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A Review on: Chronic Kidney Disease

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ABSTRACT

The morbidity and death rates of chronic kidney disease (CKD) are on the rise, making it a major worldwide health burden. Diabetes and hypertension are known to be the main risk factors for chronic kidney disease (CKD), and they are also substantially to blame for its rising prevalence. Progressive loss of kidney function linked to chronic kidney disease (CKD) eventually results in end-stage renal disease (ESRD), which necessitates dialysis or kidney transplantation. In order to decrease the course of the disease and improve patient outcomes, early diagnosis and efficient care are essential. Currently used treatment approaches include renal replacement treatments, medication, and lifestyle changes. This review discusses the epidemiology, risk factors, pathophysiology, and management approaches for CKD while emphasizing the need for early intervention and preventive measures. Understanding these aspects is vital for healthcare providers to implement appropriate therapeutic strategies and reduce disease burden.

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INTRODUCTION:

Chronic kidney disease (CKD) is one of the leading causes of mortality and morbidity worldwide,

according to the Global Burden of Disease collaboration. The frequency and mortality of chronic kidney disease (CKD) rose by 29.3% and 41.5%, respectively, between 1990 and 2017. 2001–03 and 2010–13, India's renal failure-related mortality rate rose by 38%.[1]

One prevalent non-communicable illness that is contributing to a rise in morbidity in India is chronic renal disease. It has been demonstrated that the two most prevalent risk factors for chronic kidney disease are hyperglycemia and high blood pressure. [2]

Chronic kidney disease patients also have a number of other co-morbidities, including high blood sugar levels, coronary artery disease, hypertension, and infection. These co-morbidities have two effects: they raise the cost of treatment and make caring for patients with chronic kidney disease more difficult. Patients with chronic kidney disease are more likely to have drug-related problems because they take a lot of medications.. [2] CKD has an impact on HRQOL, or health-related quality of life. There aren't many research on HRQOL in CKD patients from low- and middle-income nations, such as India.. [3]

DEFINITION: The term "chronic renal disease" refers to any kidney impairment or damage that lasts longer than three months, regardless of the etiology. Reduced glomerular filtration rate (GFR), which is often determined from the serum creatinine concentration (eGFR), is indicative of impaired kidney function. An increase in albuminuria (albumin-to-creatinine ratio (ACR) >30 mg/g (3.4 mg/mMol)) or changes in urine sediment are examples of pathologic changes in the native or transplanted kidney that are typically identified by imaging, biopsy, or clinical findings.[4]

According to the K/DOQI, chronic kidney disease (CKD) is defined as kidney damage that lasts for three months or more and is characterized by abnormalities in the structure or function of the kidney, with or without a decrease in GFR. These abnormalities, which include variations in blood or urine chemistry or in imaging studies GFR, may be pathogenic or indicators of renal disease. [5]

Chronic kidney disease (CKD), a debilitating condition that permanently changes the structure and function of the kidney over months or years, is caused by a variety of disease pathways. Evidence of persistently compromised kidney function and altered renal structure is used to identify chronic kidney disease (CKD). The most precise indicator of overall kidney function is the estimated glomerular filtration rate (eGFR), which is the total volume of the fluid filtered by all active nephrons in a given period of time. [6.]

STAGE	DESCRIPTION	GFR mL/min/1.73 m2	Associated Words	Treatment-based classification
1	Damaged kidneys with normal or higher GFR	≥90	proteinuria, hematuria Albuminuria,	T If the recipient of a kidney transplant D of hemodialysis or peritoneal dialysis
2	Mild ↓ GFR kidney damage	60–89	hematuria, proteinuria Albuminuria	
3	Mild kidney injury ↓ GFR	30–59	Long-term renal failure,	
4	Severe ↓ GFR	15–29	pre- ESRD, late-stage renal failure, Long-term renal failure,	
5	Kidney failure	Less than 15 (or dialysis)	uremia, end-stage renal disease, Renal failure,	

TABLE.NO 1 Classification of CKD [5,9]

ETIOLOGY:

The following basic conditions are the most common causes of chronic kidney disease (CKD) and, ultimately, end-stage renal disease (ESRD): [8]

- 3.9% have type 1 diabetes.
- 27.2% hypertension
- 8.2% have primary glomerulonephritis.
- 3.6% of patients had chronic tubulointerstitial nephritis.

- Secondary glomerulonephritis or vasculitis (2.1%).
- Plasma cell dyscrasias or neoplasms (2.1%).
- Neoplasms or plasma cell dyscrasias (2.1%)

Chronic kidney disease (CKD) can result from any of the three types of disease processes: prerenal (decreased renal perfusion pressure), postrenal (obstructive), or intrinsic renal (vascular, or tubule-interstitium pathology).

