A Pharmacovigilance Study of Rates of Adverse Clinical Events in Patient with Chronic Kidney Disease

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Abstract
Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min per 1.73 square meters, persisting for 3 months or more. It is a state of progressive loss of kidney function, ultimately resulting in the need for renal replacement therapy (dialysis or transplantation). This report reviews the etiology, evaluation, and Adverse effects of chronic kidney disease and emphasizes the roles of the interprofessional team in caring for patients with chronic kidney disease.

Objectives
- Describe the risk factors for developing chronic kidney disease.
- Review the drug classification of chronic kidney disease.
- Outline the treatment and management options available for chronic kidney disease.
- Explain the occurrence of adverse effects and the severity of it by doing pharmacovigilance survey in super speciality hospital.

Introduction
Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 mt2, persisting for 3 months or more, irrespective of the cause. It is a state of progressive loss of kidney function, ultimately resulting in the need for renal replacement therapy (dialysis or transplantation).

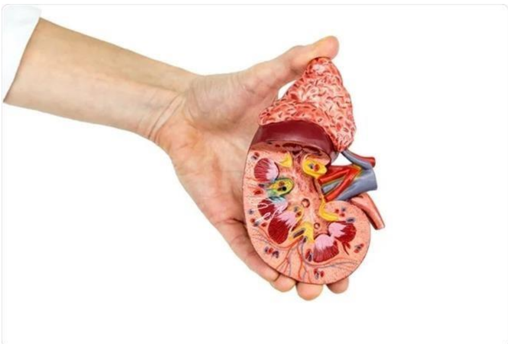


Fig No.1 Diagrammatic representation of CKD

Kidney damage refers to pathologic abnormalities either suggested by imaging studies or renal biopsy, abnormalities in urinary sediment, or increased urinary albumin excretion rates. The 2012 KDIGO CKD classification recommends details about the cause of the CKD and classifies it into 6 categories based on glomerular filtration rate (G1 to G5 with G3 split into 3a and 3b). It also includes the staging 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 6 categories include:

- G1: GFR 90 ml/min per 1.73 m^2 and above
- G2: GFR 60 to 89 ml/min per 1.73 m^2
- G3a: GFR 45 to 59 ml/min per 1.73 m^2
- G3b: GFR 30 to 44 ml/min per 1.73 m^2
- G4: GFR 15 to 29 ml/min per 1.73 m^2
- G5: GFR less than 15 ml/min per 1.73 m^2 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).

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 older people.[1]

Etiology

The causes of CKD vary globally, and the most common primary diseases causing CKD and, ultimately, end-stage renal disease (ESRD) are as follows:

- Diabetes mellitus type 2 (30% to 50%)
- Diabetes mellitus type 1 (3.9%)
- Hypertension (27.2%)
- Primary glomerulonephritis (8.2%)
- Chronic Tubulointerstitial nephritis (3.6%)
- Hereditary or cystic diseases (3.1%) Secondary glomerulonephritis or vasculitis (2.1%)
- Plasma cell dyscrasias or neoplasm (2.1)
- Sickle Cell Nephropathy (SCN) which accounts for less than 1% of ESRD patients in the United States.

CKD may result from disease processes in any of the three categories: prerenal (decreased renal perfusion pressure), intrinsic renal (pathology of the vessels, glomeruli, or tubules-interstitium), or postrenal (obstructive).

Prenenal Disease: Chronic prerenal disease occurs in patients with chronic heart failure or cirrhosis with persistently decreased renal perfusion, which increases the propensity for multiple episodes of an intrinsic kidney injury, such as acute tubular necrosis (ATN). This leads to progressive loss of renal function over time.
Intrinsic Renal Vascular Disease: The most common chronic renal vascular disease is nephrosclerosis, which causes chronic damage to blood vessels, glomeruli, and tubulointerstitial.
The other renal vascular diseases are renal artery stenosis from atherosclerosis or fibro-muscular dysplasia, which over months or years, cause ischemic nephropathy, characterized by glomerulosclerosis and tubulointerstitial fibrosis.
Intrinsic Glomerular Disease (Nephritic or Nephrotic): A nephritic pattern is suggested by abnormal urine microscopy with red blood cell (RBC) casts and dysmorphic red cells, occasionally white blood cells (WBCs), and a variable degree of proteinuria. The most common causes are post-streptococcal GN, infective endocarditis, shunt nephritis, IgA nephropathy, lupus nephritis, Goodpasture syndrome, and vasculitis.
A nephrotic pattern is associated with proteinuria, usually in the nephrotic range (greater than 3.5 gm per 24 hours), and an inactive urine microscopic analysis with few cells or casts. It is commonly caused by minimal change disease, focal segmental glomerulosclerosis, membranous GN, membranoproliferative GN (Type 1 and 2 and associated with cryoglobulinemia), diabetic nephropathy, and amyloidosis [2]

Pathophysiology

Unlike acute kidney injury (AKI), where the healing process is complete with complete functional kidney recovery, chronic and sustained insults from chronic and progressive nephropathies evolve to progressive kidney fibrosis and destruction of the normal architecture of the kidney. This affects all the 3 compartments of the kidney, namely the glomeruli, the tubules, the interstitium, and the vessels. It manifests histologically as glomerulosclerosis, tubulointerstitial fibrosis, and vascular sclerosis.

