ISSN NO: 2770-2936
March, 2026

Analysis of the relationship between hemodynamic parameters and markers of renal dysfunction, Klotho protein, vitamin D, and parathyroid hormone in hypertension.

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Abstract:
Globally, targeted scientific research is being conducted aimed at a deeper study of the origin and pathogenesis of renal dysfunction (RD), determining the role of Klotho protein in the mechanism of its development. This protein plays an important role in kidney function and the vascular system. A decrease in the amount of Klotho protein intensifies the pathological process in these systems. This study examines the relationship between Klotho protein and RD development.

Keywords: Klotho protein, HD, RD, ECG, EchoCG, BMI, GFR, CKD-EPI, Student's t-test, Pearson correlation analysis, creatinine, significance level.

Despite the development of modern medicine, hypertension (HD) is still one of the most pressing problems among cardiovascular diseases. According to the World Health Organization (WHO) and the European Society of Cardiology (ESC), patients with AH constitute 27% of the adult population. In the conclusions of experts from the above-mentioned authoritative organizations, it is predicted that by 2030 this indicator will exceed 29%, and their number will exceed 1.5 billion. The incidence of hypertension increases with age, reaching 50-65% among people over 65. [13]. In some countries, it has been shown that these figures exceed 50% [11]. When analyzing the disease depending on gender characteristics, it was noted that its incidence is 37% among women and 58% among men. According to Prospective Urban Rural Epidemiology (PURE) (Prospective Cohort Study, n=135335), the prevalence of AH in European countries is 40.7% among the adult population [3].

It is known that in most patients, hypertension affects the kidneys and ultimately leads to the development of CKD. In developed countries of Europe and North America, hypertension is one of the main causes of severe renal dysfunction (RD), and the number of patients belonging to this group is increasing [2, 8].

According to international epidemiological data, renal dysfunction in the USA, Western Europe, Australia, and China is found in the range of 11-16% among the adult population, depending on race, living conditions, and a number of other factors. [2, 12]. In them, in 3.0% - 9.5% of cases, the disease is in the initial stage, and when comparing these figures with the world's population, it is confirmed that about 5% of the adult population of the Earth has early stages of RD. With age, these figures increase, reaching 15-20%, and even 30% [6, 7, 9]. According to observations conducted in the Russian Federation, RD is observed in almost 50% of patients with hypertension [1].

Purpose of the research. Study of renal dysfunction (RD) developing depending on Klotho protein indicators in patients with hypertension (HD) and determination of the relationship between them.

Materials and methods. We involved 169 patients with developing RD with hypertension in our study. Of these, 97 (57.40%) were men and 72 (42.60%) were women. The average age of the patients was 63.09±0.65 years. The subjects were divided into the following groups depending on the stage of hypertension: Group 1: 76 patients with stage II hypertension, of which 53 were men and 21 were women. Group 2: 93 patients with stage III AH, of which 61 were men and 32 were women. All our patients underwent generally accepted physical, laboratory, and instrumental (ECG, EchoCG) studies. Excess body weight and its levels, body mass index (BMI) were determined. The content of Klotho protein and the concentration of creatinine were

ISSN NO: 2770-2936
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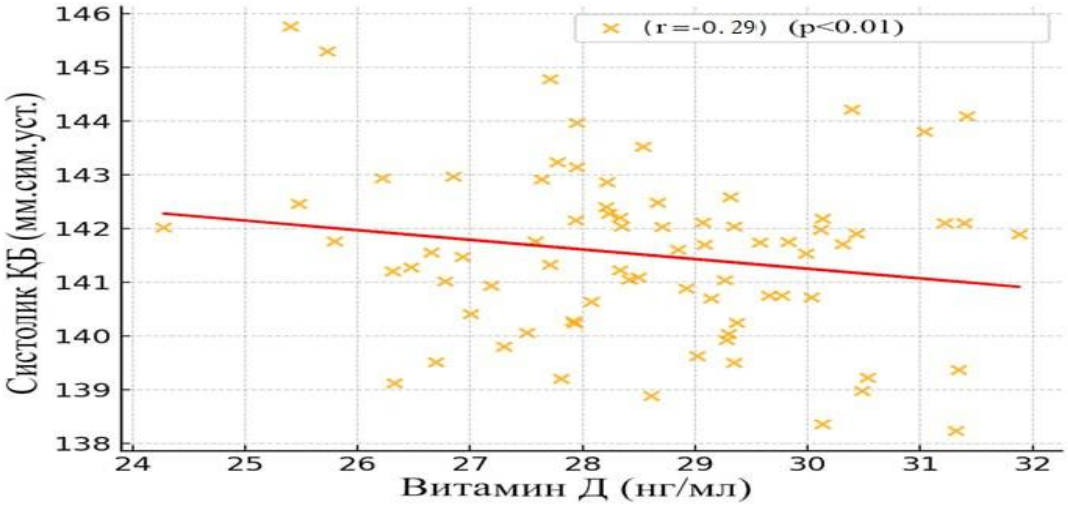
determined in the blood serum. Glomerular filtration rate (GFR) was calculated according to the formula CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). The reliability of the differences between the groups was determined by applying the odd and even differences of Student's t-test. Correlation analysis was carried out using Pearson's correlation coefficient and determining its significance based on reliability tables.

