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Early Detection of Chronic Kidney Disease: Current Diagnostic Strategies, Barriers to Timely Recognition, and Emerging Innovations

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ABSTRACT:

Chronic kidney disease (CKD) represents a major and growing global public health challenge, affecting approximately 10–15% of the global population. Characterized by progressive and often irreversible decline in renal function, CKD is associated with increased risks of cardiovascular morbidity, end-stage renal disease (ESRD), premature mortality, and reduced quality of life. Despite the availability of accessible and cost-effective diagnostic tools such as estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (uACR), CKD is frequently detected only at moderate or advanced stages. Delayed diagnosis is largely attributed to the asymptomatic nature of early disease, limitations of conventional biomarkers, inconsistent implementation of screening strategies, and persistent disparities in healthcare access. This review provides an overview of the global burden, etiological factors, staging criteria, and conventional diagnostic approaches in CKD, with particular emphasis on factors contributing to delayed recognition. Structural, educational, and healthcare system related barriers to early detection are examined. Emerging diagnostic approaches including cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and multi-omic biomarker panels are discussed alongside advances in artificial intelligence and predictive risk modeling aimed at improving early identification of kidney injury. Population based evidence demonstrating a high prevalence of undiagnosed stage 3 CKD highlights the need for systematic and proactive screening strategies. Integrating novel biomarkers, digital health technologies, and structured clinical pathways may facilitate a shift from late-stage disease management toward earlier detection, intervention, and prevention.

Keywords: Chronic Kidney Disease (CKD); Early Detection; Diagnostic Biomarkers; Artificial Intelligence; CKD Screening.

1. INTRODUCTION:

1.1 What is CKD?[1]

CKD is defined as abnormalities of kidney structure or function present for more than three months, with implications for health. It is classified according to cause, glomerular filtration rate (GFR) category, and albuminuria category.

Chronic kidney disease (CKD) is diagnosed when either markers of kidney damage or a decreased glomerular filtration rate (GFR) persists for more than 3 months. Markers of kidney damage include one or more of the following: albuminuria (albumin excretion rate [AER] ≥30 mg/24 hours or albumin-to-creatinine ratio [ACR] ≥30 mg/g [≥3 mg/mmol]), urine sediment abnormalities, electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, or a history of kidney transplantation. Additionally, a decreased GFR (≤60 ml/min/1.73 m², corresponding to GFR categories G3a–G5) confirms the diagnosis.

1.2 Global Burden and Prevalence of Chronic Kidney Disease (CKD): [2-4]

Chronic kidney disease (CKD) is a major and growing global health challenge affecting a substantial proportion of the world's population. Current estimates indicate that CKD affects approximately 10–15% of the global population, corresponding to nearly 850 million individuals worldwide, highlighting its widespread prevalence and significant contribution to the global disease burden. This high prevalence places CKD among the most common chronic diseases globally and underscores its importance as a major public health concern.Global estimates further indicate that approximately 843.6 million people were living with CKD in 2017, demonstrating the extensive worldwide distribution of the disease.

CKD affects populations across all regions and continues to represent a substantial portion of the global burden of non-communicable diseases. The magnitude of CKD prevalence worldwide highlights the growing impact of kidney disease on global health systems and populations.Projections suggest that the global burden of CKD will continue to increase in the coming decades. Forecasting studies indicate that by 2040 CKD may become the fifth leading cause of years of life lost globally, reflecting its rapidly rising global impact. These findings highlight the substantial and increasing global burden of CKD, reinforcing the need for greater awareness and prioritization of kidney health at the international level.

Despite its high prevalence, a substantial proportion of patients remain undiagnosed until late stages, when irreversible damage has already occurred. Early detection of CKD is therefore critical to slow disease progression, reduce complications, and improve long-term outcomes.Early detection of kidney disease can lower the chance of developing end-stage renal disease (ESRD) by as much as 50%, according to research. This review focuses on the current strategies for early diagnosis of CKD, highlights the key challenges in implementing these approaches, and discusses emerging technologies and future perspectives.

1.3 Economic Burden and Healthcare Impact of CKD:[4,6]

Apart from its clinical consequences, chronic kidney disease (CKD) has a substantial financial impact on healthcare systems across the globe. Costly renal replacement treatments like dialysis or kidney transplantation are necessary for the management of advanced chronic kidney disease (CKD), especially end-stage renal disease (ESRD). Haemodialysis and peritoneal dialysis are among the most costly long-term treatments in contemporary healthcare because they require ongoing care and specialized medical infrastructure.

