IMPORTANCE OF VITAMIN D LEVELS IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE C2 AND C3

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Abstract. *Purpose of the study: to study the importance of vitamin D levels in patients with stages 2–3 CKD, as well as the relationship between vitamin D levels and bone-mineral metabolism markers. 105 patients with chronic kidney disease (CKD) stages C2 and C3, aged from 35 to 69 years, of inflammatory and vascular etiology were examined. All examined patients were under dispensary observation at the Republican Specialized Scientific and Practical Medical Center of Nephrology and kidney transplantation of the Ministry of Health of Uzbekistan. Our study revealed that patients with CKD and vitamin D deficiency had significantly lower serum albumin levels. It is proposed to determine the serum level of "nutritional" vitamin D in patients not receiving dialysis and carry out correction in case of its deficiency.*
Keywords: *chronic kidney disease, vitamin D, glomerular filtration rate.*

The prevalence of chronic kidney disease (CKD) today has a steady upward trend, reaching 10-15%. Despite the fact that modern medical technologies help slow its progression, the need for renal replacement therapy tends to increase [2,4,5]. Modern researchers report a relationship between cases of premature death in patients with kidney dysfunction and disorders of vitamin D metabolism [6,9,11].

It is known that with the degree of progression of CKD, the risk of calcium metabolism disorders increases. At the same time, the risk of developing cardiovascular diseases in patients with CKD increases, maintaining it even after kidney transplantation [4,8,9,11]. A number of scientific studies to determine the level of vitamin D in patients with chronic kidney disease, including in patients after transplantation, have shown that from 30% to 50% of patients with CKD have vitamin D deficiency [11,14,15,16].

Purpose of the study: to study the importance of vitamin D levels in patients with CKD stages 2–3, as well as the relationship between vitamin D levels and markers of bone and mineral metabolism.

Materials and research methods

105 patients with chronic kidney disease (CKD) stages C2 and C3, aged from 35 to 69 years, of inflammatory and vascular etiology were examined. All examined patients were under dispensary observation at the Republican Specialized Scientific and Practical Medical *Center of Nephrology* and kidney transplant. The mean age of the patients were 41.3±14.7 years.

The diagnosis of CKD was established in accordance with the KDIGO criteria (2012) [17]. Stage 2: GFR 89–60 ml/min/1.73 m ^{2} (n = 35 patients), stage 3: GFR 59–30 ml/min/1.73 m ^{2} (n = 33 patients with stage C3a and n = 37 patients with stage C3b CKD). Assessment of the functional state of the kidneys was carried out on the basis of determining the level of serum creatinine (Cr), urinary albumin excretion (determination of microalbuminuria (MAU ≥300 mg/l) in a single morning urine, glomerular filtration rate (GFR), calculated using the GFR EPI formula , which takes into account race, gender , age, serum creatinine level [4,5,12]. To calculate GFR using the CKD - EPI formula, you can use special applications for mobile devices (QxMDCalculator). The paraclinical spectrum also included the determination of the following biochemical markers, such as parathyroid hormone (PTH), calcium (Ca), phosphorus (P), calcium-phosphorus product (

Ca×P), alkaline phosphatase (ALP), total protein, albumin, urea (on the SIEMENS biochemical analyzer ADVIA 2400", Germany).

When assessing vitamin D levels, we were guided by the KDOQI recommendations for the treatment of disorders of bone and mineral metabolism in patients with CKD from 2005 and on the nutrition of patients with CKD from 2008 [2,3,4,5]. According to these recommendations, we have created options for the level of serum calcidiol: normal – ≥ 30 ng /ml; deficiency – 15–29 ng /ml; deficiency – ≤15 ng /ml.

Statistical analysis of the results were carried out using the Statistica program v 7.0" ("StatSoft Inc ", USA). Methods of descriptive statistics were used to determine the frequency of occurrence of a sign, arithmetic mean, median and standard deviation (SD). Differences in biological markers between CKD groups were calculated using the nonparametric Mann–Whitney test. Correlations were determined using the Spearman correlation coefficient. Frequency indicators were analyzed with using the χ 2 test or Fisher's test, respectively.

Research results and discussion

The clinical characteristics of the examined patients with stage C2-3 CKD are presented in Table No. 1. As can be seen from the presented data, the average age and gender composition of the examined patients were comparable. Analysis of the etiological structure of the patient data showed that in all groups of patients with CKD stages C2, C3a and C3b, patients with chronic glomerulonephritis and tubulointerstitial nephritis prevailed. The smallest percentage of the etiological factor of CKD was made up of patients with hypertensive and atherosclerotic etiology (from 4-7%) (Table 1).

Analysis of the distribution of patients with CKD depending on the level of VitD showed that as the severity of CKD increased, there was an increase in the number of patients with insufficiency and deficiency of vitamin D. Analysis of serum levels of vitamin D revealed that in 56.2% of patients there was a decrease in it, and Vitamin D deficiency was found in 26.7% of patients. At the same time, in the 1st group with CKD C2, 22 patients (59.5%) had normal Vitamin D values, while in the 2nd group of patients with CKD stage 3a there were 4 (10.2%), and in the 3rd group this contingent of patients was equal to 0. The number of patients with insufficient levels of Vit. D in the 1st group was detected in 3 (8.1%) patients, in the 2nd group in 9 (23.1%) and in the 3rd group with CKD stage C3b in 17 (44.7%) patients (Table 1).

Table 1.