Prerenal Disease

Patients with cirrhosis or chronic heart failure are at risk for acute tubular necrosis and other intrinsic kidney damage due to chronic prerenal illness, which is characterized by a consistently reduced renal perfusion. As a result, renal function may progressively decline. [8]

Renal vascular disease that is intrinsic

Intrinsic renal disease Nephrosclerosis, the most prevalent chronic renal vascular disease, progressively damages the tubulointerstitium, blood vessels, and glomeruli.. Other renal vascular diseases that might progress to ischemic nephropathy over months or years include fibromuscular dysplasia or renal artery stenosis caused by atherosclerosis. Tubulointerstitial disease and glomerulosclerosis are the hallmarks of this condition. [8]

Nephrotic or nephritic intrinsic glomerular disease

The features of a nephrotic pattern include varying degrees of proteinuria and dysmorphic red blood cells, and sometimes white blood cells (WBCs).The most common causes include infective endocarditis, vasculitis, post-infectious glomerulonephritis, lupus nephritis, IgA nephropathy, and Goodpasture syndrome.

Nephrotic patterns are linked to an inactive urine microscopic examination with few cells or casts, as well as proteinuria, which is often in the nephrotic range (>3.5 g/24 h). Amyloidosis, focal segmental glomerulosclerosis, minimal change disease, diabetic nephropathy, and membranous glomerulonephritis are among the common causes. [8,9]

Intrinsic interstitial and tubular disease

A chronic tubulointerstitial illness, polycystic kidney disease (PKD) is the most prevalent. A relatively high incidence of CKD with an uncertain cause is mesoAmerican nephropathy, also known as chronic interstitial nephritis in agricultural communities, among agricultural workers from Central America and some parts of Southeast Asia. Additional reasons include nephrocalcinosis (often caused by

hypercalcemia and hypercalciuria), sarcoidosis, Sjögren syndrome, and reflux nephropathy in children and young adults. [8]

Obstructive Nephropathy (postrenal):

Chronic blockage can be brought on by nephrolithiasis, prostatic disease, or a tumor in the abdomen or pelvis that puts pressure on the ureter or ureters. Congenital abnormalities are also often the source of obstructions at the ureterovesical or ureteropelvic junctions. Prolonged ureteral obstruction is seldom caused by neurogenic bladder or retroperitoneal fibrosis. [8]

SIGN AND SYMPTOMS OF CKD:

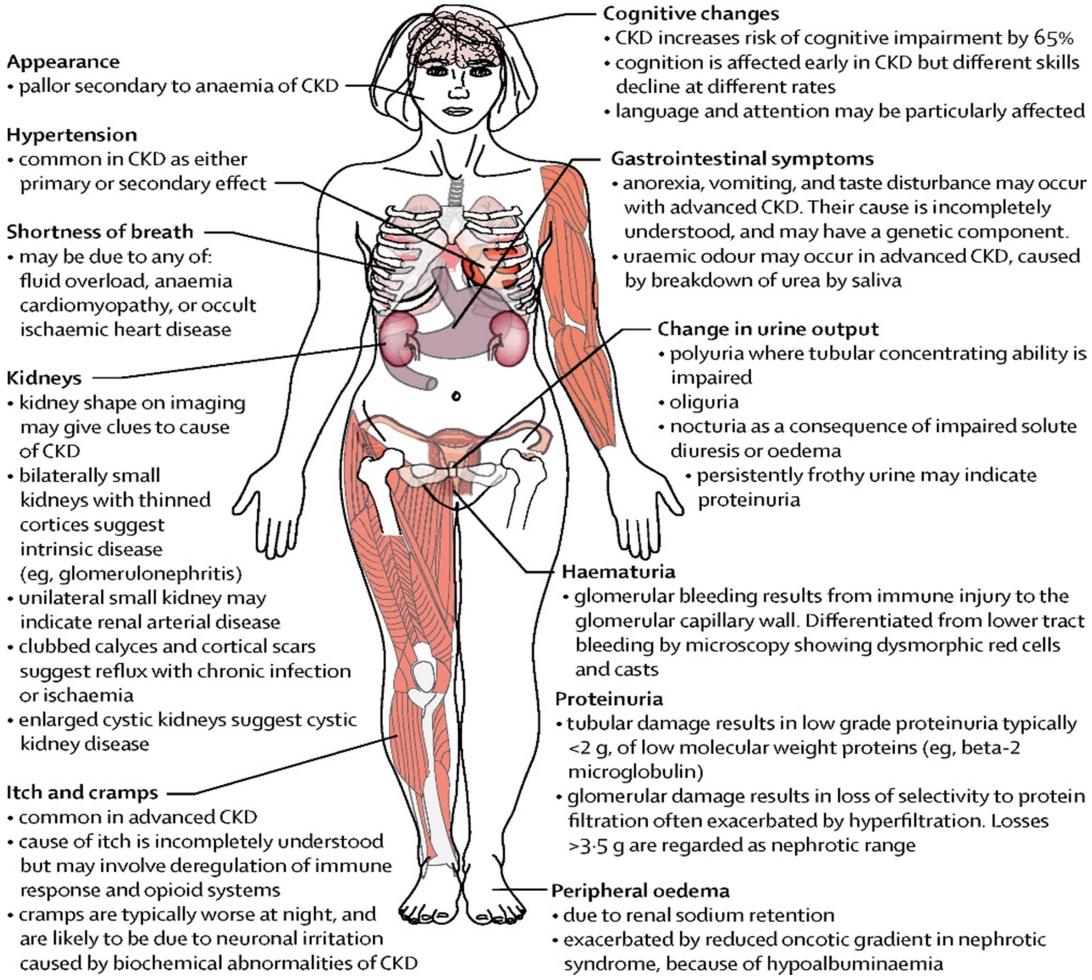

FIG.NO.1 SIGN ND SYMPTOMS OF CKD [7]

RISK FACTORS

Type	Definition	Examples
Susceptibility factors	An increased risk of kidney damage	Low birth weight, renal mass loss, advanced age, a family history of chronic kidney disease, being a member of a racial or ethnic minority, and having little money or education
Initiation factors	directly cause renal damage.	Drug toxicity, autoimmune illnesses, diabetes, hypertension, kidney stones, infections in the urinary tract, and obstruction of the lower urinary tract, systemic infections, and genetic disorders
Progression factors	cause kidney damage to worsen and renal function to diminish more quickly after kidney damage has started.	Increased blood pressure, smoking, excessive proteinuria, poor glycemic control in diabetes, and perhaps dyslipidemia
End-stage factors	a rise in kidney failure morbidity and death	Low blood albumin, high serum phosphorus, anemia, temporary vascular access, lower dialysis dosage (Kt/V), and delayed referral

TABLE NO.2 RISK FACTORS OF CKD

PATHOPHYSIOLOGY[9]:

The persistent and irreversible disorder referred to as chronic kidney disease (CKD), results in the kidneys gradually losing their ability to function normally. Numerous underlying illnesses and disorders, including diabetes, hypertension, and glomerulonephritis, are the cause of it. Numerous interconnected

processes, such as glomerular damage, tubulointerstitial fibrosis, vascular injury, and progressive nephron loss, are part of the complicated pathophysiology of chronic kidney disease (CKD).

- **Glomerular Injury Causes the Progression of CKD**

Podocyte Loss & Proteinuria

- The filtration barrier is maintained by podocytes, which are specialized cells in the glomerulus.
- The glomerular basement membrane leaks when podocytes are destroyed as a result of injury, letting proteins (albumin) into the urine.
- The toxic effects of proteinuria on tubules cause inflammation and renal fibrosis.

Glomerular Hypertension & Sclerosis

- The surviving healthy nephrons attempt to make up for it by raising the filtration pressure.
- Glomerulosclerosis results from the capillary walls being harmed by this elevated intraglomerular pressure. As more nephrons are lost over time, CKD advances more quickly.

Inflammation & Immune Activation

- Antibodies or immunological complexes build up in the glomeruli, which causes leukocyte recruitment (neutrophils, T-cells, and macrophages) and complement activation.
- Release of cytokines (TNF-α, IL-6, and TGF-β)
- Chronic inflammation causes fibrosis, which further impairs kidney function.

Tubulointerstitial Spread of Damage

- Because tubules and glomeruli are intimately related, tubulointerstitial compartment damage frequently results from glomerular injury.
- Proteinuria, hypoxia, and inflammatory mediators can promote tubular atrophy and interstitial fibrosis, leading to renal failure.

- **Proteinuria Causes CKD Progression**

1. **Direct Tubular Toxicity**
    - Albumin and other proteins are typically kept in the blood in a healthy kidney.
    - Proteins leak into the urine when the glomerular filtration barrier is compromised (by diabetes, hypertension, or glomerulonephritis).
    - These extra proteins are reabsorbed by tubular cells, but this exceeds their processing capabilities
        - resulting in lysosomal rupture and cell injury.
        - malfunctioning mitochondria, which lowers cellular energy.
        - Cell death, or apoptosis, is a factor in tubular atrophy.

