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Article

Evaluation of vitamin D and inflammatory markers in elderly

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Vitamin D is an immune modulator, in addition to being interrelated with calcium homeostasis and bone metabolism. Recent studies have associated vitamin D with inflammatory processes. C-reactive protein (CRP), platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) have been used to determine inflammation. There is no consensus on the use of these markers to determine an association between inflammation and vitamin D levels. The objective of this study was to evaluate the association between inflammatory markers and vitamin D in the elderly. A cross-sectional, descriptive study was performed based on the analysis of vitamin D, CRP (quantitative determination of C-Reactive Protein by the ultra-sensitive method) and blood count of institutionalized elderly. In this study, 64% showed vitamin D deficiency, with mean value of 22 ng/mL. In the vitamin D deficient group, the mean values found were: CRP 4.5 mg/L; NLR 2.35 and PLR 119. In the group without vitamin D deficiency the mean values were: CRP 4 mg/L; NLR 1.87 and PLR 111 without statistical difference between the values of the analyzed parameters. The results point to a predominant profile of vitamin D deficiency in the evaluated individuals. No association was found between vitamin D values and the inflammatory markers analyzed.

Keywords: Inflammatory Markers. Vitamin D. Elderly.

INTRODUCTION

Vitamin D is considered a fat-soluble pre-hormone related to calcium homeostasis, bone metabolism and immune system modulation (Chang, Lee, 2019).

After its absorption by diet or synthesis in the epidermis, cholecalciferol (vitamin D_3) undergoes enzymatic conversion in the liver to 25-hydroxyvitamin D (25-OHD), which is the preferred analyte for determining nutritional status, as it is the primary form of storage in the human body The 25-OHD coupled to the carrier protein, is taken to various tissues and through the enzyme 1-α-hydroxylase, is converted into the active form 1-α, 25-dihydroxy-vitamin D (1.25 $(OH)_2$ D), (Holick, 2009; Terushkin *et al*., 2010).

The main site of conversion of 25-OHD is the kidney. In addition, vitamin D receptors are present in various tissues such as brain, heart, skin, bones, parathyroids, intestines, gonads, prostate, breasts and in all cells of the immune system (Monteiro Júnior *et al*., 2014).

In immune cells, the conversion of the 25-OHD to 1.25$(OH)_2$ D is stimulated by interleukins such as the tumor necrosis factor alpha (TNF-α) and the interferon-gamma (INF -γ). Its performance involves aspects related to innate and adaptive immunity (Marques *et al*., 2010).

In innate immunity, vitamin D acts on neutrophils, stimulates the action of macrophages and promotes the differentiation of macrophages into monocytes, leading to acute inflammation in tissues through the synthesis of pro-inflammatory and anti-inflammatory molecules (Cruvinel *et al*., 2010).

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In the context of adaptive immune response, vitamin D appears to act on T lymphocytes inhibiting the proliferation and production of pro-inflammatory cytokines such as interleukin 2 (IL-2), interleukin 6 (IL-6), INF-γ, TNF-α and stimulates the production of anti-inflammatory cytokines (Interleukins 4, 5 and 10). It also inhibits proliferation and recognition of lipid antigens by NK lymphocytes. In B lymphocytes, it inhibits differentiation into IgE plasmacytes cells and induces apoptosis and also inhibits the synthesis and release of autoantibodies (Marques *et al*., 2010).

Thus, according to the cell type it interacts, vitamin D produces substances capable of inhibiting the inflammatory process.

Akbas *et al*. (2016) found vitamin D deficiency associated with high concentrations of cytokines (TNF-α, IL-6) and C-reactive protein (CRP), corroborating the anti-inflammatory action of the vitamin D.

The interaction of CRP with macrophages/monocytes induces tumoricidal activity and IL-1 and TNF-α secretion, stimulating the inflammatory response. On the other hand, CRP seems to decrease neutrophil activity because when degraded by lysosomal enzymes, it suppresses superoxide production and inhibits its degranulation and chemotaxis actions, endothelium adhesion, migration, and phagocytosis. Thus, CRP seems to directly influence the regulation of the inflammatory reaction, presenting pro and anti-inflammatory activity and contributing to the resolution of the process (Du Clos, 2000; Kushner, 1990).

