https://doi.org/10.1590/1678-9865202235e210219

ORIGINAL

Vitamin D concentrations and their relationship with iron parameters in patients with chronic kidney disease

Concentrações de vitamina D e sua relação com parâmetros de ferro em pacientes com doença renal crônica

Letícya Thaís Mendes VIANA[1] 0000-0002-9707-0931
Betânia de Jesus e Silva de Almendra FREITAS[1] 0000-0002-7797-735X

ABSTRACT

Objective

To investigate the relationship between calcidiol (25(OH)D3) concentrations and iron parameters in patients with chronic kidney disease.

Methods

This is a cross-sectional, descriptive, and quantitative study. The sample consisted of 86 adult patients of both sexes undergoing dialysis. 25(OH)D3 concentrations were determined by chemiluminescence; food consumption was assessed using 24-hour recalls, and the serum levels of hemoglobin, iron, ferritin, and transferrin saturation were assessed. Data analysis was performed using the program Stata, with a significance level of $p<0.05$.

Results

The results pointed to 25(OH)D3 concentrations compatible with sufficiency, iron levels consistent with normality, and ferritin and transferrin saturation above the reference values. The consumption of carbohydrates and lipids was

[1] Universidade Federal do Piauí, Centro de Ciências da Saúde, Departamento de Nutrição. *Campus* Ministro Petrônio Portella, Ininga, 64049-550, Teresina, PI, Brasil. Correspondence to: BJSA FREITAS. E-mail: <betaniafreitas2004@yahoo.com.br>.

Article based on the dissertation of LTM VIANA, entitled "*Concentrações de vitamina D e sua relação com parâmetros de ferro, níveis de cálcio, fósforo e paratormônio na doença renal crônica*". Universidade Federal do Piauí; 2021.

How to cite this article

Viana LTM. Freitas BJSA. Vitamin D concentrations and their relationship with iron parameters in patients with chronic kidney disease. Rev Nutr. 2022;35:e210219. https://doi.org/10.1590/1678-9865202235e210219

higher in females. There was no relationship between the adequacy of 25(OH)D3 and the presence of anemia and iron parameters.

Conclusion

Considering that the mean serum levels of iron and 25(OH)D3 were adequate, it is suggested that resistance to erythropoietin and the inflammatory process may have contributed to the percentage of anemic individuals found in the study.

Keywords: Anemia. Cholecalciferol. Chronic kidney disease-mineral and bone disorder. Iron. Renal dialysis.

RESUMO

Objetivo

Investigar a relação entre as concentrações de calcidiol (25(OH)D3) e os parâmetros de ferro em pacientes com doença renal crônica.

Métodos

É um estudo transversal, descritivo e quantitativo. A amostra foi composta por 86 pacientes, adultos, de ambos os sexos, em terapia dialítica. As concentrações de 25(OH)D3 foram determinadas pelo método de quimioluminescência; o consumo alimentar foi avaliado pela aplicação de Recordatórios de 24 horas e foram avaliados os níveis séricos de hemoglobina, ferro, ferritina e saturação de transferrina. A análise dos dados foi realizada no programa Stata, com nível de significância p<0.05.

Resultados

Os resultados apontaram para concentrações de 25(OH)D3 compatíveis com suficiência, níveis de ferro compatíveis com a normalidade e ferritina e saturação de transferrina superiores à referência. O consumo de carboidratos e lipídios foi superior no sexo feminino. Não foi verificada relação entre a adequação de 25(OH)D3 e a presença de anemia e parâmetros de ferro.

Conclusão

Tendo em vista que os níveis médios séricos de ferro e 25(OH)D3 estavam adequados, sugere-se que a resistência à eritropoietina e o processo inflamatório podem ter contribuído para o percentual de anêmicos constatado no estudo.

Palavras-chave: *Anemia. Colecalciferol. Distúrbio mineral e ósseo na doença renal crônica. Ferro. Diálise renal.*

INTRODUCTION

Chronic Kidney Disease (CKD) is a world health problem [1]. Global estimates of CKD indicate its prevalence in 14,3% of the general population and 36,1% of risk groups. In Brazil, the estimated prevalence of CKD in adults is 6,7%, tripling among those 60 years old or older [2].

