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RESEARCH

Use of vitamin D and infection in patients with chronic kidney disease

Uso da vitamina D e infecção em pacientes com doença renal crônica

Uso de la vitamina D e infección en pacientes con enfermedad renal crónica

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ABSTRACT

Objective: To evaluate the effectiveness of vitamin D supplementation as protection factor against infection of patients with chronic kidney disease on conservative treatment. **Method:** Retrospective cohort study carried out between 2013 and 2016 in the Conservative Treatment Outpatient Clinics (*Ambulatório de Tratamento Conservador*) of the Hypertension and Kidney Hospital (*Hospital do Rim e Hipertensão*) of the Universidade Federal de São Paulo. Data on sociodemographic factors, comorbidity, infection episodes and use or nonuse of vitamin D supplementation for at least 6 months were collected from medical records. The primary outcomes considered in both groups were: presence or absence of infection anywhere on the body (bloodstream, urinary, respiratory and surgical sites). **Results:** A total of 263 patients were included and those who received (n=43) vitamin D had 59% less chance of developing infections (OR=0.41; 95%CI; 0.15–0.99), when compared to those who did not receive. **Conclusion:** Vitamin D supplementation was a protective factor against infections of all causes.

Descriptors: Renal Insufficiency; Conservative Treatment; Vitamin D; Infection; Nephrology.

RESUMO

Objetivo: avaliar a efetividade da suplementação de vitamina D em pacientes com doença renal crônica em tratamento conservador como fator de proteção contra infecções. **Método**: Estudo de Coorte retrospectiva realizado entre 2013 e 2016 no Ambulatório de Tratamento Conservador do Hospital do Rim e Hipertensão da Universidade Federal de São Paulo. Foram coletados dos prontuários os dados sociodemográficos, de comorbidade, episódios de infecção, em uso ou não de suplementação de vitamina D por no mínimo 6 meses. Os desfechos primários considerados nos dois grupos foram: a presença ou não de infecção em qualquer sítio: urinário, respiratório, corrente sanguínea e sítio cirúrgico. **Resultados**: Foram incluídos 263 pacientes e os que receberam (n=43) vitamina D tiveram 59% menos chance de desenvolver infecção (OR=0,41; IC95% 0,15-0,99), quando comparados aos que não receberam. **Conclusão**: A suplementação de vitamina D foi fator de proteção contra infecções de todas as causas.

Descritores: Insuficiência Renal; Tratamento Conservador; Vitamina D; Infecção; Nefrologia.

RESUMEN

Objetivo: evaluar la efectividad de la suplementación de vitamina D en pacientes con enfermedad renal crónica en tratamiento conservador como factor de protección contra infecciones. **Método:** Estudio de Cohorte retrospectiva realizado entre 2013 y 2016 en el Ambulatorio de Tratamiento Conservador del Hospital do Rim e Hipertensão da Universidade Federal São Paulo. Se recogieron de los prontuarios los datos sociodemográficos, de comorbilidad, episodios de infección, en uso o no de suplementación de vitamina D por lo menos 6 meses. Los resultados primarios considerados en los dos grupos fueron: la presencia o no de infección en cualquier sitio: urinario, respiratorio, corriente sanguínea y sitio quirúrgico. **Resultados:** Se incluyeron 263 pacientes y los que recibieron (n = 43) vitamina D tenían un 59% menos de posibilidades de desarrollar infección (OR = 0,41, IC95% 0,15-0,99), en comparación con los que no recibieron. **Conclusión:** La suplementación de vitamina D fue factor de protección contra infecciones de todas las causas.

Descriptores: Insuficiencia Renal; Tratamiento Conservador; Vitamina D; Infección; Nefrología.

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INTRODUCTION

Kidney disease has become a global public health problem in recent decades. Researchers estimate that prevalence of kidney disease in world population ranges from 8 to 16%[1-2]. Among several metabolic implications, the kidney disease is a risk factor for the decrease in levels of vitamin D, which means there is a significant number of people with potential risk of presenting complications resulting from vitamin D deficit/insufficiency[3-5].

