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Review Article

The Burden of Chronic Kidney Disease: Risk Factors, Therapeutic Approaches, and Prevention

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Abstract

Chronic kidney disease (CKD) is a progressive condition affecting millions worldwide, leading to significant morbidity, mortality, and a growing healthcare burden. Without timely intervention, CKD advances to end-stage renal disease (ESRD), necessitating dialysis or kidney transplantation, both of which are often costly and inaccessible, particularly in resource-limited settings. Early detection and effective management are critical in slowing disease progression and reducing associated complications. Individuals with diabetes and hypertension are at the highest risk and require routine kidney function monitoring. Pharmacological interventions, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and sodium-glucose cotransporter-2 (SGLT2) inhibitors, have demonstrated efficacy in delaying CKD progression and lowering cardiovascular risks. However, socioeconomic barriers, inadequate healthcare infrastructure, and high treatment costs remain significant obstacles to optimal CKD management, especially in low-income regions. In addition to medical therapy, lifestyle modifications such as smoking cessation, weight management, and strict glycemic and blood pressure control play a crucial role in preventing CKD onset and progression. Addressing these challenges requires a multidisciplinary approach that emphasizes early diagnosis, effective treatment, and equitable access to healthcare. Strengthening screening programs, improving the affordability of renoprotective therapies, and promoting preventive strategies are essential to mitigating the global burden of CKD.

Keywords: Chronic kidney disease, CKD, ESRD, CKD complications, nephrotoxicity, dialysis, kidney transplant

Introduction

Chronic kidney disease (CKD) is a progressive condition characterized by the gradual loss of kidney function over time, leading to the accumulation of waste products and fluid imbalances in the body. Globally, CKD has emerged as a significant public health concern, affecting approximately 10% of the population and ranking as the seventh leading cause of death worldwide (Jager et al., 2019). The prevalence of CKD is on the rise, driven by factors such as aging populations, increasing rates of diabetes mellitus, hypertension, obesity, and exposure to nephrotoxic agents. Notably, diabetes and hypertension are the leading causes of CKD, accounting for a substantial proportion of cases (Kazancioğlu, 2013). Other risk factors include genetic predisposition, smoking, and socioeconomic status.

The economic burden associated with CKD is considerable and escalates with disease progression. In Spain, for instance, the economic burden of diagnosed CKD is expected to increase by 13.8% to 4.89 billion euros in 2027, representing 5.56% of total Spanish public health expenditure. (Navarro González et al., 2024) Similarly, in the United States, CKD has been associated with substantial healthcare costs, particularly in the management of end-stage renal disease (ESRD) requiring dialysis or transplantation (Jager et al., 2019). Early diagnosis of CKD is crucial for implementing interventions that can slow disease progression and improve outcomes. Diagnostic approaches typically involve assessing the glomerular filtration rate (GFR), measuring serum creatinine levels, and detecting proteinuria. Despite the availability of these diagnostic tools, CKD often remains underdiagnosed, leading to delayed treatment and poorer prognoses (Webster et al., 2017).

Management strategies for CKD focus on controlling underlying risk factors, such as optimizing blood pressure and glycemic control and utilizing medications like renin-angiotensin-aldosterone system inhibitors to reduce proteinuria and slow progression. In advanced stages, renal replacement therapies, including dialysis and kidney transplantation, become necessary to sustain life. Recent advancements in weight-loss medications, such as GLP-1 receptor agonists, have shown promise in improving kidney health and reducing the risk of CKD progression. This review aims to provide a comprehensive overview of CKD, encompassing its prevalence, risk factors, economic burden, diagnostic methodologies, and current treatment modalities.

Epidemiology and Prevalence of CKD

Chronic kidney disease has emerged as a global public health challenge, with a rising prevalence and substantial economic and healthcare burdens. It is associated with increased risks of cardiovascular disease, end-stage renal disease (ESRD), and premature mortality. The epidemiology of CKD is shaped by demographic factors, regional healthcare disparities, and the prevalence of risk factors such as diabetes mellitus, hypertension, obesity, and environmental toxins. Understanding the global and regional burden of CKD is essential for developing targeted interventions and healthcare policies to mitigate its impact.

Global Prevalence of CKD

The global prevalence of CKD is estimated to be around 13.4%, affecting nearly 700 million individuals worldwide (Hill et al., 2016). However, this figure varies significantly across regions, reflecting differences in risk factors, diagnostic practices, and healthcare access. CKD prevalence is increasing in both developed and developing nations, primarily due to aging populations and the rising burden of non-communicable diseases such as diabetes and hypertension (Bikbov et al., 2020).

Despite growing awareness, CKD often remains underdiagnosed and undertreated, particularly in low- and middle-income countries where limited healthcare resources hinder early detection and intervention. The burden of CKD is further exacerbated by socioeconomic factors, dietary habits, and environmental exposures, particularly in regions with high rates of infectious diseases and nephrotoxic agents (Bello et al., 2017a).