Hypovitaminosis D is a growing social problem, affecting a large part of the population of every ethnicity and age and more than 50% of the healthy population. It is also frequently seen in CKD patients submitted to dialytic therapy [3]. According to the 2019 Brazilian Dialysis Census, 10,8% of patients presented serum calcidiol levels (25(OH)D3) <20 ng/mL, characterizing vitamin D deficiency [4]. This restriction contributes to the manifestation of relevant metabolic disorders, such as oxidative stress, insulin resistance, chronic low-grade inflammation, as well as to muscular weakness, and falls. Although low levels of (25(OH)D3) occur in both men and women, it is more prevalent among women [5].

The deficiency is associated with high levels of Fibroblast Growth Factor 23 (FGF-23) and Parathormone (PTH), low bone mineral density, lack of exposure to sunlight, reduced skin synthesis of cholecalciferol in response to sunlight, reduced intake of foods that are sources of vitamin D, urinary loss of (25(OH) D3), and high blood pressure in proteinuric kidney diseases. Also, megalin, a 25(OH)D3-binding protein

in the proximal tubule, decreases as the Glomerular Filtration Rate (GFR) falls, thus reducing 25(OH)D3 tubular reabsorption. Moreover, phosphorus retention in the kidneys during the first stages of CKD might contribute to increasing FGF-23, given the reduced production of calcitriol ($1,25(OH)2D_3$) resulting from the inhibition of the 1α-hydroxylase enzyme [6,7].

The reduction of the GFR limits the supply of 25(OH)D3 for the 1α-hydroxylase enzyme in the proximal tubule, limiting the kidney's ability to produce $1,25(OH)2D_3$. In the initial stages of CKD, the expression of the co-receptor FGF-23, αKlotho, progressively decreases with nephron loss. As a compensatory mechanism, FGF-23 levels increase to 1000 times their normal values, attempting to preserve a neutral distribution of phosphate and suppressing the production of ($1,25(OH)2D_3$). That, in turn, favors the rise of PTH and secondary hyperparathyroidism, intensifying the evident hyperphosphatemia as the damaged kidney shows resistance to FGF-23 [6,8].

Anemia of inflammation, also known as anemia of chronic disease, occurs precociously during CKD. More expressive in men, it may become unmanageable with the decline of renal function [9]. Its main causes are the reduction of erythropoietin production, iron deficiency, inflammation, and vitamin D deficiency [10-12]. Anemia of inflammation may lead to erythropoietin resistance, a common problem associated with amplified rates of mortality among patients undergoing Hemodialysis Therapy (HD). As renal mass and red blood cells diminish, the kidneys may not produce sufficient erythropoietin, leading to anemia [13].

Vitamin D may have positive effects in controlling anemia of inflammation, as it stimulates erythroid progenitor cell proliferation, positively regulating the erythropoietin receptors in these cells, and provokes the reduction of pro-inflammatory cytokines, avoiding inflammation [14-17]. Decreasing the liberation of cytokines, vitamin D may increase iron's bioavailability for erythropoiesis and hemoglobin synthesis, preventing iron sequestration in macrophages, correcting absorption deficiencies, and protecting from anemia [18,14]. Studies suggest that inadequate concentrations of 25(OH)D3 may hinder the production of iron in the bone marrow, limiting erythropoiesis.

Given CKD's impact on world mortality and vitamin D's recognized effect on anemia, the present study aimed to assess the relationship between 25(OH)D3 concentrations and iron parameters in CKD patients.

METHODS

This is a cross-sectional, descriptive, and quantitative study with 86 both-sex CKD patients in HD in Centers for Dialytic Therapy in the city of *Teresina*, state of *Piauí*, Brazil. The study was carried out in accordance with the Declaration of Helsinki's guidelines and the Resolution nº 466/2012 of the *Conselho Nacional de Saúde* (National Health Council), and it was approved by the Committee of Ethics and Research of the Federal University of *Piauí* under opinion nº 3.993.938.