2. **Induction of Inflammation**
    - Reabsorbed proteins cause tubular cells to release inflammatory mediators, such as:
    - Tumor necrosis factor-alpha (TNF-α) increases inflammation;
    - interleukin-6 (IL-6) stimulates the immune system;
    - and monocyte chemoattractant protein-1 (MCP-1) attracts macrophages.

3. **Promotion of Fibrosis (Scarring of Kidney Tissue)**
    - One of the main causes of fibrosis, TGF-β, or Transforming Growth Factor-beta **,** is released more often when proteinuria occurs.
    - Overproduction of extracellular matrix (ECM) by activated fibroblasts results are:
        - tubulointerstitial fibrosis, which causes scar tissue to replace healthy kidney tissue.
        - Glomerulosclerosis: glomerular scarring that lowers filtration capacity.

4. **Endothelial Dysfunction and Vascular Damage**
    - The peritubular capillaries are harmed by proteinuria, which causes hypoxia, or a decreased oxygen supply, in the renal tissue.

- This is the activation of Hypoxia-Inducible Factor-1 (HIF-1), which exacerbates nephron loss and fibrosis.

DIAGNOSIS:

Diagnostic aspect	Summary
Historyand symptoms	Ask about symptoms (such as edema or exhaustion) and medical history (such as diabetes or high blood pressure).
Physical examination	Check for signs of renal illness (edema, pallor, etc.), blood pressure, and fluid balance.
Blood tests	Examine the CBC, serum creatinine, BUN, eGFR, and electrolytes.
Urine tests	To evaluate proteinuria, hematuria, and urine sediment, do a urinalysis. Calculate the ACR.
Imaging studies	Perform an MRI, CT scan, or renal ultrasonography to assess the size, shape, and anomalies of the kidneys.
Biopsy (if needed)	Perform an MRI, CT scan, or renal ultrasound to evaluate the kidneys' dimensions, form, and abnormalities. For an accurate CKD diagnosis and staging, think about kidney biopsy.
Staging	usually saved for situations with severe illness or an unknown origin. Based on eGFR and albuminuria, divide CKD into phases using the KDIGO criteria.

TABLE.NO.3 DIAGNOSIS TEST FOR CKD[10]

EPIDEMIOLOGY:

People all throughout the world are aware of the growing prevalence of chronic kidney disease (CKD) and its detrimental implications on health. However, between 7% and 12% of persons globally suffer with CKD. [12]

In the geographically unique rural coastal region of Uddanam in Srikakulam District, Andhra Pradesh,

which is home to several cashew and coconut farms, chronic kidney disease (CKD) has been shown to be common. 3. 4. In the past decade, there have been an estimated 34,000 cases of CKD, also known as "Uddanam nephropathy," with more than 4,500 deaths. Not much is known about the features of Uddanamnephropathy. Unpublished cross-sectional studies indicate that between 30% and 60% of persons suffer from chronic kidney disease. A recent survey found that chronic renal disease affects 18.3% of the population.The absence of uniform study designs, methodology, and criteria made comparisons difficult. 5. Theories on possible causal factors have been developed based on extrapolation of results from CKD patients in other parts of the world. [12]

40–60% of CKD patients in India currently have diabetes and hypertension as their primary causes. According to recent data from the Indian Council of Medical Research, the prevalence of diabetes in Indian adults has increased to 7.1%, with rates ranging from 5.8% in Jharkhand to 13.5% in Chandigarh. In urban populations (those over 40), the rate can even approach 28%. [14]

The incidence of chronic kidney disease (CKD) has risen by 30% in the US over the past 10 years due to rising life expectancy and the prevalence of lifestyle issues. Regretfully, there are no longitudinal studies and scant information on the prevalence of CKD in India..[13]

In tropical and subtropical agricultural regions, particularly in Central America and Sri Lanka, high rates of chronic kidney disease of unclear cause (CKD) among working-age populations have been often documented in recent decades. [14]

The Indian CKD registry, which records event cases of CKD from 2006 to 2010, shows that CKD was the second most frequent kind of CKD, behind diabetic nephropathy. [14]

Treatment

The KDIGO group offers the most recent CKD management guidelines. The most recent revision to these rules was made in 2020. The following are some of KDIGO's main suggestions for controlling CKD:[11]

1. The first step is to properly and quickly identify and stage chronic kidney disease (CKD) using the Kidney Disease Outcome Quality Initiative (KDOQI) or KDIGO criteria.
2. Determining and controlling risk factors for the advancement of chronic kidney disease (CKD), such as blood pressure regulation, diabetes glycemic control, lipid management, quitting smoking, and weight management.