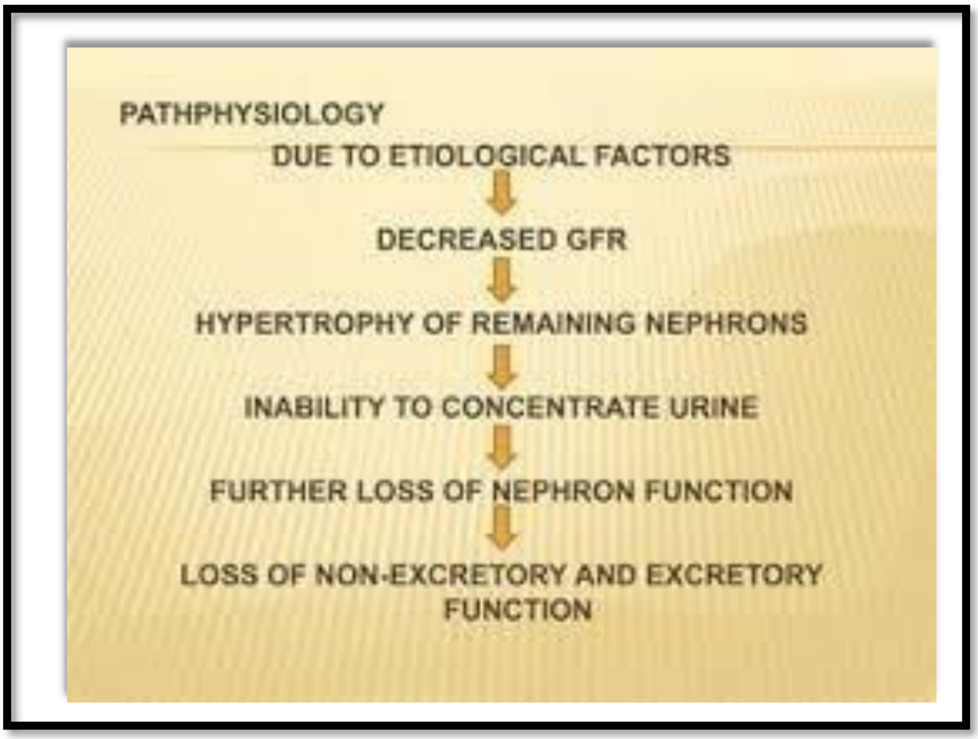


Fig No.2 Pathophysiology of Chronic Kidney Disease

The sequence of events that lead to scarring and fibrosis are complex, overlapping, and multistage phenomena.

- Infiltration of damaged kidneys with extrinsic inflammatory cells
- Activation, proliferation, and loss of intrinsic renal cells (through apoptosis, necrosis, mesangiolysis, and podocytopenia)
- Activation and proliferation of extracellular matrix (ECM) producing cells including myofibroblasts and fibroblasts
- Deposition of ECM replacing the normal architecture

Mechanisms of Accelerated Progression of CKD

- Systemic and intraglomerular hypertension
- Glomerular hypertrophy
- Intrarenal precipitation of calcium phosphate
- Altered prostanoid metabolism
- All these mechanisms lead to a histological entity called focal segmental glomerulosclerosis.[3]

Signs and symptoms

Who is more likely to develop CKD?

- **Diabetes.** Diabetes is the leading cause of CKD. High blood glucose, also called blood sugar, from diabetes can damage the blood vessels in your kidneys. Almost 1 in 3 people with diabetes has CKD.[1]
- **High blood pressure.** High blood pressure is the second leading cause of CKD. Like high blood glucose, high blood pressure also can damage the blood vessels in your kidneys. Almost 1 in 5 adults with high blood pressure has CKD.[1]
- **Heart disease.** Research shows a link between kidney disease and heart disease. People with heart disease are at higher risk for kidney disease, and people with kidney disease are at higher risk for heart disease. Researchers are working to better understand the relationship between kidney disease and heart disease.

- **Family history of kidney failure.** If your mother, father, sister, or brother has kidney failure, you are at risk for CKD. Kidney disease tends to run in families. If you have kidney disease, encourage family members to get tested. Use tips from the family health reunion guide and speak with your family during special gatherings.

Identifying cause of CKD: Cause of CKD is classified based on presence or absence of systemic disease and the location within the kidney of observed or presumed pathologic-anatomic findings on kidney biopsy or imaging.

- Determining the cause of CKD distinguishes whether the patient has a systemic condition or a localized condition in the kidney such as glomerular disease because this functionality affects management.
- It is anticipated that the cause of disease will not be known with certainty for many patients with CKD but can be either inferred or not known.
- Patients with CKD stages 1-3 are generally asymptomatic. Typically, it is not until stages 4-5 (GFR < 30 mL/min/1.73 m^2) that endocrine/metabolic derangements or disturbances in water or electrolyte balance become clinically manifest.

Signs of metabolic acidosis in stage 5 CKD include the following:

- Protein-energy malnutrition
- Loss of lean body mass
- Muscle weakness

Signs of alterations in the way the kidneys are handling salt and water in stage 5 include the following:

- Peripheral edema
- Pulmonary edema

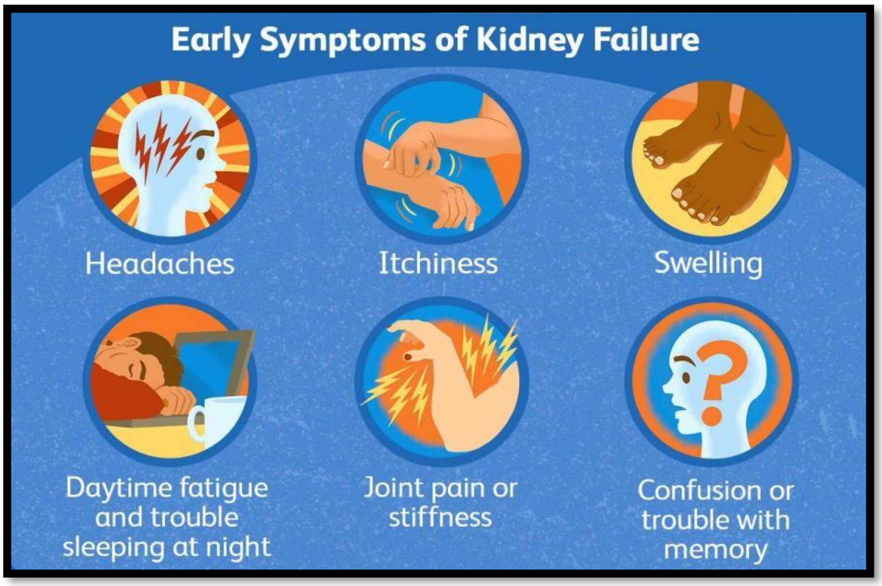


Fig No.3 Diagrammatic representation of symptoms of kidney failure

Anaemia in CKD is associated with the following:

- Fatigue
- Reduced exercise capacity
- Impaired cognitive and immune function
- Reduced quality of life
- Development of cardiovascular disease
- New onset of heart failure or the development of more severe heart failure

- Increased cardiovascular mortality. [4]

Diagnosis

Checking for CKD is easy with two simple tests:

- a **blood test** known as the estimated glomerular filtration rate (eGFR)
- a **urine test** known as the urine albumin-creatinine ratio (uACR)

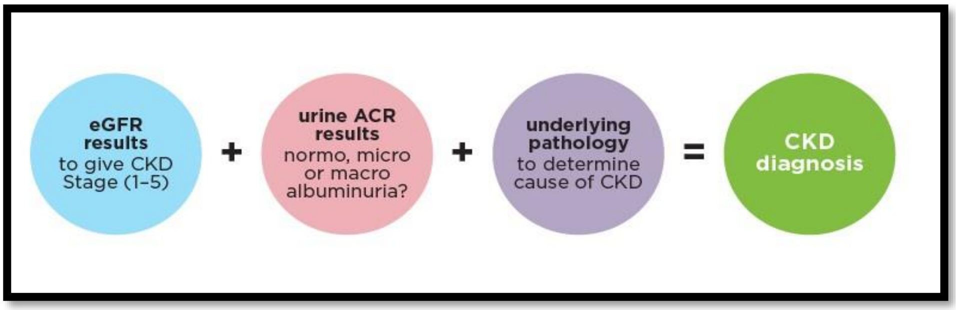


Fig. No.4 Tests for CKD diagnosis

Both tests are needed to have a clear picture of your kidney health. Having an eGFR under 60 and/or a uACR over 30 for three months or more is a sign you may have kidney disease.

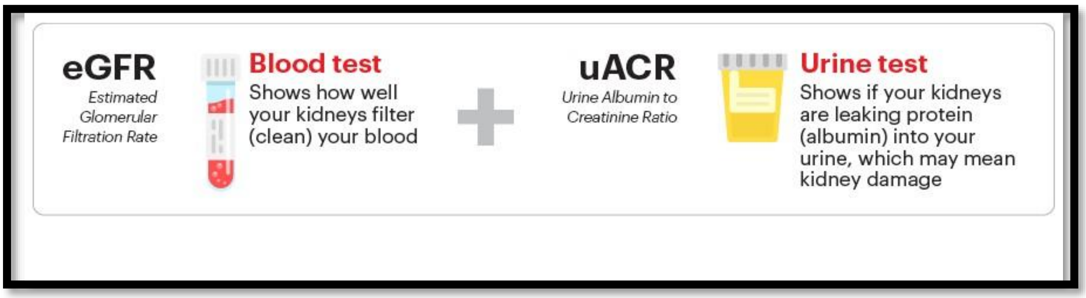
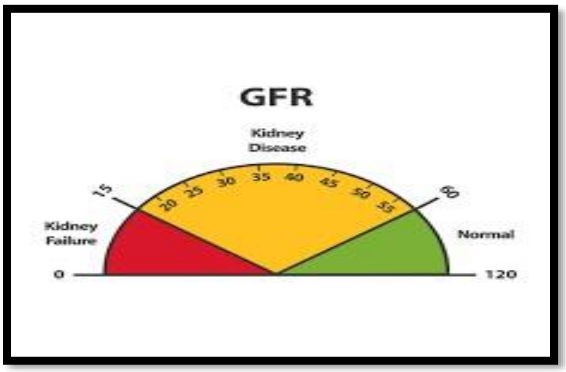


Fig No.5 Color indicating CKD tests positive

The eGFR is an estimate of how well your kidneys are removing waste products from the blood. It is calculated using your serum creatinine level, age, and sex. It can also be calculated using your cystatin C level. A "normal" eGFR varies according to age – it decreases as you get older. For this test, a **higher number** is better. Your eGFR number is used to determine your stage of CKD.

The uACR measures the amount of two different substances in your urine – albumin (protein) and creatinine. Healthy kidneys keep the albumin in your blood while filtering the creatinine out into the urine. So, there should be very little or no albumin in your urine. The uACR is calculated by dividing the amount of urine albumin by the amount of urine creatinine to find the ratio. For this test, a **lower number** is better. Your uACR number is used to test for albuminuria - a significant risk factor for complications.

In some cases, your healthcare professional may order additional_tests to get more information about your kidney health. Some examples include a kidney biopsy or medical imaging (CT scan, ultrasound, or MRI).