Regional Prevalence of CKD

Asia bears a significant burden of CKD, with wide variations in prevalence among different countries. A meta-analysis estimated the overall prevalence of CKD in Asia to be approximately 11-13%. In China, CKD affects around 10.8% of the population, with an estimated 120 million people suffering from some stage of the disease (Lv and Zhang, 2019). Similarly, India reports a high prevalence, with studies suggesting a national estimate ranging between 8% and 17% (Agarwal and Srivastava, 2009).

Diabetes and hypertension are the leading causes of CKD in Asia, particularly in rapidly urbanizing countries like China and India, where sedentary lifestyles and dietary changes have led to an increase in metabolic disorders. Additionally, exposure to nephrotoxic substances, such as herbal medications and environmental toxins (e.g., insecticides, arsenic, and micorplastics), further exacerbates the CKD burden in this region (Kazancioğlu, 2013). Countries such as Thailand, Indonesia, and the Philippines report rising cases of CKD, primarily attributed to the increasing incidence of diabetes and hypertension. In Thailand, CKD prevalence is around 17.5%, with ESRD cases rising annually (Ingsathit et al., 2010). In Bangladesh, the prevalence of CKD is around 18%, with rates as high as 25% in areas where drinking water is contaminated with arsenic (Argos et al., 2010). In India, the prevalence of CKD among adults is higher (17-21%) in states like Andhra Pradesh and Tamil Nadu due to exposure to toxic substances in agriculture (Liyanage et al., 2015).

The burden of CKD in Africa is substantial, with prevalence estimates ranging from 10% to 15% (Kaze et al., 2018). The major contributing factors include infectious diseases (such as HIV-associated nephropathy), glomerulonephritis, hypertension, and diabetes. The prevalence of CKD is particularly high in sub-Saharan Africa, where limited healthcare infrastructure and high rates of undiagnosed hypertension contribute to a growing epidemic (George et al., 2017). Additionally, genetic factors, such as APOL1 risk variants, have been linked to increased susceptibility to CKD among people of African descent (Freedman et al., 2018).

South America has an increasing prevalence of CKD, with estimates ranging from 12% to 18% in different countries (Gonzalez-Bedat et al., 2015). In Brazil, CKD prevalence is around 11%, with hypertension and diabetes being the leading causes. Similarly, in Argentina and Colombia, CKD prevalence is estimated to be between 10% and 15%, with significant regional disparities in disease burden and access to care. A unique form of CKD, often referred to as CKD of unknown origin (CKDu), has been identified in agricultural communities in Central and South America, particularly in El Salvador, Nicaragua, and Guatemala. This condition primarily affects young male workers in sugarcane fields and is believed to be linked to chronic heat stress, dehydration, and environmental toxins (Gifford et al., 2017).

Thus, the burden of CKD has increased significantly over the past three decades. Between 1990 and 2017, CKD-related mortality increased by 41.5%, making it one of the fastest-growing causes of death globally (Bikbov et al., 2020). The rising incidence of diabetes, hypertension, obesity and aging populations are major contributors to this trend. Additionally, environmental and occupational exposures, particularly in low- and middle-income countries, are further exacerbating the CKD epidemic.

Economic Burden of CKD

Chronic kidney disease imposes a substantial economic burden on healthcare systems worldwide, with costs rising dramatically as the disease progresses. The direct medical expenses increase significantly from early CKD stages to end-stage renal disease (ESRD), largely due to the resource-intensive nature of renal replacement therapies such as dialysis and kidney transplantation (Jha et al., 2023). In high-income countries like the United States and those in Europe, CKD and ESKD account for billions in healthcare expenditures. According to data referenced by the Centers for Disease Control and Prevention, treatment costs for Medicare beneficiaries with CKD reached nearly $87 billion in 2019, with additional expenses for ESRD (CDC, 2024). European studies have similarly highlighted that dialysis, while representing a small fraction of the total CKD population, consumes a disproportionately high share of national healthcare budgets (Kerr et al., 2012; Roggeri et al., 2014). In Australia, Wyld et al. found that CKD patients incur 85% higher healthcare costs than the general population, underscoring the heavy economic impact of managing the disease even in developed health systems (Wyld et al., 2015).

The economic challenges are even more pronounced in low- and middle-income countries. In Southeast Asia, the out-of-pocket costs for kidney transplantation and dialysis are catastrophic relative to average incomes, often driving households into financial crisis (Ramachandran & Jha, 2013). Similarly, the costs associated with hemodialysis and kidney transplantation place a significant strain on the public health system in Brazil (Silva et al., 2016). In China, many patients face catastrophic health expenditures despite widespread insurance coverage that forces families to divert resources from consumption to healthcare savings (Yang et al., 2022).

