

# Chronic Kidney Disease - An Overview

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## ABSTRACT

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Chronic kidney disease (CKD) is a worldwide public health problem. It is recognized as a common condition that is associated with risk Development of ESRD (end stage renal disease). In India, there is a rising incidence and prevalence of kidney failure, with poor outcomes.

The most common causes of CKD are Diabetes mellitus, systemic hypertension and chronic Glomerulonephritis. Together, these cause approximately 75% of all adult cases.

CKD may be initially without specific symptoms. As the kidney function declines steadily symptoms appear progressively which may be fatigue, anorexia, nausea, pruritis, i.e. CKD can have multisystem manifestations.

Early identification of patients with kidney disease is recommended, as measures may be instituted to slow progression and mitigate cardiovascular risk.

**Keywords:** CKD, Identification, Complications

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Chronic kidney disease (CKD) is a worldwide public health problem. It is recognized as a common condition that is associated with risk Development of ESRD (end stage renal disease). In India, there is a rising incidence and prevalence of kidney failure, with poor outcomes.

The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines chronic kidney disease as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m<sup>2</sup> for 3 or more months. Whatever the underlying etiology, the destruction of renal mass with irreversible sclerosis and loss of nephrons leads to a progressive decline in GFR. The different stages of chronic kidney disease form a continuum in time.

In 2002, K/DOQI published its classification of the stages of chronic kidney disease, as follows:

- Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m<sup>2</sup>)
- Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m<sup>2</sup>)
- Stage 3: Moderate reduction in GFR (30-59 mL/min/1.73 m<sup>2</sup>)
- Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m<sup>2</sup>)
- Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m<sup>2</sup> or dialysis) (End stage renal disease)

In stage 1 and stage 2 chronic kidney diseases, GFR alone does not clinch the diagnosis. Other markers of kidney damage, including abnormalities in the composition of blood or urine or abnormalities on

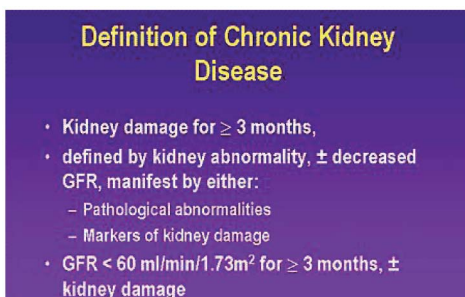


Figure 1. Definition of Chronic Kidney Disease

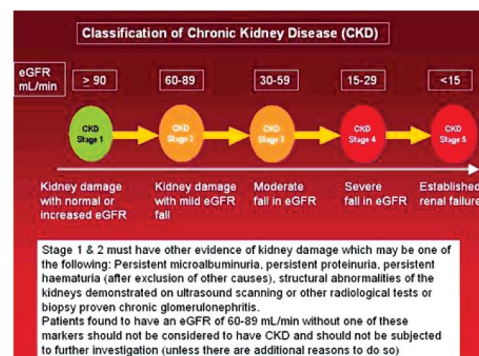


Figure 2. Classification of Chronic Kidney Disease (CKD)

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imaging studies, should also be present in establishing a diagnosis of stage 1 and stage 2 chronic kidney disease.

The K/DOQI definition and classification of chronic kidney disease allow better communication among physicians and facilitate intervention at the different stages.

### Pathophysiology

Approximately 1 million nephrons are present in each kidney, each contributing to the total GFR. In the face of renal injury (regardless of the etiology), the kidney has an innate ability to maintain GFR, despite progressive destruction of nephrons, by hyperfiltration and compensatory hypertrophy of the remaining healthy nephrons.

This nephron adaptability allows for continued normal clearance of plasma solutes. Plasma levels of substances such as urea and creatinine start to show significant increases only after total GFR has decreased to 50%, when the renal reserve has been exhausted. The plasma creatinine value will approximately double with a 50% reduction in GFR. The hyperfiltration and hypertrophy of residual nephrons, although beneficial for the reasons noted, has been hypothesized to represent a major cause of progressive renal dysfunction. This occurs due to the increased glomerular capillary pressure, which damages the capillaries and leads initially to focal glomerulosclerosis and eventually to global glomerulosclerosis.

### Causes

The most common causes of CKD are Diabetes mellitus, systemic hypertension and chronic Glomerulonephritis. Together, these cause approximately 75% of all adult cases.

