Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 2s, https://carcinogenesis.com/

"Chronic Kidney Disease: A Comprehensive Review of Pathophysiology, Diagnosis, and Management"

Dr. Vinay Gaurav[1], Dr. Jyoti Yadav[2], Dr. Savita Kumari[3]

[1]M.B.B.S.,NIMS University Jaipur

Email ID : Vinnaayyyyy333@gmail.com

[2]M.B.B.S.,NIMS University Jaipur

Email ID : Jyotiiyadavv10@gmail.com

[3]M.B.B.S., School of Medical Sciences & Research (SMS&R), Sharda University

Email ID : Kumarisavita200897@gmail.com

Corresponding author:

Dr. Vinay Gaurav

M.B.B.S.,NIMS University Jaipur

ABSTRACT

Chronic kidney disease (CKD) is a chronic disorder defined by persistent abnormalities in kidney structure or function that have serious health effects, such as increased cardiovascular morbidity and mortality and the ultimate need for renal replacement treatment. Globally, the prevalence of CKD is large and increasing, owing to an ageing population and increased rates of diabetes, hypertension, and obesity. Pathophysiology reveals a final common process that includes nephron loss, maladaptive repair, inflammation, oxidative stress, and fibrosis. KDIGO's CGA (Cause-GFR-Albuminuria) framework remains the norm for diagnosing kidney disease, which is characterized by lower glomerular filtration rate (GFR) and/or kidney damage markers (mostly albuminuria) lasting at least 3 months. Management consists of risk-factor modification (blood pressure and glycemic control, lifestyle), disease-modifying pharmacotherapy (RAAS blockade, SGLT2 inhibitors, and mineralocorticoid receptor antagonists in selected patients), complication treatment, and timely preparation for renal replacement therapy when indicated. Recent trials have extended disease-modifying possibilities while also refining blood-pressure targets and monitoring systems. This review outlines current knowledge of CKD epidemiology, pathophysiology, diagnosis, and evidence-based management, highlighting research and implementation objectives-

Keywords: *Chronic kidney disease, CKD, eGFR, albuminuria, KDIGO, SGLT2 inhibitors, RAAS inhibitors, fibrosis, inflammation*

How to Cite: Dr. Vinay Gaurav, Dr. Jyoti Yadav, Dr. Savita Kumari, (2025) "Chronic Kidney Disease: A Comprehensive Review of Pathophysiology, Diagnosis, and Management", *Journal of Carcinogenesis*, *Vol.24, No.2s*, 1117-1123

1. INTRODUCTION

Chronic Kidney Disease (CKD) is a chronic disorder characterized by persistent structural or functional abnormalities of the kidneys that last three months or longer and have serious health consequences. A sustained reduction in glomerular filtration rate (GFR) and/or evidence of kidney damage such as albuminuria, urinary sediment abnormalities, electrolyte disturbances due to tubular dysfunction, imaging-detected structural abnormalities, or a history of kidney transplantation are the most common indicators of CKD.[1] Because the kidneys play critical roles in waste elimination, fluid and electrolyte balance, acid-base homeostasis, endocrine function (including erythropoietin and vitamin D activation), and blood pressure management, CKD has far-reaching systemic implications.

Chronic kidney disease (CKD) affects hundreds of millions of people globally and is a primary cause of morbidity and mortality. KD, also known as chronic renal failure (CRF), describes all degrees of reduced kidney function, ranging from damaged-at-risk to mild, moderate, and severe chronic kidney failure[2]. A patient is diagnosed with CKD when their

estimated glomerular filtration rate (eGFR) falls below 60 ml/min per 1.73 square meters for three months or more. It typically advances silently until later stages and is strongly associated with diabetes, hypertension, cardiovascular disease, and aging. The clinical and public-health effects include increased cardiovascular risk, decreased quality of life, high healthcare expenditures, and the necessity for dialysis or transplantation in end-stage kidney disease (ESKD). Recent international guidelines and landmark randomized studies have transformed CKD care, particularly with the introduction of sodium-glucose co-transporter-2 (SGLT2) inhibitors as renal-protective medicines for a wide variety of patients. This review combines guideline recommendations with recent findings to provide clinicians and researchers with an up-to-date, practical summary.[3]