Definition and Classification of CKD

CKD is defined as an abnormality in the structure or function of the kidneys, which is present for more than three months and affects health. In CKD, the glomerular filtration rate (GFR) drops below 60 ml/min/1.73 m^2. In addition, the rate of albumin excretion in the urine (albuminuria) can be 30 mg or more in 24 hours. CKD is classified into five stages based on the GFR level. In the first stage (stage 1), GFR is almost normal, and in the last stage (stage 5), the kidney function is severely reduced, and dialysis has to be resorted to for sustenance of life. This stage is called end-stage renal disease (ESRD) (Inker et al., 2014).

Risk Factors for CKD

Chronic Kidney Disease is a multifactorial condition influenced by genetic, clinical, environmental, and socioeconomic determinants. Below is an expanded synthesis of key risk factors, supported by peer-reviewed evidence, organized to highlight mechanisms, epidemiological trends, and clinical implications.

- ***Genetic Predisposition***

Genetic factors significantly influence CKD susceptibility. Variants in the APOL1 gene, prevalent in individuals of African ancestry, are strongly associated with CKD progression due to their role in podocyte injury and altered lipid metabolism (Freedman et al., 2018). These risk alleles (G1/G2) confer a 2- to 4-fold increased risk of kidney failure, independent of hypertension or diabetes. Hereditary conditions such as polycystic kidney disease (PKD) and Alport syndrome disrupt renal architecture through cyst formation or collagen defects, accelerating nephron loss (Bergmann et al., 2018).

- ***Aging***

Aging correlates with structural and functional decline in the kidneys, including reduced nephron mass, glomerulosclerosis, and diminished renal blood flow. By age 70, approximately 45% of adults exhibit CKD, compared to 5% in those under 40 (Hallan et al., 2006). Age-related oxidative stress and vascular stiffness further impair the glomerular filtration rate (GFR), exacerbating susceptibility to acute kidney injury (AKI) and CKD progression.

- ***Ethnic and Socioeconomic Disparities***

Ethnic minorities, including African Americans, Hispanics, and Indigenous populations, face disproportionately higher CKD rates. For example, African Americans are 3–4 times more likely to develop kidney failure than White Americans due to genetic (APOL1 variants) and systemic factors such as healthcare inequities and environmental toxin exposure (Norton et al., 2016). Socioeconomic disparities, including limited access to preventive care and nutrient-poor diets, amplify CKD risk in low-income communities (Crews et al., 2019).

- ***Diabetes Mellitus***

Diabetes mellitus drives 30–50% of CKD cases globally. Chronic hyperglycemia induces glomerular hyperfiltration, advanced glycation end-products (AGEs), and oxidative stress, leading to diabetic nephropathy characterized by proteinuria and glomerulosclerosis (Alicic et al., 2017). Poor glycemic control (HbA1c >7%) doubles the risk of CKD progression, with 40% of diabetics developing kidney damage within 10–20 years of diagnosis.

- ***Hypertension***

Uncontrolled hypertension accelerates CKD by inducing glomerular capillary hypertension, endothelial injury, and tubulointerstitial fibrosis. Systolic blood pressure >140 mmHg increases CKD progression risk by 2- to 3-fold (Whelton et al., 2018). The renin-angiotensin-aldosterone system (RAAS) plays a central role, with angiotensin II promoting vasoconstriction and inflammatory pathways.

- ***Obesity and Metabolic Syndrome***

Obesity contributes to CKD through mechanisms such as glomerular hypertrophy, insulin resistance, and chronic inflammation mediated by adipokines (e.g., leptin). A BMI >30 kg/m² elevates CKD risk by 2.7-fold, even after adjusting for diabetes and hypertension (Kovesdy et al., 2017). Visceral adiposity also exacerbates renal hypoxia and fibrosis, compounding kidney damage.

- ***Environmental Toxins***

Exposure to nephrotoxic agents, such as aristolochic acid (found in herbal remedies), cadmium, and lead, is linked to tubulointerstitial nephritis and CKD. Aristolochic acid induces DNA mutations and

interstitial fibrosis, contributing to endemic CKD of unknown origin (CKDu) in agricultural regions (Grollman, 2013). Pesticide exposure in farming communities further elevates CKD risk, particularly in low-income countries.

Microplastics and nanoplastics (MNPs) are emerging environmental pollutants that may contribute to the progression of chronic kidney disease (CKD) through oxidative stress, inflammation, and nephrotoxicity. Studies suggest that MNPs can accumulate in tissues, including kidneys, leading to cellular damage and fibrosis (Prata, 2023). Additionally, MNPs may act as carriers for toxic chemicals and heavy metals, exacerbating kidney injury (Wright and Kelly, 2017). Animal models indicate that prolonged exposure to MNPs disrupts renal function and enhances proteinuria, further implicating their role in CKD pathophysiology (Huang et al, 2022). However, more human-based studies are needed to establish a definitive link between MNP exposure and CKD progression.