Also, in the context of the inflammatory process, platelets interact with T lymphocytes through CD62P (P-selectin), with a reduction in lymphocyte proliferation and consequently a decrease in pro-inflammatory cytokines such as IFN-γ, TNF-α and IL-17 and an increase in anti-inflammatory cytokines such as IL-10. Several studies in vitro have shown that platelets regulate neutrophil chemotactic and cytotoxic activities by expressing P-selectin on their surface and subsequent formation of platelets and neutrophils conjugates (Gasparyan *et al*., 2019).

In elderly, vitamin D deficiency and chronic subclinical inflammatory state often coexist. However, the evidence on the anti-inflammatory role of vitamin D in this group is still inconclusive (Llewellyn *et al*., 2010).

In studies with elderlies, low vitamin D levels are related to reduced mobility, worsening muscle function and increased risk of falls. In addition, a low vitamin D intake is associated with cognitive decline, Alzheimer's disease and depression, as there are several vitamin D receptors in the central nervous system (Llewellyn *et al*., 2010).

The Brazilian Societies of Clinical Pathology/Laboratory Medicine and Endocrinology and Metabolism recommends serum levels of 25-OHD above 20 ng/mL for a healthy population up to 60 years old and between 30 and 60 ng/mL for the elderly.

Most patients with moderate to mild vitamin D deficiency (15-20 ng/mL) are asymptomatic. Prolonged deficiency reduces intestinal calcium and phosphorus absorption leading to hypocalcemia and secondary hyperparathyroidism, bone mass loss and consequent fracture. Vitamin D levels <10 ng/mL cause bone demineralization, rickets and osteomalacia (Ferreira *et al*., 2017).

Although vitamin D is primarily associated with osteomineral physiology, especially with calcium metabolism, its role in systemic homeostasis, as well as adequate blood levels has aroused great interest in the scientific community, especially its role in the inflammatory process (Barral, 2007).

Many strategies have been used to assess the relationship between vitamin D levels and inflammation, such as the dosage of vitamin D associated with the quantification of inflammatory markers.

The number of cells and cellular products generated in the inflammatory process can be used as biomarkers in the follow up of several pathologies. Recently, the neutrophil/lymphocyte ratio (NLR) has attracted the interest of researchers as a new inflammatory marker for diagnosis and prognosis of malignant tumors, infectious diseases, diabetic nephropathy, cardiovascular disease, autoimmune disorders, and other inflammatory diseases. Meanwhile, an increasing number of studies have focused on the role of platelet/lymphocyte ratio (PLR) played in different types of neoplasms, cardiovascular disease, and terminal renal disease (Zhang *et al*., 2017).

NLR and PLR are laboratory parameters easy to be measured and are reproducible and inexpensive markers to determine inflammation. In addition, CRP dosage, due to its high sensitivity (hs-CRP), may help to demonstrate inflammatory processes.

Many studies have addressed these markers but there is little data on the relationship between hypovitaminosis D and inflammatory processes in the elderlies.

The worldwide aging of the population is increasing and thus, studies involving elderly individuals and the role of vitamin D in homeostatic processes are relevant to define strategies for vitamin supplementation in order to minimize the negative impacts produced for this disability.

The objective of this study was to evaluate the association between vitamin D levels and inflammatory markers CRP, neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in institutionalized elderlies, comparing the values found in elderlies with no vitamin D deficiency and with vitamin D deficiency.

MATERIAL AND METHODS

A cross-sectional, descriptive study was carried out from the analysis of laboratory data of individuals living in the São Vicente de Paulo Nursing Home, a long-term care institution of Ponta Grossa, Paraná, Brazil, throughout 2018.

The nursing home is a private philanthropic and non-profit association. The financial resources come from the municipality (50%) and from the institution itself (50%). It is a well-organized structure with a multidisciplinary professional team. Many of the elderly who lives were abandoned by family members in the childhood caused for presenting some kind dementia and deaf-mute disability. Currently the institution receives elderly people in situations of vulnerability and risks due to violation of rights such as referred by the Specialized Reference Center for Social Assistance (CREAS) of the municipality. Many of them have two or more comorbidities such as diabetes, hypertension, dementia syndromes and depression among others, which leads to polypharmacy.

All residents received the same diet, except for the one suffering from diabetes (36 individuals; 41.4%) and others with special occasional situations were exposed to the sun daily, for at least 15 to 30 minutes, except when weather conditions were adverse or the elderly was unable, such as those confined to bed (3 individuals; 3.4%).