Such complications involve the development of metabolic bone, cardiovascular, infectious and autoimmune diseases, neoplasms, hyperparathyroidism, type 2 diabetes mellitus, and increase in albuminuria (essential marker for predicting decrease in renal function and, consequently, renal insufficiency)[3,5-7].

The determination of vitamin D levels in the organism must be carried out through serum dosage of 25-hydroxyvitamin D (25(OH) D), given that 1,25-dihydroxyvitamin D ($1,25OH_2D_3$) is in lesser quantity in the bloodstream and has half-life less than the one of 25(OH)D. We highlight that the vitamin D deficit increases the secretion of parathyroid hormone (PTH), which consequently causes the kidney to produce more $1,25OH_2D_3$. In other words, serum levels of $1,25OH_2D_3$ will remain unchanged or, in some cases, increased[8-9].

From the discovery that several other tissues and cells feature vitamin D receptors, being able to convert (25(OH)D) into ($1,25(OH)_2D_3$), active form of vitamin D, it became imperative to study its various functions and the mechanism of action of these receptors[4,7-8].

The immune system has an important role in the mechanisms of action of vitamin D. It regulates the inhibition and/or activation of several defense cells (monocytes, lymphocytes, among others) through differentiation and activation of CD4; expands the action of regulatory T cells; and inhibits the differentiation of monocytes in dendritic cells, thus decreasing the production of interferon-γ, IL-2 and TNF-α, which stimulates Th2 helper cells, inhibiting the generation of IL-17 originating from Th1720 and promotes the increase of natural killer T cells[6,8,10].

Thus, vitamin D deficiency has been associated with the increase in prevalence of autoimmune diseases as: rheumatoid arthritis, systemic lupus erythematosus, undifferentiated connective tissue disease, inflammatory bowel disease, multiple sclerosis and type 1 diabetes[6,8]. Additionally, one can relate the function of $1,25(OH)_2D_3$-VDR (innate and adaptive) immunity to infections through the immunoregulatory action of vitamin D in the parathyroid. Therefore, a vitamin D deficit can result in hyperparathyroidism and increase the risk of infection[7-8].

The Healthcare-Associated Infections (HAI) are related to high mortality and morbidity rates[11]. The chronic kidney disease (CKD) is an important risk factor for the development of HAI. Urinary tract infection and pneumonia were reported with higher incidence in patients with chronic kidney diseases[11-12]. The unfavorable clinical picture of vitamin D deficit in kidney disease favors and potentiates the occurrence of HAI. Vitamin D deficiency has been related to the increase in morbidity by cardiovascular and infectious diseases in patients diagnosed with kidney disease[5]. Evidence show that there are functional deficit and hyperstimulation of the immune system. This fact is related to the increase in the risk of people with chronic kidney disease developing local and generalized infections, as well as to the interference in the expected immune response after immunization[6].

There is no consensus about vitamin D supplementation being associated with decrease in infection rates of all causes. Studies conducted in 2013 and 2015 on patients with chronic kidney disease undergoing hemodialysis[13-14] found no association between use of oral vitamin D and reduction of infection. On the other hand, studies conducted in the United States of America (USA) in 2003 and 2005[15-16] considered the replacement of vitamin D a valid strategy to reduce morbidity and mortality of people with kidney diseases, especially the ones of cardiovascular and infectious causes[5].

Recently, *in vivo* studies have shown that $1,25(OH)_2D_3$ assists the stimulation of monocytes and macrophages, potentializing their antibacterial effect and acts as immunosuppressant in lymphocytes. A preclinical study showed that $1,25(OH)_2D_3$ helped to inhibit transplant rejection, being more effective than cyclosporine A (heart transplantation), and to reduce the risk of infection. For kidney transplantation, the vitamin D prolonged the function of the transplanted organ[9-10].

Given this panorama, the therapeutic use of vitamin D has been considered not only for treatment of hyperparathyroidism, but also as strategy to reduce morbidity and mortality associated with cardiovascular and infectious diseases, considering its role as important immune modulator[6]. In addition, the use of calcitriol as an adjuvant of influenza vaccine was effective to enhance the immune response[5,10].