Methods (Search strategy for this review)

We conducted a targeted literature search (until September 29, 2025) using PubMed and KDIGO to find high-quality materials on CKD epidemiology, pathophysiology, diagnosis, and management. Search phrases include "chronic kidney disease prevalence" , "KDIGO CKD guideline" , "CKD pathophysiology fibrosis inflammation" , "SGLT2 inhibitors CKD DAPA-CKD EMPA-KIDNEY" , or "CKD diagnosis eGFR albuminuria" . Priority was given to international guidelines (KDIGO), large randomized trials (e.g., DAPA-CKD, EMPA-KIDNEY), systematic reviews/meta-analyses, and recent authoritative studies on mechanisms. The main sources utilized are referenced throughout. (A non-systematic narrative synthesis was conducted; this is not a conventional systematic review or meta-analysis.)

Etiology of CKD

1. Diabetic Nephropathy (Most Common Cause Worldwide)

The kidney's filtration units are full of tiny blood vessels. High blood sugar levels might cause these arteries to constrict and clog over time. When there is insufficient blood, the kidneys are damaged, and albumin gets through these filters and ends up in the urine, where it shouldn't be. Chronic hyperglycemia affects the glomeruli and renal microvasculature. Causes proteinuria, glomerulosclerosis, and a gradual reduction in GFR.[4]

2. Hypertensive Nephrosclerosis

High blood pressure can constrict and weaken blood vessels throughout the body, including the kidneys. The constriction causes a reduction in blood flow. If the blood arteries in your kidneys are damaged, they may cease to work correctly. When this happens, the kidneys fail to eliminate all waste and excess fluid from the body. Extra fluid in the blood arteries raises blood pressure even higher, triggering a deadly cycle that can lead to renal failure. Long-term uncontrolled hypertension causes vascular and glomerular damage. This results in ischemia, interstitial fibrosis, and tubular atrophy.[5]

3. Glomerular Diseases

Chronic glomerulus inflammation causes long-term kidney damage and functional impairment. Chronic renal disease is characterized as kidney damage or impaired function for three months or more. Chronic kidney disease can lead to end-stage renal disease, necessitating dialysis or a kidney transplant.

4. Polycystic Kidney Disease & Other Genetic Disorders

Autosomal dominant polycystic kidney disease (ADPKD).Alport syndrome, Fabry disease, and other inherited nephropathies.

5. Chronic Tubulo-interstitial Diseases

GFR is lowered in acute TIN because to interstitial edema, lymphocyte and plasma cell infiltration, and impaired tubular function. The decrease in GFR in chronic TIN is driven by interstitial fibrosis rather than edema. If acute interstitial inflammatory reactions are continued, extracellular matrix accumulation can induce irreversible renal function impairment, including interstitial fibrosis and tubular atrophy. Chronic pyelonephritis, reflux nephropathy, and obstructive uropathy. NSAIDs, lithium, and heavy metals can all cause nephropathy.[6]

6. Obstructive Uropathy

Prolonged obstruction due to:

Kidney stones Benign prostatic hyperplasia (BPH)

Ureteric strictures or malignancy

7. Environmental & Lifestyle Factors

Chronic painkiller abuse (analgesic nephropathy). Heavy metals (lead and cadmium). Smoking, obesity, a high-salt diet, and dehydration all contribute indirectly.

Epidemiology and burden

Global prevalence estimates vary by population and methodology, but systematic reviews and global burden studies show that CKD affects a sizable proportion of the global population and that prevalence and related mortality have increased in recent decades. The global prevalence of all-stage CKD is estimated to be between 9 to 13%, with greater rates in older populations and those with diabetes and hypertension. CKD has significant regional and socioeconomic variations in prevalence, access to care, and outcomes. The condition imposes significant costs on health systems and families, and disparities in access to dialysis and transplantation persist in low- and middle-income nations.[7]

Pathophysiology: from injury to progressive kidney failure

Compared to other well-perfused arterial beds like the heart, liver, and brain, the rate of renal blood flow roughly 400 ml/100 g of tissue per minute is noticeably higher. Renal tissue is more likely to be exposed to dangerous drugs or agents when they are in circulation[8]. CKD is caused by a variety of main insults that share common processes of progressive nephron loss, such as diabetic nephropathy, hypertensive nephrosclerosis, glomerulonephritides, polycystic kidney disease, and obstructive uropathy.

