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The Relationship Between Celiac Disease and Kidney Disease: Immunological, Endothelial and Pathophysiological Mechanisms With Clinical Implications

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ABSTRACT

Celiac disease is a systemic autoimmune disorder with growing recognition of extraintestinal involvement, including endothelial dysfunction and renal disease. Recent studies highlight a gut-vascular-renal axis driven by immune activation, oxidative stress, and cytokine signaling. This review integrates epidemiological, immunological, endothelial, and renal mechanisms, with emphasis on immunoglobulin A nephropathy and chronic kidney disease.

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Abbreviations

CD: Celiac Disease
IgAN: Immunoglobulin A Nephropathy
IL-17: Interleukin-17

Introduction

Celiac Disease (CD) is a T cell-mediated autoimmune disorder affecting approximately 1% of the population. It is increasingly recognized as a systemic disease with vascular and renal implications [1,2].

Recent evidence suggests that chronic inflammation in CD contributes to endothelial dysfunction and systemic complications through immune-mediated pathways and oxidative stress [3].

Epidemiological Associations

Immunoglobulin A nephropathy (IgAN): the strongest association exists with IgAN. Cohort and screening studies confirm increased co-prevalence and shared immunological mechanisms [4,5].

Chronic kidney disease: patients with CD have a modest but significant increased risk of chronic kidney disease [6]. Chronic inflammation and endothelial dysfunction appear central to disease progression [3].

Other renal manifestations: metabolic disturbances such as hyperoxaluria contribute to nephrolithiasis and renal injury.

Immunopathogenesis

Adaptive immunity: gluten peptides activate CD4+ T cells, leading to cytokine release [interferon (IFN)-γ, tumor necrosis factor-α (TNF-α)], which promotes systemic inflammation and endothelial activation [1].

Innate immunity and interleukin-15 (IL-15): IL-15-mediated activation of intraepithelial lymphocytes amplifies inflammation and epithelial damage [7].

Emerging role of interleukin-17 (IL-17) and systemic inflammation: recent studies highlight IL-17A as a key mediator linking gut inflammation to vascular dysfunction, promoting oxidative stress and endothelial injury. Experimental models show that gluten exposure induces vascular inflammation and hypertension through IL-17-driven pathways [8].

Autoantibodies: anti-tissue transglutaminase antibodies may directly interact with endothelial cells, contributing to vascular injury [9].

Endothelial Dysfunction

Mechanisms: chronic inflammation in CD leads to endothelial activation, increased adhesion molecule expression, and leukocyte recruitment. Oxidative stress plays a central role, reducing nitric oxide availability and impairing vascular function [8].

Oxidative stress and vascular inflammation: recent experimental and translational studies demonstrate that gut-derived inflammation induces systemic oxidative stress, endothelial dysfunction is mediated by nitro-oxidative pathways and vascular inflammation is reversible with gluten withdrawal [8]. These findings support a direct gut-vascular inflammatory axis.

Prothrombotic state: CD is associated with hypercoagulability due to inflammation and micronutrient deficiencies, increasing thrombotic risk [10].

Clinical evidence from both individual studies and meta-analyses confirms that patients with active CD exhibit impaired endothelial function, along with increased vascular permeability and reduced vasodilation. Importantly, these alterations appear to be at least partially reversible following adherence to a gluten-free diet [3].

Renal Pathophysiology

Immune-mediated mechanisms: increased intestinal permeability leads to systemic immune activation and production of aberrant immunoglobulin A (IgA), which deposits in the kidney in IgAN [4].

Endothelial-renal link: endothelial dysfunction contributes to renal microvascular injury, promoting progression to chronic kidney disease [3].

Metabolic mechanisms: malabsorption leads to oxalate accumulation and hyperoxaluria, increasing risk of nephrolithiasis and renal damage.

The Gut-Endothelium-Kidney Axis

Recent research supports a unified pathogenic model: intestinal inflammation → increased permeability, immune activation → cytokines (IL-15, IL-17, tumor necrosis factor-α (TNF-α), systemic oxidative stress and endothelial dysfunction and renal microvascular damage and immune complex deposition. This axis explains the systemic nature of CD and its vascular-renal complications [3,8].

Clinical Implications

Screening: screening for CD is recommended in IgAN, unexplained chronic kidney disease, recurrent nephrolithiasis or hyperoxaluria [5].

Gluten-free diet: reduces systemic inflammation, improves endothelial function, and may reverse vascular dysfunction and stabilize renal disease [8].

Monitoring: patients require monitoring of renal function (estimated glomerular filtration rate - eGFR, creatinine), urinalysis and cardiovascular risk factors.

Conclusion

Celiac disease is a systemic disorder with significant immunological, endothelial, and renal implications. Recent evidence highlights the role of IL-17-mediated inflammation, oxidative stress, and endothelial dysfunction in linking CD to kidney disease. Early diagnosis and strict gluten-free diet remain essential to prevent long-term vascular and renal complications.

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None.

Conflict of interest

None.

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