CKD has an economic impact that goes beyond immediate medical expenses. Indirect costs to society are significant because patients with CKD frequently have lower work productivity, disability, and early retirement. Furthermore, CKD often coexists with other chronic conditions like diabetes and cardiovascular disease, which raises healthcare costs and utilization.

These financial expenses could be significantly reduced with early CKD diagnosis and treatment. Controlling Blood pressure, improving glycaemic control, and albuminuria reduction can slow the progression of the disease and delay the need for dialysis or transplantation. Consequently, strengthening screening programs, preventive strategies, and early diagnostic tools has been identified as a key priority for healthcare systems seeking to mitigate the long-term impact of CKD.

2. Pathogenesis and Progression of Chronic Kidney Disease: [5-8]

2.1 Etiology of CKD:[5]

There are several causes of chronic kidney disease (CKD) in the world, but the most prevalent ones are:

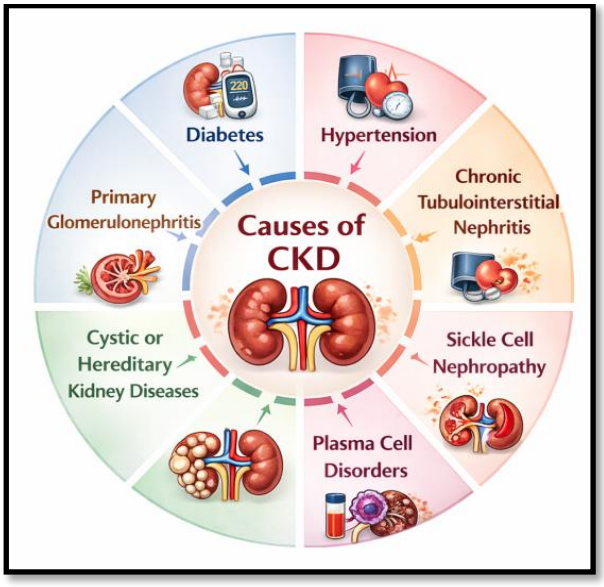

Figure 1: Major etiological factors contributing to chronic kidney disease.

i. **Type 1 and Type 2 diabetes:** Elevated blood sugar affects the kidney's small blood capillaries, decreasing filtration and resulting in the release of protein (albumin) into urine. Kidney failure affects roughly 30% of Type 1 individuals and 10% to 40% of Type 2 patients.

ii. **Hypertension:** High blood pressure reduces filtration by damaging and narrowing renal blood channels. Renal failure may result from a cycle of elevated blood pressure brought on by fluid retention.

iii. **Primary glomerulonephritis:** Prolonged glomerular inflammation results in a progressive decline in kidney function and can develop to end-stage renal disease that necessitates dialysis or a kidney transplant.

iv. **Chronic tubulointerstitial nephritis:** Renal function irreversibly declines as a result of interstitial fibrosis and tubular shrinkage brought on by ongoing inflammation.

v. **Cystic or hereditary kidney diseases:** Kidney failure may result from fluid-filled cysts that hinder the kidneys' capacity to filter blood or sometimes it may be hereditary.

vi. **Plasma Cell Disorders:** Proteinuria, renal insufficiency, and occasionally tubular dysfunction are caused by plasma cell diseases, such as myeloma.

vii. **Sickle Cell Nephropathy:** Recurrent vaso-occlusion, hypoxia, hemolysis, and anemia-related alterations damage kidney structure and function in sickle cell nephropathy, which leads to chronic kidney disease (CKD).

2.2 Pathophysiology of Chronic Kidney Disease[5,9]

Chronic kidney disease is characterized by the progressive and irreversible loss of functional nephrons, which initiates a cascade of adaptive and maladaptive processes within the remaining renal tissue. In early CKD, compensatory hyperfiltration occurs in surviving nephrons, leading to increased intraglomerular pressure and enhanced single-nephron glomerular filtration rate. Although initially adaptive, sustained hyperfiltration promotes glomerular hypertension, endothelial dysfunction, and structural damage to the glomerular basement membrane. Over time, persistent hemodynamic stress and metabolic injury stimulate inflammatory and profibrotic pathways, including activation of transforming growth factor-β (TGF-β) and other cytokines, resulting in extracellular matrix accumulation, tubulointerstitial fibrosis, and glomerulosclerosis. Progressive fibrosis ultimately reduces functional renal mass, further exacerbating nephron loss and accelerating decline in glomerular filtration rate. This self-perpetuating cycle contributes to the gradual progression from early, often asymptomatic disease to advanced CKD and eventual end-stage renal disease.