3. If it is not contraindicated, individuals with albuminuria and hypertension should use renin-angiotensin-aldosterone system (RAAS) blocking.
4. When treating CKD patients, use non-steroidal anti-inflammatory therapies with caution and stay away from nephrotoxic substances at all costs.
5. Assessment and treatment of problems related to chronic kidney disease (CKD), such as anemia, abnormalities of the bones and minerals, cardiovascular disease, and infectious infections.
6. Providing CKD patients with education and counseling to encourage self-management and treatment compliance.
7. Depending on the patient's CKD stage and risk of progression, refer them to a nephrologist as necessary.

These suggestions provide a comprehensive approach to CKD treatment and can be used to improve patient outcomes and quality of life.

Pharmacological treatment:

Managing CKD requires a combination of medications to control symptoms, slow disease progression, and address complications. Below is a detailed breakdown of commonly used drug classes in CKD patients.

1. **Antihypertensive Medications**

   Antihypertensive drugs are typically also necessary. Certain pharmaceutical treatments have extra renoprotective and/or cardioprotective activity in addition to their direct BP-lowering benefits, which may be separate from these effects . Therefore, while choosing a drug, the person's need for risk reduction should be considered.The dangers of polypharmacy must also be taken into account because combination medication therapy is usually required to meet blood pressure objectives.[20]

   - **Renin-Angiotensin-Aldosterone System Blockade**

The cardioprotective and renoprotective properties of ACE inhibitors and ARBs can help patients with chronic kidney disease (CKD). They, like diuretics and calcium channel blockers (CCBs), reduce systolic blood pressure (BP) by around 20 mmHg. However, because they lower proteinuria without changing blood pressure, ACE inhibitors and ARBs are first-line treatments for proteinuric CKD.[20]

The renoprotective impact of RAAS blocking is less clear for non-proteinuric CKD. Other antihypertensives (CCBs, thiazides) may be just as beneficial since, according to a comprehensive review, the improved renal outcomes are mostly caused by BP lowering rather than a particular RAAS-blocking action.

Up to 50% of patients may experience angiotensin II reactivation as a result of long-term ACE inhibitor therapy, which would decrease effectiveness. ACE inhibitors, ARBs, and combination treatment were compared in the ONTARGET study, which included 25,620 patients with a 56-month follow-up. Despite the lack of any cardiovascular advantages, combination treatment produced greater negative side effects. Similarly, there was no discernible advantage to combining ACE inhibitors and ARBs in the VA NEPHRON-D research, which looked at patients with diabetic CKD.

It is no longer advised to use combination treatment with ACE inhibitors and ARBs since it increases adverse effects without providing appreciable benefits for CKD. Although its long-term effects are unknown, dual blocking in IgA nephropathy lowers proteinuria more than monotherapy.

AKI and hyperkalemia brought on by RAAS blockage frequently result in a brief increase in serum creatinine. Losartan initially decreased eGFR, but the reduction slowed with time, according to the RENAAL research. As it may suggest long-term renal protection, a creatinine increase of up to 30% is usually considered acceptable if it stabilizes.[20]

- **Diuretics:**

Diuretics are essential for controlling volume overload in chronic kidney disease (CKD), which affects more than 50% of patients and raises the risk of cardiovascular disease. Potential first-line treatments for non-proteinuric CKD include thiazide like diuretics (such as Indapamide and bendroflumethiazide), whilst loop diuretics (like furosemide) are necessary for individuals with lower eGFR but need greater dosages. Although combining loop and thiazide diuretics can be

very beneficial, Care must be made to prevent fluid loss. Because Diuretics might hasten the formation of cysts, they should typically be avoided in patients with polycystic kidney disease.[20]

- **Calcium Channel Antagonists (Blockers)**

In chronic kidney disease (CKD), Calcium channel blockers (CCBs), including non-dihydropyridines like verapamil and dihydropyridines like amlodipine)—are useful in controlling hypertension. In non-proteinuric chronic kidney disease, dihydropyridine CCBs can be used alone or in combination as a first-line treatment. Although they are less effective than RAAS blockers in proteinuric CKD, they can improve blood pressure (BP) management when combined with RAAS blocking without exacerbating proteinuria. ACE inhibitors combined with CCBs are advised as the first-line treatment for proteinuric CKD by the ESC/ESH guidelines. In addition to being similarly efficient in controlling blood pressure, non-dihydropyridine CCBs offer superior proteinuria reduction.[20]

