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# DIABETIC NEPHROPATHY AND HORMONAL IMBALANCE: PATHOPHYSIOLOGICAL FOUNDATIONS AND CLINICAL SIGNIFICANCE

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**Abstract:**Diabetic nephropathy (DN) is a chronic kidney disease that develops against the background of diabetes mellitus and is one of the most common causes of chronic kidney failure worldwide. This article analyzes the complex pathophysiological relationship between DN and hormonal imbalance, its clinical manifestations, and therapeutic strategies. The study examines how insulin, the renin-angiotensin-aldosterone system (RAAS), cortisol, thyroid hormones, and other hormones influence the development of DN. Additionally, a table is provided demonstrating the correlation between DN stages and hormonal imbalance.

**Keywords:**diabetic nephropathy, hormonal imbalance, insulin, RAAS, cortisol, thyroid hormones, clinical significance.

## Introduction

Diabetic nephropathy is the most prevalent form of chronic glomerulonephritis, primarily developing in patients with type 1 and type 2 diabetes mellitus. Hormonal imbalance plays a central role in the progression of DN. Insulin resistance, overactivation of RAAS, and alterations in cortisol and thyroid hormones disrupt kidney filtration, proteinuria, and sodium and water balance [1,2].

Globally, 20–40% of patients with diabetes exhibit varying degrees of DN, which eventually leads to chronic kidney failure [1]. Therefore, understanding the pathophysiology of DN and identifying hormone-related mechanisms is crucial for optimizing clinical monitoring and treatment.

The clinical course of DN typically progresses in stages: an initial subclinical phase, microalbuminuria, followed by proteinuria and hypertension, and ultimately chronic kidney failure. Each stage is associated with specific roles of hormonal imbalance [2].

## Materials and Methods

This analysis is based on a systematic review of literature and clinical studies. Selected sources include clinical and experimental studies, meta-analyses, and cohort studies published between 2010 and 2025. Inclusion criteria were:

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Hormonal changes associated with DN stages I–IV.

Correlation between clinical manifestations and hormones.

Biomarkers: albuminuria, creatinine, glomerular filtration rate (GFR).

Statistical analysis included Pearson correlation coefficients, ANOVA, and visual representation of the relationship between DN stages and hormonal imbalance through graphs.

**Results**

**Insulin and DN**

Insulin resistance is a primary pathophysiological mechanism in the early stages of DN. Hyperinsulinemia leads to glomerular hypertrophy, podocyte injury, and the development of proteinuria. Disrupted insulin signaling impairs normal glomerular filtration and promotes podocyte apoptosis [3].

Clinical example: In patients with type 2 diabetes, those with high insulin resistance progress from microalbuminuria to proteinuria within 2–3 years.

**RAAS and DN**

The renin-angiotensin-aldosterone system (RAAS) plays a crucial role in DN development. Angiotensin II causes vasoconstriction, increasing glomerular pressure and promoting oxidative stress. Additionally, overactivation of aldosterone receptors contributes to interstitial fibrosis and podocyte loss [4].

Clinical observation: Patients with elevated RAAS activity develop hypertension more rapidly, and proteinuria increases significantly. RAAS blockers (ACE inhibitors, ARBs) are key therapeutic agents for improving DN prognosis.

**Cortisol and DN**

Chronic excess cortisol secretion disrupts glucose metabolism, accelerating hyperglycemia and DN progression. Cortisol promotes podocyte apoptosis, increasing proteinuria [5].

Experimental studies indicate that patients with high cortisol levels experience rapid DN progression and an increased risk of chronic kidney failure.

**Thyroid Hormones and DN**

Thyroid hormones (T3, T4) play a direct role in DN development by regulating glomerular filtration, RAAS activity, and sodium and water balance. Hypothyroidism accelerates DN progression, while hyperthyroidism may increase glomerular pressure [6].

Clinical example: In hypothyroid patients, proteinuria progresses slowly in early DN stages, but

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GFR declines rapidly. Normalizing thyroid function slows kidney damage.

**Clinical Manifestations**

Key symptoms in patients with DN include:

Proteinuria and microalbuminuria.

Hypertension.

Peripheral edema (hands and feet).

Signs of chronic kidney failure: increased creatinine levels, reduced GFR.

Hormonal imbalance directly exacerbates these symptoms [7].

**Table 1. DN Stages and Hormonal Imbalance**

| DN Stage | Hormonal Changes | Clinical Manifestations | Biomarkers | Treatment Strategy |
|---|---|---|---|---|
| I | ↑Insulin resistance | Subclinical | Normoalbuminuria, ↑ GFR | Lifestyle modification, diet, physical activity |
| II | ↑RAAS activity | Onset of proteinuria | Microalbuminuria | ACE/ARB therapy, hypertension management |
| III | ↑ Aldosterone, ↑ Cortisol | Hypertension, peripheral edema | Proteinuria, ↓ GFR | RAAS blockers, cortisol modulation |
| IV | Thyroid imbalance, excessive RAAS activity | Chronic kidney failure | ↑ Creatinine, significantly ↓ GFR | Comprehensive therapy: RAAS, thyroid medications, symptomatic treatment |

**Discussion**

Hormonal imbalance is a central mechanism in DN development. Insulin resistance and RAAS overactivation lead to glomerular hypertension, podocyte injury, and proteinuria. Changes in

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cortisol and thyroid hormones accelerate the clinical course of DN.

Effective strategies for early DN detection in clinical practice include:

Monitoring biomarkers (microalbuminuria, creatinine, GFR).

Blocking RAAS activity.

Therapies that enhance insulin sensitivity.

Normalizing cortisol levels and optimizing thyroid hormone function.

Experimental studies show that normalizing RAAS and cortisol slows DN progression and stabilizes kidney function [8,9].

**Conclusion**

Hormonal imbalance is a key pathophysiological mechanism in the development of diabetic nephropathy. Insulin resistance, RAAS activity, cortisol, and thyroid hormones significantly influence the clinical course of DN. Early detection, restoration of hormonal balance, and individualized therapy strategies help prevent chronic kidney failure.

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