2.3 Stages and Clinical Classification of CKD[7-9]

The estimated glomerular filtration rate (eGFR), a blood test that measures renal filtration capacity, is used to categorize chronic kidney disease (CKD) into five stages (1–5). At every stage, kidney function gradually deteriorates, necessitating various therapies to mitigate the harm. Renal replacement therapy, such as hemodialysis, peritoneal dialysis, or kidney transplantation, is necessary to maintain life in cases of kidney failure.

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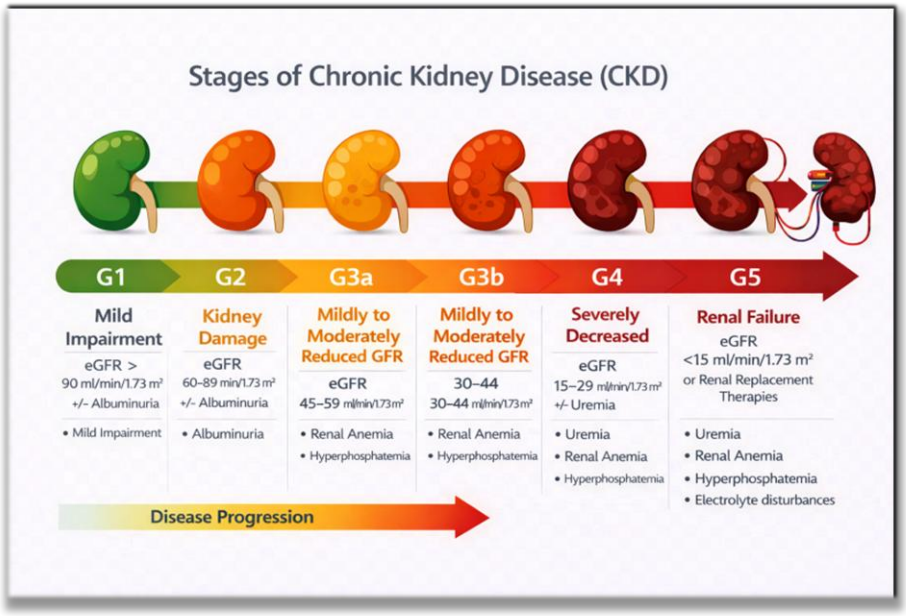

Figure 2: Staging of CKD based on eGFR categories.

Stage 1:

Mild illness with few symptoms. Proteinuria, microalbuminuria, or ultrasonography abnormalities could be present; frothy urine could happen. In diabetes, management include individualized blood pressure control according to current hypertension guidelines, consuming no more than 2300 mg of salt per day, and maintaining adequate glucose control.

Stage 2:

Little impairment with diminished functionality. One of the symptoms could be frothy urine. Weight loss, a balanced diet, quitting smoking, getting enough sleep, managing stress, and, for the right patients, taking drugs like ACE inhibitors, ARBs, SGLT2 inhibitors, or Kerendia are the main goals of management.

Stage 3:

Moderate damage accompanied by symptoms.

3a (45–59): dry or itchy skin, appetite loss, weight loss, polyuria or oliguria.3b (30–44): peripheral edema, peripheral neuropathy, shortness of breath, cramping in the muscles, and poor focus. Renal bone disease and anemia are possible complications. Iron, calcium/vitamin D, diuretics, and statins are possible forms of treatment.

Stage 4:

Severe impairment accompanied by a higher risk of consequences, including metabolic acidosis, anemia, hypertension, bone disease, hyperkalemia, hyperphosphatemia, and cardiac dysrhythmia. Hematuria, ammonia breath, back pain, and insomnia are possible symptoms. Erythropoiesis-stimulating therapies for anemia, avoiding nephrotoxic medications, and restricting protein, phosphate, and potassium are all part of management.

Stage 5:

End-stage renal disease is known as kidney failure. Dyspnea, pruritus, chest discomfort, nausea, vomiting, restless legs, bruises, hiccups, seizures, and coma are some of the symptoms of uremia. Dialysis or a kidney transplant is necessary for treatment.Cardiovascular events, higher mortality, and a lower quality of life are all linked to chronic kidney disease.

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3. Methods of Diagnosing CKD:[11-13]

The diagnosis of chronic kidney disease (CKD) is based on the evaluation of kidney function and the presence of structural or functional abnormalities. Core diagnostic measures include estimation of glomerular filtration rate (eGFR) using serum creatinine and assessment of urine albumin-to-creatinine ratio (uACR) to detect albuminuria, with abnormalities persisting for at least three months confirming CKD. Additional investigations, such as imaging studies and emerging biomarkers, may further aid in determining disease severity and etiology. The different methods used in diagnosing CKD are explained below.