The sample size was estimated considering the total number of patients (n=1056) registered in all the units of hemodialytic treatment in Teresina in 2018. It adopted a confidence interval of 95% and a relative error of 10%. The resulting sample was 88 patients.

We employed the following criteria of eligibility for the selection of patients: patients diagnosed with CKD who were in HD therapy for at least three months, with preserved cognitive capacity, ages ≥18 and ≤59, not undergoing vitamin D supplementation (confirmed in interviews with the patient), and not being chronic smokers or drinkers. Out of 89 patients selected, 3 were lost in the course of research, due to a kidney transplantation surgery, absence at the day of drawing blood, and death. Thus, 86 patients were considered for the sample.

Samples of 5 mL of blood were collected in the morning from patients who had fasted for at least 8 hours. The analysis of vitamin D blood concentrations by dosing 25(OH)D3 was determined by

chemiluminescence. Concentrations of 25(OH)D3 ≥30 ng/mL, between 21 and 29 ng/mL, and <20 ng/mL were considered, respectively, sufficient, insufficient, and deficient, according to the recommendations of Hollick, Inda and Melamed [19,6].

The patients' medical records were consulted for information on biochemical exams: hemoglobin, ferritin, transferrin saturation, and serum iron. The collected information refers to the last monthly blood draw carried out in the clinics that perform exams with proven periodicity.

Following the criteria of the World Health Organization, anemia was defined as hemoglobin levels below 13 g/dL for men and 12 g/dL for women, regardless of the CKD stage [20]. Hemoglobin was measured with the cyanomethemoglobin method, using cyanide-free sodium lauryl sulfate, as recommended by the International Committee for Standardization in Haematology.

Ferritin was analyzed with the immunoturbidimetric method, with 200 to 500 ng/dL as reference values [13]. Transferrin saturation (%) was calculated as (iron/TIBC) x 100 and the reference value was below 20% [13]. The Total Iron-Binding Capacity (TIBC) was calculated as (TIBC (µmol/L) = 25,1 x Transferrin (g/L). The serum iron was determined with the modified Goodwin colorimetric system (Ferrozine), with the following reference values: 65 to 175 µg/dL in men and from 50 to 170 µg/dL in women [11].

The patients eating habits were assessed with two 24-hour recalls (R24h). The first R24h included all the patients in the study, and for the second, 40% of the previously selected population was picked randomly [21]. The consumption of energy, macronutrients, vitamin D, and iron were calculated with the software Dietbox®. The results were adjusted for intrapersonal and interpersonal variability, avoiding distortions caused by differences in energy consumption.

To verify the adequation of energy food consumption, macro and micronutrients, we considered the daily recommendations for HD patients: energy: 35 kcal/kg/day <60 years-old; protein: 1,2 g/kg/day; carbohydrates: 4 – 6 g/kg/day; lipids: 1 – 1,5 g/kg/day; dietary vitamin D: 10 µg/day and dietary iron: 8mg/day for men and 15 mg/day for women [22,20,23].

The data were analyzed in the software Stata® version 14 (Stata Corp., College Station, United States). The Shapiro-Wilk test was applied to check the normality of data. Pearson's chi-square (χ^2) or, when suitable, Fisher's exact test were used to evaluate the categorical variables. The differences in means were compared among groups with Student's *t*-test and ANOVA for parametric variables. For the non-parametric ones, we used the Mann-Whitney or the Kruskal-Wallis tests. The correlation between 25(OH)D3, the iron parameters, and eating habits was examined by Pearson's correlation coefficient. The significance level was $p<0.05$.

RESULTS

This study included 86 patients with an average of 42.5 years of age. Among the patients, 49 were male (57%) and 37 were female (43%). Table 1 introduces the mean values of 25(OH)D3 as consistent with sufficiency; the average serum iron values were compatible with normality; ferritin and transferrin saturation were above the reference values. No statistically significant difference was found between the sexes.