Markers of kidney failure

Proteinuria: Proteinuria refers to increased excretion of any urinary protein, including albumin and other serum proteins (tubular proteins). A normal urinary protein/creatinine ratio is less than 200 mg per g; proteinuria is a predictor of total mortality and CKD progression, and can help determine the type of CKD. A normal urinary albumin/creatinine ratio is less than 30 mg per g. Patients with albumin/creatinine ratios of 30 to 300 mg per g are classified as having microalbuminuria, and those with ratios greater than 300 mg per g are classified as having macroalbuminuria.

Urine dipstick testing is insensitive for the measurement of small amounts of albumin and is not recommended for CKD screening in patients at risk. This test is positive when a large amount (greater than 500 to 1,000 mg per day) of protein is excreted. Patients with positive urine dipstick results should repeat the test in the absence of urinary tract infection, ketosis, and hypovolemia. If the second result is positive, the urinary protein/creatinine ratio should be obtained within three months. Persistent proteinuria can be diagnosed by two positive protein/creatinine ratios one to two weeks apart.[9] Diabetes, the leading cause of nephrotic syndrome in the United States, is diagnosed when the protein/creatinine ratio is greater than 3,000 mg (3.0 g) per g.

Albuminuria: Albumin is a sensitive marker of CKD caused by diabetes, hypertension, and glomerular diseases. Microalbuminuria was the most common abnormality associated with the diagnosis of stages 1 and 2 CKD in the National Health and Nutrition Examination Survey. Microalbuminuria is an inherent part of the diabetes disease process but also can be present with nonrenal conditions (e.g., obesity, inflammation, cancer). Microalbuminuria may indicate increased vascular permeability rather than kidney injury.

Patients with diabetes and microalbuminuria who progress to macroalbuminuria are more likely to progress to end-stage renal disease. Diabetic kidney disease can be diagnosed based on the urinary albumin/creatinine ratio, duration of diabetes, and presence of diabetic retinopathy. When albuminuria reaches the range of macroalbuminuria, albumin becomes the dominant urinary protein, and the advantage of measuring albuminuria over proteinuria is generally lost. Two out of three abnormal readings are required to confirm persistent albuminuria.[5]

Evaluation of CKD: A thorough initial investigation includes determining the etiology and type of CKD and evaluating for comorbidities. The patient and family histories, physical examination, and blood pressure and weight measurements are the most valuable parts of the CKD evaluation (Table 1). Laboratory tests should include measurement of serum electrolytes and glucose, and a fasting lipid panel. Urinalysis should be performed to evaluate urinary sediment and the urinary albumin/creatinine or protein/creatinine ratio(Table 2).Additional testing may be required to identify rare causes of CKD. Renal ultrasonography is recommended to evaluate kidney size and assess for possible structural abnormalities.

Cardiovascular disease risk assessment—especially smoking status and lipid levels—is important because death is more likely than progression to dialysis in any stage of CKD.[9] Electrocardiography is recommended to identify left ventricular hypertrophy.

Patients with an estimated GFR of less than 60 mL per minute per 1.73 m^2 require further evaluation to assess for complications. Evaluation for anaemia is recommended in women with haemoglobin levels less than 12 g per dL (120 g per L) and in men with levels less than 13.5 g per dL (135 g per L), in addition to nutritional assessment and evaluation for bone disease (Table 3)

Examination component	*Diagnostic clues*	*Findings suggestive of CKD risks and etiology*
Review of systems	Recent infections	Poststreptococcal glomerulonephritis
	Risk factors for sexually transmitted disease	HIV infection, hepatitis B or C
	Skin rash or arthritis	Autoimmune disease (e.g., systemic lupus erythematosus, cryoglobulinemia)
	Symptoms during urination	Urinary tract infection, obstruction, or stone
Medical history	Diabetes mellitus (5 to 10 years' duration)	Microalbuminuria with evidence of retinopathy and elevated BP
	Diabetes (10 to 15 years' duration)	Albuminuria, retinopathy, hypertension
	Hypertension	Severe BP elevation, often with target organ damage
Family history of kidney disease	Males and females are affected equally in every generation	Autosomal dominant polycystic kidney disease
	Males in every generation are affected	Sex-linked recessive disease (e.g., Alport syndrome)
	Less frequent than every generation	Autosomal recessive polycystic kidney disease
Physical examination	Abdominal findings	Bruit (renal artery stenosis, fibromuscular dysplasia), flank pain, distended bladder
	Cardiovascular findings	Heart failure, ventricular hypertrophy
	Carotid bruit	Carotid artery disease
	Decreased peripheral pulses	Peripheral vascular disease
	General findings	Cushingoid appearance, edema
	Increased BP and weight	Hypertension, obesity
	Musculoskeletal findings	Arthritis, synovitis
	Ophthalmoscopic findings	Hypertensive or diabetic retinal disease
	Skin changes	Rash and skin changes in autoimmune disease or neurofibromatosis
Laboratory tests	Abnormal serum and urine protein electrophoresis	Multiple myeloma, amyloidosis, light-chain deposition disease
	Decreased serum complement levels C3 and C4	Poststreptococcal glomerulonephritis, membranoproliferative glomerulonephritis, lupus nephritis, cryoglobulinemia
	Eosinophiluria	Atheroembolic disease, tubulointerstitial disease
	Positive antiglomerular basement membrane antibody test	Goodpasture syndrome, antiglomerular basement membrane–associated rapidly progressive glomerulonephritis
	Positive antineutrophil cytoplasmic antibody test	Wegener granulomatosis, microscopic polyangiitis, pauci-immune rapidly progressive glomerulonephritis
	Positive antinuclear antibody test	Lupus nephritis
	Positive cryoglobulin test	Cryoglobulinemia
	Positive hepatitis B serology	Membranous nephropathy, membranoproliferative nephritis
	Positive hepatitis C serology	Mixed cryoglobulinemia, membranoproliferative glomerulonephritis, membranous nephropathy
	Positive HIV serology	Focal and segmental glomerulosclerosis
Ultrasonography	Doppler ultrasonography	May be useful in investigation of venous thrombosis, less so in arterial stenosis
	General findings	May show nephrocalcinosis, discrete stones, hydronephrosis, cysts,* or masses
	Increased echogenicity	May indicate cystic disease or medical renal disease
	Large kidneys	Generally indicate tumors, infiltrating diseases, or diseases causing nephrotic syndrome
	Size disparities and scarring	Suggest vascular, urologic, or tubulointerstitial diseases due to stones or infection
	Small hyperechoic kidneys	Generally indicate CKD

