Analysis of the relationship between kidney dysfunction markers Klotho protein and vitamin D in hypertension.

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Abstract

In the context of this article, the prevalence of hypertension worldwide, including among the population of Uzbekistan, is explained, the consequences of which are the observed complications. Alternatively, with the development of renal dysfunction and chronic kidney disease in this disease, the effectiveness of Klotho protein and vitamin D is considered in detail.

ABBREVIATED WORDS

HD - hypertension

RD - renal dysfunction

CVSD - cardiovascular system disease

PTH - Parathormone

EGFR - Estimated Glomerular Filtration Rate

CKD EPI - Chronic Kidney Disease Epidemiology Collaboration

LDV - Latest diastolic volume

LSV - Latest systolic volume

LDS - Latest diastolic size

LSS - Latest systolic size

BShF - Blood shot fraction

IVBT - Inter-ventricular barrier thickness

TRWLV - Thickness rear wall of the left ventricle

LVMW - Left ventricle myocardial weight

LVMWI - Left ventricular myocardial weight index

WTRI - Wall thickness ratio index

A - Left ventricle final diastolic filling

E - Left ventricle early diastolic filling

According to the World Health Organization, people with hypertension make up 27% of the adult population. By 2030, this figure is projected to exceed 29%, and their number will exceed 1.5 billion. The incidence of hypertension increases with age, reaching 50-65% among people over 65 [15].

In most patients, hypertension affects the kidneys, ultimately leading to the development of chronic kidney disease. In developed countries of Europe and North America, it is one of the main causes of severe renal dysfunction, and the number of patients belonging to this group is increasing [4, 9].

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 [14]. In them, in 3.0% - 9.5% of cases, the disease is in the initial stage, and if these figures are compared with the world population, it is confirmed that about 5% of the adult population of the globe has early stages of renal dysfunction. With age, these figures increase, reaching 15-20%, and even 30% [6, 10, 7, 13].

According to the latest data provided in the sources, signs of renal dysfunction were observed in 18% of patients with hypertension in the territory of Uzbekistan. According to their conclusions, this indicator is projected to double in the next decade. There is a "closed loop" between hypertension and the kidney, in which the kidney is simultaneously a factor leading to an increase in blood pressure and a target organ being damaged as a result [1].

The above data confirm that the prevention of renal changes in hypertension and its early detection are of great practical importance, as well as the need for scientific research in this area. Based on this, the comprehensive assessment of AH and its complications, in particular, kidney processes, changes in the last organ, which have a sharply negative impact on the outcome of the disease, and the improvement of effective treatment methods are of great importance.

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 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.

RESUTS

In patients with hypertension, as a result of its exacerbation, organic changes in the cardiovascular system accelerate in the transition from one stage to the next and lead to hemodynamic disorders. The pre-diagnosis of this process and conditions and the development of necessary treatment measures are considered one of the pressing problems of modern medicine. Foreign articles published in recent years provide information on the importance of Klotho protein and vitamin D in the development of RD, exacerbation and complication of CVSD [2, 11, 12]. Based on these data, we studied the relationship of Klotho protein and vitamin D with hemodynamic indicators and RD factors in patients with hypertension based on the purpose and function of our study. The blood serum Klotho protein and vitamin D indicators of those in the main and control group are reflected in table 1.1.

Table 1.1.

Serum Klotho protein, vitamin D, well as parathormone indicators in patients

Specification	1-group hypertension II (n=76)	1-group hypertension III (n=93)	Control group without hypertension (n=23)
Klotho, ng/ml	43,28±3,27	27,20±3,23*** p1-2<0,001	64,57±2,3*** p1<0,001 p2<0,001
Vitamin D, ng/ml	28,73±1,70	20,03±1,96*** p1-2<0,001	38,35±1,05*** p1<0,001 p2<0,001
Parathormone, ng/ml	45,11±2,34	76,75±2,41*** p1-2<0,001	32,31±0,83*** p1<0,001 p2<0,001