Table 2 shows the characteristics of the patients' diets. Regular food ingestion indicated a high probability of inadequate consumption of energy, macronutrients, vitamin D, and iron, especially with the statistically higher average lipid and carbohydrate consumption among females.

Table 3 did not relate 25(OH)D3 sufficiency with the presence of anemia or iron classification ($p>0.05$). Table 4 presents a significant negative correlation between 25(OH)D3 and dietary lipids.

Table 1 – Distribution of mean serum concentrations of biochemical variables according to the total of patients. *Teresina* (PI), Brazil, 2021.

Variables	N=86		*p*-value
	Male (n=49)	Female (n=37)	
	Means (95%CI)	Means (95%CI)	
Vitamin D (ng/mL)*	41.2 (3.6-45.8)	36.9 (33.1-40.7)	0.167
Hemoglobin (g/dL)*	12.2 (11.5-12.9)	11.8 (11.0-12.7)	0.534
Iron (ug/dL)#	80.2 (69.3-91.2)	69.3 (59.4-79.1)	0.173
Ferritin (ng/dL)#	567.5 (392.6-742.4)	493.6 (350.9-635.2)	0.947
Transferrin saturation (%)#	32.0 (26.6-37.4)	31.8 (25.6-38.0)	0.946

Note: *Student's *t* test; #Mann-Whitney's test. CI: Confidence Interval.

Table 2 – Distribution of mean values and standard deviation of energy, macronutrients, vitamin D, and dietary iron intake. *Teresina* (PI), Brazil, 2021.

Variables	Total (N=86)		Male (n=49)		Female (n=37)		*p*-value
	Mean	SD	Mean	SD	Mean	SD	
Energy (kcal/kg/day)#	22.93	9.08	23.32	8.42	22.41	10.0	0.297
Carbohydrates(g/kg/ day)*	2.69	0.75	2.46	0.73	3.00	0.67	<0.001
Protein (g/kg/ day)*	1.00	0.39	0.96	0.43	1.05	0.34	0.302
Lipids (g/kg/ day)*	0.76	0.25	0.69	0.21	0.86	0.27	0.001
Vitamin D (µg/ day)#	2.0	2.0	2.3	2.4	1.5	1.2	0.059
Iron (mg/day)#	7.3	2.0	7.2	2.7	7.4	5.1	0.678

Note: *Student's *t* test; #Mann-Witney test. SD: Standard Deviation.

Table 3 – Relation between 25(OH)D3 concentrations and the presence of anemia and serum iron. *Teresina* (PI), Brazil, 2021.

Variables	25(OH)D3						*p*-value
	Total		Sufficient		Insuf/Deficient		
	n	%	n	%	n	%	
Anemia							0.644
Absence	32	37.2	24	38.7	8	33.3	
Presence	54	61.3	38	61.3	16	66.7	
Serum iron							0.246
Deficient	29	34.5	23	38.3	6	25.0	
Normal	55	65.5	37	61.7	18	75.5	

Note: <Pearson's Chi-square.

Table 4 – Simple linear correlation between 25(OH)D3, iron parameters, and eating habits. *Teresina* (PI), Brazil, 2021.

Variables	Coefficient of correlation	*p*-value
Hemoglobin (g/dL)	-0.1148	0.292
Serum iron (ug/dL)	-0.0692	0.531
Ferritin (ng/dL)	0.0713	0.513
Transferrin sat. (%)	-0.0977	0.397
Energy (kcal)	0.0345	0.752
Carbohydrates (g)	0.2014	0.063
Protein (g)	-0.0311	0.776
Lipids (g)	-0.2197	0.042
Vitamin D (mcg)	0.1720	0.113
Iron (mg)	0.0050	0.963

Note: >Pearson's correlation test.

 https://doi.org/10.1590/1678-9865202235e210219

DISCUSSION

Although the sample included patients in stages 4 and 5 of CKD (data not shown), in which the patient displays low vitamin D concentration and dialytic therapy is required, most studied subjects presented sufficient values of 25(OH)D3. Many factors may influence 25(OH)D3 concentrations, such as race, skin pigmentation, age, season, latitude, climate conditions, eating habits, and exposure to sunlight. The city where the study was carried out has warm and sunny weather for the entire year, which presumably means high sun exposure and vitamin D endogenous biosynthesis through the skin, possibly justifying the concentration of 25(OH)D3 found in patients. Similarly, another recent study in the same region, Marreiro *et al.* [24], found predominantly adequate concentrations of 25(OH)D3 in the studied sample.