- **β-Blockers**

β-Blockers effectively lower blood pressure in people with chronic renal disease by altering the dysregulated sympathetic nervous system**..** In animal studies, they have demonstrated renoprotective effects, such as lowering interstitial fibrosis, and offer well-established cardioprotective advantages. Despite clinical trials showing a survival advantage, β-blockers are still neglected in CKD patients because of worries regarding systemic buildup, renal excretion, and glycemic management. Although many β-blockers necessitate modifying dosage, hepatically excreted alternatives such as carvedilol are especially advantageous. Studies such as AASK show that metoprolol is more effective than amlodipine in CKD patients, despite the fact that β-blockers provide less renoprotection than ACE inhibitors. Therefore, in individuals who also have cardiovascular disease, β-blockers are useful, especially when used in conjunction with RAAS blocking.**[20]**

- **α-Blockers**

In combination treatment, alpha-blockers such doxazosin are frequently used for the treatment of hypertension among those suffering from chronic kidney disease (CKD). Along with possible advantages for glycemic management, its efficacy is ascribed to a constant pharmacokinetic profile that is unaffected by a diminishing estimated glomerular filtration rate (eGFR). Alpha-blockers have been found to be a useful adjunctive therapy for hypertension in people with

long-term renal illness**.** However, because They are less effective than other antihypertensive medications at lowering the risk of cardiovascular disease (CVD), they are not advised as first-line treatment.[20]

2. **Antidiabetic Medications**

Glycemic management improves clinical outcomes for those with diabetes and renal disease and postpones the onset of albuminuria.

Maintaining blood sugar control is crucial in diabetic CKD patients to prevent further kidney damage. [21]

- **Metformin:**

A first-line antidiabetic drug, metformin, is safe for the majority of individuals whose estimated glomerular filtration rate (eGFR) is greater than 30 mL/min/1.73 m². In peripheral tissues, it increases insulin sensitivity and decreases hepatic gluconeogenesis as a biguanide. According to the UKPDS research, metformin reduces mortality from diabetes, cardiovascular disease, and all causes when compared to insulin and sulfonylureas. In individuals with diabetic kidney disease (DKD), it is also associated with a lower risk of bad cardiovascular outcomes and end-stage kidney disease (ESKD**).**[22]

eGFR **(mL/min per 1.73 m²)**	**Metformin use**
Above 60 (CKD 1 ,CKD 2)	Not contraindicated
	Annual renal function check
45 to 60 (CKD 3a)	Metformin use: lower dosage (no more than 1.5–2 g per day)
	Regular evaluation of renal function (every three to six months)
30 to 45 (CKD 3b)	Lower the dosage (no more than 1–1.5 g per day).
	No new cases

eGFR (mL/min per 1.73 m^2)	Metformin use
	Regular evaluation of renal function (every three to six months)
Less than 30 (CKD 4 , 5)	Give up taking metformin.

- **Inhibitor of sodium-glucose cotransporter-2**

SGLT2 inhibitors (SGLT2i) cause natriuresis and glucosuria by blocking the proximal convoluted tubule's ability to reabsorb glucose and salt. They dramatically reduce the risk of cardiovascular mortality, heart failure hospitalization, and end-stage kidney disease (ESKD). Their advantages for the heart and kidneys happen without the glucose-lowering effects, which go away when eGFR drops. Additionally, SGLT2i may improve tissue energetics, lower oxidative stress, and improve glomerular hemodynamics.[21,22,23]

- **Pioglitazone :**

Theoretically, pioglitazone is safe for all phases of CKD without dosage modification because it is only metabolized in the liver and does not result in hypoglycemia. However, in diabetic CKD patients, its adverse effects—osteoporosis, anemia, and fluid retention—can exacerbate pre-existing problems. Its usage is often restricted to a lower dosage of 15 mg once day as a result of these worries.[23]

- **Sulfonylurea in CKD**

Sulfonylureas are ancient medications that are used all over the world. These medications reduce insulin secretion and are linked to a higher risk of hypoglycemia, a serious problem for those with chronic kidney disease.[21,22,23]

1. **Glibenclamide** (also known as gliburide) is broken down in the liver and then removed via the kidneys and intestines.. [21,22,23]

In CKD, active metabolites can build up and raise the risk of hypoglycemia.

In CKD stage ≥3 (eGFR < 60 mL/min), it is not advised.

When treating moderate CKD (eGFR 60-90 mL/min), use cautious, reduce dosage, and check often.