Hyperfiltration and hemodynamic stress: When the number of surviving nephrons decreases, the remaining nephrons hyperfilter, raising intraglomerular pressure and encouraging sclerosis.

Inflammation and immune activation: Chronic inflammation is one of the main factors driving progression, and tissue damage is sustained by persistent inflammatory signals (innate and adaptive immunity).

Oxidative stress and mitochondrial dysfunction: Tubular damage and interstitial fibrosis are caused in part by reactive oxygen species and compromised antioxidant responses.

Maladaptive repair and fibrosis: Interstitial fibrosis and permanent loss of functional renal parenchyma are caused by extracellular matrix deposition and fibroblast/myofibroblast activation.

Cellular senescence and metabolic reprogramming: Tubular epithelial cells undergo maladaptive changes that impair regenerative capacity.[9]

These processes interact, and many treatment approaches focus on fibrosis, inflammation, and maladaptive hemodynamics. Recent mechanistic reviews emphasize the importance of tubular damage and the NF-κB, TGF-β, and Nrf2 pathways in the pathogenesis.

Stages of CKD

Five phases and six categories, ranging from 1 to 5, can be used to categorize chronic kidney disease. The estimated glomerular filtration rate (eGFR), a blood test, is used to determine the stages of chronic kidney disease (CKD). An estimated glomerular filtration of 90 or above and progressive renal involvement lasting longer than three months are characteristics of stage 1 kidney disease. An absolute measure of the kidneys' ability to filter extra fluid from blood is the estimated glomerular filtration rate (10). The kidneys' function gradually declines at each stage of chronic kidney disease (CKD), necessitating various treatments to minimize kidney damage and prolong kidney function. A patient with renal failure will need to go on renal replacement therapy such as hemodialysis, peritoneal dialysis, or renal transplant to sustain life [11].

Stage 1

Since there are no notable clinical symptoms to treat stage 1 CKD, it is regarded as moderate. GFR is 90 milliliters per minute. This stage is regarded as mild. It might have proteinuria, a condition in which glomeruli permit protein to flow into the urine. Microalbumin in the urine or ultrasonography can occasionally reveal alterations. Patients frequently complain of having foamy urine, which is brought on by an excess of urine albumin[12].

Stage 2

The kidneys will be operating at their best with 20–40% normal function, even though the damage is still regarded as minor. GFR is between 60 and 89 ml/min. Foamy pee is still one of the symptoms. Losing weight and thinking about a healthy diet are suggested lifestyle changes. A few conservative management strategies are suggested to slow the progression of stage 2 CKD. It is advised that obese patients use exercise to reduce their weight. Giving up smoking can help lower blood pressure and lessen renal strain. Blood pressure will also be impacted by encouraging the patient to manage stress and get adequate sleep. It is advised that diabetic people take medications that can reduce the progression of chronic kidney disease (CKD), such as ACE inhibitors, angiotensin II receptor blockers (ARBs), sodium-glucose cotransporter 2 (SGLT2) inhibitors, or Kerendia.[13]

Stage 3

The patient will have symptoms at this point that show sufficient damage to cause symptoms. This occurs when the kidneys reach 15% of their usual function. Stage 3 falls into one of two categories: 3a or 3b. GFR 45–59 mL/min indicates mild-to-moderate renal function loss in stage 3a, while GFR 30–44 mL/min indicates moderate-to-severe kidney function loss in stage 3b. At this stage, renal osteodystrophy and anemia may have developed in a CKD patient [14].