The Indian CKD Registry report published in 2012 confirms the emergence of diabetic nephropathy as the pre-eminent cause of CKD in India. A significant proportion has CKD of undetermined etiology. These patients are younger, have a lower income and more advanced CKD. Patients presenting to public sector hospitals are poorer, younger, and more likely to have CKD of unknown etiology as per the registry report

Historically, kidney disease has been classified according to the part of the renal anatomy that is involved-important ones are

- Vascular disease -large vessel disease such as bilateral renal artery stenosis, small vessel disease such as ischemic nephropathy, hemolytic uremic syndrome

and vasculitis

- Glomerular, comprising a diverse group and sub classified into
  - o Primary Glomerular disease such as IgA nephropathy, focal segmental glomerulosclerosis
- Secondary Glomerular disease such as and diabetic nephropathy, lupus nephritis
- Drug and toxin-induced chronic tubulointerstitial nephritis , Reflux nephropathy
- Polycystic kidney disease
- Obstructive nephropathy with bilateral urolithiasis and diseases of the prostate

Factors other than the underlying disease process and glomerular hypertension that may cause progressive renal injury include the following:

- Systemic hypertension
- Acute insults from nephrotoxins or decreased perfusion
- Proteinuria
- Increased renal ammoniogenesis with interstitial injury
- Hyperlipidemia
- Smoking
- Uncontrolled diabetes

### Symptoms and signs

CKD may be initially without specific symptoms. As the kidney function declines steadily symptoms appear progressively which may be fatigue, anorexia, nausea, pruritis, i.e. CKD can have multisystem manifestations.

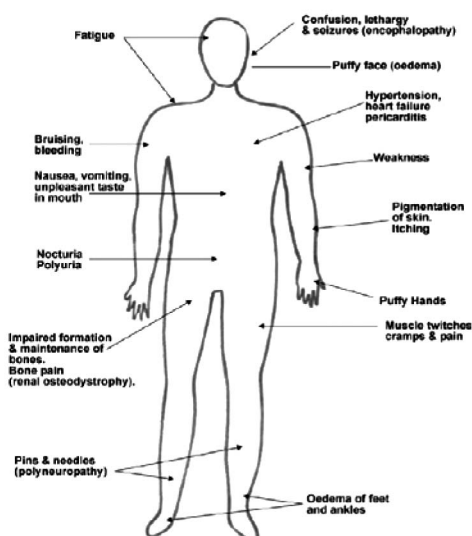


Figure 3. Symptoms and Signs of Chronic Kidney Disease

- o Hypertension due to fluid overload and production of vasoactive hormones created by the kidney via the rennin angiotensin system, increasing one's risk of developing congestive heart failure
- o Urea and other uremic toxins accumulate, leading to azotemia and ultimately uremia (symptoms ranging from lethargy to pericarditis and encephalopathy. Urea may be excreted by sweating and crystallizes on skin ("uremic frost") seen in advanced uremia
- o Potassium accumulates in the blood (hyperkalemia potentially cause fatal cardiac arrhythmias
- o Erythropoietin synthesis is decreased ( leading to normocytic normochromic anemia)
- o Volume overload- symptoms may range from mild oedema to life-threatening pulmonary oedema
- o Hyperphosphatemia and hypocalcemia- due to reduced phosphate excretion and 1.25 dihydroxy vitamin D3 deficiency. The renal 1 alpha hydroxylase is deficient. Also the enzyme is inhibited due to stimulation of Fibroblast growth factor 23 (FGF23)
- Later this progresses to secondary hyperparathyroidism and bone disease ie. renal osteodystrophy((CKD- MBD) and vascular calcification that further impairs cardiac function.
- o Metabolic acidosis- In chronic kidney disease, the kidneys are unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium. In chronic kidney disease stage 5,accumulation of phosphates, sulfates, and other organic anions are the cause of the increase in anion gap. Me

Patients with chronic kidney disease suffer from accelerated atherosclerosis and are more likely to develop cardiovascular disease than the general population

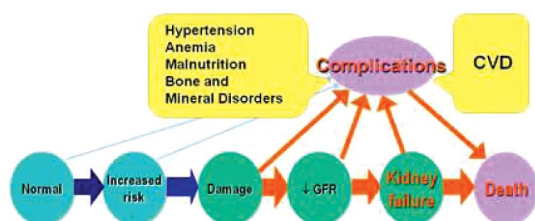


Figure 4. Outcomes of CKD

## Diagnosis

In many CKD patients, previous renal disease or other underlying diseases are already known. A small number

present with CKD the cause may not be obvious.

It is important to differentiate CKD from acute renal failure (ARF) because ARF can be reversible. Abdominal ultrasound, in which the size of the kidneys is measured, should be performed. Kidneys with CKD are usually smaller than normal kidneys or may be significantly contracted, with notable exceptions such as diabetic nephropathy and polycystic kidney disease. Another diagnostic clue that helps differentiate CKD from ARF is a gradual rise in serum creatinine (over several months or years) as opposed to a sudden increase in the serum creatinine (several days to weeks). If these levels are unavailable (because the patient has been well and has had no blood investigations in the past), it is occasionally necessary to treat a patient briefly as having ARF until it has been established that the renal impairment is irreversible.

## Screening and referral

Early identification of patients with kidney disease is recommended, as measures may be instituted to slow progression and mitigate cardiovascular risk.

Among those who should be screened are objects with hypertension or history of cardiovascular disease, those with diabetes or marked obesity, those aged > 60 years, those with a history of renal disease in the past, as well as subjects who have relatives who had kidney disease requiring dialysis.

