



Global Conference on Medical and Health Sciences

Hosted Online from Madrid, Spain

Date: 14th May, 2026

Website: <https://econferencia.com>

KLOTHO PROTEIN AND VITAMIN D AS NOVEL BIOMARKERS FOR EARLY RENAL DYSFUNCTION IN HYPERTENSIVE PATIENTS: DIAGNOSTIC VALUE AND THERAPEUTIC IMPLICATIONS

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Abstract

This study investigated the diagnostic value of Klotho protein and vitamin D in the early detection of renal dysfunction in patients with hypertension. Serum levels of cystatin-C, Klotho protein, vitamin D, and parathyroid hormone were evaluated in 169 hypertensive patients and 23 healthy volunteers. Correlations between these biomarkers across different stages of hypertension were established. The addition of vitamin D supplementation (Detrimax 5000 IU) to standard therapy demonstrated a statistically significant positive effect on hemodynamic parameters and markers of renal dysfunction.

Keywords: Hypertension, renal dysfunction, Klotho protein, vitamin D, cystatin-C, early diagnosis, nephroprotection.

Hypertension (HTN) remains one of the most pressing challenges in modern medicine. According to the World Health Organization, it affects 27% of the adult population globally, with projections exceeding 29% by 2030. In Uzbekistan, HTN prevalence is recorded at an average of 3,099.7 per 100,000 adults, representing 32.26% of the general population. HTN causes renal damage in a substantial proportion of patients and ultimately leads to the development of



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chronic kidney disease (CKD). Studies in Russia report that nearly 50% of hypertensive patients present with renal dysfunction (RD) [1, 2].

Conventional markers for early RD detection — creatinine and creatinine-based estimated glomerular filtration rate (eGFR) — provide limited diagnostic value in patients with reduced muscle mass, vegetarian diets, varying body constitution, or comorbid conditions. For this reason, cystatin-C, Klotho protein, and vitamin D have attracted growing research interest as more sensitive and reliable biomarkers [3, 4].

Aim: To evaluate the diagnostic role of Klotho protein and vitamin D in early detection of renal dysfunction across different stages of hypertension and to optimize treatment based on standard therapy.

Material and methods: The study enrolled 169 hypertensive patients treated in the cardiology, nephrology, and internal medicine departments of the National Medical Center, along with 23 healthy volunteers. Patients were stratified into two groups based on eGFR: Group 1 — eGFR ≥ 90 ml/min/1.73 m² (n=87); Group 2 — eGFR ≤ 89 ml/min/1.73 m² (n=82). All participants underwent standard biochemical analysis (complete blood count, urinalysis, lipid panel, urea, creatinine, glucose) alongside serum cystatin-C, Klotho protein, vitamin D, parathyroid hormone, microalbuminuria, coagulogram, ECG, and echocardiography. Statistical analysis was performed using contemporary methods.

Results. Cystatin-C-based eGFR proved superior to creatinine-based calculation in detecting renal dysfunction: in Group 1, RD prevalence was 9.12% by



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creatinine versus 12.92% by cystatin-C; in Group 2, the figures were 11.16% and 15.81%, respectively.

Serum Klotho protein was 43.28 ng/ml in patients with eGFR ≥ 90 ml/min/1.73 m² versus 27.2 ng/ml in those with eGFR ≤ 89 ml/min/1.73 m² ($p < 0.001$). Cystatin-C levels were 5.15 ng/ml in Group 1 and 6.56 ng/ml in Group 2 ($p < 0.05$). These findings confirmed that Klotho protein has higher sensitivity than cystatin-C for the early detection of renal dysfunction in hypertension.

Vitamin D levels were 28.73 ± 1.70 ng/ml in Group 1 and 20.03 ± 1.96 ng/ml in Group 2. A significant positive correlation between Klotho protein and vitamin D was identified across both groups: $r = 0.88$ ($p < 0.001$) in Group 1 and $r = 0.77$ ($p < 0.001$) in Group 2. Rising cystatin-C reflected deteriorating glomerular filtration, while declining Klotho protein indicated parenchymal damage and increasing disease severity [5].

Adding vitamin D (Detrimax 5000 IU) to standard therapy produced a statistically significant improvement across all hemodynamic and renal dysfunction markers ($p < 0.001$): eGFR increased by 18.4 ml/min/1.73 m², Klotho protein by 5.36 ng/ml, and vitamin D by 10.5 ng/ml. Systolic and diastolic blood pressure reached target levels [6].

These results demonstrate that Klotho protein can detect developing renal dysfunction even in patients with eGFR ≥ 90 ml/min/1.73 m², where clinical manifestations are not yet apparent. This enables subclinical-stage diagnosis before conventional markers become abnormal, and carries significant potential to reduce rehospitalization rates and treatment costs [7].

Conclusion:

1. Cystatin-C-based eGFR is a more effective marker for detecting renal dysfunction compared to creatinine-based calculation.



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2. Klotho protein demonstrates higher sensitivity than cystatin-C in early renal dysfunction detection (43.28 vs 27.2 ng/ml, $p < 0.001$).
3. The significant correlation of vitamin D with hemodynamic and renal function parameters confirms its value as a prognostic marker for disease course and outcome.
4. Addition of vitamin D to standard therapy reliably improves hemodynamic parameters and renal dysfunction markers ($p < 0.001$).
5. Klotho protein and vitamin D should be incorporated into clinical protocols as early diagnostic markers for renal dysfunction in hypertensive patients, and vitamin D supplementation should be included in standard treatment guidelines to prevent CKD progression.

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