Stage 4

The kidneys are moderately to severely damaged at this point, with an eGFR of 15–29 mL/min. Disease complications such as anemia, hypertension, bone disease, and metabolic acidosis have significantly increased. Additionally, there will be hyperphosphatemia and hyperkalemia, which cause cardiac dysrhythmia. Patients may have microscopic or extensive hematuria, ammonia breath odor, sleeplessness, and chronic lower back discomfort. Treatment is required at this point, which includes dietary changes to help patients who are protein-restricted. A low-potassium and low-phosphate diet will reduce the risk of electrolyte imbalance complications. Avoid nephrotoxic medications, including insulin, statins, cephalosporins, proton pump inhibitors, and nonsteroidal anti-inflammatory medicines (NSAIDs). We can use erythropoiesis-stimulating agents (ESAs) to address low hemoglobin levels.[15]

Stage 5

The most concerning stage of CKD is stage 5, when the patient has renal failure with an eGFR of less than 15 milliliters per minute. At this point, GFR falls to fewer than 15 mL/min, and End-Stage Renal Disease (ESRD) is diagnosed if only 10% of the residual kidney is present. Uremia, in which the waste product builds up in the blood, is linked to stage5. Dyspnea, pruritus, chest discomfort, nausea, vomiting, restless legs syndrome, hiccups, seizures, and coma are all symptoms that the patient will encounter.[16] Dialysis, either hemodialysis or peritoneal dialysis, or a kidney transplant will be part of the treatment at this point.

Screening for CKD

Given that most patients with CKD are asymptomatic, screening may be important to early detection of disease.[17] A kidney profile test created by the National Kidney Foundation measures urine ACR in addition to serum creatinine for determining GFR. Many clinical practice guidelines support a risk-based approach to screening, with screening being advised for individuals over 60 or with a history of diabetes or hypertension. 18–20 Individuals with clinical risk factors, such as autoimmune disease, obesity, kidney stones, recurrent UTIs, decreased kidney mass, exposure to certain medications like lithium or NSAIDs, and previous acute kidney injury episodes, should also be screened (Box). Randomized clinical trials, however, have not shown that screening asymptomatic patients for CKD leads to better results.[18]

Other Risk Factors for CKD

Food insecurity, low income, low education, and nonwhite race are some of the sociodemographic characteristics that raise the risk of chronic kidney disease. Pacific Islanders and African Americans are far more likely to develop ESKD than white people. This is partly because obesity, diabetes, and hypertension are more common.[19] But genetics probably plays a part as well. More precisely, risk alleles in the apolipoprotein L1 (APOL1) gene may raise the hereditary risk of kidney disease in a recessive fashion. 7,8: Compared to people with 0 or 1 risk allele, those with 2 APOL1 risk alleles (found in roughly 13% of African Americans) have a 2-fold increased risk of developing chronic kidney disease (CKD) and a 29-fold increased risk of developing certain CKD etiologies, such as focal-segmental glomerulosclerosis and HIV-associated nephropathy.[20] An elevated risk of kidney illness has also been linked to sickle cell trait, which affects about 8% of African Americans. Sickle cell trait carriers are 1.8 times more likely to experience incident chronic kidney disease (CKD), 1.3 times more likely to experience a reduction in eGFR of more than 3 mL/min/1.73 m2, and 1.9 times more likely to experience albuminuria..[21]

Evaluation and diagnostic approach

Initial assessment

History and examination: risk factors (autoimmune illness, diabetes, hypertension, family history), drugs (nephrotoxins), symptoms related to the urinary system, and systemic disease.

Baseline labs: serum creatinine and eGFR, lipid profile, glycemic indices, hemoglobin, electrolytes, calcium/phosphate, PTH if necessary, and urine ACR.

Urinalysis and imaging: renal ultrasound to evaluate size or obstruction, certain serologic tests (autoimmune serologies), kidney biopsy if the diagnosis is ambiguous, or urine for hematuria or protein.[22]

Management- principles and evidence-based interventions[23,24,25,26]

General principles

Goals:

(1) Slow development of CKD

(2) Lower the risk of cardiovascular disease

(3) Address problems (e.g., electrolyte imbalances, acidosis, mineral bone disease, anemia).

(4) get ready for renal replacement therapy if necessary.

Individualized evaluation of the patient's values, comorbidity, and etiology is necessary for management.