2. **Glimepiride** is metabolized in the liver, and CKD is characterized by an accumulation of active metabolites. [21,22,23]

Severe hypoglycemia lasting >24 hours may result from this.

With a dosage decrease for eGFR 30-60 mL/min, it is safe if eGFR > 60 mL/min.

It is not recommended in CKD stages 4 or 5 (eGFR < 30 mL/min).

3.Gliclazide

Inactive metabolites are eliminated in urine after being metabolized in the liver. [21,22,23,] less chance of hypoglycemia than other sulfonylureas. Safe for people with eGFR > 30 mL/min and CKD stages 1-3.

There is little information on severe CKD, however lower dosages are thought to be acceptable.

4. **Glipizide**

For mild to severe CKD, there is no need to change the dosage.

can be utilized without harm; the risk of hypoglycemia is the primary issue.

- **Glinides :**

Short-acting secretagogues called glides, including nateglinide and repaglinide, are suitable for diabetic patients with chronic kidney disease (CKD) because to their lower risk of hypoglycemia compared to sulfonylureas**.** [22,23] Repaglinide is absorbed in the gastrointestinal system, converted into M1, M2, and M4 metabolites in the liver, and then eliminated through bile without causing hypoglycemia. Without lowering dosage, it can be used in stages 4 and 5 of CKD.[22,23,]

Nateglinide is also broken down into nine metabolites in the liver, with only M7 showing significant action. 84% are eliminated as metabolites and 16% are eliminated unaltered in urine. While the dosage is modified (60 mg × 3) in stage 4, it is avoided in stage 5 CKD.[23]

- **GLIPTINES (INHIBITORS OF DIPEPTIDYL PEPTIDASE 4)**

This class includes Linagliptin, Adolliptin, Vildagliptin, Sitagliptin, and Saxagliptin, all of which are currently on the market. They play a crucial role in algorithms for CKD and diabetic patients. For most members of this class, we can use them all in CKD, although with dosage adjustments. (At any stage of CKD, linagliptin is the only medication that does not require dosage modification.)[23]

3. **Phosphate Binders**

Phosphate binders come in three primary varieties: calcium-containing binders, aluminum-containing binders, which have been widely used and are reasonably priced, and the recently developed non-calcium-based binders.[24]

In both dialysis or nondialysis chronic kidney disease (CKD),

- The most common phosphate binder **is calcium carbonate**. It should be used in conjunction with mild dietary phosphate restriction and is most effective when taken with meals under a dietitian's supervision. While high-quality protein sources like meat and eggs should be preserved, processed meals with excessive phosphate should be avoided. When it comes to nondialysis CKD, [24]
- **aluminum-based binders** are the second-line therapy. Sevelamer, lanthanum, and sucroferric oxyhydroxide are newer non-calcium-based binders that are exclusively accessible to dialysis patients under the PBS.[24]

4. **Agents that stimulate erythropoiesis (ESAs)**

Erythropoiesis-stimulating agents (ESAs) are recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) recommendations for the treatment of anemia in patients with treatment-responsive anemia who have chronic kidney disease (CKD). Monitoring of hemoglobin (Hb) should be done at least once a year, and more frequently if CKD progresses. Because there is not enough data to justify habitually aiming levels of 13 g/dL or higher, the recommendations recommend maintaining Hb levels between 11 and 12 g/dL. Targeting Hb above 12 g/dL may raise cardiovascular risks and death, according to recent research and meta-analyses. According to the KDOQI Anemia Work Group, damage happens when hemoglobin levels above 13 g/dL. In September 2007, updated target hemoglobin recommendations were released.[25]

Erythropoietin and Darbepoetin: These agents boost red blood cell production, reducing anemia-related symptoms. However, excessive use can increase the risk of high blood pressure and blood clots, so hemoglobin levels should be carefully monitored. [25]

Daprodustat: An oral alternative to injectable ESAs, recently approved for treating anemia in CKD patients on dialysis. [25]

5. **Vitamin D Analogs**

Chronic kidney disease mineral and bone disorder (CKD-MBD) is a common consequence of chronic kidney disease**.** which involves problems in vascular calcification, bone health, and mineral metabolism. [26]

Its growth is influenced by disturbances in the metabolism of vitamin D. CKD-MBD raises the risk of cardiovascular illness, bone pain, fractures, and mortality. The main causes of cardiovascular disease, the leading cause of death for those with chronic renal disease, are endothelial dysfunction, vascular calcification, arterial stiffness, and left ventricular hypertrophy.[26,27]

