**A REVIEW OF CHRONIC KIDNEY DISEASE**

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**Abstract**

Chronic kidney disease (CKD) is distinguished by a persistent impairment of kidney structure or function lasting over three months (e.g., with albuminuria of 30 mg per 24 hours or a glomerular filtration rate [GFR] of 60 mL/min/1.73 m2). In developed nations, diabetes and hypertension are the primary causes of CKD. However, awareness of early-stage CKD is reported by less than 5% of affected individuals. Globally, CKD ranks as the sixteenth largest cause of premature death and is intricately linked to systemic diseases such as cardiovascular disease and end-stage renal disease. Diagnosing CKD involves a comprehensive approach, including a thorough patient history, cutting-edge risk assessment through Glomerular Filtration Rate testing, and Albuminuria testing. Treatment strategies may involve the use of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, and preventive measures include avoiding potential nephrotoxins, such as non-steroidal anti-inflammatory drugs, and monitoring albuminuria.

**Keywords:** Chronic Kidney diseases, GlomerularFiltrate Rate, Albuminuria, Angiotensin Converting Enzyme Inhibitors, Angiotensin II Receptors, , Hypertension, Anti-Inflammatory Medications.

1. **Introduction**

Chronic kidney disease (CKD), affecting approximately 8% to 16% of individuals globally, is frequently underreported, both by patients and medical professionals [1-4]. The determination of CKD prevalence relies on criteria such as a glomerular filtration rate (GFR) below 60 mL/min/1.73 m², albuminuria exceeding 30 mg in a 24-hour period, or the presence of kidney damage symptoms like persistent hematuria, along with anatomical abnormalities such as polycystic or dysplastic kidneys persisting for more than three months [5]. Notably, CKD is more prevalent in low- and middle-income countries than in high-income ones [6]. Recent professional guidelines recommend adopting a risk-based approach for the management and assessment of CKD [4].

1. **Methods**

This concerns chronic renal failure, and up until April 2019, an investigation was carried out in the Medline and PubMed databases using various terms related to chronic renal insufficiency. These terms encompassed epidemiology, incidence, prevalence, occurrence, diagnosis, assessment, identification, screening, workup, etiology, causes, management, treatment, intervention, therapy, and prevention. The search focused on scholarly papers, guidelines, and human studies published in English. The initial search yielded 998 publications, including clinical trials, meta-analyses, practice recommendations, and systematic reviews. Subsequently, the search criteria were expanded to include review papers, observational research, such as cross-sectional studies, and more recent publications identified in the reference lists of the located articles. All clinical studies addressing the treatment or prevention of CKD were considered, irrespective of study size or the age of the patient population.

1. **Clinical presentations**

Regular screening with urine and serum chemical profiles often leads to the inadvertent or routine discovery of chronic renal disease. Other symptoms that patients may suffer include nocturia, flank pain, extensive haematuria, "foamy urine" (which is a sign of albuminuria), nocturia, or decreased urine production. Dyspnea, peripheral edema, fatigue, low appetite, nausea, vomiting, metallic taste in the mouth, inadvertent weight loss, itching, and mental abnormalities are further signs of severe chronic kidney disease (CKD).

When evaluating an individual with confirmed or suspected chronic kidney disease (CKD), medical professionals should investigate additional symptoms that might indicate a urinary obstruction (such as urinary hesitancy, urgency, or frequency, or incomplete bladder emptying) or a systemic cause (such as hemoptysis, rash, lymphadenopathy, hearing loss, neuropathy) [7].

This entails taking into account whether they have ever been exposed to substances that could be harmful to the kidneys, such as chemotherapy, nonsteroidal anti-inflammatory drugs (NSAIDs), bowel preparations with phosphate, herbal remedies with aristolochic acid, bowel preparations with phosphate, and herbal remedies without aristolochicacid.The presence of other medical conditions like hypertension, diabetes, autoimmune disease, or chronic infections, a family history of kidney disease, and any known genetic risk factors like sickle cell trait, if this information is available, are additional factors to take into account [11,15].