Considering the magnitude of kidney disease and its association with vitamin D deficit/insufficiency, our study proposes to answer the following question: is there an association between vitamin D supplementation in patients under conservative treatment with decrease in the occurrence of infections? The choice of this subject can be explained by the non-standardization of vitamin D utilization as prophylaxis of infections in patients with kidney disease and by the need of seeking evidence that could corroborate this practice.

OBJECTIVE

To evaluate the effectiveness of vitamin D supplementation as protection factor against infections of patients with chronic kidney disease on conservative treatment.

METHOD

Ethical Aspects

This project was approved by the Research Ethics Committee of the Universidade Federal de São Paulo, in compliance with the standards[17] of the Brazilian National Health Council.

Study design and location

Retrospective cohort study[18] carried out in the Conservative Treatment Outpatient Clinics (*Ambulatório de Tratamento Conservador*) of the Hypertension and Kidney Hospital (HRim – *Hospital do Rim e Hipertensão*) of the Universidade Federal de São Paulo. This outpatient clinics is part of the HRim infrastructure, which consists of clinical analysis laboratories, services of pathologic anatomy, imaging and hemodynamic diagnostic unit and surgical center, where transplantations

and videolaparoscopies of urinary and digestive apparatus are performed, in addition to cardiac and vascular surgeries.

The several outpatient clinics that are part of the HRim treat approximately 500 people/day, providing healthcare in pre- and post-transplantations, dialysis, conservative treatment and appointments conducted by a multidisciplinary team. It is an institution of national and international reference in teaching, research and healthcare.

Population

A convenience sample was used. The initial sample of the study consisted of medical records of patients treated in the outpatient clinics for at least one year and who attended at least one medical appointment between January 01, 2013 and December 31, 2016. Subsequently, patients were subjected to the inclusion criteria listed below:

1. Patient's medical record available at the time of data collection;
2. Patients on conservative treatment older than 18 and of both sexes;
3. Patients with or without previous infection episode reported in the medical record;
4. Patients on use or nonuse of vitamin D supplementation for at least 6 months;

Patients whose medical records were not located during data collection or whose treatment was other than the conservative one were excluded from the sample.

Study protocol

The instrument used for data collection consisted of sociodemographic variables (age, sex, race, profession); comorbidities (high blood pressure, diabetes mellitus, cardiovascular diseases, others); infection episodes; and vitamin D supplementation.

Infection was considered as dependent variable, and *use or nonuse of vitamin D*, *sociodemographic data* age, sex, race, profession), and comorbidity (high blood pressure, diabetes mellitus, cardiovascular diseases, others) were considered as independent variables. Two groups were considered:

Group A – patients on use of vitamin D supplementation for at least 6 months;

Group B – patients on nonuse of vitamin D supplementation.

The primary outcome considered in both groups was the presence or absence of infection. *Infection* is a medical condition caused by pathological microorganisms that, due to the pathophysiology of chronic kidney disease, may cause negative impact on the health status of this population, contributing to increase morbidity and mortality[19-20].

Thus, this study considered as *infection episode* the occurrence of any infectious process anywhere on the body. The option in using the delimitation of the Brazilian Health Regulatory Agency (Anvisa) regarding the classification of Healthcare-Associated Infections (HAI) is justified by the shortage of literature that could support the methodological approach adopted and because it was impossible to determine, in all cases, whether the source of the infection was the community or associated with the healthcare service[11].

Thus, the infection episodes identified were grouped into four large groups, considering the current recommendations regarding the HAI used in Brazil. They are: urinary tract infection (UTI), respiratory tract infection (RTI), bloodstream infection (BSI) and surgical site infection (SSI). The infection episode was validated through confirmation of registration in the medical record of the doctor's evaluation and clinical diagnosis and/or result of one or more positive cultures of any micro-organism through blood culture, urine culture, bronchoalveolar lavage or surgical wound secretion[11].