Differently from the present study, the literature shows a high prevalence of hypovitaminosis D among CKD patients with renal function decrease. Subih *et al.* [25] confirmed the prevalence of inadequate 25(OH)D3 levels in HD patients, with concentrations <30 ng/mL before the study began. Chen *et al.* [26] found that 80% of patients had insufficient vitamin D levels (25(OH)D3 < 30 ng/mL) and 11.6% had severe deficiency (25(OH)D3 <10 ng/mL).

The results show elevated mean values of ferritin and transferrin saturation, compatible with the results of Signori *et al.* [27]. As ferritin is an acute-phase protein, its high levels may be related to the underlying disease and its inherent inflammatory process. Elevated transferrin saturation may suggest high iron levels in the body, a parameter of iron availability for erythropoiesis. In fact, some patients received occasional iron and erythropoietin supplementation, following medical advice.

Male patients predominated in the study, as supported by many studies pointing out that women postpone therapy due to the slow progression of the disease or die before starting dialysis. Female patients' lives are usually more affected by the disease during treatment, as they tend to have more associated symptoms [28-30].

The mean values of hemoglobin, serum iron, ferritin, and transferrin saturation were inferior in women, without significant differences. We observed that 43% of the women in the sample had been diagnosed with anemia because of hemoglobin levels. Usually, hemoglobin levels remain lower among women in all stages of CKD, requiring more erythropoietin [28]. Iron and blood loss during menstrual periods may contribute to anemia.

In this study, the mean 25(OH)D3 concentrations were inferior in women, although the difference between the sexes was not significant. The literature broadly recognizes consistently low levels of 25(OH)D3 in the population with CKD. Nevertheless, some studies have found that the deficiency is more pronounced in women and as age progresses [31,32]. For instance, in a study of 25(OH)D3 concentrations with Palestinian HD patients, Nazzal [33] found that women presented lower 25(OH)D3 levels, supporting the present investigation's results.

The dietary intake of vitamin D was below the recommendations in both sexes, without significant differences [34]. However, as this form of ingestion only accounts for 10% to 20% of the total vitamin D absorbed in the organism, it is not decisive to justify 25(OH)D3 values [35]. Moreover, the results of the correlational analysis did not show statistically significant associations between dietary vitamin D and its serum concentrations. A diversified diet generally does not supply large quantities of vitamin D, and food fortification is modest. In this context, the largely inadequate levels of dietary vitamin D found may reflect the insufficient consumption of food items that contain it, such as fish, dairy, eggs, salmon, tuna, and liver [36]. It is worth pointing out that another study, Lee *et al.* [37], investigated the factors determining the increase of 25(OH)D3 in HD patients, including dietary intake. The average dietary intake of vitamin D was

found to be below the recommended 3,25 µg/day for men and 2,47 µg/day for women, and no association was found with its serum concentrations.

As for the patients' food intake, we found a good probability of inadequate caloric and macronutrient intake, suggesting that the present sample did not follow the specific dietary guidelines for HD patients. This may be justified by self-imposed diet restrictions, reduced sense of hunger, associated comorbidities, the effects of drug interactions, uremia, and endocrine and metabolic alterations that accompany the disease, making the nutritional goals hard to attain, as Gebretsadik and Shahar also state [38,39].

The statistical superiority of the dietary consumption of carbohydrates and lipids in females may be explained by having more meals a day and presenting increased consumption of bread, rice, and pasta, canned and industrialized foods, as well as meats, compared to males. It may also be related to women's higher probability of adapting to the effects of uremia.