Results

According to the literature published in recent years, vitamin D participates in maintaining normal blood pressure in the human body by affecting the renin-angiotensin-aldosterone system (RAAS) in the kidneys. With a decrease in its level below 30 ng/ml, an increase in BP to 5-10 mm Hg was observed [4, 5, 10]. In the main group of patients with stage II and III hypertension, a correlation was observed between vitamin D and SBP. According to the analysis conducted based on the obtained results, it was established that in patients with stage II AH, an increase in the level of vitamin D in the blood has a reliable (r=-0.29), (r<0.01) weak negative correlation with SBP. In patients with stage III hypertension, this dependence was significantly higher than in group 1. In these cases, an increase in the level of vitamin D in blood serum leads to a decrease in systolic pressure (Pic. 1.1).

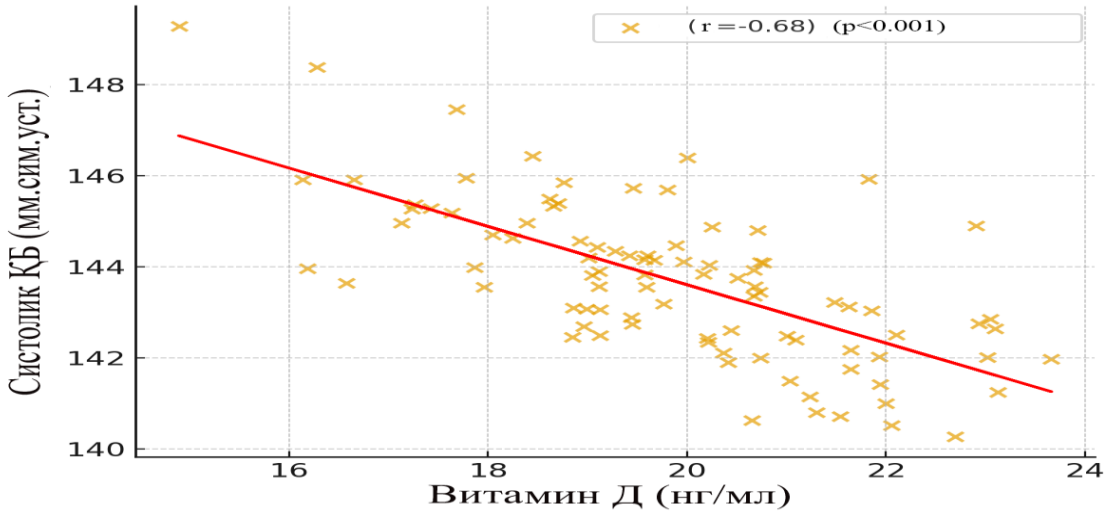


Pic. 1.1. Correlation between vitamin D and systolic blood pressure in patients with stage II hypertension.

At the same time, in the second group of patients with stage III hypertension, a significant negative correlation (r=-0.68) (r<0.001) was also found between vitamin D and SBP (Pic. 1.2). This result was significantly higher compared to the 1st group. This reflects the high probability of an increase in blood

