THE ROLE OF OXIDATIVE STRESS IN KIDNEY STONE DISEASE

Anvarjon Mamashakirov *Assistant*
Azizbek Otajonov *Assistant*
Department of Normal and Pathological Physiology, Andijan Branch of Kokand University, Andijan, Uzbekistan

Abstract

Kidney stone disease (urolithiasis) remains one of the most significant challenges in contemporary urology, with metabolic, genetic, inflammatory, and molecular factors playing crucial roles in its development. In recent years, oxidative stress has been recognized as one of the key pathogenic mechanisms involved in both stone formation and disease progression. Excessive production of reactive oxygen species leads to damage of cellular membranes, proteins, and nucleic acids, thereby impairing the functional integrity of renal epithelial cells. By promoting inflammatory responses, crystal adhesion to the epithelium, and fibrotic remodeling, oxidative stress creates a favorable microenvironment for stone formation. This study analyzes the pathophysiological and molecular mechanisms of oxidative stress in kidney stone disease. The available evidence suggests that oxidative stress markers may serve as promising biomarkers for predicting disease progression and recurrence.

Keywords: urolithiasis, kidney stone, oxidative stress, reactive oxygen species, lipid peroxidation, inflammation, NF-κB, renal epithelium, crystal adhesion.

Introduction. Kidney stone disease is one of the most common urological disorders worldwide and is characterized by a high rate of recurrence. The etiopathogenesis of the disease involves not only physicochemical properties of urine, metabolic abnormalities, genetic predisposition, and environmental influences, but also complex cellular and molecular mechanisms [1].

According to the traditional concept, stone formation results from urinary supersaturation with specific salts, followed by crystal nucleation, growth, and aggregation. However, crystal formation alone cannot fully explain the processes by which crystals adhere to and are retained within the renal epithelium. Consequently, increasing attention has been directed toward understanding the molecular mechanisms underlying kidney stone disease [2].

Oxidative stress develops when the balance between reactive oxygen species production and antioxidant defense mechanisms is disrupted. This condition leads to structural and functional damage to cellular membranes, proteins, enzymes, and DNA. In kidney stone disease, enhanced oxidative stress may facilitate crystal adhesion to epithelial cells, stimulate inflammatory responses, and promote structural alterations within renal tissues [3,4].

The aim of this study was to analyze the pathophysiological and molecular role of oxidative stress in kidney stone disease.

Materials and Methods. The theoretical framework of this study was based on contemporary scientific evidence concerning the pathogenesis of kidney stone disease, mechanisms of oxidative stress, and their molecular consequences. Particular attention was given to the role of reactive oxygen species, mitochondrial dysfunction, lipid peroxidation, antioxidant defense systems, and inflammatory signaling pathways in the development of nephrolithiasis.

Information regarding the generation of reactive oxygen species, lipid peroxidation, mitochondrial dysfunction, impairment of antioxidant defense mechanisms, activation of inflammatory mediators, and interactions between urinary crystals and renal epithelial cells was comparatively analyzed and systematically synthesized using analytical approaches.

Results. Enhanced oxidative stress in kidney stone disease contributes significantly to both functional and structural injury of renal epithelial cells. Contact between calcium oxalate crystals and epithelial cells results in a marked increase in

the generation of reactive oxygen species. Consequently, lipid peroxidation intensifies, leading to disruption of cellular membrane integrity [2,5].

Mitochondria represent one of the principal sources of oxidative stress. Crystal internalization into epithelial cells causes a reduction in mitochondrial membrane potential, impaired ATP synthesis, and the release of cytochrome c. These alterations activate apoptotic pathways and contribute to a reduction in the number of viable epithelial cells [4].

Oxidative stress also activates the NF-κB signaling pathway, resulting in increased production of pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6. As a consequence, a chronic inflammatory microenvironment develops within renal tissues. These inflammatory mediators facilitate crystal attachment to epithelial surfaces and accelerate the process of stone formation [6].

Furthermore, oxidative stress increases the expression of molecules such as osteopontin, CD44, and hyaluronic acid. These molecules function as adhesive substrates that promote crystal retention within the renal epithelium. As a result, favorable conditions are created for crystal aggregation and stone nidus formation [7].

Reduced activity of antioxidant defense components, including superoxide dismutase, catalase, and glutathione peroxidase, further exacerbates oxidative stress. This impairment represents an important factor contributing to the persistence and progression of pathological processes associated with nephrolithiasis [8].

Discussion. Explaining the development of kidney stone disease solely through crystallization processes does not fully reflect the complexity of its pathogenesis. Cellular and molecular mechanisms mediate the transition from crystal formation to crystal retention within the renal epithelium. Among these mechanisms, oxidative stress occupies a central position.

Excessive production of reactive oxygen species contributes to cellular injury and amplifies inflammatory responses. These changes facilitate crystal adhesion to

renal epithelial cells while simultaneously impairing crystal clearance. From this perspective, oxidative stress should be regarded not merely as a consequence of stone formation but also as an active participant in the pathogenic process.

At the molecular level, NF-κB signaling, mitochondrial dysfunction, and impaired antioxidant defense mechanisms form an interconnected pathogenic network. Sustained activation of these pathways promotes chronic inflammation, fibrotic remodeling, and progressive deterioration of renal function. Therefore, the assessment of oxidative stress biomarkers may provide valuable diagnostic information regarding disease severity and the risk of recurrence.

Conclusion. Oxidative stress represents a critical molecular component in the pathogenesis of kidney stone disease. Excessive generation of reactive oxygen species contributes to epithelial cell injury, inflammatory responses, and enhanced crystal adhesion.

Mitochondrial dysfunction, activation of the NF-κB signaling pathway, and impairment of antioxidant defense systems play important roles in both stone formation and disease recurrence. Identification of oxidative stress biomarkers and the development of antioxidant-based therapeutic strategies may improve the prevention and treatment of urolithiasis.

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