BP = blood pressure; CKD = chronic kidney disease; HIV = human immunodeficiency virus.

**—Simple cysts and duplicated collection systems are considered normal variants and are not indicative of kidney damage. Complex cysts or masses require urologic evaluation to rule out malignancy.*

Information from references 9, 27, and 28.

Table No.1 Initial Diagnostic Evaluation in Patients with Suspected CKD

BP = blood pressure; CKD = chronic kidney disease; HIV = human immunodeficiency virus. *—Simple cysts and duplicated collection systems are considered normal variants and are not indicative of kidney damage. Complex cysts or masses require urologic evaluation to rule out malignancy.

Associated kidney disease	Predominant abnormality on urinalysis: ACR or PCR (mg per g creatinine)	RBCs	RBC casts*	WBCs	WBC casts	Tubular cells	Granular casts
Cystic kidney disease	PCR 200 to 1,000	+					
Diabetic kidney disease, earlier stages	ACR 30 to 300						
Diabetic kidney disease, later stages	ACR > 300 or PCR > 500 to 1,000						
Hereditary nephritis or disease of small vessels (microangiopathy)	PCR < 1,000	+				+	+
Hypertensive disease	PCR 200 to 1,000						
Noninflammatory glomerular disease (minimal change disease, focal segmental glomerulosclerosis, associated with neoplasm)	PCR > 1,000						
Proliferative glomerulonephritis (systemic lupus erythematosus, vasculitis, infections) or hereditary nephritis	PCR > 500	+	+	±	±		
Tubulointerstitial nephritis	PCR 200 to 1,000	±		+	+		

ACR = albumin/creatinine ratio; PCR = protein/creatinine ratio; RBCs = red blood cells; WBCs = white blood cells; + = abnormality present; ± = abnormality may or may not be present.

**—Detection of RBC casts requires careful preparation and thorough and repeated examination of sediment from freshly obtained urine specimens. Even under ideal conditions, RBC casts may not always be detected in patients with proliferative glomerulonephritis.*

Adapted with permission from Levey AS, Perrone RD, Madaio MP. Laboratory assessment of renal disease: clearance, urinalysis and renal biopsy. In: Brenner BM, Rector FR. The Kidney. *Philadelphia, Pa.: W.B. Saunders; 1991:919-968, with additional information from references 9 and 11.*

Table No.2 Urinary Sediment Abnormalities and Associated Kidney Disease

ACR = albumin/creatinine ratio; PCR = protein/creatinine ratio; RBCs = red blood cells; WBCs = white blood cells; + = abnormality present; ± = abnormality may or may not be present.
*—Detection of RBC casts require careful preparation and thorough and repeated examination of sediment from freshly obtained urine specimens. Even under ideal conditions, RBC casts may not always be detected in patients with proliferative glomerulonephritis.

Clinical finding	CKD stage	Parameters to assess	Frequency of evaluation
Anemia	All	Complete blood count with differential; reticulocyte count; iron, ferritin, and transferrin levels	Once per year (more frequently if abnormal)
Malnutrition	3 to 5	Weight, serum albumin level, dietary history	Every 6 to 12 months in stage 3; every 1 to 3 months in stages 4 and 5
Metabolic bone disease	3 to 5	Alkaline phosphatase level	Once in stage 3; every 12 months in stages 4 and 5
		Calcium and phosphorus levels	Every 6 to 12 months in stage 3; every 3 to 6 months in stage 4; every 1 to 3 months in stage 5
		Consider duel energy x-ray absorptiometry	No routine testing
		25-hydroxyvitamin D level	Once, then as indicated
		Parathyroid hormone level	Once, then as indicated in stage 3; every 6 to 12 months in stage 4; every 3 to 6 months in stage 5
Neuropathy	3 to 5	Paresthesias, mental status, sleep disturbances (e.g., restless legs syndrome); consider sleep study and nerve conduction study	As indicated
Reduced level of functioning and well-being	3 to 5	Health literacy assessment, social support, standardized self-administered instruments (e.g., Dartmouth-Northern New England Primary Care Cooperative Information Project charts, Duke Health Profile, 36-item Medical Outcomes Study [SF-36], Kidney Disease Quality of Life scale)	Once, then as indicated

CKD = chronic kidney disease.

Information from references 9, 30, and 31.

Table No.3 Additional Clinical Interventions for Adults with CKD

Treatment

There's no cure for chronic kidney disease (CKD), but treatment can help relieve the symptoms and stop it getting worse.

Your treatment will depend on the stage of your CKD.