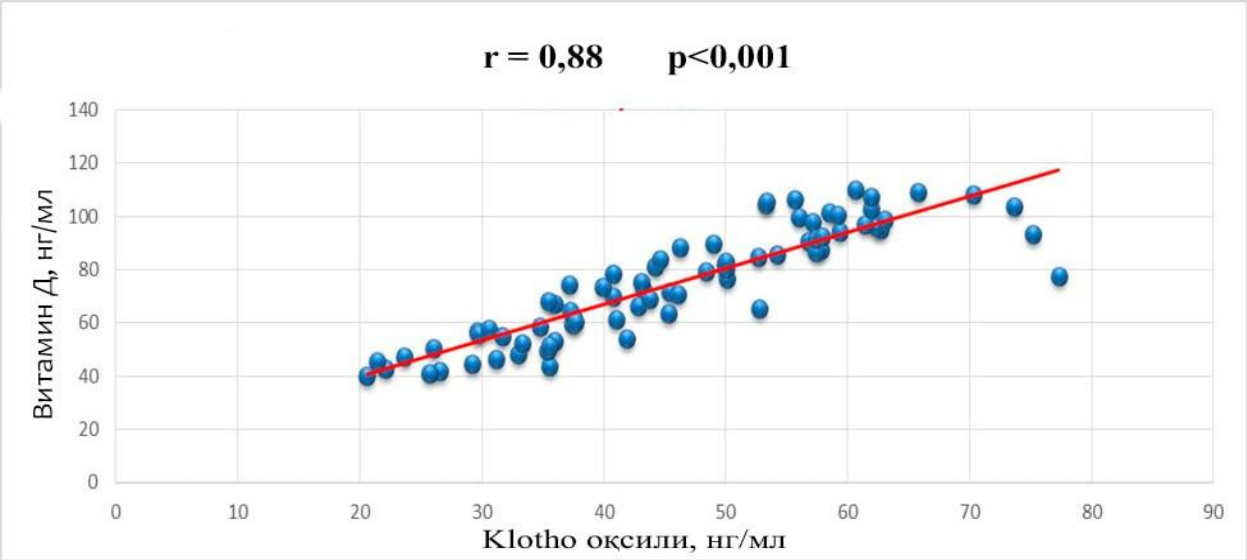
*Note: * - reliability of differences in relation to the main and control groups:*- p<0,05; **- p<0,01; ***- p<0,001.*

A strong reliable discrepancy was found between the groups (r1-2<0,001) with the Klotho protein group 1 hypertension phase II present in patients with group 43,28±3,27 ng/ml in group 2 hypertension phase III patients with 27,20±3,23 ng/ml. In the control group, Klotho protein was observed to be 64,57±2,3 ng/ml, reliably high compared to group 1 and group 2 (r1<0,001; r2<0,001). This result showed a decrease in the amount of Klotho protein in the stage-dependent Chol of hypertension.

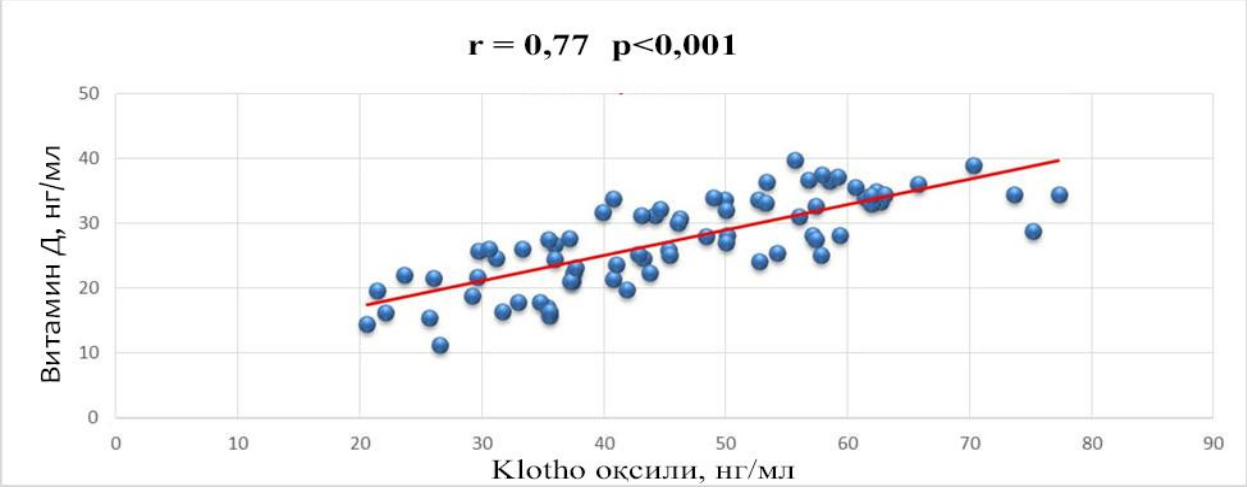
It is known that there are data on vitamin D and its influence on the development of parathormone (PTH) hypertension, which is important in its absorption in the body, as well as RD [3, 8, 5, 2]. Taking into account this information, we examined these active biological substances and obtained the following results. In group 1 patients, vitamin D was 28,73±1,70 ng/ml, while the PTH was 45,11±2,34 ng/ml in group 2, these indicators were 20,03±1,96 ng/ml and 76,75±2,41 ng/ml, respectively. Compared to the cross section of groups, Klotho protein and vitamin D were found to be significantly higher in the first group (r1-2<0.001), while PTH was noted to be higher in the second group instead (r1-2<0.001).