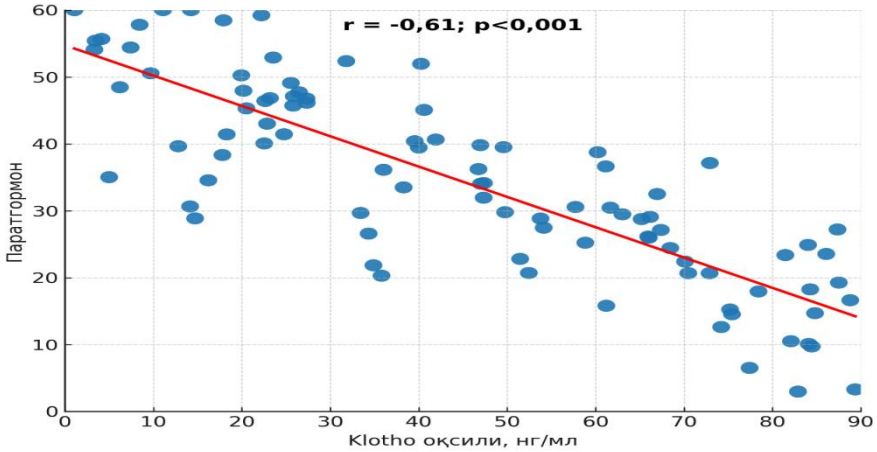
ISSN NO: 2770-2936
March, 2026

pressure and a decrease in vitamin D levels as the disease stage progresses.



Pic. 1.2. Correlation between vitamin D and systolic blood pressure in patients with stage III hypertension.

In our study, the relationship between cystatin C, PTH, and the Klotho protein was also studied. In the control group of patients with RD, a decrease in the content of Klotho protein and vitamin D, an increase in the concentration of cystatin C and PTH were revealed. Taking this into account, we studied the relationship between them. According to the obtained results, in the first main group, PTH was 45.11±2.34 ng/ml, in the second - 76.75±2.41 ng/ml (p1-2<0.001), and an increase was observed, contrary to the decrease in the content of Klotho protein. The results of the analysis showed a significant negative correlation between these indicators in the 1st group (r=-0.61), (r<0.001) and in the 2nd group (r=-0.74), (r<0.001) (Pic. 1.3 a and b). This relationship is associated with the fact that Klotho balances the protein's calcium channels (TRPV5), enhancing the reabsorption of PTH. Through this mechanism, PTH prevents excessive calcium excretion from bones and prevents calcium-phosphorus balance disruption.



Pic. 1.3 a. Correlation between Klotho protein and parathyroid hormone in group 1