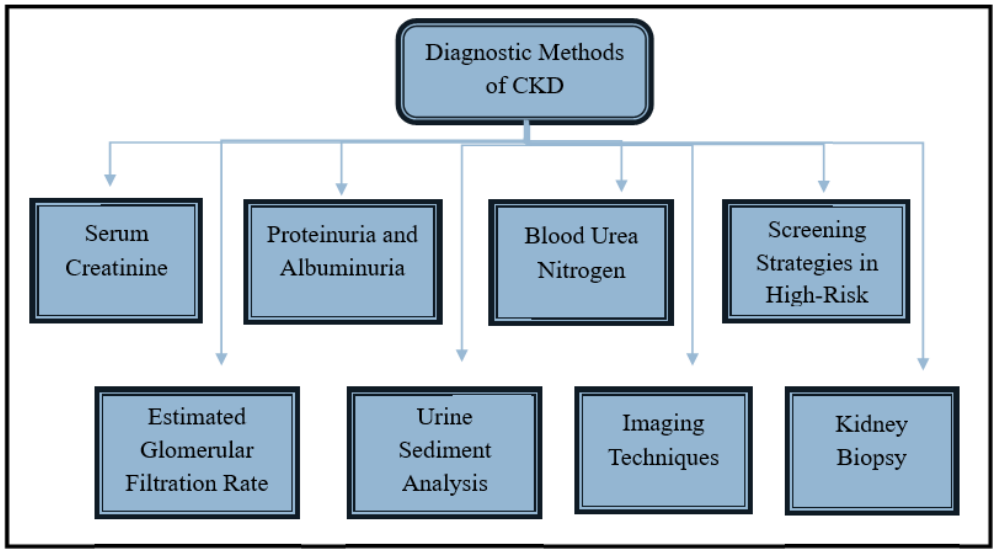

Figure 3: Overview of major diagnostic methods used in CKD detection, including laboratory markers, imaging techniques, and screening strategies for high-risk populations.

3.1 Serum Creatinine

One frequently measured biochemical indicator used to assess renal function is serum creatinine. Serum creatinine is one of the most commonly used laboratory markers for assessing renal function in clinical practiceand represents the kidneys' ability to remove metabolic waste products from the blood.Its widespread use is largely attributed to its low cost and broad availability. However, the sensitivity of serum creatinine levels for identifyingearly renal disease may be limited by variations in muscle mass, age, sex, and dietary variables.

3.2 Estimated Glomerular Filtration Rate(eGFR)

Estimated glomerular filtration rate provides a quantitative measure of renal filtration capacity and constitutes a central parameter for diagnosing and staging CKD. It allows evaluation of total renal function and is mostly computed from serum creatinine levelseGFR is a cheap, readily available, and practical way to track kidney function over time. Variability in creatinine's non-renal determinants can impair eGFR calculations and, in some patient populations, theaccuracy of the diagnosis.

3.3 Proteinuria and Albuminuria

The urine albumin-to-creatinine ratio (UACR), which is commonly used to measure albuminuria, is a crucial indicator of early kidney impairment and a significant predictor of the course of the disease and cardiovascular risk.

Albuminuria is particularly useful for early diagnosis since it can identify kidney damage before a noticeable drop in eGFR takes place. However, albuminuria testing is not always done in routine practice, and if repeated testing is not done to confirm the results, temporary elevations brought on by things like exercise, infection, or fever could result in false-positive results.

3.4 Urine Sediment Analysis and Urinalysis

A routine part of the clinical assessment for suspected CKD is urinalysis. It makes it possible to detect hematuria, protein excretion, and anomalies in urine sediment. These results aid in the diagnostic evaluation and offer proof of structural or functional renal damage.

3.5 BUN (Blood Urea Nitrogen)

The kidneys' capacity to eliminate nitrogenous waste products from the blood is assessed by measuring blood urea nitrogen. It is frequently measured together with serum creatinine when evaluating renal excretory function in a lab setting.

3.6 Imaging Techniques

Renal ultrasound is one imaging modality that can be used to detect structural abnormalities such as congenital malformations, asymmetry, blockage, or decreased kidney size. Imaging is useful in identifying the underlying cause of chronic kidney disease (CKD), but it is not a good stand-alone technique for early diagnosis due to its low sensitivity for identifying early functional abnormalities. It also helps detect structural causes such as obstruction, cysts, or changes in kidney morphology. Instead of being used for routine screening, advanced imaging techniques are mostly employed in specific instances.

3.7 Screening Strategies in High-Risk Populations

An efficient method for early CKD identification is targeted screening of high-risk groups, such as those with diabetes, hypertension, cardiovascular illness, a family history of CKD, or advanced age. It has been demonstrated that screening, which usually consists of eGFR evaluation and albuminuria testing, can detect CKD earlier than opportunistic testing alone. Nonetheless, there are still issues because of inconsistent implementation, limited awareness, variable access to healthcare, and lack of standardized screening protocols across healthcare systems.