A thorough physical examination is crucial for assessing the patient's volume status, providing valuable insights into the underlying etiology of chronic kidney disease (CKD). Signs indicative of volume overload may be associated with decompensated heart failure, liver failure, or nephrotic syndrome, while symptoms of volume depletion may arise from inadequate oral intake, vomiting, diarrhea, or excessive urine output. Arterial-venous nicking or retinopathy observed during an eye examination suggests the potential presence of chronic hypertension or diabetes. Patients with abdominal or carotid bruits may have renovascular disease. Considerations for flank pain or kidney enlargement should include obstructive uropathy, nephrolithiasis, pyelonephritis, or polycystic kidney disease. Neuropathy, less frequently caused by amyloidosis, diabetes, and vasculitis, may be present. Skin signs such as rash, visible purpura, cryoglobulinemia, vasculitis, systemic lupus erythematosus, and acute interstitial nephritis should also be taken into account [7].

1. **STAGING**

Chronic kidney disease (CKD) is characterized by the prolonged presence of structural and functional abnormalities in the kidneys, lasting for a duration exceeding three months. These abnormalities may manifest through various indicators, including a glomerular filtration rate (GFR) below 60 mL/min/1.73 m², albuminuria (urine albumin levels below 30 mg per 24 hours or a urine albumin-to-creatinine ratio [ACR] below 30 mg/g), anomalies in urine sediment, histological or imaging evidence suggestive of kidney damage, renal tubular disorders, or a history of kidney transplantation [5].

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Figure 1 : Testing For CKD

After CKD has been identified, the next step is to stage the condition, which is dependent on GFR, albuminuria, and the underlying etiology .GFR is staged as shown in the figure 1.

Additionally, it is crucial to assess patients for any risk factors that could lead to kidney disease, such as prior exposure to chemicals that could affect the kidneys for instance, [5, 7, 11].

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Figure 2 : GFR categories & Albuminuria Categories

Ideally, the evaluation of albuminuria should include the measurement of urine albumin-to-creatinine ratio (ACR). Albuminuria is classified into three stages: A1 (urine ACR <30 mg/g), A2 (30-300 mg/g), and A3 (>300 mg/g) as depicted in Figure 2. The use of urine protein-to-creatinine ratio for staging CKD is discouraged according to five guidelines. This is because urine ACR assays are more likely to be standardized and exhibit better precision, particularly at lower levels of albuminuria. Due to significant biological variation in daily urine albumin excretion, the most accurate results are obtained from measurements taken from the first morning sample or a 24-hour collection [5,8,9]. Nevertheless, initial screening can also utilize random urine samples, and urine ACR is considered a more sensitive and specific indicator for assessing glomerular disease compared to urine protein-to-creatinine ratio.

Urine protein electrophoresis or testing for the particular protein (such as immunoglobulin heavy and light chains, 1-microglobulin, and 2-microglobulin) may be pursued if tubular or overflow proteinuria is predicted. For every CKD patient, imaging using a kidney ultrasonography to evaluate morphology and rule out urinary blockage should be considered.The two basic criteria used to categorize the etiology of CKD are the location of anatomic abnormalities and the existence or absence of systemic illness. Systemic diseases include those that affect other organs in addition to the kidney, such as diabetes, autoimmune disorders, cancer, persistent infections, and genetic ailments. The classifications used to classify anatomic locations are vascular, tubulointerstitial, glomerular, and cystic/congenital illnesses [5].

1. **REDUCING RISK OF CARDIOVASCULAR DISEASES**

Individuals diagnosed with CKD display a markedly elevated prevalence of cardiovascular disease compared to those without CKD. For instance, among a Medicare 5% sample, 65% of the 175,840 individuals aged 66 or older with CKD had cardiovascular disease, whereas only 32% of those without CKD presented with this condition. Importantly, the presence of CKD is linked to more unfavorable cardiovascular outcomes. In the same population, individuals with CKD demonstrated lower 2-year survival rates for various conditions, including coronary artery disease (77% vs. 87%), acute myocardial infarction (69% vs. 82%), heart failure (65% vs. 76%), atrial fibrillation (70% vs. 83%), and cerebrovascular accident/transient ischemic attack (73% vs. 83%) [10]. Actively supporting initiatives aimed at smoking cessation is crucial.