Screening should include calculation of estimated GFR/1.73 m<sup>2</sup> from the serum creatinine level, and measurement of urine-to-albumin creatinine ratio in a first-morning urine specimen as well as dipstick screen for hematuria. Guidelines for Nephrologist referral vary among different countries. Nephrology referral is useful when eGFR/1.73m<sup>2</sup> is less than 30 or decreasing by more than 3 mL./min/year, when urine albumin-to-creatinine ratio is more than 30 mg/g, when blood pressure is difficult to control, or when hematuria or other findings suggest either a primarily glomerular disorder or secondary disease amenable to specific treatment.

Other benefits of early nephrology referral include proper patient education regarding options for renal replacement therapy as well as pre-emptive transplantation, and timely workup and placement of an arteriovenous fistula in those patients opting for future hemodialysis

Table 1. Action Plan according to CKD - Stage

Stage	Action plan
1	Diagnosis and treatment of comorbid conditions, slow progression, CVD risk reduction
2	Estimate progression
3	Evaluate and treat complications
4	Prepare for renal replacement therapy (Av fistula creation)
5	Renal replacement

## TREATMENT

The presence of chronic kidney disease confers a markedly increased risk of cardiovascular disease, and people with CKD often have other risk factors for heart disease.

Apart from controlling other risk factors, the goal of therapy is to slow down or halt the progression of CKD to stage 5.

**Diet-** Protein restriction has been advocated to reduce symptoms associated with uremia. It also slows the rate of renal decline at earlier stages of renal disease.

KDOQI clinical practice guidelines include a daily protein intake of between 0.60 and 0.75 g/kg per day, depending upon patient adherence, co morbid disease, presence of proteinuria, and nutritional status. It is further advised that at least 50% of the protein intake be of high biologic value. As patients approach stage 5 CKD, spontaneous protein intake tends to decrease, and patients may enter a state of protein- energy malnutrition. In these circumstances, a protein intake of up to 0.90 g/kg per day might be recommended

Sufficient energy intake is important to prevent protein-calorie malnutrition, and 35 kcal/kg is recommended.

Salt, and water restriction is generally required along with controlling the dietary potassium intake according to the electrolyte profile of the patient

### Control of Blood Pressure and Proteinuria

Hypertension is found in the majority of type 2 diabetic patients at diagnosis. This finding correlates with the presence of albuminuria and is a strong predictor of cardiovascular events and nephropathy. Micro-albuminuria, the finding of albumin in the urine not detectable by the urine dipstick, precedes the decline in GFR and heralds renal and cardiovascular complications. Testing for micro albumin is recommended in all diabetic patients, at least annually. If the patient already has established proteinuria, then testing for micro albumin is not necessary. Antihypertensive treatment reduces albuminuria and diminishes its progression

even in normotensive diabetic patients. In addition to treatment of hypertension in general, the use of ACE inhibitors and ARBs in particular is associated with additional renoprotection. These salutary effects are mediated by reducing intraglomerular pressure.

However patients have to be closely monitored while on ACE/ARB in view of possibility of hyperkalemia and may need to withdraw in case of rapid decline in GFR.

### Control of Blood Glucose

Excellent glycemic control reduces the risk of kidney disease and its progression in both type 1 and type 2 diabetes mellitus. It is recommended that plasma values for preprandial glucose be kept in the 5.0–7.2mmol/L (90–130 mg/dL) range and hemoglobin A1C should be < 7%.

Replacement of erythropoietin and calcitriol is necessary in people with advanced disease. A target hemoglobin level of 11-12 g/dL is recommended. Phosphate binders are also used to control the serum phosphate levels, which are usually elevated in advanced chronic kidney disease. Aggressive treatment of hyperlipidemia is warranted

When one reaches CKD stage 5 renal replacement therapy is usually required, in the form of either dialysis (hemodialysis or peritoneal dialysis) or kidney transplantation

### Prognosis

While renal replacement therapies can maintain patients indefinitely and prolong life the quality of life is compromised. Renal transplantation increases the survival of patients with stage 5 CKD significantly when compared to other therapeutic options and delivers excellent quality of life (1, 2, 3). Annually, while over 100, 000 Indians suffer from End Stage Renal Disease, only a mere 3,000 are recipients of a donor kidney, The cadaver organ sharing programme is yet to gain momentum in our country. Transplantation aside, high intensity home hemodialysis appears to be associated with improved survival when compared to the conventional three times a week hemodialysis or peritoneal dialysis

The prognosis of patients with chronic kidney disease is guarded as epidemiologic data has shown that all cause mortality (the overall death rate) increases as kidney function decreases. The leading cause of death in patients with chronic kidney disease is cardiovascular disease.

## CONCLUSION

Chronic kidney disease is one of the most important public health problems in the last decade with our nation becoming the Diabetic capital of the world. CKD management consumes a disproportionately large fraction of the available health care resources. The treatment of end stage renal disease is expensive and beyond the reach of average Indian. Thus it is crucial that prevention of chronic kidney disease has to be the goal of medical fraternity, government of India and the general public. Healthcare agencies must plan for improved screening for early detection, prevention, and retarding the progression of CKD.

## END NOTE

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