- ***Medication-Induced Nephrotoxicity***
  - *NSAIDs:* Inhibit prostaglandin synthesis, reducing renal blood flow and causing ischemic injury. Long-term use increases CKD risk by 32% (Perazella and Rosner, 2022).
  - *PPIs:* Prolonged use is linked to chronic interstitial nephritis, elevating CKD risk by 28% (Xie et al., 2016).
  - *Chemotherapy agents:* Cisplatin and ifosfamide cause tubular necrosis and chronic fibrosis, with 20–30% of cancer survivors developing CKD (Perazella and Rosner, 2022).

- ***Infections***

Chronic infections such as HIV and hepatitis C (HCV) promote CKD through direct viral toxicity, immune complex deposition, and antiretroviral drug nephrotoxicity. HIV-associated nephropathy (HIVAN) is 5–10 times more prevalent in African Americans with APOL1 risk alleles (Jha et al., 2013).

Pathophysiology of Kidney Dysfunction

The kidneys maintain homeostasis through filtration, reabsorption, secretion, and endocrine functions. Disruption of these processes underpins kidney disease progression. Below is an integrated analysis of key pathophysiological mechanisms.

- ***Loss of Nephrons and Hyperfiltration***

The initiation of kidney dysfunction in CKD begins with the loss of functioning nephrons due to injury from various insults (e.g., diabetes, hypertension, glomerulonephritis). As the number of healthy nephrons declines, the remaining nephrons compensate by increasing their filtration rate - a process known as hyperfiltration. While this adaptive mechanism initially preserves overall renal function, the increased glomerular capillary pressure over time results in damage to the glomerular structure. This elevated pressure contributes to mesangial expansion, thickening of the glomerular basement membrane, and ultimately glomerulosclerosis, which further reduces the number of functioning nephrons and sets up a vicious cycle of injury (Anderson et al., 1985).

- ***Glomerular Injury and Proteinuria***

The hyperfiltration-induced injury to the glomeruli is accompanied by increased permeability of the glomerular filtration barrier. Consequently, proteins - primarily albumin—leak into the urine, resulting in proteinuria. Proteinuria is not only a marker of glomerular injury but also an active contributor to further kidney damage. Filtered proteins trigger an inflammatory response in the tubular epithelial cells, leading to the release of cytokines and growth factors that promote fibrosis and further damage the renal parenchyma (Alicic et al., 2017; Hill, 2008). Thus, proteinuria both reflects and accelerates the progression of kidney dysfunction.

- ***Tubulointerstitial Fibrosis***

In response to glomerular injury and proteinuria, the tubulointerstitial compartment becomes increasingly affected. Damaged tubular cells and the influx of filtered proteins stimulate the production of proinflammatory cytokines, including transforming growth factor-β (TGF-β), which is a key mediator in the development of fibrosis. The resultant deposition of extracellular matrix components in the interstitial space leads to tubulointerstitial fibrosis - a process that is strongly correlated with the decline in renal function. Over time, fibrotic tissue replaces normal parenchyma, leading to further loss of kidney function and structural integrity (Alicic et al., 2017; Hill, 2008).

- ***Activation of the Renin–Angiotensin–Aldosterone System and Oxidative Stress***

A central feature in the progression of CKD is the maladaptive activation of the renin–angiotensin–aldosterone system (RAAS). The loss of nephrons and subsequent hyperfiltration contribute to intraglomerular hypertension, which in turn activates RAAS. This activation not only perpetuates systemic hypertension but also directly promotes inflammatory and fibrotic pathways within the kidney. Furthermore, RAAS activation enhances oxidative stress by increasing the production of reactive oxygen species, which further injures renal cells and exacerbates both glomerular and tubulointerstitial damage. Together, these mechanisms drive the progressive decline in renal function and contribute to the systemic complications associated with CKD (Anderson et al., 1985).

- ***Systemic Consequences and Progressive Decline***

The culmination of nephron loss, glomerular injury, tubulointerstitial fibrosis, and RAAS-mediated oxidative stress leads to a gradual, yet inexorable, decline in kidney function. As the kidneys lose their ability to filter waste products, regulate electrolyte balance, and maintain acid–base homeostasis, patients develop uremia and other metabolic disturbances. These systemic consequences not only impair the excretory and endocrine functions of the kidney but also contribute to the high cardiovascular risk and overall morbidity observed in CKD patients.

Long-Term Complications of CKD

1. *Cardiovascular Complications*

Cardiovascular complications in CKD arise from a complex interplay of hemodynamic, metabolic, and inflammatory factors. The reduction in renal function leads to volume overload, hypertension, and anemia, which together increase both preload and afterload on the heart. This chronic burden contributes to left ventricular hypertrophy and eventually heart failure. Overactivation of the renin–angiotensin–aldosterone system and disturbances in calcium–phosphate metabolism further promotes vascular remodeling, atherosclerosis, and vascular calcification. These changes, combined with electrolyte imbalances such as hyperkalemia, predispose CKD patients to arrhythmias and sudden cardiac death, thereby markedly increasing their overall cardiovascular risk (Romagnani et al., 2025).