The main treatments are:

A. lifestyle changes – to help you stay as healthy as possible
B. medicine – to control associated problems, such as high blood pressure and high cholesterol
C. dialysis – treatment to replicate some of the kidney's functions, which may be necessary in advanced (stage 5) CKD
D. kidney transplant – this may also be necessary in advanced (stage 5) CKD

Lifestyle changes: The following lifestyle measures are usually recommended for people with kidney disease:

- stop smoking if you smoke
- eat a healthy, balanced diet
- restrict your salt intake to less than 6g a day – that's around 1 teaspoon
- do regular exercise – aim to do at least 150 minutes a week
- manage your alcohol intake so you drink no more than the recommended limit of 14 units of alcohol a week
- lose weight if you're overweight or obese
- avoid over-the-counter non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, except when advised to by a medical professional – these medicines can harm your kidneys if you have kidney disease

Find out more about living with CKD and what you can do to stay healthy.

Medicine: There's no medicine specifically for CKD, but medicine can help control many of the problems that cause the condition and the complications that can happen as a result of it.

You may need to take medicine to treat or prevent the different problems caused by CKD.

High blood pressure: Good control of blood pressure is vital to protect the kidneys. People with kidney disease should usually aim to get their blood pressure down to below 140/90mmHg, but you should aim to get it down to below 130/80mmHg if you also have diabetes.

There are many types of blood pressure medicines, but medicines called angiotensin converting enzyme (ACE) inhibitors are often used. Examples include ramipril, enalapril and lisinopril.

If the side effects of ACE inhibitors are particularly troublesome, you can be given a medicine called an angiotensin-II receptor blocker (ARB) instead. Find out more about how high blood pressure is treated.

Diabetes or high ACR: If you also have type 2 diabetes or a high albumin to creatinine ratio (ACR) you may be offered a type of medicine called an SGLT2 inhibitor, such as dapagliflozin, as well as medicines for high blood pressure.

Dapagliflozin helps to lower your blood sugar and can reduce damage to your kidneys.

You may also be given an additional medicine called finer none to take with dapagliflozin. Finer none works by blocking the action of certain hormones that can damage your kidneys.

High cholesterol: People with CKD have a higher risk of cardiovascular disease, including heart attack and stroke. This is because some of the causes of kidney disease are the same as those for cardiovascular disease, including high blood pressure and high cholesterol.

You may be prescribed medicines called statins to reduce your risk of developing cardiovascular disease. Examples include atorvastatin and simvastatin. Find out more about how high cholesterol is treated.

High potassium levels: People with CKD can develop high potassium levels in their blood, called hyperkalaemia, because their kidneys do not work properly. Hyperkalaemia can cause muscle weakness,

stiffness and tiredness. If it becomes severe, it can cause an irregular heartbeat (arrhythmia) which can lead to a heart attack.
If you have CKD, it's important to avoid taking potassium supplements and some medicines used to treat high blood pressure and heart failure because they can make your potassium levels too high. Talk to a GP about the medicines you take if you're worried.
A medicine called sodium zirconium cyclosilicate can be used to treat hyperkalaemia in adults, but only if it's used:

- in emergency care for acute life-threatening hyperkalaemia alongside standard care
- in people with hyperkalaemia that does not get better, CKD stage 3b to 5, or heart failure
- People with hyperkalaemia that does not get better (called persistent CKD) who also have CKD stage 3b to 5, or heart failure, should only take sodium zirconium cyclosilicate if they: have a serum potassium level of at least 6.0 mmol/litre and are not also taking a certain amount of renin-angiotensin-aldosterone system
- (RAAS) inhibitor because of hyperkalaemia and are not on dialysis.

You should stop taking sodium zirconium cyclosilicate if RAAS inhibitors are no longer suitable for you.

Water retention: You may get swelling in your ankles, feet and hands if you have kidney disease.
This is because your kidneys are not as effective at removing fluid from your blood, causing it to build up in body tissues (oedema). You may be advised to reduce your daily salt and fluid intake, including fluids in food such as soups and yoghurts, to help reduce the swelling. In some cases, you may also be given diuretics (tablets to help you pee more), such as furosemide.
Anaemia: Many people with advanced-stage CKD develop anaemia, which is a lack of red blood cells.
If you have anaemia, you may be given injections of a medicine called erythropoietin. This is a hormone that helps your body produce more red blood cells.
If you have an iron deficiency as well, iron supplements may also be recommended. Find out more about how iron deficiency anaemia is treated.
If you have anaemia but do not have iron deficiency, you may be given a medicine called Roxadustat. This medicine helps your body to produce more red blood cells and comes as tablets.

Bone problems: If your kidneys are severely damaged, you can get a build-up of phosphate in your body because your kidneys cannot get rid of it.
Along with calcium, phosphate is important for maintaining healthy bones. But if your phosphate level rises too much, it can upset the balance of calcium in your body and lead to thinning of the bones.
You may be advised to limit the amount food you eat which are high in phosphate, such as red meat, dairy products, eggs and fish.
If this does not lower your phosphate level enough, you may be given medicines called phosphate binders. Commonly used medicines include calcium acetate and calcium carbonate.
Some people with CKD also have low levels of vitamin D, which is necessary for healthy bones. If you're low in vitamin D, you may be given a supplement called cholecalciferol or ergocalciferol to boost your vitamin D level.

Glomerulonephritis: Kidney disease can be caused by inflammation of the filters inside the kidneys, known as glomerulonephritis. In some cases this happens as a result of the immune system mistakenly attacking the kidneys.
If a kidney biopsy finds this is the cause of your kidney problems, you may be prescribed medicine to reduce the activity of your immune system, such as a steroid or a medicine called cyclophosphamide.
Improving muscle strength:
If you are having a bad flare-up and are unable to exercise, you may be offered electrical stimulation to make your muscles stronger.
This is where electrodes are placed on your skin and small electrical impulses are sent to weak muscles, usually in your arms or legs.