Laboratory tests were done at the University Clinical Laboratory of the State University of Ponta Grossa. The parameters analyzed were dosage of total 25 hydroxyvitamin D in serum, quantitative determination of C-Reactive Protein (ultra-sensitive method – hs-CRP) and Complete Blood Count.

Total 25 hydroxyvitamin D quantification was performed in a Vidas/Biomérieux automated device using the Enzyme-Linked Fluorescent Assay (ELFA) technique. The measurement of hs-CRP was performed by the Wiener Lab immunoturbidimetric method on the Wiener Lab CT300i automated equipment. The blood counts including total leukocytes, neutrophils, lymphocytes, and platelets were performed on a Wiener Lab Counter 19 automated hematology analyzer.

The NLR and PLR ratios were calculated as the relationship between the absolute number of neutrophils and lymphocytes, and between the platelet count and absolute lymphocyte, respectively.

Subjects under 60 years of age with leukopenia or leukocytosis were excluded from the study (reference values: 4,000/mm^3 to 10,000/mm^3). Among individuals with normal number of leukocytes, those with abnormal counts of neutrophil (reference values: 2,255/mm^3 to 8,244/mm^3), lymphocytes (reference values: 848/mm^3 to 3,969/mm^3) and platelets (reference values: 150,000/mm^3 a 450,000/mm^3) were excluded.

The age and gender of the participants of the study were provided by the nursing home.

Groups were defined according to vitamin D level and classified as a deficiency (<30 ng/mL) and non-deficiency (>30 ng/mL), according to Endocrine Society, National Osteoporosis Foundation, International Osteoporosis Foundation and American Geriatrics Society (Cosman *et al.*, 2014).

The research protocol number 12.235.227/2018 was approved by the Ethics Committee in Research of the State University of Ponta Grossa and was conducted in accordance with the Helsinki Declaration.

In the statistical analysis, data normality was verified by the Kolmogorov-Smirnov test. The vitamin

D parameters, lymphocytes, neutrophils, CRP, NLR and PLR did not present normal distribution. Therefore, continuous variables were described as average and interquartile range and categorical variables as number and percentage. Possible differences between groups for continuous variables were assessed by the Mann-Whitney test, while categorical variables were evaluated by Chi-square (χ^2). The correlation of vitamin D with the other parameters of the study was carried out using the Spearman correlation coefficient. The statistical program employed was the SPSS 20.0® (Chicago, USA). Regardless of the test used, the significance level was set at $p < 0.05$.

RESULTS AND DISCUSSION

The studied population consisted of 87 individuals, 55 of whom (63.2%) female, with an average of 77 (71 - 81) years old and 32 (36.8%) male, average of 75 (69 - 83) years old. The results of the participants' demographic characteristics and the serum levels of the inflammatory markers analyzed can be seen in Table I, categorized according to the status of total 25 hydroxyvitamin D, in two groups, insufficient vitamin D levels <30 ng/mL (56 individuals; 64.4%) and sufficient levels of vitamin D ≥30 ng/mL (31 individuals; 35.6%).

TABLE I - Demographic and laboratory data of the individuals, according to the groups formed according to the presence or absence of vitamin D deficiency

Parameters	**Vitamin D <30 ng/mL 22 (15 - 26) (n = 56)**	**Vitamin D ≥30 ng/mL 36 (33 - 44) (n = 31)**	***P* value**
Age, median (years) [a]	77 (71 - 81)	75 (69 - 83)	0.763
Gender, n (%.) [b]			
Male	23 (41)	9 (29)	0.265
Female	33 (59)	22 (71)	
Leukocytes (cells /mm^3) [a]	6,000 (5,100 – 7,550)	5,700 (4,900 – 7,200)	0.549
Lymphocytes (cells /mm^3) [a]	1,669 (1,317 – 2,049)	1,806 (1,375 – 2,375)	0.334
Neutrophils (cells /mm^3) [a]	3,756 (3,235 – 4,471)	3,381 (2,993 – 4,350)	0.184
Platelets (10^{3}cells /mm^3) [a]	215 (179 - 252)	208 (167 - 254)	0.859

[a]Test Mann-Whitney, median and interquartile range (25th Quartile - 75th Quartile);
[b]Chi-square test, number and percentage (%);

Most individuals had vitamin D deficiency, with an average of 22 (15 - 26) ng/mL. Among non-disabled individuals, an average of 36 (33-44) ng/mL was found.

