Ref: Ro Med J. 2024;72(2)
DOI: 10.37897/RMJ.2025.2.12

Chronic kidney disease in the elderly: Unraveling the complexities of aging and renal decline

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ABSTRACT

Background. The prevalence of chronic kidney disease (CKD) increases with age, primarily characterized by a decline in glomerular filtration rate (GFR) and elevated albuminuria. CKD in the elderly is influenced by both age-related changes in kidney function and the presence of common comorbidities.

Objective. This literature review aims to explore the etiology and pathogenesis of CKD in the elderly population, focusing on the underlying mechanisms that contribute to kidney decline and disease progression.

Results. Aging kidneys exhibit structural and functional alterations, such as reduced GFR and nephron loss, making the elderly more vulnerable to CKD. Common comorbidities, including hypertension, diabetes mellitus, and the use of medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, exacerbate kidney function deterioration in older adults. Pathophysiological mechanisms underlying CKD in the elderly include premature aging driven by senescence-associated secretory phenotype (SASP) secretion, reduced autophagy in podocytes, mitochondrial dysfunction, and epigenetic modifications such as DNA methylation, histone modification, chromatin remodeling, and noncoding RNA (ncRNA) regulation. Additionally, inflammation and immunosenescence increase pro-inflammatory cytokine production, contributing to renal damage and muscle wasting, further accelerating kidney aging and the development of CKD.

Conclusion. The pathogenesis of CKD in the elderly is multifactorial, involving aging-related cellular and molecular changes alongside the impact of comorbidities and medications. Targeting cellular senescence and other molecular pathways may offer novel therapeutic strategies to mitigate CKD progression in older populations.

Keywords: elderly, etiology, pathogenesis, chronic kidney disease, senescence, inflammation, autophagy

Abbreviations (in alphabetical order):

AGE	– advanced glycation end products
AKI	– acute kidney injury
CKD	– chronic kidney disease
ECM	– extracellular matrix
FF	– filtration fraction
GFR	– glomerular filtration rate
PI 3-kinase	– phosphatidylinositol 3-kinase
RAS	– renin-angiotensin-aldosterone system
RFR	– renal functional reserve
RPF	– renal plasma flow
SASPs	– senescence and its associated secretory phenotypes

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Article History:
Received: 29 December 2024
Accepted: 23 March 2025

INTRODUCTION

A glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m² for three months or longer is indicative of chronic kidney disease (CKD). GFR markers are used based on age: individuals under 40 should have a GFR of 75 ml/min/1.73 m², those between 40 and 65 should have 60 ml/min/1.73 m², and those over 65 should have 45 ml/min/1.73 m², according to the American Society of Nephrology [1]. While CKD can affect individuals at any age, it predominantly impacts the elderly [2]. Between 2017 and 2020, 33.2% of people aged 65 and older were diagnosed with CKD [3].

Anatomical changes in the kidneys, such as glomerulosclerosis, tubular atrophy, and atherosclerosis, contribute to the development of CKD in older adults. Diagnostic tools, including urine albumin excretion and creatinine levels, help confirm the diagnosis of CKD in the elderly [4]. In individuals aged 18–29 years, the kidney has around 1 million nephrons, but by age 65, this number drops to approximately 500,000, reflecting the decline in nephron count with aging. As renal function declines with age, early intervention and management become critical [1,5].

Recent projections indicate that the global elderly population is rising rapidly [6]. By 2050, one in six people will be 65 or older, increasing the risk of CKD [2]. Currently, 71.6% of CKD cases in the elderly are undiagnosed, with age ≥65 being a significant risk factor [7]. The presence of CKD in older adults presents unique challenges for primary care providers, as they must differentiate between the normal, age-related decline in kidney function and pathological causes of CKD. Understanding the etiology and pathogenesis of CKD in the elderly is crucial for improving diagnosis and management. This literature review aims to explore the specific mechanisms behind CKD in the elderly, focusing on the underlying factors that contribute to its development.

METHODS

A comprehensive literature search was conducted in the PubMed and Cochrane databases to identify relevant studies published in the last 15 years. The following Medical Subject Headings (MeSH) terms were used to search for articles in English: “chronic kidney disease,” “elderly,” “etiology,” “pathogenesis,” “aging,” “kidney,” and “inflammation.” Titles and abstracts were screened for relevance. The “related articles” function in both databases was employed to expand the scope of the search and ensure broader inclusion of pertinent studies. Additionally, a manual search of reference lists from relevant articles was carried out to identify additional studies not captured through the database search.