Nonpharmacologic interventions

Lifestyle: lowering salt intake (KDIGO recommends limiting sodium), controlling weight, getting regular exercise, quitting smoking, and consuming protein in moderation depending on stage and nutritional condition.

Medication review: Nephrotoxins (NSAIDs, some radiocontrast exposures, and some herbal medicines) should be avoided or stopped.

Blood pressure control

Lowering blood pressure slows the course of CKD and cardiovascular events. To balance the benefits and dangers, the KDIGO 2021 BP guideline suggests personalized objectives with urine albumin ≥30 mg/day and systolic blood pressure typically <120 mmHg using standardized measurement in many patients with CKD (especially in frail/elderly patients). For patients with albuminuria, RAAS inhibitors (also known as ACE inhibitors or ARBs) are the first line of treatment.

Glycemic management in diabetes

Microvascular problems are decreased by strict glycemic control. SGLT2 inhibitors have become important renoprotective medicines in diabetic CKD, and metformin is typically taken with eGFR thresholds and dose modifications (see below). GLP-1 receptor agonists are taken into consideration when required and may have weight and cardiovascular benefits. Adjust glycemic goals according to comorbidities and life expectancy.

Renin–angiotensin–aldosterone system (RAAS) blockade

In proteinuric CKD (especially in diabetics and many non-diabetic proteinuric etiologies), ACE inhibitors or ARBs decrease albuminuria and limit the disease's progression. Keep an eye on potassium and creatinine levels; a sudden increase of up to 30% after starting may be tolerated but needs to be monitored. Recent studies have demonstrated context-dependent renal and cardiovascular advantages of mineralocorticoid receptor antagonists (finerenone) in diabetics with chronic kidney disease.

SGLT2 inhibitors - paradigm shift

SGLT2 inhibitors (dapagliflozin, empagliflozin) have been shown in large randomized controlled studies (DAPA-CKD, EMPA-KIDNEY, and others) to lower the risk of cardiovascular events and the progression of CKD in patients with and without diabetes, as well as across a broad range of eGFR. These medications decrease albuminuria, moderate the drop in eGFR, and diminish kidney-related death, sustained reduction in eGFR, and composite outcomes of kidney replacement therapy. According to updated guidelines, many CKD patients should use SGLT2 inhibitors in addition to RAAS blocking when necessary. Track the risk of genital infections and volume status.

Other pharmacologic therapies

SGLT2 + RAAS combination: complementary mechanisms.

Nonsteroidal mineralocorticoid receptor antagonists (e.g., finerenone): evidence of improved cardiovascular and renal outcomes in a subset of patients with diabetic kidney disease.

Bicarbonate therapy: to treat CKD's metabolic acidosis (which in certain situations may halt its progression).

Anemia management: In order to balance thrombotic risk, erythropoiesis-stimulating drugs and iron therapy (oral/IV) are used for symptomatic anemia or severe hemoglobin reduction.

Phosphate and PTH control: PTH-modulating techniques, vitamin D analogs, and phosphate binders are used to treat CKD-mineral bone disease in accordance with recommended thresholds.

When to initiate dialysis or transplant evaluation

In cases of increasing CKD (often G4–G5) or when problems or eGFR decline indicate an impending need, consult a dialysis or transplant planning specialist. Results are enhanced by prompt vascular access creation, transplant evaluation, and instruction on available modalities (hemodialysis, peritoneal dialysis). Access to RRT equity is still a global concern.

Complications and their management[27]

CKD has many systemic complications that require proactive management:

Cardiovascular disease: primary cause of death in CKD; vigorous management of blood pressure, cholesterol, volume, and the use of cardioprotective drugs (SGLT2i, RAAS inhibitors) as necessary.

Anemia: Assess your iron levels and adjust your treatment to meet your specific Hb goals.

Acid-base disorders: When metabolic acidosis persists, treat it with oral bicarbonate, for example.

Electrolyte disturbances: RAAS dosage adjustments, potassium binders, and dietary changes may all be part of the

therapy of hyperkalemia.

Mineral bone disorder: Track PTH, calcium, and phosphate levels and treat in accordance with KDIGO guidelines.