Marreiro *et al.* [24] observed that the habitual dietary intake tended to be inadequate in terms of energy and lipids. On the other hand, protein consumption was found adequate, given that these patients' protein needs are enlarged by the losses during dialysis.

Patients' habitual diets revealed a low consumption of red meats, fish, poultry, and offal, thus were low in heme iron. Other dietary components found could interfere in the bioavailability of minerals – specifically, having a fiber-rich diet increases the availability of oxalates, phosphates, phytates, tannins, and polyphenols that inhibit iron, compromising its effective use in the organism [40].

The association between the presence of anemia and 25(OH)D3 concentrations was not evidenced in the present study. However, a trend was distinguished, as among the anemic patients, 66,7% presented insufficient/deficiency of 25(OH)D3. From this perspective, Sim *et al.* [18] found that 49% of the patients with insufficient concentrations of 25(OH)D3 had anemia, while 36% of those with adequate concentrations did.

Against the results of the present study, López-Ramiro *et al.* [16] showed a strong and independent correlation between 25(OH)D3 concentrations and the levels of hemoglobin, serum iron, transferrin saturation, and ferritin. Also, the findings of Patel *et al.* [41] and Madar *et al.* [42] showed that low concentrations of 25(OH)D3 and 1,25(OH)2D3 were independently associated with reduced hemoglobin and the development of anemia.

The lack of association between the adequacy of 25(OH)D3 and anemia in this study may be explained by a damaged production of erythropoietin as CKD progresses and by the coexistence of other chronic diseases. As an inflammatory condition, the direct action of pro-inflammatory cytokines is presumably able to inhibit erythropoietin expression, thus hindering the expression and regulation of specific transcription factors involved in controlling erythrocyte differentiation [43,11].

The study has some limitations worth pointing out. First, as a cross-sectional study without a control group of healthy people, it presents difficulties in noting causes and effects. Although it employed different strategies present in the literature to ensure a trustworthy evaluation of the patients' eating habits, the bias created by subjects self-reporting their intake persists. The reduced expression of pro-inflammatory cytokines is the proposed mechanism through which vitamin D may affect erythropoiesis. However, in our study, it was not possible to evaluate the concentrations of pro-inflammatory cytokines, which is another limitation.

Given the complexity of the mechanisms involved in the interaction of 25(OH)D3 with the parameters of the iron state, this study is important to guide professionals and patients with CKD. It also shows the

importance of diversifying the dietary intake with foods rich in iron and vitamin D, avoiding self-imposed and unnecessary restrictions, as well as having clear behavioral guidelines that prioritize adequate sun exposure.

CONCLUSION

We did not find a relation between adequate levels of 25(OH)D3 and anemia. As the mean values of serum iron and vitamin D were adequate or compatible with sufficiency, we suggest that augmented resistance to erythropoietin and inflammatory processes may have contributed to the substantial percentage patients with anemia in the study.

CONTRIBUTORS

LTM VIANA planned the research, designed the study, collected and analyzed the data, and prepared the manuscript. BJSA FREITAS supervised and coordinated the research, analyzed the data, revised the manuscript, and participated in the approval of the final version.