Inclusion criteria focused on studies addressing the etiology, pathogenesis, or mechanisms underlying chronic kidney disease in the elderly population, specifically those investigating age-related renal changes, comorbidities, and associated risk factors. **Exclusion criteria** were applied to remove studies not directly relevant to the aging process or CKD in elderly individuals, as well as studies published in languages other than English.

This literature review aimed to synthesize findings from both observational and experimental studies to provide a comprehensive overview of the current understanding of CKD pathogenesis in elderly individuals. Data were extracted on the etiology, molecular mechanisms, and clinical outcomes associated with CKD in older populations.

RESULTS AND DISCUSSION

Structural and functional changes of the kidney in the elderly

The main organs responsible for eliminating excess fluid and metabolic waste are the kidneys. The kidneys receive 20–25% of the cardiac output, filter 200 L of blood daily, and produce 1.5 L of waste-containing urine. The kidney is a highly metabolic organ under physiological conditions that can tolerate a great deal of oxidative stress but is also vulnerable to aging. During normal aging, the kidney is one of the organs that undergo some of the most noticeable alterations [8].

Systemic comorbidities, including diabetes mellitus and hypertension, as well as underlying or pre-existing renal disease, exacerbate the kidney's steady functional decline and the macro- and microscopic histological alterations that occur with aging. Although kidney damage is not directly caused by aging, the physiological changes associated with normal aging tend to decrease the kidney's capacity to heal, increasing the risk of acute, long-term, and other renal diseases in the elderly [8].

Kidney mass declines by roughly 10% every ten years between the ages of 30 and 80. Each decade of aging is linked to a 10% loss in renal cortex thickness, which is accompanied by a reduction in the number of functioning nephrons. GFR declines at the same rate after age 40, and renal blood flow declines by roughly 10% every ten years. Nonetheless, glomerular volume and single-nephron GFR remain mostly unchanged with age [9].

The glomerular basement membrane thickens, tubulointerstitial alterations occur, glomerulosclerosis increases, and as we age, our nephrons become smaller. As people age, their GFR falls. Renal function declines at a rate of 3.8 ml/min per year per 1.73 m², which can drop as low as 0.4 ml/min per year per 1.73 m². The decline in GFR accelerates with age. Decreas-

ing potassium excretion and progressive tubular dysfunction, including reduced salt reabsorption and urine-concentrating capacity, are all signs of aging that may make a person more vulnerable to acute renal failure. In response to fludrocortisone or hyperkalemia, elderly individuals fail to enhance distal tubular potassium excretion and exhibit reduced transtubular potassium gradients. Reduced potassium excretion may result from a slower rate of sodium and chloride transport to the distal cortical tubule, which correlates with decreased GFR.

The aging kidney also shows changes in vascular anatomy and function. The cortex is primarily affected by increased intrarenal shunts and capillary bypass, increased proliferation of intimal cells in preglomerular arterioles, and greater extracellular matrix (ECM) deposition. While the sensitivity of aortic baroreceptors to sympathetic tone decreases with age, elevated renal sympathetic tone encourages vasoconstriction [10].

The following describes the structural and functional alterations of the aging kidney [9]:

1. Structural changes
   a. Glomerulus
      1. Decreased glomerular number
      2. Elevated global and localized glomerulosclerosis (but not segmental)
      3. Gradual decrease followed by increase in glomerular size
      4. Afferent and efferent arterioles form a shunt
      5. Thickening of the glomerular basement membrane
      6. Greater matrix and mesangial volume
   b. Tubules
      1. Decreased number, volume, and length of tubules
      2. Tubular atrophy with thickened basement membranes and simplified tubular epithelium
      3. Increased presence of tubular diverticula
      4. Acquired cysts
   c. Interstitial and blood vessels
      1. Interstitial fibrosis and increased interstitial volume
      2. Pericapsular fibrosis
      3. Arteriosclerosis
2. Functional changes
   a. Decline in GFR
   b. Stabilized single-nephron GFR
   c. Stable urinary output and minimal albumin excretion
   d. Impaired renal blood flow
   e. Reduced sodium reabsorption
   f. Decreased potassium excretion
   g. Impaired urine-concentrating capacity
   h. Increased renal sympathetic tone
   i. Decreased nitric oxide production
   j. Diminished hemodynamic response to vasodilatory agents

Characteristics of chronic kidney disease in the elderly

Numerous etiologies of chronic kidney disease (CKD) can coexist with the physiological alterations in the kidneys brought on by aging. In contrast to patients with CKD, healthy individuals experience aging-related changes in their kidneys that are distinct in both pattern and severity. Apoptosis or cellular senescence can occur in response to stress or trauma and is characterized by changes in morphology, gene expression, secretory activity, and resistance to apoptosis. As the body's ability to generate new cells and tissues declines with age, the balance between cellular damage and repair becomes progressively impaired.