2. *Metabolic Acidosis and Electrolyte Imbalances*

The kidneys' reduced ability to excrete acid in CKD leads to metabolic acidosis - a chronic state of acid retention that promotes protein catabolism, muscle wasting, and the use of bone minerals as buffers, resulting in further demineralization. Concurrently, impaired potassium excretion often causes hyperkalemia, an electrolyte imbalance that can trigger life-threatening cardiac arrhythmias. These metabolic disturbances worsen the overall metabolic state of the patient and contribute significantly to both cardiovascular and musculoskeletal complications (Chen et al., 2019).

3. *Hematologic Complications*

Anemia is nearly ubiquitous in CKD, largely due to the diminished production of erythropoietin by damaged kidneys. In addition, iron deficiency and chronic inflammation impair red blood cell production by limiting iron availability and suppressing bone marrow function. The resulting anemia reduces the oxygen-carrying capacity of the blood, leading to persistent fatigue and exercise intolerance. Furthermore, reduced

oxygen delivery increases the workload on the heart, exacerbating cardiac strain and contributing to the development of left ventricular hypertrophy and heart (Chen et al., 2019; Thomas et al., 2008).

4. Mineral and Bone Disorders (CKD-MBD)

Disorders of mineral and bone metabolism in CKD, collectively referred to as CKD-MBD, result from a disruption in the homeostasis of calcium, phosphate, parathyroid hormone, and vitamin D. As kidney function declines, the conversion of vitamin D to its active form diminishes, leading to hypocalcemia and compensatory secondary hyperparathyroidism, while impaired phosphate excretion results in hyperphosphatemia. These biochemical derangements contribute to bone demineralization, increasing the risk of fractures and bone pain, and they promote vascular calcification, which further heightens cardiovascular risk. The interrelation of skeletal and vascular abnormalities is a central feature in the increased morbidity observed in CKD patients (Bello et al., 2017b; Thomas et al., 2008).

5. Neurological Complications

Neurological complications in CKD affect both the central and peripheral nervous systems. The accumulation of uremic toxins may lead to cognitive impairments, such as difficulties with concentration, memory, and executive function, and can even progress to vascular dementia. Simultaneously, many patients develop peripheral neuropathy, which manifests as numbness, tingling, and muscle weakness in the extremities. Additionally, autonomic dysfunction may lead to blood pressure instability and other dysregulations. Together, these neurological issues markedly impair daily functioning and overall quality of life in CKD patients (Krishnan & Kiernan, 2009).