According to the results of numerous scientific studies, Klotho protein is mainly synthesized in the kidneys, and as RD develops, its production decreases sharply. This condition leads to impaired phosphate metabolism. Active vitamin D (calcitriol) enhances the expression of the Klotho protein in the kidneys. If this protein decreases vitamin D over-activation or calcium-phosphorus imbalance occurs **[2].** Based on the

conclusions obtained in the patients we involved in our study, we observed a positive correlation relationship between Klotho protein and vitamin D. This correlation was r=0,88 in group 1 (r<0,001), and r=0,77 in group 2 (r<0,001). They did not make a convincing difference when compared with each other. In doing so, it was found that vitamin D increased the Klotho protein in line with an increase in body levels (1.1 a and b - pic).

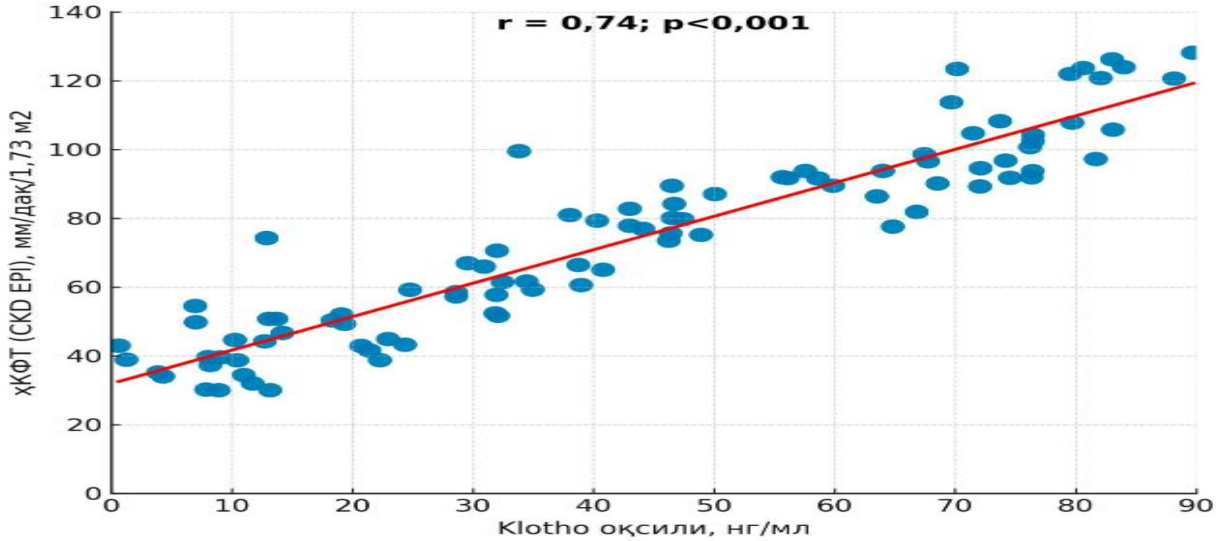


1.1 a- pic. Correlation relationship between Klotho protein and vitamin D in patients with hypertension phase II