3.8 Kidney Biopsy

When the cause of chronic kidney disease (CKD) is unknown or specific disease characterization is needed, kidney biopsies are characterized as a diagnostic procedure. In certain situations, itfacilitates conclusive diagnosis and staging and offers direct histopathological assessment of renal tissue.

4. Conventional Approaches vs Emerging Approaches:

Conventional diagnostics for chronic kidney disease (CKD) rely on serum creatinine, eGFR, proteinuria, and imaging like renal ultrasound, but they often detect disease late due to influences like muscle mass and variability. Emerging approaches use biomarkers such as NGAL, KIM-1, cystatin C, and multi-omics with AI for earlier, more precise detection.

Table 1: Comparison of Conventional and Emerging Diagnostic Approaches in Chronic Kidney Disease.

Aspect	Conventional Approaches	Emerging Approaches
Examples	Serum creatinine, eGFR, BUN, urine albumin/protein (ACR), renal ultrasound	NGAL, KIM-1, cystatin C, suPAR, multi-biomarker panels, AI models, CEUS/SWE
Detection Timing	Late-stage; normal until significant damage (e.g., creatinine insensitive early on)	Early-stage; detects tubular injury before eGFR decline (e.g., NGAL rises in hours)
Sensitivity/Specificity	Low sensitivity for early CKD; affected by age, muscle mass, diet	Higher sensitivity/specificity; less confounded (e.g., cystatin C independent of muscle mass)
Invasiveness	Mostly non-invasive (blood/urine tests, ultrasound)	Non-invasive (urine/serum biomarkers, imaging advances)
Limitations	Variable (hydration, comorbidities); poor for progression prediction	Assay standardization needed; limited routine availability
Clinical Utility	Standard staging, widely available, cost-effective	Risk stratification, prognosis, personalized medicine

While these conventional and emerging diagnostic approaches provide essential tools for CKD identification, their real-world impact remains limited by multifaceted barriers that hinder timely early detection, as explored next.

5. Barriers to Early CKD Diagnosis:[14-19]

A complex issue resulting from biological, diagnostic, healthcare system, and socioeconomic factors is the delayed identification of chronic kidney disease (CKD). In contrast to many acute illnesses, chronic kidney disease (CKD) develops gradually over years, and standard diagnostic instruments are not sensitive enough to detect early structural damage. Under-recognition is further exacerbated by inequities in healthcare access, inconsistent screening implementation, and low patient and healthcare provider awareness. A significant percentage of patients are only detected atmoderate to advanced stages, when permanent nephron loss has already taken place, as a result of several interrelated circumstances. The major barriers contributing to delayed CKD diagnosis are outlined below:

5.1 Asymptomatic Nature of Early CKD

- **Slow progression:** CKD usually doesn't show any symptoms until it's late (usually when GFR drops below ≈25 mL/min/1.73 m²). In fact, people frequently do not seek medical assistance because they feel good despite significant kidney impairment.

- **Widespread unawareness:** Surveys reveal that the great majority of those impacted by CKD are ignorant because the disease is silent in its early stages.Many individuals remain unaware of their condition because early CKD is clinically silent. Without overt signs, chronic kidney disease sometimes goes unnoticed until it is discovered by accident or through consequences.

5.2 Conventional biomarker's limitations

- **Development of CKD biomarkers throughout time:** Serum creatinine and creatinine-based eGFR are the cornerstones of conventional CKD diagnosis. These markers miss early disease because they are influenced by age, sex, and muscle mass and only increase after severe nephron loss.

- **Low creatinine/eGFR sensitivity:** Serum creatinine levels may remain normal until about 50% of function is lost. CKD is already mild when eGFR (based on creatinine) is less than 60 mL/min/1.73 m². As a result, many common tests are not sensitive enough in the beginning.

- **Underutilized protein markers:** The urine albumin to creatinine ratio (uACR)is frequently overlooked despite being a reliable early sign of kidney impairment. For example, only about 53% of diabetic patients in real-world U.S. data had a urine albumin test within a year. Many cases of early CKD, which are frequently accompanied by albumin urea, go undiagnosed if this test is skipped.

- **Emerging biomarkers not currently in use:** Studies have found multi-omics techniques and novel markers (cystatin C, NGAL, KIM-1, etc.) that can identify harm earlier. They haven't been extensively accepted or incorporated into therapeutic practice, though. Reliance on indicators that date back decades effectively postpones the early detection of CKD.