Clinical characteristics of patients with CKD stage C2-C3

Options	***CKD stage 2 n= 37***	***CKD stage 3a n= 39***	***CKD stage 3b n= 38***
Age, years	40.82±12.67	39.7±11.37	35.63±13.55
Gender distribution			
Men, n (%)	16 (29.4%0	21 (53.8%)	22 (57.9%)
Women, n (%)	21 (56.6%)	18 (46.1%)	16 (42.1%)
Distribution of patients by etiology			
Chronic glomerulonephritis	13 (35.2%)	14 (35.9%)	16 (42.1%)
Chronic tubulointerstitial nephritis	15 (40.5%)	15 (38.5%)	13 (34.2%)
Hypertensive nephroangiosclerosis	5 (13.5%)	7 (17.9%)	5 (13.2%)
Atherosclerosis of renal vessels	4 (10.8%)	3 (7.7%)	4 (10.5%)
Distribution of patients depending on VitD level			
Norm VitD (≥ 30 ng /ml)	22 (59.5%)	4 (10.2%)	-

VitD deficiency (15–29 ng /ml)	12 (32.4%)	26 (66.7%)	21 (55.3%)
VitD deficiency (≤15 ng /ml)	3 (8.1%)	9 (23.1%)	17 (44.7%)
Biochemical indicators of kidney function			
GFR, ml / min /1.73 m²	7 3.36 ±12.4	5 2 .6+ 7 .7 5**	3 6.7+ 6.5 9 *** _
Urea, mmol / l	10.3±1.8	12.4±2.2**	13.7±2.6***
Creatinine, µmol / l	122.55±13.58	167.4±18.37**	203.5±22.52***
Total protein, g / l	52.67±5.5	46.23±6.66**	42.51±6.93***
Albumin , g/l	36.2+4, 72	31.45±4.34	26.7±5.6***
Alkaline phosphatase , U/l	2 5 7.43+ 6 8.15	2 86.7+ 59.7 _ _	32 1.5+ 6 3.4 ***

Note: significance level ** p< 0.01 and *** p<0.001

Analysis of the biochemical parameters of the functional state of the kidneys (creatinine and GFR level) and the biochemical composition of the blood (urea, total protein level) corresponded to the stages of CKD, differed significantly in the 2nd and 3rd study groups, in contrast to the data of the 1st group with CKD stage 2 (** p < 0.01 and *** p<0.001 – table 1.). However, alkaline phosphatase, despite a slight tendency to increase the level of the latter, did not differ significantly in patients with stages 2 and 3a of CKD. The results of the analysis of serum albumin levels also did not reveal a significant difference in patients with different stages of CKD. (Table 1.).

The level of PTH increased significantly, starting from stage 3 CKD (** p < 0.01 and *** p < 0.001 - table 2.) by 72.6% and 1.2 times in the 2nd and 3rd groups of patients with CKD 3a and stage 3b. As for the level of serum calcium and phosphorus, as well as their ratio (Ca x P), there was no significant difference between the presented study groups (p>0.05).

Table 2.

Indicators of calcium -phosphorus metabolism in patients with CKD stage C2-C3

Options	***CKD stage 2 n= 37***	***CKD stage 3a n= 39***	***CKD stage 3b n= 38***
Vit.D , ng / ml	26.6+ 6.96 _	20.2 +5.7 *	19.7+4.3 ***
Calcium , mmol /l	2.4 6 +0.1 4	2.3 3 +0.3 1	2.1 5 +0.3 4 _
Phosphorus , mmol /l	1.4 4 +0.2 7	1.52 +0.3 3 _	1.6 5 +0.2 2
Ca x P	3.4 9 +0.7 2 4	3.5 4 + 0.7 7	3, 6 3+0, 6 9
iPTH , pg / ml	54.2+ 2 3.8	9 3.6+ 3 7.1 **	12 8.3+34.5 ***

Note: level of significance * p< 0.05; **p<0.01 and ***p<0.001.

Mineral and bone disorders can be detected when GFR decreases to less than 70 ml/min/1.73 m² even before stage III CKD is established. The deterioration of renal function and the progression of mineral-bone disorders in CKD are complicated by the development of secondary hyperparathyroidism. Patients with CKD are at risk of developing earlier and more severe disorders of mineral-bone metabolism, which are the leading cause of cardiovascular morbidity and mortality in this category of patients. Despite an attempt to actively correct mineral metabolism disorders in patients with CKD, more than half of them had vitamin D deficiency. In patients with CKD, decreased serum vitamin D levels are due to increased glomerular filtration and the result of low protein diets and proteinuria [11,14,15,16]. These factors often accompany CKD, leading to loss of vitamin D -binding protein in the urine [7,8,9,15, 16]. Vitamin D deficiency leads to low intestinal calcium absorption, hypocalcemia and increased PTH secretion with the development of secondary hyperparathyroidism, which is an independent risk factor for death in patients with CKD [2, 3, 10, 11, 12].

Conclusion. Our study revealed that patients with CKD and vitamin D deficiency had significantly lower serum albumin levels. However, the question remains about the definition of vitamin D in patients with severe stages of CKD and in need of hemodialysis, since the effect of dialysis on bone-mineral metabolism is large and it is difficult to assess the true picture of bone-mineral metabolism in such patients. Determination of serum vitamin D and its correction in patients with CKD has been the subject of controversy due to different results obtained by different researchers [10,11,14,16]. It is proposed to determine the serum level of "nutritional" vitamin D in patients not receiving dialysis and carry out correction in case of its deficiency.

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