Analysis of results and statistics

Initially, the descriptive analysis of quantitative and categorical variables were conducted and results were presented in absolute and relative frequencies. In the bivariate exploratory analysis (Table 2), the association between infection (outcome variable) and other variables (exposure variables) was tested, being the use of Vitamin D the main variable. The chi-square test considered significant the results with $p < 0.05$. Odds Ratio (OR) was the measure of association used in the bivariate analysis and its confidence interval was set at 95%.

RESULTS

A total of 263 medical records were analyzed, of which 52.85% were male patients, 60.46% were white and 56.65% were 66 or older. Regarding the associated comorbidities, most patients of both sexes had systemic high blood pressure (88.21%). Of the total, 45.25% of patients had diabetes mellitus and 69.58% had other diseases (Table 1).

Table 1 – Sociodemographic data of patients with chronic kidney disease on conservative treatment, São Paulo, Brazil, 2018

Variables	n	%
Sex		
Male	139	52.85
Female	124	47.14
Age group		
18–33	13	4.94
34–49	21	7.98
50–65	77	29.28
66 or older	149	56.65
Without information	3	1.14
Race		
White	159	60.46
Black	84	31.94
Without information	20	7.60
Occupation		
Retired patients/pensioners	55	20.21
Other	116	44.11
Without information	92	34.99
Comorbidities		
Diabetes mellitus	119	45.25
High blood pressure	232	88.21
Cardiovascular diseases	57	21.67
Other	183	69.58

Source: Database of patients on conservative treatment.

Table 2 – Bivariate analysis of the relationship between main exposure variable (vitamin D) and outcome (infection), São Paulo, Brazil, 2018

Variables	Use of Vitamin D	Nonuse of Vitamin D	Total (n)	%	Proportion Exposure
With infection	7	71	78	29.65	0.1628
Without infection	36	149	185	70.34	0.3237
Total	43	220	263	100	0.2966

Source: Database of patients on conservative treatment.

Table 3 – Distribution of infection cases among people with chronic kidney disease on conservative treatment by site, São Paulo, Brasil, 2018

Site	Use of Vitamin D	Nonuse of Vitamin D	Total	
			n	%
Bloodstream infection	2	5	7	8.97
Urinary tract infection	3	65	68	87.18
Respiratory tract infection	2	1	3	3.85
Total	07	71	78	100

Source: Database of patients on conservative treatment.

Table 4 – Microorganisms identified in cultures performed in patients with chronic kidney disease on conservative treatment who presented site infection, São Paulo, Brazil, 2018

Microorganisms	Urinary tract infection	Respiratory tract infection	Total	
			n	%
Gram-positive bacteria				
Staphylococcus aureus	1		1	1.41
Coagulase-negative staphylococcus	1		1	1.41
Enterococcus spp.	4		4	5.63
Gram-negative bacteria				
Escherichia coli	35	1	36	50.70
Klebsiella pneumoniae	12		12	16.90
Klebsiella oxytoca	1		1	1.41
Morganella morganii	1		1	1.41
Proteus mirabilis	3		3	4.23
Pseudomonas aeruginosa	1		1	1.41
Enterobacter spp.	3		3	4.23
Culture not available	6	2	8	11.26
Total	68	3	71	100

Source: Database of patients on conservative treatment.

Approximately 29.66% of patients had hypovitaminosis D, to whom a vitamin replacement therapy was established. Table 2 shows that among the 43 patients who used vitamin D supplementation, only 7 (16.27%) had infection. Among the 185 who used no vitamin D supplementation, 71 (32.27%) had infection somewhere on the body.

Table 3 shows the distribution of infection cases by type. The UTI was the most common among patients, regardless of use or nonuse of vitamin D supplementation, corresponding to 87.18% of the total.

Table 4 demonstrates which microorganisms were isolated in the cultures performed in patients with respiratory and urinary tract infection. Most of them, 91.55%, consisted of gram-negative microorganisms. The most frequent bacteria was the *Escherichia coli* (50.70%), followed by the *Klebsiella pneumoniae* which appeared in 16.90% of cases.