Damage may be compounded by the accumulation of harmful elements such as mitochondrial dysfunction and oxidative stress (e.g., oxygen radicals and profibrogenic mediators), which worsen intrinsic age-related changes. These processes may be further intensified by disease-specific mechanisms, including ischemia and inflammation. Thus, physiological aging and disease-related injury commonly coexist [11].

Aging affects the kidney's structure and regulatory functions in multiple ways, increasing the likelihood of developing CKD or acute kidney injury. While both aging kidneys and CKD share some pathophysiological and clinical features, aging tends to involve a gradual process, whereas CKD involves progressive damage due to genetic, immune, or toxic factors. The interplay of diminished protective factors (e.g., reduced vascular density, lower antioxidant capacity, telomere shortening, decreased PPARγ and Klotho expression) and elevated stress factors (e.g., hypoxia, overexpression of collagen I and III, TGF-β, oxidative stress) can trigger pathways leading to renal fibrosis and inflammation. These changes promote microvascular rarefaction and senescence, accelerating kidney damage.

Vascular alterations in the kidneys may also be influenced by advanced glycation end products (AGEs), which accumulate in both diabetic and non-diabetic individuals as they age or develop CKD. AGEs promote tubular epithelial cell aging and reduce insulin sensitivity, potentially contributing to the onset of type 2 diabetes. These mechanisms collectively modify the structure and impair the function of the kidneys [12].

Age-related declines in GFR occur gradually and follow a relatively normal distribution, implying that they stem largely from physiological aging. Interest-

ingly, renal function remains relatively stable in approximately one-third of elderly individuals, with an average annual GFR loss of 0.4 to 2.6 ml/min. Under normal conditions, the aging kidney is generally able to maintain fluid and electrolyte balance. However, vulnerability to acute kidney injury increases as renal reserve declines.

Specifically, healthy older adults often exhibit mildly decreased GFR and significantly decreased renal plasma flow (RPF), which alters renal hemodynamics. When RPF declines more than GFR, the filtration fraction (FF) typically rises. This is partly due to redistribution of blood flow from the cortex to the medulla. In addition, renal functional reserve (RFR) is diminished with age due to increased glomerular sclerosis and a reduced ability to raise RPF in response to maximal vasodilation.

Two main functional characteristics shared by the aging and the injured kidney are low GFR and reduced tubular sodium and water reabsorption. However, in healthy older adults, levels of calcium, magnesium, and phosphorus typically remain within normal limits, and both erythropoietin and hemoglobin levels are preserved, reflecting maintained proximal tubular function. Notably, serum erythropoietin levels tend to rise with age, possibly compensating for a blunted erythropoietic response [12].

A decreased GFR is the hallmark of renal failure, while kidney injury is indicated by an increased albumin-to-creatinine ratio. Diagnosing CKD in the elderly can be aided by identifying comorbid conditions such as diabetes, musculoskeletal disorders, cardiovascular and respiratory diseases, and polypharmacy. Albuminuria is present in approximately 19% of elderly individuals with CKD. Table 1 summarizes key similarities and differences between renal aging and CKD based on renal function parameters [12].

Other studies support the association between albuminuria and CKD. Molecular research suggests biological overlaps between renal aging and CKD of diverse origins. Proteomic analyses of rat and human kidneys reveal that age-related and disease-related changes involve increased deposition of extracellular matrix (ECM) proteins – such as collagens I, III, VI, and XV, fibrinogen, and nephronectin – compared to baseline membrane components (e.g., laminin, collagen types IV and VIII). Elevated collagen VI levels may reflect an adaptive response to basement membrane weakening in early aging and disease models.

The absence of albuminuria in age-related GFR decline suggests that podocyte loss is not the primary driver of functional decline in healthy aging. In contrast, albuminuria is more strongly associated with podocyte injury and glomerular hyperfiltration in disease states. Elevated albuminuria also correlates with other structural and functional abnormalities of the aging kidney, such as tubular atrophy, glomerulosclerosis, arterial sclerosis, reduced RPF, impaired acidification, and decreased maximum urine concentration – features that would be considered pathological in younger individuals.