REFERENCES

1. Daimon M, Fujita T, Murabayashi M, Mizushiri S, Murakami H, Nishiya Y, *et al.* Exacerbation of hyperparathyroidism, secondary to reduced renal function, in individuals with vitamin D deficiency. Front Med. 2020;7:221.
2. Silva PAB, Silva LB, Santos JFG, Soares SM. Política pública brasileira na prevenção da doença renal crônica: desafios e perspectivas. Rev Saude Publica. 2020;54:86.
3. Afifeh MAS, Verdoia, M, Nardin M, Negro F, Viglione F, Rolla R, *et al.* Determinants of vitamin D activation in patients with acute coronary syndromes and its correlation with inflammatory markers. Nutr Metab Cardiovasc Dis. 2021;31(1):36-43.
4. Neves PDMM, Sesso RCC, Thomé FS, Lugon JR, Nascimento MM. Inquérito brasileiro de diálise 2019. J Bras Nefrol. 2021;43(2):217-27.
5. Azizieh F, Alyahya KO, Raghupathy R. Association between vitamin D levels and inflammatory markers in healthy women. J Inflamm Res. 2016;27(9):51-7.
6. Inda AJF, Melamed ML. Vitamina D e doença renal: o que nós sabemos e o que nós não sabemos. J Bras Nefrol. 2013;35(4):323-31.
7. Obi Y, Hamano T, Isaka Y. Prevalence and prognostic implications of Vitamin D deficiency in chronic kidney disease. Dis Markers. 2015;2015(1):1-9.
8. Czaya B, Faul C. The role of fibroblast growth factor 23 in inflammation and anemia. Int J Mol Sci. 2019;20(17):4195.
9. Nalado AM, Mahlangu JN, Waziri B, Duarte R, Paget G, Olorunfemi G, *et al.* Ethnic prevalence of anemia and predictors of anemia among chronic kidney disease patients at a tertiary hospital in Johannesburg, South Africa. Int J Nephrol Renovasc Dis. 2019;12:19-32.
10. Bueno CS, Frizzo MN. Anemia na doença renal crônica em hospital da região noroeste do estado do Rio Grande do Sul. J Bras Nefrol. 2014;36(3):304-14.
11. Agarwal AK. Iron metabolism and management: focus on chronic kidney disease. Kidney Int Suppl. 2021;11(1):46-58.
12. Al-shaer OS, Behiry EG, Ahmed AA, Moustafa H. Association between the genetic variant of the vitamin D receptor (FokI) rs2228570 and iron profile in hemodialysis patients. Mol Biol Rep. 2020;47(1):545-53.
13. Ministério da Saúde (Brasil). Portaria nº 365, de 15 de fevereiro de 2017. Aprova o Protocolo Clínico e Diretrizes Terapêuticas para Anemia na Doença Renal Crônica. Brasília: Ministério; 2017.
14. Smith EM, Tangpricha V. Vitamin D and anemia: insights into an emerging association. Curr Opin Endocrinol Diabetes Obes. 2015;22(6):432-38.

15. Naini AE, Hadaiati ZP, Gholami D, Pezeshki AH, Moinzadeh F. The effect of vitamin D administration on the treatment of anemia in patients with terminal renal disease with vitamin D deficiency in hemodialysis: a double-blind, placebo-controlled clinical trial. J Res Med Sci. 2015;20(8):745-50.

16. López-Ramiro E, Rubert M, González-Parra E, Mahillo I, De la Piedra C. Correlation between 25-hydroxy-vitamin D levels and the degree of anemia in patients with chronic kidney disease. Am J Clin Exp Med. 2017;5(4):151-56.

17. Sah SK, Adhikary LP. Prevalence of abnormal serum 25-hydroxyvitamin D and its association with hemoglobin level in patients with pre-dialysis CKD: a cross-sectional study in the Himalayas. BMC Nephrol. 2019;20:267.

18. Sim JJ, Lac PT, Liu ELA, Meguerditchian SO, Kumar VA, Kujubu DA, *et al.* Vitamin D deficiency and anemia: a cross-sectional study. Ann Hematol. 2010;89(5):447-52.

19. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357:266-81.

20. World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation. Geneva: Organization; 2000.

21. Fisberg RM, Vilar BS, Marchiori DML, Martini LA. Inquéritos alimentares: métodos e bases científicas. 1st ed. Barueri: Manole; 2005.

22. Mahan LK, Escott-Stump S, Raymond JL. Krause: alimentos, nutrição e dietoterapia. 13th ed. Rio de Janeiro: Elsevier; 2013.

23 Mira AR, Garagarza C, Correia F, Fonseca I, Rodrigues R. Manual de Nutrição e doenças renais. 1st ed. Porto: Associação Portuguesa de Nutricionistas; 2017.

24. Marreiro CS, Nogueira TR, Braz DC, Nascimento PP, Paz SMRS, Freitas BJSA. Glycoinsulinemic parameters associated with vitamin D status in patients with chronic kidney disease undergoing dialysis therapy. Rev Chil Nutr. 2021;48(4):534-44.