	*Dosage adjustment based on GFR (mL per minute per 1.73 m^2)**		
Medication	*> 50*	*10 to 50*	*< 10*
Acyclovir (Zovirax; oral)	100%	100%	200 mg every 12 hours
Allopurinol (Zyloprim)	75%	50%	25%
Amoxicillin	Every 8 hours	Every 8 to 12 hours	Every 24 hours
Amoxicillin/clavulanate (Augmentin)	Every 12 hours	Estimated GFR 10 to 30 mL per minute per 1.73 m^2: every 12 hours Estimated GFR < 30 mL per minute per 1.73 m^2: do not use 875-mg/125-mg tablets	Every 24 hours
Atenolol (Tenormin)	100%	50%	25%
Cefazolin	Every 8 hours	Every 12 hours	50% every 24 to 48 hours
Cephalexin (Keflex)	Every 8 hours	Every 8 to 12 hours	Every 12 to 24 hours
Ciprofloxacin (Cipro)	100%	50 to 75%	50%
Clarithromycin (Biaxin)	100%	50 to 100%	50%
Famotidine (Pepcid)	50%	25%	10%
Fluconazole (Diflucan)	100%	50%	50%
Gabapentin (Neurontin)	Estimated GFR 30 to 60 mL per minute per 1.73 m^2: 200 to 700 mg twice daily Estimated GFR 16 to 29 mL per minute per 1.73 m^2: 200 to 700 mg daily Estimated GFR ≤ 15 mL per minute per 1.73 m^2: 100 to 300 mg daily		
Glyburide	100%	Avoid	Avoid
Levofloxacin (Levaquin)	100%	Estimated GFR 20 to 49 mL per minute per 1.73 m^2: 500- to 750-mg initial dose, then 250 to 750 mg every 24 to 48 hours Estimated GFR 10 to 19 mL per minute per 1.73 m^2: 500-mg initial dose, then 250 to 500 mg every 48 hours	—
Metformin (Glucophage)	Avoid if serum creatinine level is greater than 1.5 mg per dL (132.60 μmol per L) in men or greater than 1.4 mg per dL (123.76 μmol per L) in women, and in patients older than 80 years		
Metoclopramide (Reglan)	100%	75%	50%
Ranitidine (Zantac)	75%	50%	25%
Rosuvastatin (Crestor)	—	GFR < 30 mL per minute per 1.73 m^2: 5 mg per day initially; 10 mg per day maximum	
Simvastatin (Zocor)	—	GFR < 30 mL per minute per 1.73 m^2: 5 mg per day initially	
Thiazide diuretics†	100%	100%	Avoid
Valacyclovir (Valtrex)	100%	Every 12 to 24 hours	500 mg every 24 hours

GFR = glomerular filtration rate.

**—Percentages refer to percentage of usual dosage.*

†—Thiazides should not be used in patients with estimated GFR < 30 mL per minute per 1.73 m^2; however, metolazone (Zaroxolyn) retains effectiveness at GFR < 30 mL per minute per 1.73 m^2.

Information from references 9 and 26.

Table no.4 Medication used in chronic kidney disease with Dose Adjustments.

Dialysis

For a small proportion of people with CKD, the kidneys will eventually stop working.

This usually happens gradually, so there should be time to plan the next stage of your treatment.

One of the options when CKD reaches this stage is dialysis. This is a method of removing waste products and excess fluid from the blood.

There are 2 main types of dialysis:

- **haemodialysis** – this involves diverting blood into an external machine, where it's filtered before being returned to the body
- **peritoneal dialysis** – this involves pumping dialysis fluid into a space inside your tummy to draw out waste products from the blood as they pass through vessels lining the inside of your tummy

Haemodialysis is usually done about 3 times a week, either at hospital or at home. Peritoneal dialysis is normally done at home several times a day, or overnight.
If you don't have a kidney transplant, treatment with dialysis will usually need to be lifelong.
Talk to your doctor about the pros and cons of each type of dialysis and which type you would prefer if your kidney function becomes severely reduced.[6]

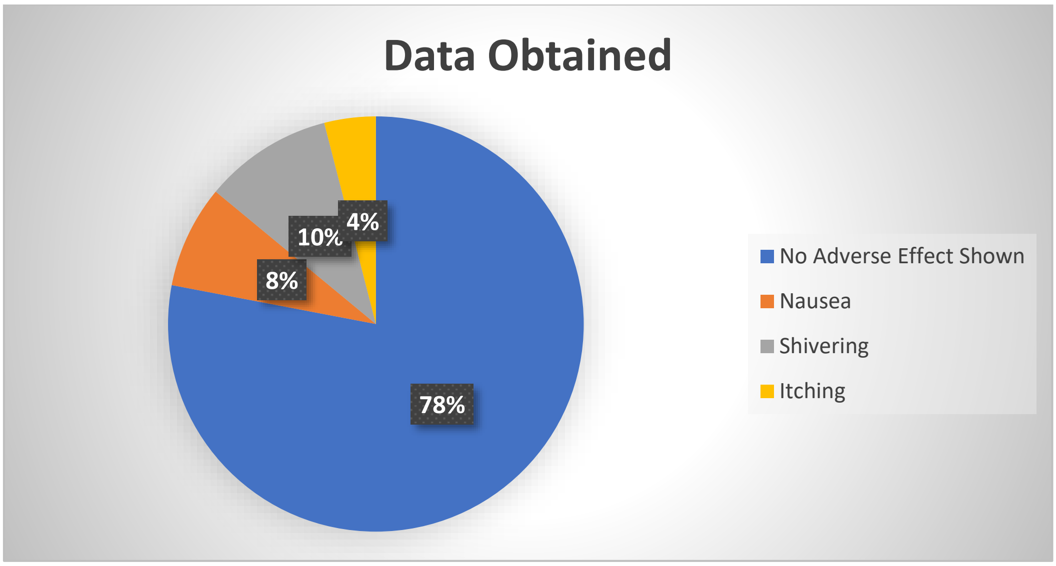
Complications
Chronic kidney disease can affect almost every part of your body. Potential complications include:

- 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 (hyperkalaemia), which could impair your heart's function and can be life-threatening
- Anaemia
- Heart disease
- Weak bones and an increased risk of bone fractures
- Decreased sex drive, erectile dysfunction or reduced fertility
- Damage to your central nervous system, which can cause difficulty concentrating, personality changes or seizures
- Decreased immune response, which makes you more vulnerable to infection
- Pericarditis, an inflammation of the saclike membrane that envelops your heart (pericardium)
- Pregnancy complications that carry risks for the mother and the developing foetus
- Irreversible damage to your kidneys (end-stage kidney disease), eventually requiring either dialysis or a kidney transplant for survival.[7]

Prevention
To reduce your risk of developing kidney disease:

- Follow instructions on over-the-counter medications. When using nonprescription pain relievers, such as aspirin, ibuprofen (Advil, Motrin IB, others) and acetaminophen (Tylenol, others), follow the instructions on the package. Taking too many pain relievers for a long time could lead to kidney damage.
- Maintain a healthy weight. If you're at a healthy weight, maintain it by being physically active most days of the week. If you need to lose weight, talk with your doctor about strategies for healthy weight loss.
- Don't smoke. Cigarette smoking can damage your kidneys and make existing kidney damage worse. If you're a smoker, talk to your doctor about strategies for quitting. Support groups, counseling and medications can all help you to stop.
- Manage your medical conditions with your doctor's help. If you have diseases or conditions that increase your risk of kidney disease, work with your doctor to control them. Ask your doctor about tests to look for signs of kidney damage.[7]

Case Study
Aim: To Study Adverse Drug Reaction Monitoring Among Chronic Kidney Disease In Super Specialty Hospital
Collection of Data: Five days retrospective study was conducted among chronic kidney disease (CKD) patients at multi-wards in a Super speciality hospital. Data collected included physical examination results, laboratory tests and medications taken. Only medication prescribed during the hospital stay were considered in this study.
Collection Of Data: In Hospital Survey, We found that there are various Adverse drug reaction in patients suffering from Chronic Kidney Disease. We have taken 50 patients for observation. They are:



Result: Fifty CKD patients evaluated out of which 4 patients were showing Nausea, 5 patients were showing Shivering and 2 patients were showing Itchy skin. The study reveal that CKD patients were mostly among the age group of 40-65. Ten patients had a history of acute Alcoholism 13 patients were of High Blood Pressure, 12 patients were of Diabetic history and only 15 patients did not had any history of disease.

Methodologies: A Validated self administer questionnaires that was created with assistance from professor from college and several articles was given to 3 pharmacist in Amravati district as part cross sectional study. There were 24 questions in this cross sectional questionnaires based on observational survey. Data from completed questionnaires were analyse.
The study was setup as follows:

1. A questionnaire was created based on like general Pharmacovigilance questions, fundamental ADR knowledge, the process of reporting an ADR, and some of pharmacists own opinion on the ADR.
2. Completed and printed survey questionnaires forms.
3. We physically visited every medical retailer, and filled up survey questionnaires with pharmacist opinions.
4. Response of YES, NO OR MAYBE kind were collected.
5. Visited hospital and consult to the physician/ Doctor. Ask them about the dosage given to patients.
6. Noted the dosage given to patients.
7. Ask patients for permission about their personal information and their disease. It include:

- Name
- Age
- Sign and symptom
- History of patients
- Disease
- Dosage
- Diagnosis
- Treatment
- Treated physician

8. The chemist is aware of fundamentals of Pharmacovigilance and about Pharmacovigilance and its goals is the first Pharmacovigilance perspective.
9. India Pharmacovigilance programme.
10. Knowledge of ADR and its application.
11. Helpline number for reporting of ADR, new techniques to identified ADR.
12. Knowledge of ADR reporting.
13. The chemists competence in filling an ADR.
14. Whether or not pharmacist should be required to report ADRs.

15. ADR reporting practices in the work place.
16. If any training require before reporting ADR.
17. Participation in treatment selection decision.
18. Pharmacist are among the crucial health care providers of ADR reporting.ave any other disease history.

Survey To Hospital

Chronic Kidney Disease Patient Questionnaire

You have most likely been referred to this clinic by a health care professional or yourself to address concerns about impaired kidney function. This is a short questionnaire designed to help your doctor fully evaluate and manage your kidney health.

Section I: Kidney Disease

1. Have you ever been told you have kidney disease? Y / N (If no, skip to next section)
2. How long has it been since you were first diagnosed?
3. How was this diagnosed? (Check those that apply)

- Blood test (elevated creatinine)
- Protein in the urine
- Other

4. Have you been told what caused your kidney disease (e.g. diabetes, high blood pressure, glomerulonephritis, kidney stones, medication, related to surgery or severe medical illness?

Have you ever had any of the following (Check if yes):

- Kidney problems at birth or in childhood?
- Hospitalization due to kidney failure?
- Kidney failure while hospitalized for another reason?
- Kidney stones?
- Bladder or kidney infections?
- Difficulty emptying your bladder?
- Bladder or other urologic surgery?
- Radiation to the abdomen or pelvis?
- Chemotherapy for cancer?
- Family history of kidney disease?
- Blood in the urine?

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