Because of the kidney's rich vascular network, levels of GFR and albuminuria often reflect the extent of vascular disease. In healthy aging, urinary albumin excretion remains stable and low. By contrast, proteinuria is observed in approximately 3% of individuals with advanced kidney failure. Thus, albuminuria and proteinuria serve as indicators of deteriorating renal function in elderly patients [12].

Aucella et al. reported that a GFR < 60 ml/min/1.73 m² can be observed in both healthy aging kidneys and CKD. However, Mallappallil emphasized that individuals with normal urinalysis, electrolyte and acid-base balance, and kidney hormone function – even if their GFR is below 60 – should not automatically be diagnosed with CKD [13].

According to renal disease criteria, many elderly individuals, especially those aged 70 years or older, exhibit both albuminuria and a GFR below 45 ml/min/1.73 m² [14]. Notably, some aspects of renal function – such as production of the anti-aging protein Klotho – may decline early in CKD even while GFR remains above 60 ml/min/1.73 m² and albumin/creatinine ratio exceeds 30 mg/g. This decline contributes to biological aging through uremic toxin accumulation and impaired homeostasis when GFR eventually drops below 60.

The cutoffs used for GFR and albumin/creatinine ratio in defining CKD are based on their association with increased risks of mortality, progression to end-stage renal disease (ESRD), and acute kidney injury (AKI), provided the values persist for more than three months [15]. Aging-related GFR decline is a physiological event linked to oxidative stress, reduced nephron number, changes in renal volume, altered responses to vasoactive agents, and dysregulation of the renin-angiotensin system. Increased glomerular basement membrane permeability also facilitates protein leakage – including albumin – further increasing the risk of kidney damage in the elderly [14].

TABLE 1. Similarities and differences between renal aging and CKD based on renal function parameters [12]

	GFR	Urea FE[a]	Urea	Ca, Mg, P FE	K FE[a]	Erythropoietin
Aging kidney	<60 ml/m	↑	=	=	↓	=
CKD	<60 ml/m	↑	↑	↑	↑	↓

FE: Fractional excretion; [a]Decreased GFR may prevent full compensation of CKD-related increases in urea and K FE

Etiology of chronic kidney disease in the elderly

Chronic kidney disease (CKD) is more prevalent in the elderly for several reasons. Reduced renal blood flow and fewer functional nephrons are examples of the morphological and functional changes that aging causes in the kidneys. Diabetes mellitus and hypertension are among the conditions more common in older adults, and both contribute to the development and progression of CKD [16].

Regarding diabetes mellitus, a systematic review and meta-analysis of more than 5 million individuals from previous observational studies confirmed that diabetes is a strong risk factor for CKD [17]. This can be attributed to persistently high blood glucose levels disrupting the kidney's ability to filter waste and fluids from the blood, thereby causing damage [18]. While CKD is common in older adults, the rate of progression is typically slow. Older individuals with diabetes experience an annual eGFR decline of 2.42 mL/min/1.73 m², compared to 0.8–1.4 mL/min/1.73 m² in non-diabetic individuals over 65. Diabetes accelerates CKD onset in older adults. Several mechanisms may be involved, including inflammation, purinergic system modification, osmotic sodium retention, endothelial dysfunction, hyperactivity of the renin-angiotensin-aldosterone system (RAAS), extracellular signal-regulated kinase (ERK)/RAF pathway, and PI3-kinase-dependent signaling. These mechanisms cause glomerular hyperfiltration, proteinuria, glomerulosclerosis, and declining GFR [14].

Hypertension further burdens renal functional reserve and significantly accelerates CKD progression [19]. Loss of glomeruli leads to increased intraglomerular pressure, which causes hypertrophy and hyperfiltration in the remaining nephrons. This initiates a vicious cycle: nephron loss leads to compensatory hypertrophy and hyperfiltration, which in turn leads to further nephron loss, culminating in kidney failure. Cytokines and hormones such as TGF-β and angiotensin II exacerbate this process by inducing fibrosis and vasoconstriction of the efferent arterioles [13].