Table 5 shows the results for bivariate analysis and the relationship between main exposure variable (vitamin D) and outcome (infection). The relationship between main exposure variable (vitamin D) and outcome (infection) had a 95%CI less than 1, with statistical significance.

Table 5 – Occurrence of infection according to sociodemographic and clinical variables of cases, São Paulo, Brazil, 2018

	Infection		OR (95%CI)	*p* value	OR (95%CI)	*p* value
	Yes	No				
Sex						
Female	43	86	1			
Male	35	99	0.71 (0.40-1.24)	0.20	0.64 (0.37-1.11)	0.11
Age group						
18–33	1	12	1			
34–49	8	13	7.38 (0.75-354.38)	0.05	8.97 (0.92-87.41)	0.06
50–65	19	58	3.93 (0.51-176.72)	0.17	4.12 (0.48-35.55)	0.20
66 or older	50	99	6.06 (0.85-264.12)	0.05	6.04 (0.73-50.15)	0.10
Race						
White	44	115	1			
Black	23	61	0.99 (0.52-1.85)	0.96	1.00 (0.54-1.83)	0.99
Ignored	11	9	3.19 (1.11-9.31)	0.01	3.07 (1.15-8.18)	0.03
Diabetes mellitus						
No	42	102	1			
Yes	36	83	1.05 (0.60-1.85)	0.85		
High blood pressure						
No	9	21	1			
Yes	69	164	0.98 (0.41-2.56)	0.97		
Cardiovascular disease						
No	57	148	1			
Yes	21	37	1.47 (0.75-2.84)	0.22		
Use of vitamin D						
No	71	149	1			
Yes	7	36	0.41 (0.15-0.99)	0.03	0.48 (0.20-1.15)	0.10

Source: Database of patients on conservative treatment.

Thus, we can consider that the use of vitamin D is a "protection factor" for infection. The use of vitamin D is a protector factor against infection, without being adjusted by the presence of other variables (e.g., age, sex, etc). That is, cases that received vitamin D had 59% less chance of developing infection (OR = 0.41; 95%CI; 0.15–0.99) when compared to those who did not receive.

To the multivariate analysis were included the covariates sex, race, age group, in addition to the main variable, use of vitamin D. In this case, the statistical significance did not remain, probably because some of the covariates modified the effect. The main risk factors found were age in the age group 34–49 years (OR = 8.97; 95%CI; 0.92–87.41) and older than 66 (OR = 6.04; 95%CI; 0.73–50.15).

DISCUSSION

Vitamin D supplementation has been a practice in patients with chronic kidney disease (CKD), because their renal tubular cells are unable to produce 1,25-dihydroxyvitamin D, precursor substance of the 25-hydroxyvitamin D, which is the active form of vitamin D. This study noticed the additional action of vitamin D as a protective agent against healthcare-associated infections. This investigation was a pioneer among patients with chronic kidney disease on conservative treatment of a national reference institution for kidney dysfunction.

Therefore, this study had as main objective to assess whether vitamin D supplementation in patients with chronic kidney disease on conservative treatment acts as a protective factor against infections and as secondary objectives to identify the association between the occurrence of infection with use of vitamin D and to identify the microorganisms isolated in the cultures of these patients. We opted for the retrospective cohort design following the recommendations proposed by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [18] to answer the question of the study.

With the increase in Brazilians' life expectancy over the past decades, one can note the growth in incidence and prevalence of chronic diseases such as high blood pressure and diabetes mellitus, which are the main causes of chronic kidney disease, especially in older persons[20].

Brazilian and world prospects have similar increasing rates. However, in developed countries, the prevalence maintains a constant growth and the incidence remains stable or presents a discrete elevation[21-22]. In 2015, 124,114 new cases of chronic kidney disease occurred in the USA. Individuals affected the most were female (15.1%), older than 60 (33.2%), and white (13.9%). The associated comorbidities were diabetes mellitus (39.2%) and high blood pressure (31%)[21].