Biomarkers, imaging, and future diagnostics

In order to enhance early identification, prognostication, and precision medicine, researchers are investigating novel biomarkers (such as NGAL, KIM-1, and urinary proteomics), genomic risk profiling, and imaging advancements in addition to eGFR and albuminuria. Most are still in the research stage, though; additional validation and cost-effectiveness information are needed for clinical use. [28]

Implementation challenges and health equity

In order to enhance early identification, prognostication, and precision medicine, researchers are investigating novel biomarkers (such as NGAL, KIM-1, and urinary proteomics), genomic risk profiling, and imaging advancements in addition to eGFR and albuminuria. Most are still in the research stage, though; additional validation and cost-effectiveness information are needed for clinical use.[29]

2. DISCUSSION

This research article explores the complex terrain of chronic kidney disease (CKD), providing a thorough examination of its various facets. We have learned a great deal about the intricate interactions between genetic, environmental, and lifestyle factors that lead to the development of chronic kidney disease (CKD) by carefully examining its underlying causes, diagnostic standards, and progression. The explanation of the several stages of chronic kidney disease (CKD) also highlights the significance of early detection and intervention, as well as the possibility of taking preventive action to slow the progression of this silent but widespread ailment. The careful examination of various treatment approaches, such as medication and lifestyle changes, reveals how CKD therapy is changing and the encouraging opportunities for bettering patient outcomes. A comprehensive approach to patient care becomes a key topic as we traverse the complex web of consequences linked to chronic kidney disease (CKD), which includes anything from metabolic changes to cardiovascular problems. The necessity of a cooperative and patient-centered approach is highlighted by the use of interdisciplinary approaches, including nephrology, cardiology, endocrinology, and lifestyle modifications.

3. CONCLUSION

Chronic kidney disease (CKD) is a prevalent, diverse illness that has significant effects on society and health. The therapeutic landscape has been significantly enhanced by advancements in blood pressure control, risk stratification (CGA), early identification, and the addition of disease-modifying drugs, particularly SGLT2 inhibitors. However, there are still unmet needs, health disparities, and implementation gaps in anti-fibrotic treatments. Reducing the worldwide burden of chronic kidney disease requires integrated, patient-centered methods in general and specialist care, bolstered by governmental initiatives to enhance equal access to effective medicines.

REFERENCES

[1] Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260–272. doi:10.1016/S0140-6736(13)60687-X.

[2] Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. American Journal of Kidney Diseases. 2014;63(5):713-735

[3] Alesutan I, Voelkl J, Feger M, Kratschmar DV, Castor T, Mia S, et al. Involvement of vascular aldosterone synthase in phosphate-induced osteogenic transformation of vascular smooth muscle cells. Scientific Reports. 2017;7(1):1-15. DOI: 10.1038/s41598-017-01882-2

[4] Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet. 25 Mar 2017;389(10075):1238-1252

[5] Daugirdas JT, Depner TA, Inrig J, Mehrotra R, Rocco MV, Suri RS, et al. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. American Journal of Kidney Diseases. 2015;66(5):884-930

[6] Yu HT. Progression of chronic renal failure. Archives of Internal Medicine. 2003;163(12):1417-1429. DOI: 10.1001/archinte.163.12.1417

[7] Methven S, Traynor JP, Hair MD, O'Reilly St. J, Deighan CJ, MacGregor MS. Stratifying risk in chronic kidney disease: An observational study of UK guidelines for measuring total proteinuria and albuminuria. QJM. 2011;104(8):663-670. DOI: 10.1093/qjmed/hcr026. Epub 2011 Mar 7

[8] Yu HT. Progression of chronic renal failure. Archives of Internal Medicine. 2003;163(12):1417-1429. DOI: 10.1001/archinte.163.12.1417

[9] Hallan SI, Orth SR. Smoking is a risk factor in the progression to kidney failure. Kidney International. 2011;80(5):516-523. DOI: 10.1038/ki.2011.157

[10] Alshahrani S. Renin–angiotensin–aldosterone pathway modulators in chronic kidney disease: A comparative review. Frontiers in Pharmacology. 2023;14:1101068