Age-related renal function decline is frequently accompanied by multiple comorbidities, necessitating polypharmacy [20]. Older adults often take medications – such as antibiotics or nonsteroidal anti-inflammatory drugs (NSAIDs – that may harm the kidneys, especially when used in excess or over long periods. In addition, age-related changes in drug metabolism and excretion increase susceptibility to drug-induced nephrotoxicity. The elderly are also more vulnerable to kidney injury due to infections, dehydration, or surgery, owing to their reduced renal reserve [16].

Longitudinal studies show that elderly patients often take drugs targeting the cardiovascular, digestive, and metabolic systems. The five most commonly used drugs include amlodipine (16.6%), irbesartan (15.6%), acetylsalicylic acid (8.1%), metoprolol (7.4%), and metformin (7.1%). Patients using multiple medications face a higher risk of CKD. In those with knee osteoarthritis, kidney function declined by 0.39 mL/min/1.73 m² eGFR for each additional drug taken over two years [21].

NSAIDs are among the most common nephrotoxic drugs prescribed to the elderly. These drugs—including acetylsalicylic acid—are frequently contraindicated in elderly patients with impaired kidney function. NSAIDs can cause renal vasoconstriction, nephrotoxicity, and a marked reduction in GFR. Their mechanisms include inhibition of renal prostaglandins, resulting in interstitial nephritis, membranous glomerulonephritis, renal tubular acidosis, and papillary necrosis. Low-dose aspirin is contraindicated in individuals with severe CKD [20].

Healthcare providers must carefully manage medication use in the elderly to minimize renal burden [21]. For elderly patients with hypertension, it is recommended to start treatment with low-dose antihypertensive drugs, gradually titrate upward, and closely monitor side effects [22]. In primary care, limited consultation time often restricts thorough evaluation of kidney function. Swedish researchers have implemented a computerized decision support system (CDSS) to visualize kidney function and offer prescribing guidance to improve medication safety in elderly patients [20].

Pathogenesis of chronic kidney disease in the elderly

The prevalence of CKD increases with age [14]. The kidneys are metabolically active organs responsible for vital functions such as filtration, secretion, and reabsorption – all of which decline with age. Several molecular pathways contribute to renal aging, including telomere shortening, inflammation, mitochondrial dysfunction, impaired autophagy, altered sirtuin and Klotho signaling, and genomic instability [16].

The aging kidney undergoes structural, hemodynamic, physiological, and transcriptomic changes, both at rest and in response to injury. These changes impair the kidney's ability to recover from damage, increasing susceptibility to acute kidney injury (AKI) and promoting progression to CKD [10]. CKD and aging share numerous molecular stressors, including autophagy defects, epigenetic changes, and mitochondrial dysfunction, suggesting they are driven by common underlying mechanisms.

Premature aging

Premature aging in CKD is driven by inflammation, fructose intake, advanced glycation end products (AGEs), oxidative stress, and gut microbiota imbalances. Oxidative stress accelerates both renal

aging and muscle wasting [19]. Premature cellular aging may result from acute insults such as ischemia or oxidative injury, triggering activation of the p16Ink4a and/or p53-p21 pathways. These pathways halt the cell cycle, allowing time for DNA repair and preventing unchecked proliferation. Immune surveillance mechanisms also help clear prematurely aging cells.

However, chronic stress transforms this temporary arrest into irreversible senescence, accompanied by the development of senescence-associated secretory phenotypes (SASPs). Prolonged stress leads to the accumulation of senescent cells that perpetuate tissue damage and impair repair, contributing to CKD and kidney aging. SASP plays a dual role: it may help tissue regeneration after AKI, but chronic exposure promotes fibrosis and sterile inflammation, worsening CKD [23,24].

Autophagy

Autophagy is a lysosome-mediated process that maintains cellular homeostasis by degrading damaged organelles and proteins. In renal cells, basal autophagy preserves structure and function. Decreased autophagy in proximal tubules leads to tubular atrophy, interstitial fibrosis, and accelerated renal aging. In podocytes, reduced autophagy promotes SASP production, further driving CKD [24].

Mitochondrial dysfunction

The inner and outer membranes of mitochondria, which are intracellular organelles, are separated by an intermembrane gap. Cellular homeostasis throughout aging and the preservation of normal mitochondrial structure and function is essential for chronic renal disease. The development of CKD and aging can be accelerated by a variety of endogenous and external insults that cause mitochondrial dysfunction, mitochondria-mediated inflammation, and reduced mitophagy [24].