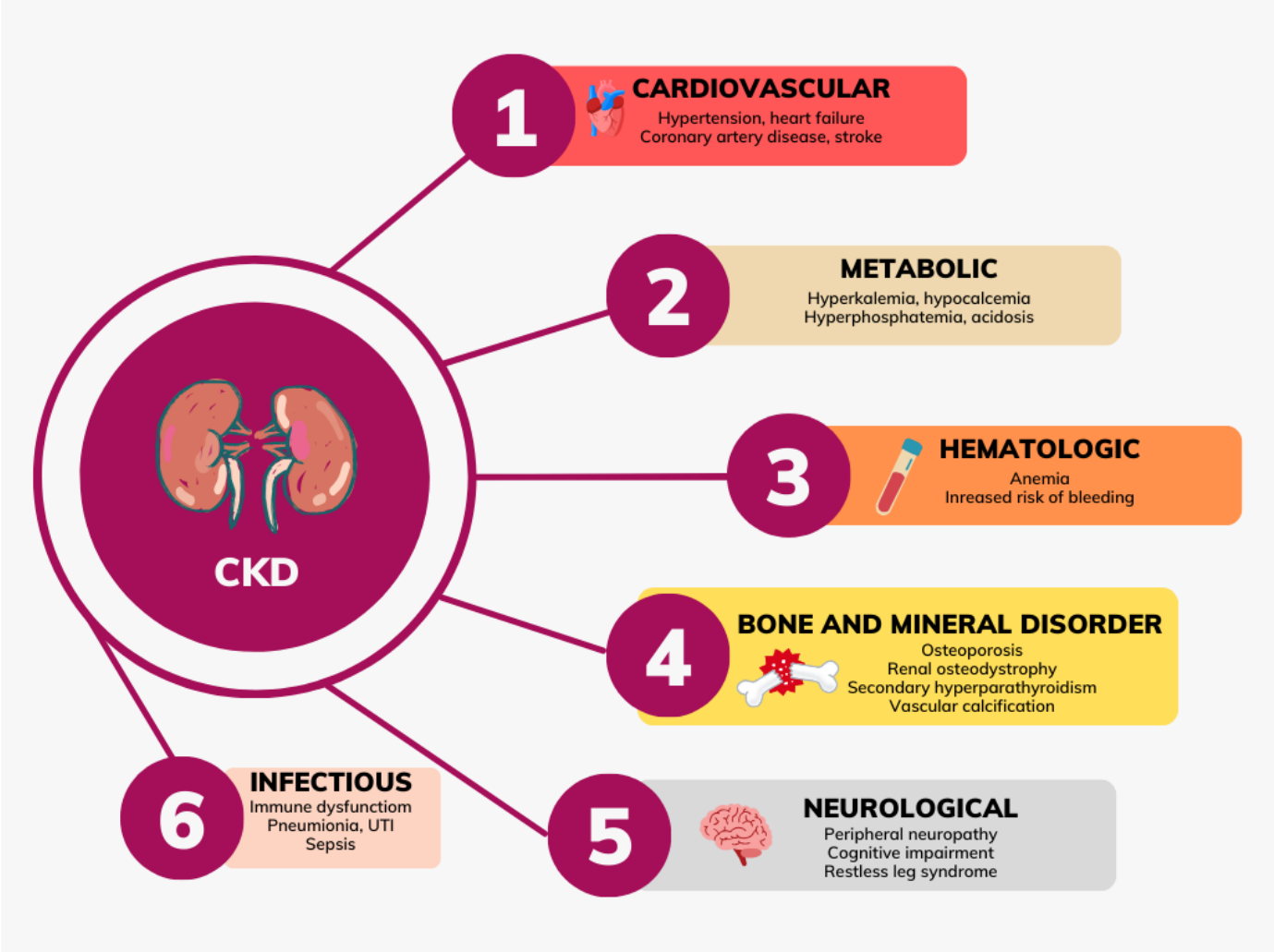

Figure 1. Long-term complications of CKD

6. *Infectious Complications*

Chronic Kidney Disease is associated with a state of immune dysfunction that increases the risk of infections considerably. Uremia and malnutrition impair both innate and adaptive immune responses, making patients more susceptible to infections such as pneumonia, sepsis, and urinary tract infections. These infectious complications occur at rates three to four times higher than in the general population, often resulting in increased hospitalization and a higher risk of mortality. Moreover, suboptimal vaccination rates further exacerbate this susceptibility, underscoring the importance of proactive preventive measures in CKD management (Naqvi & Collins, 2006).

Diagnosis of CKD

The evaluation of CKD involves a systematic approach, including a thorough assessment of the patient's symptoms, laboratory investigations such as blood tests, and imaging techniques such as X-rays, ultrasounds, or CT scans. Timely and accurate diagnosis is essential to mitigate disease progression and prevent complications.

Blood tests

Blood tests are essential for diagnosing CKD and evaluating kidney function. Key blood tests include:

- *Determination of serum creatinine and glomerular filtration rate (GFR)*: High levels of creatinine in the blood are an important indicator of decreased kidney function. GFR is calculated using formulas such as the CKD-EPI equation. A patient with a GFR below 60 mL/min/1.73 m² for three months or more is considered to have CKD. (Inker et al., 2014; Levey et al., 2000) CKD is classified into several stages based on GFR.
- *Blood urea nitrogen (BUN)*: This test measures urea nitrogen in the blood, which is another waste product excreted by the kidneys. High levels of urea nitrogen are another indicator of decreased kidney function.
- *Electrolytes, minerals, and parathyroid hormone (PTH)*: Evaluating the electrolytes (such as sodium, potassium, and chloride) and minerals (such as calcium and phosphorus) in the blood helps identify imbalances resulting from CKD. CKD also increases the amount of PTH, which indirectly helps in diagnosing kidney function (Moe et al., 2007; Palmer, 2020).

Urine tests

Urine tests are crucial for detecting abnormalities that indicate signs of CKD. Important urine tests include:

- *Urinalysis:* This test checks the chemical and microscopic properties of urine. It can detect abnormalities such as the presence of proteins, red blood cells, white blood cells, or casts in the urine, which can indicate kidney damage (Perazella and Rosner, 2022).
- *Urinary albumin creatinine ratio (UACR):* This test measures the amount of albumin compared to creatinine in the urine. High levels of UACR (30 mg/g or more) indicate excessive protein secretion in the urine, which is an indication of kidney damage (Inker et al., 2014).
- *24-hour urine collection:* Kidney dysfunction can be more accurately assessed by collecting 24-hour urine and measuring the total amount of protein excreted in it.

Imaging Studies

- *Ultrasound of the kidney:* It can assess the size, shape, and structure of the kidney. Small kidneys usually indicate chronic damage, while kidneys of increased size may indicate polycystic kidney disease or urinary tract obstruction (O'Neill, 2014).
- *CT scan and MRI:* These tests provide detailed images of structural abnormalities in the kidneys, tumors, or obstructions in the urinary tract (Faubel, 2014).