5.3 Insufficient monitoring and screening

- **Low screening rates:** Many high-risk individuals remain unscreened in spite of explicit guidance. Less than 25% of individuals with type 2 diabetes in a sizable U.S. cohort underwent all of the required yearly CKD testing. This delays diagnosis because most at-risk people are never formally examined.

- **Inadequate assessment:** Even in cases where laboratory testing is conducted, it is frequently insufficient. According to one study, only about 52.9% of diabetics had their urine albumin levels checked during a one-year follow-up. Early cases of CKD are undetected when serum and urine testing are not performed.

- **Lack of population programs:** Because of logistics and cost, no nation has widely used CKD screening for the general public. Typically, recommendations are restricted to high-risk populations (such as those with diabetes or hypertension), although even these focused screenings are underutilized. Instead of using regular programs, CKD testing frequently depends on opportunistic inspections in practice.

5.4 Education and awareness gaps

- **Patient unawareness:** There is very little public awareness about CKD. Only 10–20% of persons with early or moderate chronic kidney disease (CKD) are aware that they have a kidney issue, according to surveys. Patients do not request screening or assistance if they are unaware of the hazards associated with CKD or the necessity of testing.

- **Knowledge gaps among providers:** According to qualitative research, PCPs frequently have concerns about managing CKD and whether to refer patients. They might not stay up to date with new tests and changing guidelines, or they might undervalue the significance of early diagnosis. For instance, PCPs de-prioritize CKD screening due to a general "lack of time and resources" and feeling "overwhelmed" by conflicting demands.

- **Misaligned perceptions:** Misaligned clinical perceptions persist in certain settings, where early or mild chronic kidney disease (CKD) is frequently regarded as a normal consequence of aging rather than a pathological condition warranting medical evaluation. This conceptualization contributes to under-recognition and under-diagnosis of stages 1–3 CKD, which are often perceived by general practitioners as poorly defined or clinically ambiguous entities.

5.5 Inequalities in healthcare resources and access

- **Diagnostic access gaps:** Basic CKD testing may not be available, particularly in low- and middle-income nations. Only around one third of primary care settings in resource constrained nations were able to monitor blood creatinine, and quantitative proteinuria tests were much less common, according to the ISN Global Kidney Health Atlas. Access gaps are present even in high-income nations (for example, only about 58% of primary care facilities have urine albumin-creatinine tests). Many people are unable to receive any testing at all because to these shortages.

- **Insurance and financial obstacles:** Exorbitant out-of-pocket expenses discourage screening and follow-up. Due to cost, patients frequently skip lab testing in areas lacking universal coverage. In certain systems, healthcare professionals are forced to select more urgent tests since their fixed lab funds are insufficient to cover recommended CKD panels. Thus, CKD recognition is delayed for patients with poor incomes or inadequate insurance.

❖ **Case Study: Population-Level Evidence of Underdiagnosed CKD[20]**

A population-based cross-sectional analysis from the Tabari Cohort Study in Iran evaluated the prevalence of diagnosed and undiagnosed stage 3 CKD among 10,255 adults aged 35–70 years. Stage 3 CKD (eGFR 30–59 mL/min/1.73 m^2) was identified in 25.6% of participants. Notably, 98.1% of affected individuals were unaware of their condition, while only 1.9% had received a prior diagnosis. These findings highlight a substantial burden of unrecognized CKD and underscore the limitations of current screening strategies focused primarily on high-risk populations.

Collectively, these findings reinforce the urgent need for systematic, proactive, and risk-based screening approaches capable of identifying CKD prior to irreversible nephron loss.

6. Future Strategies for Early Detection of Chronic Kidney Disease:[37-41]

Identifying Chronic Kidney Disease in its early stages is difficult because conventional diagnostic indicators often reveal kidney impairment only after considerable structural harm has taken place. Currently, the diagnosis of CKD mainly depends on serum creatinine levels, estimated glomerular filtration rate (eGFR), and albuminuria, which highlight alterations in kidney filtration instead of initial cellular damage. Consequently, significant loss of nephrons may happen before these markers show any abnormalities.

As a result, extensive research has concentrated on creating new biomarkers, utilizing multi-omics methods, and designing artificial intelligence–driven prediction models that can detect kidney injury at earlier phases and enhance risk assessment.

6.1 Emerging Biomarkers for Early CKD Detection

Recent research has pinpointed various novel biomarkers that indicate early injury to the renal tubules and inflammation before any observable changes in glomerular filtration rates.

6.1.1 Neutrophil Gelatinase-Associated Lipocalin (NGAL)

NGAL is among the most extensively researched biomarkers for early kidney damage. It is quickly released by injured tubular epithelial cells and neutrophils following renal damage. Increased levels of NGAL in urine or plasma can be detected within hours after kidney injury and could act as an early signal of CKD advancement.