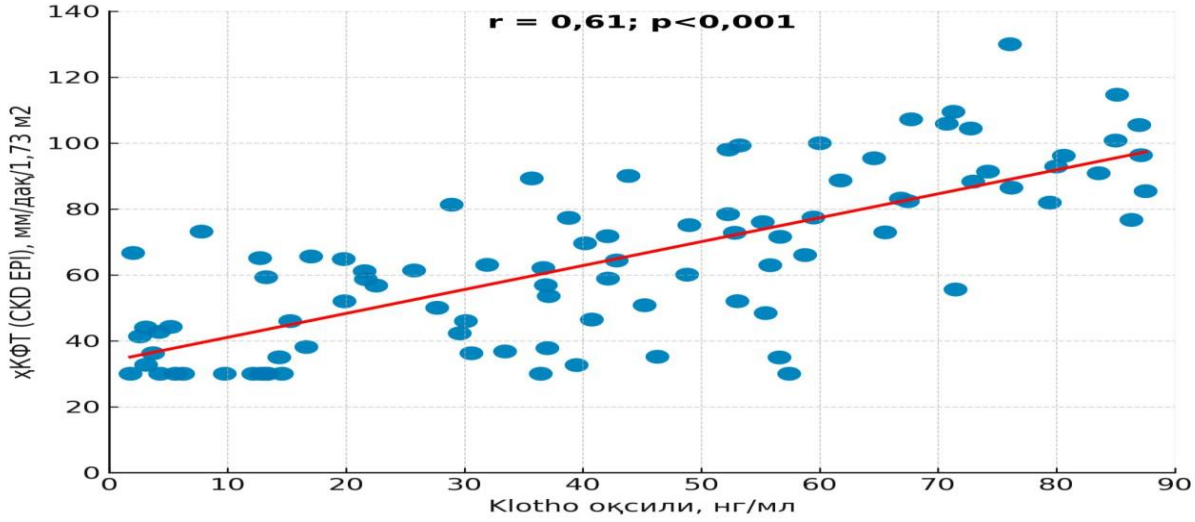


1.1 b- pic. Correlation relationship between Klotho protein and vitamin D in patients with hypertension phase III

A decrease in the estimated glomerular filtration rate (EGFR) in hypertension indicates a significant change in the kidneys. At the same time, as the early stages of hypertension, the synthesis of the Klotho protein in the kidneys begins to decrease, while during its pronounced period there is a sharp decrease. Our study found a positive correlation relationship between the amount of this protein and the EGFR (Chronic Kidney Disease Epidemiology Collaboration - CKD EPI) indicator. That is, if the amount of Klotho protein increases in the body, an increase in EGFR is observed, respectively (1.2 a and b - pic).



1.2 a- pic. Correlation relationship between Klotho protein and estimated glomerular filtration rate in group 1



1.2 b- pic. Correlation relationship between Klotho protein and estimated glomerular filtration rate in group 2

The correlation relationship between Klotho protein and EGFR was reliably high in group 2 (r=0,61), (p<0,001), group 1 (r=0,74), (p<0,001) when analyzed in cross-section of groups.

Klotho protein is not only a biomarker for early detection of RD, it is also important in the diagnosis of this system disease through its effects on the vascular system. This protein prevents damage to the vascular wall through the action of antioxidants and antifibrosis, restricts the accumulation of these salts in the walls of arteries through calcium-phosphorus homeostasis, stimulates the production of nitric oxide, positively affects hemodynamics by ensuring the expansion of vessels.

Table 1.2

Correlation relationship between Klotho protein and exocardiography indicators

Specification	Klotho protein ng/ml		P	R
	1-group hypertension II (n=76)	1-group hypertension III (n=93)		
Latest diastolic volume, ml (LDV)	112,4±2,62	116,6±2,83	p1>0,05 p1>0,05	r_1=-0,59 r_2=-0,64
Latest systolic volume, ml (LSV)	46,54±0,91	48,53±0,78	p1>0,05 p2>0,05	r_1=-0,56 r_2=-0,61
Latest diastolic size, sm (LDS)	4,26±0,51	5,26±0,53	p1>0,05 p2>0,05	r_1=-0,51 r_2=-0,57
Latest systolic size, sm (LSS)	3,07±0,04	3,12±0,04	p1>0,05 p2>0,05	r_1=-0,58 r_2=-0,65
Blood shot fraction, % (BShF)	58,5±0,49	57,5±0,54	p1>0,05 p2>0,05	r_1=0,64 r_2=0,72
Inter-ventricular barrier thickness, (mm) (IVBT)	12,2±0,14**	13,3±0,13***	p1<0,01 p2<0,001	r_1=-0,40 r_2=-0,65