ISSN NO: 2770-2936
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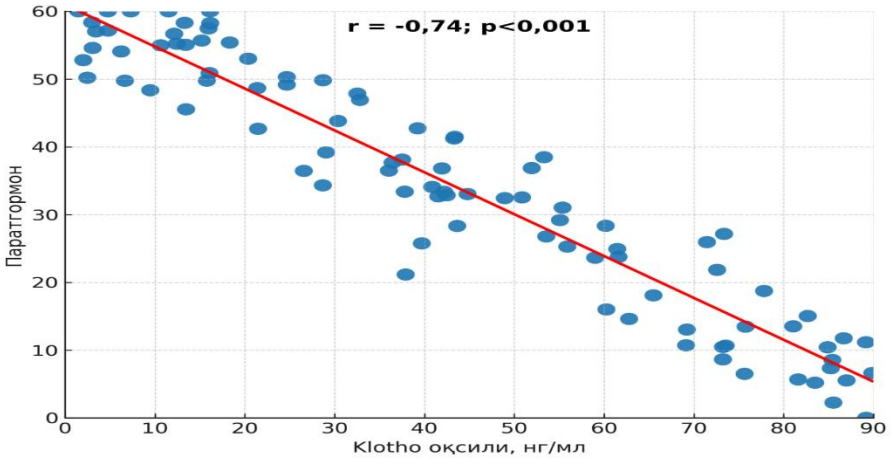
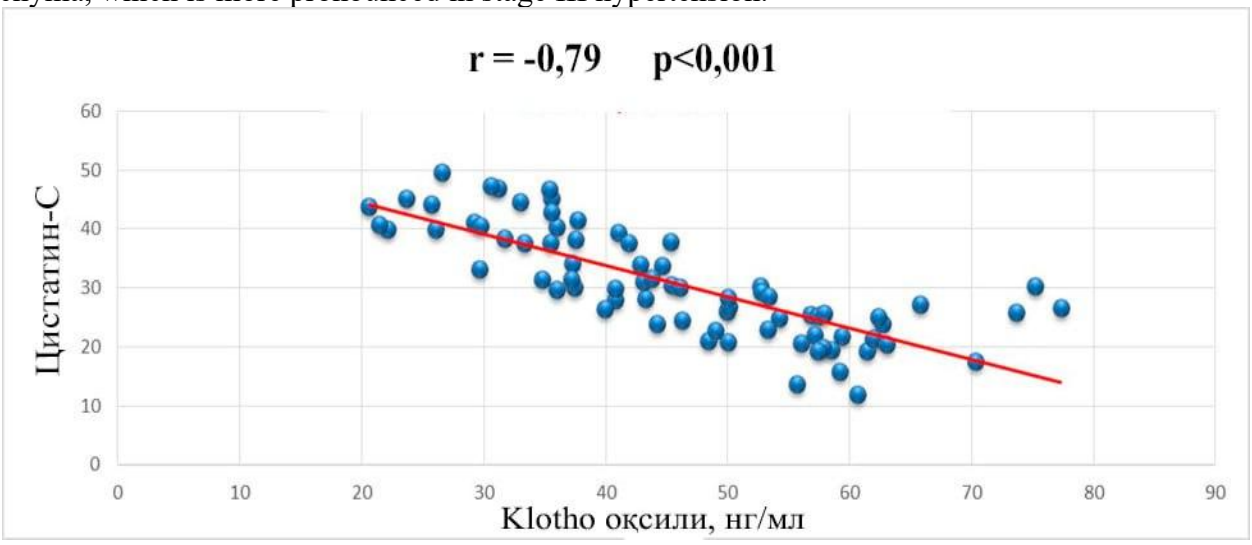
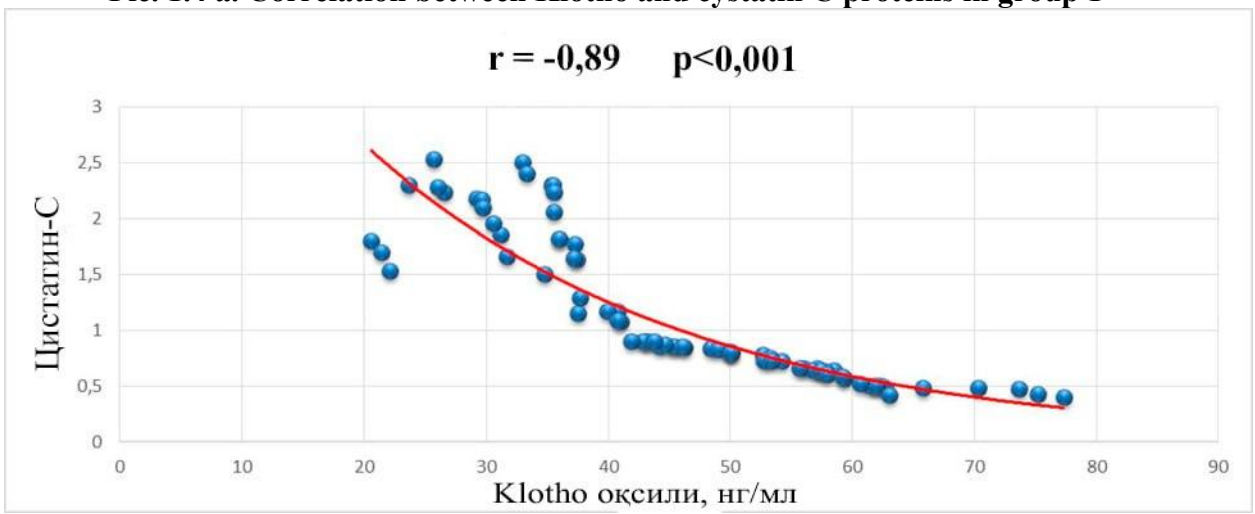


Pic. 1.3 b. Correlation between Klotho protein and parathyroid hormone in group 2

When analyzing the relationship between cystatin C and the Klotho protein, a reliable inverse correlation was observed between them (Pic. 1.4 a and b). In the second group of patients, this correlation (r=-0.89) (p<0.001) was significantly higher than in the first (r=-0.79) (p<0.001). In this case, an increase in cystatin C indicates impaired renal filtration, and a decrease in Klotho protein indicates damage to the parenchyma, which is more pronounced in stage III hypertension.



Pic. 1.4 a. Correlation between Klotho and cystatin C proteins in group 1



Pic. 1.4 b. Correlation between Klotho and cystatin C proteins in group 2

Klotho protein is not only a biomarker for early detection of RD, but also plays an important role in the diagnosis of diseases of this system through its effect on the vascular system. This protein protects the vascular wall from damage due to its antioxidant and antifibrous effect, limits the accumulation of these