Research has illustrated that NGAL concentrations rise noticeably prior to traditional markers like creatinine, highlighting its potential for early identification and monitoring of renal damage.

6.1.2 Kidney Injury Molecule-1 (KIM-1)

KIM-1is a glycoprotein that spans the membrane, found in proximal tubular epithelial cells after kidney damage occurs. In healthy kidneys, its expression is low, but it significantly increases following tubular injury.

The levels of KIM-1 detected in urine are associated with the degree of tubular damage and could assist in differentiating early chronic kidney disease (CKD) from other renal disorders. Numerous studies have shown that it serves as a sensitive biomarker for identifying early kidney injury and tracking disease progression.

6.1.3 Cystatin C

Cystatin C is a low molecular weight protein that is reabsorbed in renal tubules after being freely filtered by the glomerulus. It is a more accurate indicator of early renal dysfunction than creatinine since its levels are less affected by age, diet, or muscle mass. Before creatinine levels rise, elevated serum cystatin C concentrations may indicate subtle changes in glomerular filtration, allowing for the early detection of renal impairment.

6.1.4 Other Emerging Biomarkers

In addition to NGAL, KIM-1, and cystatin C, several other biomarkers are being investigated for early CKD diagnosis, including:

- N-acetyl-β-D-glucosaminidase (NAG)
- Liver-type fatty acid-binding protein (L-FABP)
- β2-microglobulin
- soluble urokinase plasminogen activator receptor (suPAR)
- microRNAs and extracellular vesicles

These biomarkers reflect different pathophysiological pathways such as inflammation, oxidative stress, and tubular damage, potentially enabling a multimarker approach for early CKD detection.

Table.2: Emerging and novel biomarkers for early detection of kidney dysfunction, highlighting their pathophysiological significance and potential role in identifying subclinical renal injury prior to overt decline in eGFR.

Biomarker	Biological Role	Early Detection Value
Cystatin C	A more sensitive marker of GFR than creatinine	Detects early kidney dysfunction, less affected by muscle mass.
NGAL (Neutrophil Gelatinase-Associated Lipocalin)	It is released by damaged tubular cells	Rises early after injury; signals kidney damage before eGFR drop.
KIM-1 (Kidney Injury Molecule-1)	Marker of tubular injury	Sensitive to early injury and progression.
β-Trace Protein & other novel proteins	Alternative functional markers	Under study; may improve early risk assessment.
Urine microRNAs & proteomic panels (e.g., CKD273)	Molecular signatures of early damage	Can identify at-risk individuals even before clinical CKD.

6.2 Multi-Omics Technologies in Early CKD Detection

Advances in multi-omics technologies, including proteomics, metabolomics, and transcriptomics, have expanded the understanding of CKD pathogenesis and biomarker discovery. These approaches analyze large datasets of proteins, metabolites, and gene expression patterns to identify molecular signatures associated with early kidney injury.

Multi-omics strategies may allow clinicians to detect CKD before structural damage becomes irreversible, thus facilitating early intervention and personalized treatment strategies.

6.3 Artificial Intelligence and Machine Learning Approaches

Artificial intelligence (AI) and machine learning algorithms are increasingly being applied to healthcare data for disease prediction and early diagnosis. By analyzing electronic health records, laboratory results, and imaging data, AI models can identify complex patterns associated with CKD risk.

Recent studies have demonstrated that machine learning models such as random forests, support vector machines, and deep neural networks can predict CKD onset with higher accuracy than traditional statistical models. These predictive systems can help clinicians identify high-risk individuals and initiate preventive interventions earlier in the disease course.

6.4 Future Perspectives

Despite promising advances, most emerging biomarkers and AI-based diagnostic tools are still under clinical validation. Large-scale longitudinal studies are required to establish their sensitivity, specificity, and cost-effectiveness before routine clinical implementation.

Future diagnostic strategies may combine biomarkers, multi-omics profiling, and AI-basedrisk prediction models to enable precise, early detection of CKD and personalized patient management.