Thickness rear wall of the left ventricle, (mm) (TRWLV)	12,5±0,15**	13,7±0,13***	p1<0,01 p2<0,001	r_1=-0,43 r_2=-0,69
Left ventricle myocardial weight, (g) (LVMW)	210,29±4,16**	224,66±1,76***	p1<0,01 p2<0,001	r_1=-0,55 r_2=-0,75
Left ventricular myocardial weight index, (g/m^2) (LVMWI)	97,24±1,29	103,25±1,39*	p1>0,05 p2<0,05	r_1=-0,56 r_2=-0,67
Wall thickness ratio index (WTRI)	0,71±0,06	0,76±0,03	p1>0,05 p2>0,05	r_1=-0,52 r_2=-0,58
Left ventricle final diastolic filling (A), sm/s (LVFDF)	0,56±0,02	0,55±0,02	p1>0,05 p2>0,05	r_1=-0,44 r_2=-0,51
Left ventricle early diastolic filling (E), sm/s (LVEDF)	0,70±0,02	0,71±0,02	p1>0,05 p2>0,05	r_1=0,47 r_2=0,52
E/A	0,78±0,01	0,79±0,01	p1>0,05 p2>0,05	r_1=0,56 r_2=0,62
Vitamin D, ng/ml	28,73±1,70***	20,03±1,96***	p1<0,001 p2<0,001	r_1=0,88 r_2=0,77
Parathormone, ng/ml	45,11±2,34**	76,75±2,41***	p1<0,01 p2<0,001	r_1=-0,61 r_2=-0,74

*Note: * - the degree of reliability of differences in groups *- p<0,05; **- p<0,01; ***- p<0,001.*

In controlled patients, the correlation between hemodynamic indicators and Klotho protein was analyzed. In the first group according to the results obtained Klotho protein A (r=-0,44, p>0,05), IVBT (r=-0,40, p<0,01), TRWLV (r=-0,43, p<0,01) weak negative with, E (r=0,47, p>0,05) weak positive with, LDV (r=-0,59, p>0,05), LSV (r=-0,56, p>0,05), LDS (r=-0,51, p>0,05), LSS (r=-0,58, p>0,05) indications, beyond LVMWI (r=-0,56, p>0,05), WTRI (r=-0,52, p>0,05), LVMW (r=-0,55, p<0,01) with mean negative, E/A (r=0,56, p>0,05) with mean positive, PTH (r=-0,61, p<0,01) with strong negative, BShF (r=0,64, p>0,05) with reliable positive, vitamin D (r=0,88, p<0,001) with, however, it has been found to have strong reliable

positive correlations. The second group consisted of Klotho protein A (r=-0,51, p>0,05), E (r=0,52, p>0,05) weak with, LDV (r=-0,64, p>0,05), LSV (r=-0,61, p>0,05), LDS (r=-0,57, p>0,05), LSS (r=-0,65, p>0,05), LVMWI (r=-0,67, p>0,05), WTRI (r=-0,58, p<0,05), IVBT (r=-0,65, p<0,001) mean negative with indicators, E/A (r=0,62, p>0,05) with mean positive, BShF (r=0,72, p>0,05), vitamin D (r=0,77, p<0,001) strong reliable positive with, TRWLV (r=-0,69, p<0,001), LVMW (r=-0,75, p<0,001), PTH (r=-0,74, p<0,001) it has been observed that there is a strong reliable negative correlation relationship with (table 1.2).