25. Subih HS, Behrens J, Burt B, Clement L, Pannell R, Macha L, *et al.* 25 hydroxyvitamin D is greater when a renal multivitamin is administered with cholecalciferol in hemodialysis. Asia Pac J Clin Nutr. 2016;25(4):754-59.

26. Chen MY, Ou SH, Yen MC, Lee MS, Chen NC, Yin CH, *et al.* Vegetarian diet in dialysis patients. Medicine. 2021;100(6):1-7

27. Signori D, Frizzo MN, Novicki A. Hiperferritinemia e anemia ao longo do tratamento hemodialítico. Rev Saúde Int. 2019;12(23):54-68.

28. Cobo G, Hecking M, Port FK, Exner I, Lindholm B, Stenvinkel P, *et al.* Sex and gender differences in chronic kidney disease: progression to end-stage renal disease and haemodialysis. Clin Sci. 2016;130(14):1147-163.

29. Carrero JJ, Hecking M, Chesnaye NC, Jager JK. Sex and gender disparities in the epidemiology and outcomes of chronic kidney disease. Nat Rev Nephrol. 2018;14(3):151-64.

30. Brar A, Markell M. Impact of gender and gender disparities in patients with kidney disease. Curr Opin Nephrol Hypertens. 2019;28(2):178-82.

31. Ho LT, Sprague SM. Women and CKD-mineral and bone disorder. Adv Chronic Kidney Dis. 2013;20(5):423-26.

32. Kara AV, Aldemir MN, Arslan YK, Soylu YE. Relationship between Serum Vitamin D Levels and health-related quality of life in maintenance hemodialysis patients. Blood Purif. 2019;48(1):1-9.

33. Nazzal ZA, Hamdan Z, Natour N, Barbar M, Rimawi R, Salaymeh E. Prevalence of Vitamin D deficiency among hemodialysis patients in palestine: a cross-sectional study. Int J Nephrol. 2021;2021:6684276.

34. Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington: National Academies Press; 2011.

35. Castro LCG. O sistema endocrinológico vitamina D. Arq Bras Endocrinol Metab. 2011;55(8).

36. Melo SRS, Santos RO, Santos LR, Oliveira ARS, Cruz KJC, Morais JBSM, *et al.* Dietary intake of vitamin D and its relation to an inflammatory marker in obese women. RBONE. 2020;14(90):1164-170.

37. Lee YJ, Oh IH, Baek HJ, Lee CH, Lee SS. Effects of sun exposure and vitamin D intake on diets on serum 25-hydroxyvitamin D status in hemodialysis patients. Nutr Res Pract. 2015;9(2):158-64.

38. Gebretsadik GG, Mengistu ZD, Molla BW, Desta HT. Patients with chronic kidney disease do not follow dietary recommendations well: a cross-sectional study. BMC Nutr. 2020;6:14.

39. Shahar D, Barakat RAS, Haviv Y. Determinants of the nutritional status of patients with ESRD and their quality of food intake, should we reconsider some recommendations? Clin Nutr. 2018;37:S238.

40. Cozzolino SMF. Biodisponibilidade de nutrientes. 5th ed. Barueri: Manole; 2016.

41. Patel NM, Gutiérrez OM, Andress DL, Coyne DW, Levin A, Wolf M. Vitamin D deficiency and anemia in early chronic kidney disease. Kidney Int. 2010;77(8):715-20.

42. Madar AA, Stene LC, Meyer HE, Brekke M, Lagerløv P, Knutsen KV. Effect of vitamin D3 supplementation on iron status: a randomized, double-blind, placebo-controlled trial among ethnic minorities living in Norway. Nutrition. 2016;15:74.

43. Wiciński M, Liczner G, Cadelski K, Kołnierzak T, Nowaczewska M, Malinowski B. Anemia of chronic diseases: broader diagnoses - better treatment? Nutrients. 2020;12(6):1784.

Received: October 7, 2021
Final version: April 18, 2022
Approved: July, 26, 2022