In 2016, according to data from the Brazilian Society of Nephrology (SBN – *Sociedade Brasileira de Nefrologia*), 122,825 patients with end stage renal disease (ESRD) were on hemodialysis. Prevalence and incidence rates were, respectively, 596 and 193 patients per million population (pmp). Most of these individuals (57%) were male, older than 65 (33%), whose diagnosis of primary kidney disease were, respectively, high blood pressure (34%) and diabetes mellitus (30%)[23].

A retrospective study with data on 1,120,295 people in Northern California showed that 54.6% were female and 50.9% were white. This investigation demonstrated association between lower levels of glomerular filtration rate (GFR) with mortality, cardiovascular diseases and hospitalization. In this context, 33.7% of patients with high blood pressure and 12.3% with diabetes mellitus were detected in stage 3 (GFR between 45–59 mL/min/1.73 m^2) in DRC, with considerable elevation to 50.3% with high blood pressure and 31.1% with diabetes mellitus in stage 5 (GFR < 15mL/min/1.73m^2)[24].

In our study, we observed a higher percentage of occurrences in male patients, corresponding to 52.85% of the studied population, with 60.46% being white and having high blood pressure as the main cause of primary kidney disease, as well as 88.21% of patients in our study.

Considering the data from developed countries, we noted a small discrepancy regarding the sex and the primary cause of chronic kidney disease, which can suggest specificities of the population studied. Such hypothesis can be supported by a study carried out in 2009 in Recife (PE), which showed that most individuals analyzed were female (56%)[25].

In this study, 29.66% of the sample had vitamin D deficiency. The supplementation of these patients was performed through the protocol used in the institution, which considered the serum rates of each patient: < 20 ng/mL loading dose for 3 months; 20–19 ng/mL loading dose for 3 months; > 30 ng/mL maintenance dose. Vitamin D deficiency is associated with risk factors such as black race, obesity, diabetes mellitus, among others[26].

In this context, low levels of 25-hydroxyvitamin D (25(OH) D) are common in patients with chronic kidney disease. The prevalence of this condition increases as the kidney function decreases. Factors as age and comorbidities (diabetes mellitus and high blood pressure) have been associated with low levels of 25(OH)D in patients with CKD (on dialysis or conservative treatment)[27].

A preclinical study investigated the relationship of vitamin D deficiency with progression of chronic kidney disease. The authors found an increase in gene expression of compounds of the renin-angiotensin system, in levels of aldosterone in plasma and in presence of tubulointerstitial injury with formation of interstitial fibrosis in experimental groups submitted to Vitamin D deficiency[28].

Additionally, a cross-sectional research performed in 2,895 patients with CKD assessed the relationship of vitamin D values with CKD stage. Rates of ≤ 30 ng/mL and < 10 ng/mL were set in 84.7% and 11.3% of patients classified with stage 5 of CKD. On the other hand, for the respective rates, 66.6% and 1.9% of patients were classified with stage 3. These findings demonstrate the significant association of progression of chronic kidney disease with hypovitaminosis D[29].

In Bulgaria, a comparative study conducted with patients on conservative treatment or renal replacement therapy showed that 80% of subjects had vitamin D deficiency/insufficiency[30]. Similarly, in the sample of CKD patients on conservative treatment, 73.6% of them had hypovitaminosis D, considered of high frequency[3]. In addition, another research showed that, although there is no clarity on risk factors associated with vitamin

D deficiency/insufficiency in CKD patients, its prevalence is high[27]. Such findings corroborate other studies, which showed the high prevalence of vitamin D deficiency/insufficiency in CKD patients and its association with cardiovascular diseases, hyperparathyroidism, neoplasms, type 2 diabetes mellitus, bone, immune and infectious diseases, which are the main causes of morbidity and mortality in patients with chronic kidney disease[28-31].

This investigation showed that 29.65% of patients had infection episode, regardless of the use or nonuse of vitamin D. From these infections, 87.18% affected the urinary tract, caused in their most by *E. Coli* (50.7%).