[11] Schnaper HW. Remnant nephron physiology and the progression of chronic kidney disease. Pediatric Nephrology. 2014;29:193-202

[12] Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, et al. Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements. 2013;3(1):1-50

[13] Hallan SI, Orth SR. Smoking is a risk factor in the progression to kidney failure. Kidney International. 2011;80(5):516-523. DOI: 10.1038/ki.2011.157

[14] Wheeler DC, Becker GJ. Summary of KDIGO guideline. What do we really know about management of blood pressure in patients with chronic kidney disease? Kidney International. 2013;83(3):377-383

[15] Bello AK, Alrukhaimi M, Ashuntantang GE, Basnet S, Rotter RC, Douthat WG, et al. Complications of chronic kidney disease: Current state, knowledge gaps, and strategy for action. Kidney International Supplements. 2017;7(2):122-129

[16] de Boer IH, Caramori ML, Chan JC, Heerspink HJ, Hurst C, Khunti K, et al. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. Kidney International. 2020;98(4):S1-S15

[17] Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63(5):713–735. doi:10.1053/j.ajkd.2014.01.416 [PubMed: 24647050]

[18] Naik RP, Derebail VK, Grams ME, et al. Association of sickle cell trait with chronic kidney disease and albuminuria in African Americans. JAMA. 2014;312(20):2115–2125. doi:10.1001/jama.2014.15063 [PubMed: 25393378].

[19] Grams ME, Rebholz CM, Chen Y, et al. Race, APOL1 risk, and eGFR decline in the general population. J Am Soc Nephrol. 2016;27(9):2842–2850. doi:10.1681/ASN.2015070763 [PubMed: 26966015]

[20] Peralta CA, Bibbins-Domingo K, Vittinghoff E, et al. APOL1 genotype and race differences in incident albuminuria and renal function decline. J Am Soc Nephrol. 2016;27(3):887–893. doi:10.1681/ASN.2015020124 [PubMed: 26180129

[21] Naik RP, Derebail VK, Grams ME, et al. Association of sickle cell trait with chronic kidney disease and albuminuria in African Americans. JAMA. 2014;312(20):2115–2125. doi:10.1001/jama.2014.15063 [PubMed: 25393378]

[22] Farrington K, Covic A, Aucella F, et al.; ERBP Guideline Development Group. Clinical practice guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR <45 mL/min/1.73 m2). Nephrol Dial Transplant. 2016;31(suppl 2):ii1–ii66. doi:10.1093/ndt/gfw356 [PubMed: 27807144]

[23] Skorecki K, Chertow GM, Marsden PA, Taal MW, Yu ASL. Brenner & Rector's the Kidney. 10th ed Philadelphia, PA: Elsevier; 2016.

[24] Yang B, Xie Y, Guo M, Rosner MH, Yang H, Ronco C. Nephrotoxicity and Chinese herbal medicine. Clin J Am Soc Nephrol. 2018;13(10):1605–1611. [PubMed: 29615394]

[25] Rocuts AK, Waikar SS, Alexander MP, Rennke HG, Singh AK. Acute phosphate nephropathy. Kidney Int. 2009;75(9):987–991. doi:10.1038/ki.2008.293 [PubMed: 18580858]

[26] Markowitz GS, Perazella MA. Acute phosphate nephropathy. Kidney Int. 2009;76(10):1027–1034. doi:10.1038/ki.2009.308 [PubMed: 19675530]

[27] Levey AS, Becker C, Inker LA. Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: a systematic review. JAMA. 2015;313(8):837–846. doi:10.1001/jama.2015.0602 [PubMed: 25710660]

[28] Brown SC, O'Reilly PH. Iohexol clearance for the determination of glomerular filtration rate in clinical practice: evidence for a new gold standard. J Urol. 1991;146(3):675–679. doi:10.1016/S0022-5347(17)37891-6 [PubMed: 1875470]

[29] Elwood CM, Sigman EM, Treger C. The measurement of glomerular filtration rate with 125I-sodium iothalamate (Conray). Br J Radiol. 1967; 40(476):581–583. doi:10.1259/0007-1285-40-476-581 [PubMed: 4952294].