Epigenetic regulation

The malfunction and dysregulation of the immune system, known as immunosenescence, are commonly associated with aging and inflammation. Immunosenescence is linked to low-grade sterile inflammation and diminished cellular responses to infections and vaccinations, making it hazardous. Numerous factors, including genetics, diet, exercise, exposure to microbes, gender, and status of human cytomegalovirus, affect the alterations associated with immunosenescence. Inflammation is indicated by elevated blood levels of proinflammatory cytokines in the elderly [23]. Compared to healthy controls, individuals with kidney disease exhibit greater immunosensitivity. This is demonstrated by the production of pro-inflammatory cytokines and the accumulation of immunological senescent cells, including CD28-T cells and CD14CD16 monocytes. When senescent cells accumulate in the kidney, they cause chronic low-grade inflammation, which exacerbates renal damage and accelerates renal aging. As a result, elderly individuals are more vulnerable to kidney disease [25].

High levels of innate immunity lead to inflammation, which is typified by proinflammatory cytokines including IL-6, IL-1, and tumor necrosis factor, as well as activated macrophages. Adaptive immunity has also been somewhat altered. Immunosensitivity in CKD is demonstrated by a decrease in the quantity and functionality of naïve T cells and an increase in memory T cells, particularly proinflammatory $CD4^{+}CD28^{-}$ T cells. In CKD, systemic inflammation leads to muscular atrophy. Proinflammatory cytokines, which are produced by aged cells with SASP, trigger proteolytic processes that prevent muscle regeneration [23].

The mechanisms explaining the development of CKD in the elderly are related to the role of SASP. Experimental evidence supports the idea that the accumulation of senescent cells and the SASP associated with them is a major driver of structural and functional organ degeneration in CKD [26]. The SASP includes proinflammatory cytokines, chemokines, matrix metalloproteases, growth factors, microRNAs, and small molecule metabolites, and its expression is largely controlled by transcription factors, such as p53, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB), and Janus kinase signal transducers and activators of transcription. SASP components are associated with chronic inflammation in aging and disease. SASP chemokines such as chemokine (C-C motif) ligand 2 (membrane cofactor protein-1) and cytokines like IL-1, IL-8, and TNF-α recruit immune cells, including macrophages, neutrophils, and T cells, potentially allowing senescent and damaged neighboring cells to be located and destroyed. However, age-related loss of immune competence, along with immune evasion strategies, in a chronically inflammatory environment, may allow senescent cells to escape immune clearance and persist in tissues. Through the release of SASP factors, aging may modulate pathways in neighboring cells and tissues, as well as at distant sites [27].

The implication that senescent cells are a promising target for therapeutic interventions provides an unprecedented opportunity to develop more effective senotherapies to combat CKD and other aging-related disorders. It is hoped that future therapies based on targeting cellular senescence will be translated into the clinic to improve the lives of millions of patients with aging-related diseases [26].

CONCLUSION

Chronic kidney disease (CKD) in the elderly is influenced by a complex interplay of comorbidities, such as diabetes mellitus and hypertension, along with age-related structural and functional changes in the kidneys. The use of medications that increase the risk of kidney damage, such as antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs), further compounds the problem. The aging kidney is vulnerable to a variety of stressors, including oxidative stress, inflammation, altered gut microbiota, advanced glycation end products, and increased fructose consumption. These factors contribute to premature kidney aging, a decline in podocyte autophagy, mitochondrial dysfunction that disrupts cellular homeostasis, and epigenetic changes (e.g., DNA, histone modifications, chromatin remodeling, non-coding RNA (ncRNA) regulation, and RNA modifications) that activate gene expression linked to CKD. Moreover, inflammation and immunosenescence exacerbate kidney damage through the activation of proteolytic mechanisms, impairing muscle regeneration.

A central feature of these mechanisms is the development of senescence and its associated secretory phenotypes (SASPs), which, over prolonged exposure, disrupt tissue function and repair, accelerating the progression of CKD. Understanding the underlying processes driving CKD in the elderly provides valuable insights for future therapeutic interventions. Specifically, targeting cellular senescence offers promising potential for the development of treatments aimed at halting or even reversing the progression of CKD in aging populations.

Conflict of interest:

The authors declare no conflict of interest.

Authors' contributions:

RS – conceptualization, design, sources, materials, literature search, manuscript writing
HR – conceptualization, design, supervision, literature search
NM – conceptualization, design, literature search
AS – conceptualization, design, supervision, literature search
AA – conceptualization, design, supervision, literature search

Acknowledgements:

This review was supported by the Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia.

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