Kidney Biopsy

A kidney biopsy involves obtaining a small tissue sample from the kidney for microscopic examination. This procedure is performed to diagnose specific kidney diseases, evaluate the extent of renal damage, and guide treatment decisions. It is particularly useful when the underlying cause of chronic kidney disease (CKD) is uncertain, providing a precise diagnosis to facilitate appropriate management (Stevens et al., 2024).

Classification of CKD

CKD is classified based on the glomerular filtration rate (GFR) and the presence of symptoms of kidney damage such as albumin excretion in the urine. This classification helps to understand the severity of the disease and determine the course of treatment. ("Chapter 1: Definition and Classification of CKD," 2013; Inker et al., 2014)

CKD is classified into five stages:

- *Stage 1:* This is the initial stage of the disease, where the GFR is approximately normal (≥90 mL/min/1.73 m²). Kidney damage is characterized by the presence of protein or red blood cells in the urine, or structural abnormalities in the kidneys, despite the almost normal functioning of the kidneys at this stage.
- *Stage 2:* This results in a very small decrease in GFR (60–89 mL/min/1.73 m²)
- *Stage 3:* Moderately low GFR (30–79 mL/min/1.73 m²). This stage is divided into two parts:
  - Stage 3A: GFR 45-59 mL/min/1.73 m²
  - Stage 3B: (stage 3b) GFR 30-44 mL/min/1.73 m²
- *Stage 4:* This severely reduces the GFR (15-29 mL/min/1.73 m²). Kidney function is so reduced during this stage that patients often experience physical symptoms of kidney failure.
- *Stage 5:* At this stage, the kidneys have completely lost their function (GFR <15 mL/min/1.73 m²). It is also known as end-stage renal disease or ESRD, where life is sustainable without dialysis or a kidney transplant.

Treatment of CKD

Treatment of CKD is multifaceted, aimed at delaying the progression of the disease, relieving physical symptoms, and preventing complications. This multifaceted treatment can be done by changing lifestyle and dietary habits, use of medications, dialysis, and kidney transplantation. Below is a detailed description of each aspect.

Lifestyle Changes

- *Change in Diet:* Low sodium foods (2-3 g/day) help control blood pressure and the amount of water in the body. Limiting the intake of protein (0.6-0.8 g/kg/day) helps to keep its performance longer by reducing the workload on the kidneys. To control potassium and phosphorus levels in the blood, it is essential to avoid foods that are high in them (Cupisti et al., 2018; Fouque and Mitch, 2015; Stevens et al., 2024).
- *Physical Activity:* Regular physical exercise increases heart function and reduces obesity, which enhances the overall well-being of CKD patients (Heiwe and Jacobson, 2011).
- *Avoiding Smoking and Drinking:* Smoking accelerates kidney damage. At the same time, excessive drinking can increase high blood pressure and liver dysfunction. Avoiding these two can reduce the rapid deterioration of CKD (Orth and Hallan, 2008).

Pharmacological Management

- *Blood Pressure Control:* ACE inhibitors (e.g. lisinopril) and ARBs (angiotensin receptor blocker, e.g. losartan) are the first-line treatments for high blood pressure in CKD. They reduce protein secretion and deterioration of GFR in the urine. In CKD, it is necessary to keep the blood pressure level below 130/80 mm Hg so that the pressure on the kidneys decreases (Inker et al., 2014; Jafar et al., 2001; Whelton et al., 2018).
- *Glycemic Control: Strict* control of blood sugar levels (Hb A1c<7%) reduces the risk of worsening CKD in diabetics. SGLT 2 inhibitors (such as empagliflozin or canagliflozin) help protect kidneys (Nathan, 2003a; Perkovic et al., 2019).
- *Management of Anemia:* CKD often causes anemia. To combat this, drugs that stimulate the production of red blood cells (erythropoiesis stimulating agent) and iron supplementation are used to treat anemia (Stevens et al., 2024).
- *Bone and Mineral Disorder:* Phosphate binders (such as sevelamer) and vitamin D analogues (such as calcitriol) are used to control high amounts of phosphate and parathyroid hormone in the blood (Cunningham et al., 2011).
- *Diuretic:* Loop diuretic (e.g., furosemide) plays an effective role in controlling the excess of water in the body of CKD patients (Ellison, 2001).

Advanced Therapy

- *Dialysis:* Hemodialysis and peritoneal dialysis are the main life-saving treatments for end-stage renal disease (ESRD). The type of dialysis to be used usually depends on the patient's preference, financial ability, and what other ailments the patient has (Kaplan, 2016).
- *Kidney transplant: A* kidney transplant is the best long-term treatment for CKD. This treatment greatly improves the overall quality of life of the patient compared to dialysis. However, it is very expensive, and the patient has to take immunosuppressive agents after the transplant for the rest of his life (Hart et al., 2020; Wolfe et al., 1999).