Table 1.3

Correlation relationship of vitamin D and exocardiography indicators

Specification	Vitamin D ng/ml		P	R
	1-group hypertension II (n=76)	1-group hypertension III (n=93)		
Latest diastolic volume, ml (LDV)	112,4±2,62	116,6±2,83	p1>0,05 p1>0,05	r_1=-0,57 r_2=-0,62
Latest systolic volume, ml (LSV)	46,54±0,91	48,53±0,78	p1>0,05 p2>0,05	r_1=-0,58 r_2=-0,63
Latest diastolic size, sm (LDS)	4,26±0,51	5,26±0,53	p1>0,05 p2>0,05	r_1=-0,53 r_2=-0,59
Latest systolic size, sm (LSS)	3,07±0,04	3,12±0,04	p1>0,05 p2>0,05	r_1=-0,56 r_2=-0,63
Blood shot fraction, % (BShF)	58,5±0,49	57,5±0,54	p1>0,05 p2>0,05	r_1=0,66 r_2=0,74
Inter-ventricular barrier thickness, (mm) (IVBT)	12,2±0,14	13,3±0,13	p1<0,01 p2<0,001	r_1=-0,42 r_2=-0,67
Thickness rear wall of the left ventricle, (mm) (TRWLV)	12,5±0,15	13,7±0,13	p1<0,01 p2<0,001	r_1=-0,45 r_2=-0,69
Left ventricle myocardial weight, (g) (LVMW)	210,29±4,16	224,66±1,76	p1<0,01 p2<0,001	r_1=-0,55 r_2=-0,73

Left ventricular myocardial weight index, (g/m^2) (LVMWI)	97,24±1,29	103,25±1,39	p1>0,05 p2<0,05	r_1=-0,57 r_2=-0,69
Wall thickness ratio index (WTRI)	0,71±0,06	0,76±0,03	p1>0,05 p2>0,05	r_1=-0,51 r_2=-0,59
Left ventricle final diastolic filling (A), sm/s (LVFDF)	0,56±0,02	0,55±0,02	p1>0,05 p2>0,05	r_1=-0,46 r_2=-0,54
Left ventricle early diastolic filling (E), sm/s (LVEDF)	0,70±0,02	0,71±0,02	p1>0,05 p2>0,05	r_1=0,46 r_2=0,51
E/A	0,78±0,01	0,78±0,01	p1>0,05 p2>0,05	r_1=0,57 r_2=0,64
Klotho protein, ng/ml	43,28±3,27	27,20±3,23	p1<0,001 p2<0,001	r_1=0,88 r_2=0,77
Parathormone, ng/ml	45,11±2,34	76,75±2,41	p1<0,01 p2<0,001	r_1=-0,63 r_2=-0,76

*Note: * - the degree of reliability of differences in relation to groups *- p<0,05; **- p<0,01; ***- p<0,001.*

In controlled patients, the correlation between hemodynamic indicators and vitamin D was analyzed. Vitamin D in the first group according to the results obtained LDV (r=-0,57, p>0,05), LSV (r=-0,58, p>0,05), LDS (r=-0,53, p>0,05), LSS (r=-0,56, p>0,05), BShF (r=0,66, p>0,05), LVMWI (r=-0,57, p>0,05), WTRI (r=-0,51, p>0,05), A (r=-0,46, p>0,05), E (r=0,46, p>0,05), E/A (r=0,57, p>0,05) weak with, IVBT (r=-0,42, p<0,01), TRWLV (r=-0,45, p<0,01), LVMW (r=-0,55, p<0,01), PTH (r=-0,63, p<0,01) with mean, Klotho protein (r=0,88, p<0,001) it has been found to have a reliable correlation relationship with. In the second group, vitamin D LDV (r=-0,62, p>0,05), LSV (r=-0,63, p>0,05), LDS (r=-0,59, p>0,05), LSS (r=-0,63, p>0,05), BShF (r=0,74, p>0,05), LVMWI (r=-0,69, p>0,05), WTRI (r=-0,59, p<0,05), A (r=-0,54, p>0,05), E (r=0,51, p>0,05), E/A (r=0,64, p>0,05) weak with, IVBT (r=-0,67, p<0,001), TRWLV (r=-0,69, p<0,001), LVMW (r=-0,73, p<0,001), Klotho protein (r=0,77, p<0,001), PTH (r=-0,79, p<0,001) it was observed that there is a reliable correlation relationship with (table 1.3).

CONCLUSION

The above data indicate that there was a correlation between Klotho protein and vitamin D in patients with hypertension. This correlation was observed to be more recent in hypertension phase III than in its phase II. Based on the results obtained, in determining the incidence of disease in patients with hypertension, the Klotho protein and vitamin D can be used as one of the main markers in the early diagnosis of the development of KD.

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