1. **MANAGEMENT OF HYPERTENSION**

Recommendations often involve algorithms for determining the appropriate pharmacological treatment of hypertension in CKD patients [12, 15]. It is crucial to assess the presence and severity of albuminuria. In adults with diabetes and a urine albumin-to-creatinine ratio (ACR) of at least 30 mg per 24 hours or in any adult with a urine ACR of at least 300 mg per 24 hours, it is advisable to consider the blockade of the renin-angiotensin-aldosterone system using either an ACE inhibitor (ACE-I) or an angiotensin II receptor blocker (ARB) [5, 11, 12]. Typically, dual therapy involving both an ACE-I and an ARB is avoided due to the associated risks of hyperkalemia and acute renal damage [5, 11, 16].

1. **MANAGEMNT OF DIABETES MELLITUS**

Effective diabetes management is critically important. Initially, maintaining control over blood sugar levels can impede the progression of CKD; most recommendations propose targeting a hemoglobin A1c level below 7.0%. Secondarily, it might be necessary to adjust dosages for oral hypoglycemic medications. As a general guideline, drugs primarily cleared by the kidneys (such as glyburide) should be avoided, while drugs metabolized by the liver and/or partially cleared by the kidneys (e.g., metformin and certain DPP-4 and sodium-glucose cotransporter-2 [SGLT-2] inhibitors) may require dose reduction or discontinuation, particularly when the estimated glomerular filtration rate (eGFR) falls below 30 mL/min/1.73 m² [11, 14].

1. **NEPHROTOXINS**

All people with CKD should be advised to stay away from nephrotoxins. The scope of this study does not extend to a full list, but a few stand out. Especially for individuals receiving ACE-I or ARB therapy, routine NSAID use in CKD is not recommended [5,11].

1. **DRUG DOSING**

Pharmaceuticals that frequently require dose reductions include most antibiotics, direct oral anticoagulants, insulin, pregabalin, gabapentin, oral hypoglycemic medicines, chemotherapy agents, and opiates. Patients with acute renal injury, eGFR less than 30 mL/min/1.73 m², or ESKD should refrain from using gadolinium-based contrast agents due to the risk of developing nephrogenic systemic fibrosis, a debilitating condition characterized by significant skin and occasionally other organ fibrosis. The most effective preventive measure may still be complete avoidance of gadolinium. Gadoteridol, gadobutrol, and gadoterate are examples of more recent macrocyclic chelate formulations that are far less likely to cause nephrogenic systemic fibrosis. It is essential to inform the patient about the potential risk of developing nephrogenic systemic fibrosis if gadolinium injection is deemed necessary. Consultation with a nephrologist may be considered to discuss the possibility of post-exposure hemodialysis [5,11].

1. **DIETARY MANAGEMENT**

The use of dietary therapy to prevent the onset of CKD is a topic of debate due to conflicting results from significant trials. In the MDRD trial, involving 840 patients and examining two levels of protein restriction, it was observed that a low-protein diet only exhibited a decelerated rate of GFR reduction during the initial four months. It is worth noting that a very low-protein diet was not recommended, yet it demonstrated a notable association with a reduced rate of GFR decline when compared to a low-protein diet. Although the subgroup was relatively small, those with proteinuria exceeding 3 g per day appeared to benefit from both levels of protein restriction. As per the KDIGO guidelines, protein intake should be limited to less than 0.8 g/kg per day for adults with CKD stages G4 to G5 and less than 1.3 g/kg per day for all adult CKD patients at risk of disease progression. It's important to weigh the potential advantages of dietary protein restriction against the risks of malnutrition or the development of protein wasting syndrome [5,17].