Emerging Therapy

- *SGLT2 inhibitors*: Newer drugs such as empagliflozin and dapagliflozin significantly reduce the chances of worsening of CKD and heart disease in both diabetic and non-diabetic patients (Heerspink et al., 2020; Perkovic et al., 2019).
- *GLP-1 receptor agonists*: Liraglutide and semaglutide reduce protein in the urine in diabetic CKD patients (Mann et al., 2017).
- *Anti-fibrotic agent*: Scientists are currently researching a new type of medication, such as pirfenidone, that may help delay the worsening of CKD by slowing the progression of fibrosis (Huang et al., 2023).

Prevention of CKD

CKD can be prevented by applying different strategies. These strategies aim to reduce the incidence of CKD, delay its worsening, and prevent long-term complications.

Primary Prevention: The goal of primary prevention is to reduce the chances of developing CKD by addressing modifiable risk factors and developing healthy habits.

- *Diabetes and High Blood Pressure Control:* Diabetes and high blood pressure are the two main causes of CKD. It is possible to significantly reduce the risk of CKD by strictly controlling blood sugar levels (HbA1c <7%) and blood pressure (<130/80 mm) (Nathan, 2003b; Stevens et al., 2024; Whelton et al., 2018).

- *Healthy Lifestyle:* Avoiding excessive salt, processed foods and saturated fat foods and regular exercise reduce the risk of CKD (Heiwe and Jacobson, 2011).
- *Avoidance of Nephrotoxic Agents:* Limiting the use of NSAIDs and avoiding exposure to environmental toxins (such as heavy metals, insecticides) can prevent kidney damage (Perazella and Rosner, 2022).
- *Avoidance of smoking:* Smoking reduces blood flow to the kidneys by constricting the arteries and accelerates kidney damage. Stopping smoking is essential for preventing CKD (Orth and Hallan, 2008).

Secondary Prevention: This level of prevention aims to detect and treat CKD in at-risk populations to impede disease progression.

- *Screening in high-risk populations:* Regular evaluation of kidney function for people with diabetes, high blood pressure, or a family history of kidney disease helps in the early detection and treatment of CKD. High-risk ethnic groups, such as African Americans and Hispanics, should have this test done regularly because they are more likely to develop kidney disease (Rettig et al., 2008; Stevens et al., 2024).
- *Treatment of associated diseases:* Strict control of blood pressure and blood sugar in patients with diabetes or hypertension hampers the progression of CKD. The use of some modern drugs, such as ACE inhibitors or ARBs, reduces proteinuria and delays the loss of kidney function (Jafar et al., 2001; Stevens et al., 2024; Whelton et al., 2018).
- *Avoiding Nephrotoxic Medications:* Limiting the use of NSAIDs, contrast agents, and other nephrotoxic drugs in high-risk individuals prevents kidney damage (Perazella and Rosner, 2022).

Tertiary prevention: This level of prevention helps prevent complications of CKD and improves quality of life through proper treatment.

- *Prevention of Heart-related Complications:* CKD patients have a higher risk of heart disease. The use of statins, blood pressure control, and a healthy lifestyle reduce the risk of cardiovascular complications and death (Stevens et al., 2024).
- *Prevention of Anemia and Bone Loss:* Rapid treatment of anemia with erythropoiesis-stimulating drugs and iron supplements improves the quality of life of the patient. Phosphate binders and vitamin D analogs reduce bone fragility and prevent vascular calcification (Cunningham et al., 2011; Stevens et al., 2024).

Conclusions

Chronic kidney disease remains a major global health challenge, with significant morbidity and mortality. Without timely intervention, CKD progresses to end-stage renal disease (ESRD), necessitating costly and often inaccessible treatments such as dialysis or kidney transplantation. Early detection and appropriate management, particularly in high-risk populations such as individuals with diabetes and hypertension, are crucial in slowing disease progression and reducing associated cardiovascular risks. The use of renoprotective agents, including ACE inhibitors, ARBs, and SGLT2 inhibitors, are effective in delaying CKD progression and improving clinical outcomes.

However, access to adequate and affordable medical care remains a significant barrier, particularly in low-resource settings, where dialysis and transplantation services are either scarce or prohibitively expensive. Addressing these disparities requires global efforts to improve healthcare infrastructure, enhance early screening programs, and promote cost-effective treatment strategies. Additionally, lifestyle modifications, including smoking cessation, weight management, and optimal control of diabetes and hypertension, play a critical role in CKD prevention. A multidisciplinary approach combining early diagnosis, effective pharmacological interventions, and public health initiatives aimed at lifestyle modifications is essential to

mitigate the burden of CKD. Increased awareness, policy reforms, and equitable healthcare access are imperative to improving outcomes for individuals affected by this disease worldwide.

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