Volume 3, Issue 12, December – 2025 **ISSN (E):** 2938-379X

PATHOPHYSIOLOGY OF CHRONIC KIDNEY DISEASE: MECHANISMS AND CLINICAL IMPLICATIONS

Sharafiy Tamina Floridovna
Bukhara State Medical Institute named after Abu Ali ibn Sina,
Uzbekistan, Bukhara, st. A. Navoi. 1
https://orcid.org/0000-0003-1551-0057 Tel: +998 (65) 223-00-50
E-mail: sharafi.tamina@bsmi.uz

Abstract
Chronic Kidney Disease (CKD) is a progressive condition characterized by irreversible loss of kidney function over time. It represents a major global health problem due to its increasing prevalence and association with high morbidity and mortality. The pathophysiology of CKD involves complex interactions between hemodynamic changes, inflammation, fibrosis, and metabolic disturbances. This article reviews the key pathophysiological mechanisms underlying CKD progression and highlights their clinical significance.

Keywords: Chronic Kidney Disease, pathophysiology, nephron loss, fibrosis, inflammation.

Introduction

The kidneys play a vital role in maintaining homeostasis by regulating fluid balance, electrolyte levels, acid–base balance, and waste excretion. Chronic Kidney Disease occurs when structural or functional abnormalities of the kidneys persist for more than three months. The progression of CKD is driven by multiple interrelated pathophysiological processes that ultimately lead to end-stage renal disease (ESRD).

Nephron Loss and Hyperfiltration

Initial kidney injury leads to the loss of functional nephrons. To compensate, the remaining nephrons undergo adaptive hyperfiltration, increasing glomerular pressure and filtration rate. Although this mechanism temporarily maintains renal function, prolonged hyperfiltration causes glomerular damage, podocyte injury, and sclerosis, accelerating disease progression.

Role of Hemodynamic Alterations

Hemodynamic changes play a central role in CKD pathophysiology. Activation of the renin–angiotensin–aldosterone system (RAAS) increases intraglomerular pressure and promotes sodium retention. Persistent RAAS activation contributes to hypertension, proteinuria, and further structural damage to the renal parenchyma.

Inflammation and Immune Activation

Chronic inflammation is a hallmark of CKD. Injured renal cells release pro-inflammatory cytokines and chemokines that attract immune cells such as macrophages and T lymphocytes. This inflammatory environment promotes tissue damage and stimulates fibrotic pathways, leading to progressive loss of renal function.

Renal Fibrosis

Renal fibrosis is the final common pathway of CKD progression. It is characterized by excessive deposition of extracellular matrix components, replacing normal kidney tissue. Activation of fibroblasts and transformation into myofibroblasts result in scarring and irreversible damage. Transforming growth factor-beta (TGF-β) is a key mediator in fibrotic processes.

Metabolic and Endocrine Disturbances

As kidney function declines, metabolic imbalances develop, including uremia, electrolyte disturbances, anemia, and mineral bone disorders. Reduced erythropoietin production leads to anemia, while impaired vitamin D activation contributes to secondary hyperparathyroidism and bone disease.

Clinical Implications

Understanding the pathophysiology of CKD is essential for early diagnosis and targeted therapy. Interventions aimed at controlling blood pressure, reducing proteinuria, and suppressing inflammation can slow disease progression. Early management significantly improves patient outcomes and quality of life.

Conclusion

Chronic Kidney Disease is a complex disorder driven by nephron loss, hemodynamic stress, inflammation, and fibrosis. These interconnected mechanisms contribute to progressive renal dysfunction. A deeper understanding of CKD pathophysiology provides a foundation for effective prevention and therapeutic strategies.

References

1. Brenner, B. M., & Rector, F. C. (2016). The Kidney. Elsevier.
2. Levey, A. S., et al. (2012). Chronic kidney disease. The Lancet, 379(9811), 165–180.
3. Eddy, A. A. (2014). Overview of the cellular and molecular basis of kidney fibrosis. Kidney International, 86(3), 479–489.