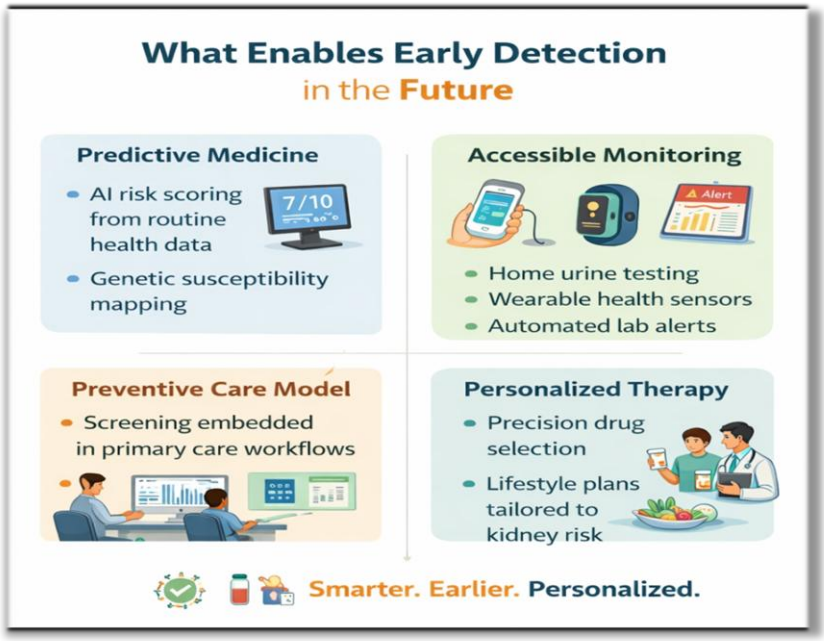

Figure 4: Conceptual model of future CKD detection pathways.

Building on these future pathways for early CKD diagnosis, the following section illustrates the broader paradigm shift in CKD detection from reactive, late-stage identification to proactive, prevention-oriented strategies.

7. Evolution of Diagnostic Paradigm Shift in Chronic Kidney Disease: [1,28-30]

Chronic kidney disease diagnosis has traditionally relied on functional markers such as estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (uACR), which often detect disease only after significant nephron loss. Emerging biomarkers, multi-omics technologies, and artificial intelligence–based models are enabling earlier identification of kidney injury. This shift represents a transition from late-stage detection toward proactive and predictive diagnosis of CKD.

Table.3: Evolution of CKD detection from reactive late-stage diagnosis to proactive prevention-oriented strategies.

Stage	Past (Traditional Pattern)	Present (Transition Era)	Future (Early-First Model)
Disease Onset	Kidney damage begins silently (no symptoms)	Risk awareness improving but screening inconsistent	Risk prediction before damage (AI + genetics + data)
Care Seeking	Patients seek care only when symptoms appear: -Fatigue -Swelling -Reduced urine	Targeted screening in high-risk groups: -Diabetes -Hypertension -Family history	Routine population screening integrated into primary care: -Wearables & home testing -Continuous monitoring
Testing Pattern	Lab testing ordered late: -Creatinine only -No urine albumin	Earlier lab panels used: -eGFR -uACR	Real-time kidney function tracking Biomarker panels Digital alerts
Treatment approach	Treatment = damage control -Dialysis planning -Transplant referral	Treatment = slow progression -BP + glucose control -RAAS inhibitors	Preventionfocused care: - Personalized therapy - Lifestyle precision plans
Outcome	High cost + high mortality	Improved outcomes	CKD largely preventable or delayed

8. Limitations and Challenges:

Although several emerging biomarkers and advanced technologies demonstrate promise for earlier detection of CKD, many remain in the research phase and have not yet been widely implemented in routine clinical practice. Challenges include limited assay standardization, variability in biomarker performance across populations, and high costs associated with advanced diagnostic platforms. Additionally, the integration of artificial intelligence–based predictive models requires robust clinical validation and careful consideration of ethical and data governance issues. Addressing these limitations will be essential to translate emerging innovations into effective population-level screening strategies.

9. Conclusion:

Chronic kidney disease remains substantially underdiagnosed worldwide, particularly during its early and potentially reversible stages. Although CKD is well-defined and diagnosable using accessible laboratory parameters, reliance on late-changing biomarkers, inconsistent screening of high-risk populations, limited awareness among patients and providers, and systemic healthcare inequities contribute to delayed detection. The consequences of late diagnosis are profound, leading to irreversible kidney damage, increased cardiovascular complications, higher healthcare costs, and reduced survival.

Emerging biomarkers and multi-omics approaches demonstrate promising potential to identify kidney injury before substantial functional decline occurs. In parallel, advances in machine learning, risk prediction algorithms, and integrated electronic health systems may enable proactive identification of individuals at risk for CKD. However, translation of these innovations into routine clinicalpractice requires standardized validation, cost-effectiveness analyses, and equitable implementation strategies.

Ultimately, improving CKD outcomes requires a transition from reactive late-stage management to proactive, prevention-oriented detection and care.Strengthening risk-based screening, enhancing education and awareness, integrating novel diagnostics, and addressing disparities in healthcare access are critical steps toward achieving earlier detection and reducing the global burden of chronic kidney disease and improving long-term patient outcomes.

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