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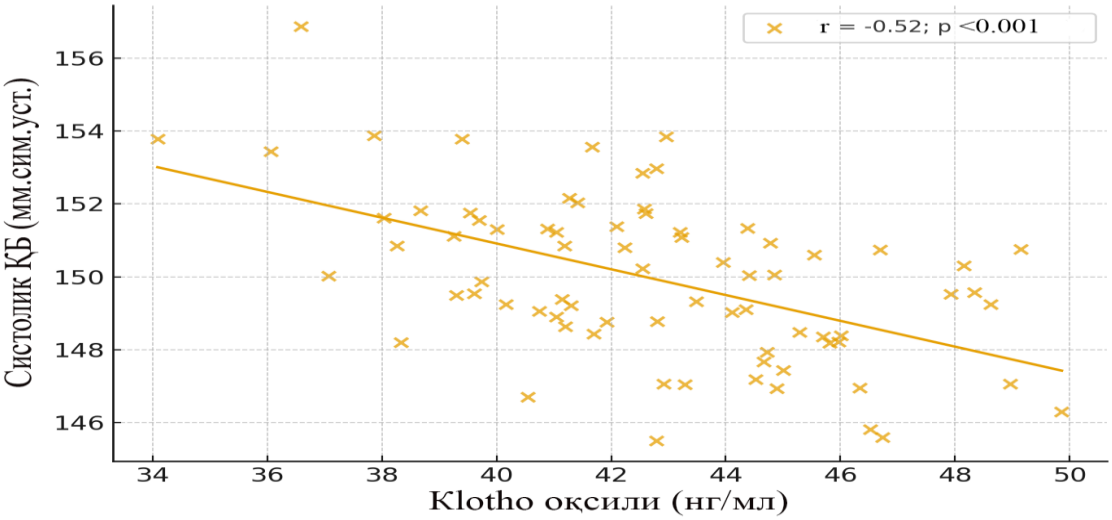
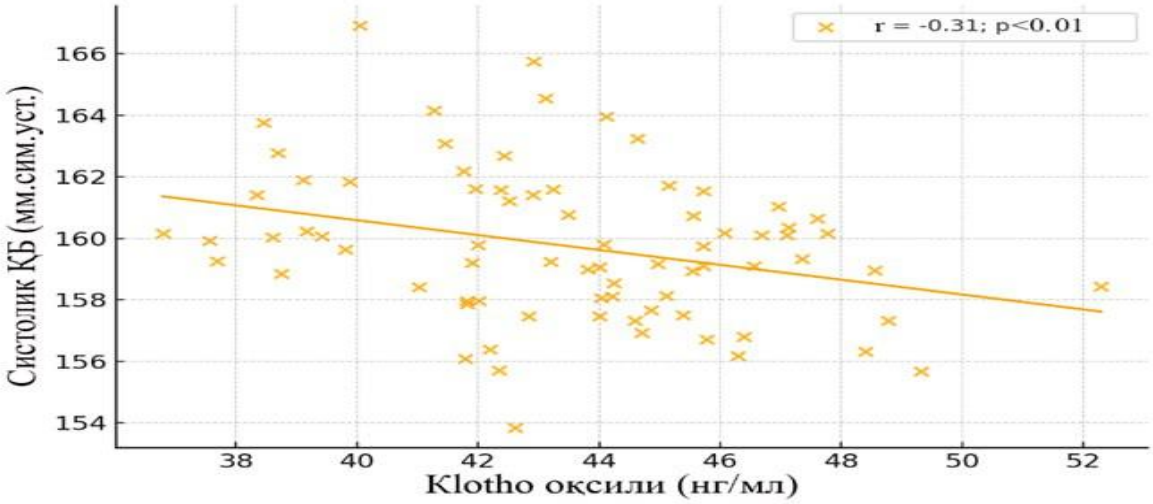
salts in the arterial wall through calcium-phosphorus homeostasis, stimulates the production of nitric oxide, and positively affects hemodynamics by ensuring vasodilation.



Pic. 1.5 a. Correlation between Klotho protein and systolic blood pressure in patients with stage II hypertension.



Pic. 1.5 b. Correlation between Klotho protein and systolic blood pressure in patients with stage III hypertension.

In the 1st and 2 nd subgroups of the main group of our study, a significant (r=-0.52; p<0.001), (r=-0.31; p<0.01) negative correlation was found between Klotho protein and SBP (Pic. 1.5 a and b). Compared to the groups, this relationship was more pronounced in the first group. In patients of both groups, a decrease in the amount of Klotho protein was accompanied by an increase in SBP. This relationship indicates that the Klotho protein can be considered not only as a pathogenetic biomarker of RD, but also of hypertension.

Conclusion

According to the above data, a correlation was observed between hemodynamic parameters and RD factors in patients with hypertension. It was established that this relationship was more pronounced in stage III of hypertension than in stage II. The obtained results confirm the significant role of renal markers in determining disease progression, hemodynamic changes, and early diagnosis of RD development in patients with hypertension.

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ISSN NO: 2770-2936
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