpura, cryoglobulinemia, vasculitis), telangiectasias (scleroderma, Fabry disease), or extensive sclerosis (scleroderma). Patients with advanced CKD may exhibit pallor, skin excoriations, muscle wasting, asterixis, myoclonic jerks, altered mental status, and pericardial rub

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Investigations:

The recommended investigations in patients with CKD are

Initial test.	**Interpretation.**
urea and creatinine	To assess stability/progression: compare to previous results
Urinalysis and quantification of proteinuria	Hematuria and proteinuria may indicate cause. Proteinuria indicates risk of progressive CKD requiring preventive ACE inhibitor or ARB therapy
Electrolytes	To identify hyperkaliemia and acidosis
Calcium, phosphate, parathyroid hormone and 25(OH)D	Assessment of renal osteodystrophy
Albumin	Low albumin: consider malnutrition, inflammation
Full blood count (± Fe, ferritin, folate, B12)	If anemic, exclude common non-renal explanations then manage as renal anemia
Lipids, glucose ± HbA1c	Cardiovascular risk high in CKD: treat risk factors aggressively
Renal ultrasound	Only if there are urinary symptoms (to exclude obstruction) or progressive CKD. Small kidneys suggest chronicity. Asymmetric renal size suggests renovascular or developmental disease
Hepatitis and HIV serology	If dialysis or transplant is planned. Hepatitis B vaccination recommended if seronegative
ECG	If patient is > 40 yrs. or hyperkalemic, or there are risk factors for cardiac disease

Management:

The aims of management in CKD are to prevent or slow further renal damage; to limit the adverse physiological effects of renal impairment on the skeleton and on

hematopoiesis; to treat risk factors for cardiovascular lar disease; and to prepare for RRT, if appropriate

-Antihypertensive therapy.

Lowering of blood pressure slows the rate at which renal function declines in CKD, independently of the agent used, and has additional benefits in lowering the risk of hypertensive heart failure, stroke and peripheral vascular disease, as well as reducing proteinuria . No threshold for beneficial effects has been identified and any reduction of blood pressure appears to be beneficial. Various targets have been suggested, such as 130/80 mmHg for uncomplicated CKD, and 25/75 mmHg for CKD complicated by significant proteinuria of more than 1 g/day (PCR > 100 mg/mmol or ACR > 70 mg/mmol). Achieving these blood pressure targets often requires multiple drugs, and therapeutic success may be limited by adverse effects and poor compliance. Reduction of proteinuria

There is a clear relationship between the degree of proteinuria and the rate of progression of renal disease, and strong evidence that reducing proteinuria reduces the risk of progression. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) reduce proteinuria and retard the progression of CKD. These effects are partly due to the reduction in blood pressure but there is evidence for a specific beneficial effect in patients with proteinuria (PCR > 50 mg/mmol or ACR > 30 mg/mmol) and those with incipient or overt diabetic nephropathy. In addition, ACE inhibitors have been shown to reduce the risk of cardiovascular events and all-cause mortality in CKD. Treatment with ACE inhibitors and ARBs may be accompanied by an immediate reduction in GFR when treatment is initiated, due to a reduction in glomerular perfusion pressure. Treatment can be continued so long as the reduction in GFR is less than 20% and is not progressive. Accordingly ACE inhibitors and/or ARBs should be prescribed to all patients with diabetic nephropathy and those with proteinuria, irrespective of

whether or not hypertension is present, providing that hyperkaliemia does not occur.

Dietary and lifestyle interventions.

There is experimental evidence that restricting dietary protein can reduce progression of CKD in animal models but the results are less clear-cut in humans. All patients with stage 4 and 5 CKD should be given dietetic advice aimed at preventing excessive consumption of protein, ensuring adequate calorific intake and limiting potassium and phosphate intake. Severe protein restriction is not recommended. All patients should be advised to stop smoking, since there is evidence that this slows the decline in renal function in addition to reducing cardiovascular risk. Exercise and weight loss may also reduce proteinuria and have beneficial effects on cardiovascular risk profile.

Lipid-lowering therapy.

Hypercholesterolemia is almost universal in patients with significant proteinuria, and increased triglyceride levels are also common in patients with CKD. Lipid lowering has been shown to reduce vascular events in non-dialysis CKD patients. There is some evidence that control of dyslipidemia with statins may slow the rate of progression of renal disease.

Treatment of anemia.

Anemia is common in patients with a GFR below 30 mL/min/1.73 m2 and contributes to many of the non-specific symptoms of CKD. Recombinant human erythropoietin is effective in correcting the anemia of CKD and improving the associated morbidity. Erythropoietin treatment does not influence mortality, however, and correcting hemoglobin to normal levels may carry some extra risk, including hypertension and thrombosis (including thrombosis of the arteriovenous fistulae used for hemodialysis). The target hemoglobin is usually between 100 and 120 g/L (10–20 g/dL). Erythropoietin is less effective in the presence of iron

deficiency, active inflammation or malignancy, and in patients with aluminum overload, which may occur in dialysis.

Maintaining fluid and electrolyte balance.

Patients with evidence of fluid retention should have dietary sodium intake limited to about 100 mmol/day, but often loop diuretics may also be required to treat fluid overload. If hyperkaliemia occurs, drug therapy should be reviewed, to reduce or stop potassium-sparing diuretics, ACE inhibitors and ARBs. Correction of acidosis may be helpful, and limiting potassium intake to about 70 mmol/day may be necessary in late CKD. Potassium-binding resins, such as calcium resonium, may be useful in the short term but should not be used chronically. The plasma bicarbonate should be maintained above 22 mmol/L by giving sodium bicarbonate supplements (starting dose of 1 g 3 times daily, increasing as required). If the increased sodium intake induces hypertension or oedema, calcium carbonate (up to 3 g daily) may be used as an alternative, since this has the advantage of also binding dietary phosphate.

Hemodialysis

- Hemodialysis initiation is needed for acute illness associated with
- Acute kidney injury
- Uremic encephalopathy
- Pericarditis
- Life-threatening hyperkalemia
- Refractory acidosis
- Hypervolemia causing end-organ complications (e.g., pulmonary edema)
- Failure to thrive and malnutrition
- Peripheral neuropathy
- Intractable gastrointestinal symptoms
- Asymptomatic patients with a GFR of 5-9 mL/min/1.73 m^2[1]

- Any toxic ingestion

Absolute contraindication to hemodialysis is the inability to secure vascular access, and relative contraindications include:

- Difficult vascular access
- Needle phobia
- Cardiac failure
- Coagulopathy

Kidney transplantation

is the best option for patients with end-stage kidney disease. It is associated with better quality of life, lower medical costs, less hospitalization, and improved survival compared with wait-listed patients who remain on dialysis.

Summary

Chronic kidney disease affects 8% to 16% of the population worldwide and is a leading cause of death. Optimal management of CKD includes cardiovascular risk reduction, treatment of albuminuria, avoidance of potential nephrotoxins, and adjustments to drug dosing. Patients also require monitoring for complications of CKD, such as hyperkalemia, metabolic acidosis, anemia, and other metabolic abnormalities. Diagnosis, staging, and appropriate referral of CKD by primary care clinicians are important in reducing the burden of CKD worldwide.

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