1. Top of Form
2. **MONITORING OF ESTABLISHED CKD AND TREATMENT OF COMPLICATIONS**

If CKD is identified, the KDIGO recommendations suggest the surveillance of albuminuria and eGFR at least once a year. Patients at high risk should undergo these assessments at least twice a year, and those at extremely high risk (as illustrated in Figure 2) should have them at least three times a year. The chronic kidney disease (CKD) stage dictates the frequency of screening and evaluation for laboratory abnormalities, encompassing assessments such as complete blood count, basic metabolic panel, serum albumin, phosphate, parathyroid hormone, 25-hydroxyvitamin D, and lipid panel (Table 1) [5].

**Table.1 Screening, Monitoring, and Management of the Complications of Chronic Kidney Disease (CKD)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Complication** | **Relevant Tests** | **Frequency of Repeat Testing** | **Management** |
| Hyperkalemia | Serum potassium | At baseline and as needed | Dietary insufficient in potassium, treatment of hyperglycemia and acidemia, and thought of potassium binders |
| Metabolic acidosis | Serum bicarbonate | At baseline and as needed | For various levels that are consistently below 22 mmol/L, oral bicarbonate supplementation (such as sodium bicarbonate, baking soda, or sodium citrate/citric acid) is necessary. |
| Cardiovascular disease | Lipid panel | At baseline and as needed | Patients with CKD under the age of 50 should take low- to moderate-dose statins.  Statin therapy for those between the ages of 18 and 49 who have CKD, coronary artery disease, diabetes, a history of ischemic stroke, or who are at high risk of myocardial infarction or cardiovascular mortality |

The initial treatment protocols typically involve dietary limitations and the prescription of supplements. Patients with hyperkalemia should be advised by primary care physicians to adhere to low-potassium diets, while those with hyperphosphatemia should follow low-phosphorus diets. Considering the association between long-term metabolic acidosis and an increased rate of CKD progression, individuals with chronically low serum bicarbonate levels below 22 mmol/L should be considered for oral bicarbonate supplementation [5,11].

1. **REFERRAL TO A NEPHROLOGIST AND KIDNEY REPLACEMNT THERAPY**

When an individual's eGFR falls below 30 mL/min/1.73 m2 (stage G4) or their urine ACR climbs above 300 mg per 24 hours (stage A3), the KDIGO guidelines state that they should be referred to a nephrologist [5]. An emergency nephrologist examination and the potential for nephrotic syndrome should be triggered by albuminuria of more than 2200 mg per 24 hours.

Other conditions include glomerulonephritis with uncontrolled hypertension despite the use of four or more antihypertensive medications and glomerulonephritis with red blood cell casts evident in the microscopic features of the urine. Anemic conditions with over 20 red blood cells per high-power field of unknown cause necessitate erythropoietin replacement. Examples of such conditions encompass recurrent or significant kidney stones, hereditary kidney disease, or acute kidney failure.

Primary care physicians should search for reversible causes because even modest increases in serum creatinine (such as moving from 0.7 mg/dL to 1.2 mg/dL) in individuals without CKD indicate significant decreases in eGFR. Kidney biopsy is indicated, among other things, by the presence of rapid or inexplicable reduction in GFR and abnormally shaped red blood cells or cellular casts in urine sediment [5]. Otherwise, dialysis treatment is started for patients who show signs of volume overload (pulmonary or lower extremity edema), electrolyte abnormalities (hypokalaemia or metabolic acidosis), uremic symptoms (nausea, vomiting, poor appetite, metallic taste, pericardial rub or effusion, asterixis, or altered mental status), or both that are resistant to medical management. [5–11]

1. **CONCLUSION**

Chronic renal disease affects 8% to 16% of the global population and stands as a prominent cause of mortality. To effectively manage CKD, it is essential to mitigate cardiovascular risk, attend to albuminuria, steer clear of potential nephrotoxic substances, and make necessary adjustments to medication dosages. Additionally, patients require ongoing monitoring for CKD-related complications, including hyperkalemia, metabolic acidosis, anemia, and other metabolic irregularities. Primary care physicians play a pivotal role in the accurate identification, staging, and referral of CKD patients to alleviate the global burden associated with this condition.

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