One important treatment for CKD-MBD has been vitamin D therapy, which contains molecules that are either nutritional or active (VDRAs). The synthetic analogs of calcitriol are alfacalcidol, maxacalcitol, paricalcitol, and doxercalciferol, whereas calcitriol is the natural VDRA. As with the general population, vitamin D insufficiency should be treated similarly, according to the 2017 KDIGO CKD-MBD recommendations (2C recommendation). Only CKD stages 4 and 5 with severe hyperparathyroidism should take calcitriol and VDRAs, while the optimal PTH target for non-dialysis patients is still uncertain**.** [26,27]

6. **Iron supplements:**

- **General Considerations**

  - Balance benefits (fewer transfusions, anemic symptoms, and ESA usage) against the hazards (acute responses, unidentified long-term consequences). (Not assigned a grade)[28]

- **Adult CKD Patients Not Receiving ESA or Iron Treatment *(2C)***

  - **Recommendation:** Trial of IV iron (or 1–3 months of oral iron for CKD ND patients) if:
    - Increasing Hb without ESA is desired.
    - TSAT ≤30% and ferritin ≤500 ng/ml.[28]

- **Iron Supplementation-Free Adult CKD Patients Receiving ESA Therapy (2C)**[28]

  - **Recommendation:** IV iron trial (or, for CKD ND patients, 1–3 months of oral iron)if:
    - Increasing Hb or reducing ESA dose is desired.

- 30% TSAT and 500 ng/ml ferritin are required.

- **Iron Administration Route in CKD ND Patients** (Not Graded) [28]

  - Considering the degree of insufficiency, venous access, and previous reaction, side effects, compliance, and cost.

- **Guiding Ongoing Iron Therapy** *(*Not Graded)[28]

  - Consider Hb response, blood loss, iron status (TSAT, ferritin), ESA responsiveness and dose,and trends.

  - **Children with Chronic Kidney Disease Not Receiving Iron or ESA Treatment (1D)**[28]

    - Oral iron (or IV iron for CKD HD patients) is advised if:
    - Ferritin concentration ≤100 ng/ml and TSAT ≤20%.

  - **Children with chronic kidney disease receiving ESA treatment without iron supplementation (1D)** [28]

    - It is advised that people with CKD HD take oral iron (or IV iron) to maintain:
    - Ferritin >100 ng/ml and TSAT >20%.

7. **Antiplatelet therapy:**

   The risk of developing cardiac disease is increased by chronic kidney disease (CKD). which can obstruct the heart's or brain's blood flow and result in a heart attack or stroke. In the general adult population, clots in the arteries can be prevented by antiplatelet medicines, which are medications that stop blood clots from forming. There could be less advantages for those with chronic kidney disease (CKD), though, as artery clots are less likely to result in mortality or hospitalization than heart failure or sudden death in these individuals. Individuals with chronic kidney disease (CKD) are also more likely to bleed because of altered blood coagulation patterns. If CKD is present, antiplatelet medications may be more dangerous.

Aspirin and clopidogrel are higjly use medicine for ckd patients.[29]

8. **Uric acid-lowerning agent:** Because CKD patients excrete less uric acid in their urine, they often develop hyperuricemia. Hyperuricemia has also been demonstrated to hasten the development and progression of chronic kidney disease (CKD). A fascinating and unsolved question for nephrologists is whether hyperuricemia is a cause of the development of renal disease, an indirect indicator of reduced kidney function, or both . The role that uric acid plays in the development of chronic kidney disease (CKD) and the need for urate-lowering therapy (ULT) in its treatment are controversial subjects.[30]

   benzbromarone and allopurinol: In patients with CKD who are hyperuricemic, it is more successful in reducing serum uric acid and regulating blood pressure.[30]

9 . **Multivitamins:** Vitamin supplements are frequently required for Chronic Kidney Disease (CKD) patients because of dietary limitations, higher losses, and decreased kidney function. The following vitamin medications are frequently suggested: Nephrocaps , Renavite, Nephro-Vite.[31]

Conclusion: Diabetes, hypertension, and other modifiable risk factors are contributing to the rising prevalence of chronic kidney disease (CKD), a serious public health problem. In order to improve patient outcomes and decrease the course of the disease, early identification and effective care are essential. Although medication, lifestyle changes, and renal replacement treatments are the mainstays of current therapeutic methods, improved patient awareness and preventative measures are desperately needed. To enable prompt diagnosis and treatment, future studies should concentrate on innovative therapeutic approaches and early biomarkers. To lessen the worldwide burden of CKD, a multidisciplinary strategy including patients, legislators, and healthcare professionals is crucial.

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