Infection is the leading cause of morbidity and the second cause of mortality among patients on hemodialysis[32]. A retrospective cohort study associated the increase in urinary tract infections with stages 4 and 5 of chronic kidney disease[12]. Grothe C et al. demonstrated a 61% incidence of bloodstream infection, with major occurrence of gram-positive bacteria, being the most prevalent the *S. aureus* (56.6%)[33]. Another study, a case-control study held in São Paulo between 2010 and 2013, showed that, among patients undergoing hemodialysis, the use of central venous catheter was a risk factor for bloodstream infection and that the most prevalent microorganisms were gram-positive bacteria[32].

The recent acknowledgment that $1,25(OH)_2D$ performs several functions as immunomodulator, brought to light the associations between alterations in vitamin D and occurrence of infections, which were previously inexplicable[34-35]. Low levels of 25(OH)D were associated with greater susceptibility to mycobacterial infections (67.68%) and with recurrence of infection in patients with rickets (16–18%). This fact reinforces the importance of studying the effects of low concentration of vitamin D in patients with chronic kidney disease and the likely increase of predisposition to the development of infections[36].

In our study, the relationship between main exposure variable (vitamin D) and outcome (infection) proved the vitamin D supplementation as a protection factor against infections. Patients on vitamin D supplementation had 59% less chance to develop an infection, when compared to those who did not receive vitamin D. This data strengthens our hypothesis by confirming that the use of vitamin D in patients with chronic kidney disease elucidates the protective action of this substance and that it can act on preventing healthcare-associated infections.

Vitamin D disability/insufficiency can negatively influence cells of the immune system, predisposing the occurrence of infections; however, there is no consensus on the relationship infections × vitamin D. In fact, among studies that analyzed the association between vitamin D deficiency/insufficiency in patients with kidney disease and morbidity, few of them focus on infectious diseases[8,37-38].

A multicenter study showed that vitamin D supplementation was a protection factor against infection and risk of mortality among patients on peritoneal dialysis[38]. Additionally, a cohort study performed in Japan with 508 patients on hemodialysis showed that vitamin D supplementation prevented respiratory infection, impacting the hospitalization rate of this population[37]. Another research showed that vitamin D supplementation resulted in prevention of infection and graft loss in patients with kidney transplantations[36].

On the other hand, a case-control study held in Canada showed no positive association of vitamin D supplementation with the risk of hospitalizations by infection among patients on hemodialysis[13]. Additionally, Phyo et al. had similar results that did not relate the reduction of infection rates of all kinds with vitamin D supplementation in US patients on dialysis treatment[14].

Summarily, despite controversial data on scientific evidence about the protective action of vitamin D against infections, our study highlighted that vitamin D supplementation in patients with chronic kidney disease on conservative treatment prevented healthcare-associated infections.

Study limitations

Given the retrospective design and data collected from medical records, even though the research was carried out in an international reference service on research, we could not collect the results for bloodstream infections (BSI) cultures because they were available only for medical records in the hospital, which we could not access. We can emphasize that the non-integration of information (sole electronic health record) or access to the report of patient discharge (counter-reference) are obstacles that cause a negative impact on the quality of data collected.

Contributions to the field of nursing, health or public policy

Considering the advances for the healthcare area, our study brings to light the need for prospective studies, randomized clinical trials and multicenter studies on populations with chronic kidney disease, regardless of the type of treatment (conservative or substitute) that corroborate these findings that, for now, are opposed to studies conducted, aiming at better understanding the action of vitamin D in the organism, as well as searching clinical evidence that can subsidize protocols that ensure quality in the diagnosis, proper supplementation and preventive measures aimed at reducing morbidity and mortality.

CONCLUSION

Vitamin D deficiency/insufficiency affects several patients with chronic kidney disease. Evidence on the role of vitamin D, beyond calcium homeostasis, have been demonstrated; in particular its possible retardant action of progression of kidney damage and it function as protection factor for several pathologies, including infectious diseases.

This study demonstrated that our epidemiological data are similar to the findings of other studies, even though there are differences possibly related to the peculiarities of the sampled population. Among the infection cases, most of them affected the urinary tract and the microorganism isolated was the *E. coli*.

This study demonstrated that vitamin D supplementation in patients with chronic kidney disease on conservative treatment was a protection factor against infections of all causes.

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