Some studies carried out with institutionalized elderly people in Brazil have also found high rates of hypovitaminosis D.

Sousa *et al.* (2019) analyzed 109 institutionalized elderly in northeastern Brazil and found a prevalence of 71.0% of hypovitaminosis D. Another study carried out in a nursing home located in the extreme south of Brazil analyzed samples of 77 elderly and found vitamin D levels below 30 ng/mL in 97.0% of individuals (Augusto, Paiva, Bettinelli, 2013).

Two studies that established values lower than or equal to 20 ng/mL for vitamin D deficiency conducted with institutionalized elderly in central-south and southern Brazil, also found a high prevalence of hypovitaminosis D with percentages of 71.2% (Saraiva *et al.*, 2007) and 85.6% (Scalco, Furlanetto, 2008), respectively.

The high prevalence of vitamin D deficiency can be explained by the aging process, where the epidermis and dermis become thinner and consequently there is a decrease in the reserve of 7-dehydrocholesterol (7DHC), a precursor of vitamin D (De Oliveira *et al.*, 2014). Thus, even under favorable environmental conditions, the bioavailability of vitamin D can be negatively affected by the reduced capacity for synthesis.

In addition, the production of vitamin D in the skin is modulated by season, latitude, time of day, pigmentation and skin thickness and use of sunscreen. The more distant from the equator, the greater the thickness of the atmospheric layer that sunlight must pass through, including UVB that must be between 290 and 315 nanometers (De Oliveira *et al.*, 2014). Thus, residents in cities far from the equator, such as Ponta Grossa (latitude 25º 05'42"), need more time of exposure to the sun (De Oliveira *et al.*, 2014).

Another variable involved in the synthesis of vitamin D is the amount of melanin present in the individual's skin. This pigment competes for the photon of UVB radiation at wavelengths between 290 and 315 nm, decreasing the availability of photons for 7DHC photolysis (De Oliveira *et al.*, 2014). Thus, individuals with greater skin pigmentation need more time of exposure to the sun to synthesize vitamin D. In the case of the sample analyzed in this study, 10 individuals had more pigmented skin (11.5%). The size of the body surface and the exposure time, necessary for an adequate synthesis of vitamin D, are difficult to define. In general, an exposure of 25% of the body surface for 15 minutes is capable of producing a minimal erythematous lesion necessary for the skin to synthesize the equivalent of 1.000 units of vitamin D (Holick, 2001).

Despite living in a confined nursing home, the individuals analyzed in this study were exposed to the sun daily, including wheelchair users, according to the climatic possibilities, for at least 15 to 30 minutes. However, for the elderly, due to all the variables involved, the standardization of the ideal time of exposure to the sun to obtain adequate levels of vitamin D still requires more studies (Ferreira *et al.*, 2017).

The different methods used to measure vitamin D should also be considered when comparing the data found in the literature.

Tolan *et al.* (2018) conducted a study comparing various $25(OH)D_3$ dosing methods and warned of the inaccuracy of results related to $25(OH)D_2$ unequal cross-reactivity issues in some immunoassays. Other researchers also drew attention to the need for standardization and maintenance of quality control to ensure a reliable measurement of vitamin D (Atef, 2018; Heijboer *et al.*, 2012**).**

There are still other factors that should be considered in this assessment, such as low vitamin D intake, reduced intestinal absorption and the use of medications (Ferreira *et al.*, 2017).

The aging process is often accompanied by comorbidities that leads to the use of a large number of medications, which can interfere with the absorption of vitamin D. Among the 87 individuals included in the study, there was a predominance of chronic non-transmissible diseases and the most prevalent among them was hypertension (64.4%), followed by dyslipidemia (44.8%) and diabetes (41.4%). The main comorbidities were: depression (27.6%), hypothyroidism (25.3%), dementia (25.3%), chronic obstructive pulmonary disease (12.6%) and Parkinson's disease (4.6%). It should also be noted that among the women studied, none used hormone replacement therapy. As for smoking and past drinking, the prevalence was 13.8% and 6.9%, respectively.

In the two groups formed according to the levels of total 25 hydroxyvitamin D, the inflammatory markers CRP, NLR and PLR were measured and the results analyzed according to the Mann-Whitney test. The results of inflammatory parameters were shown in Figure 1.

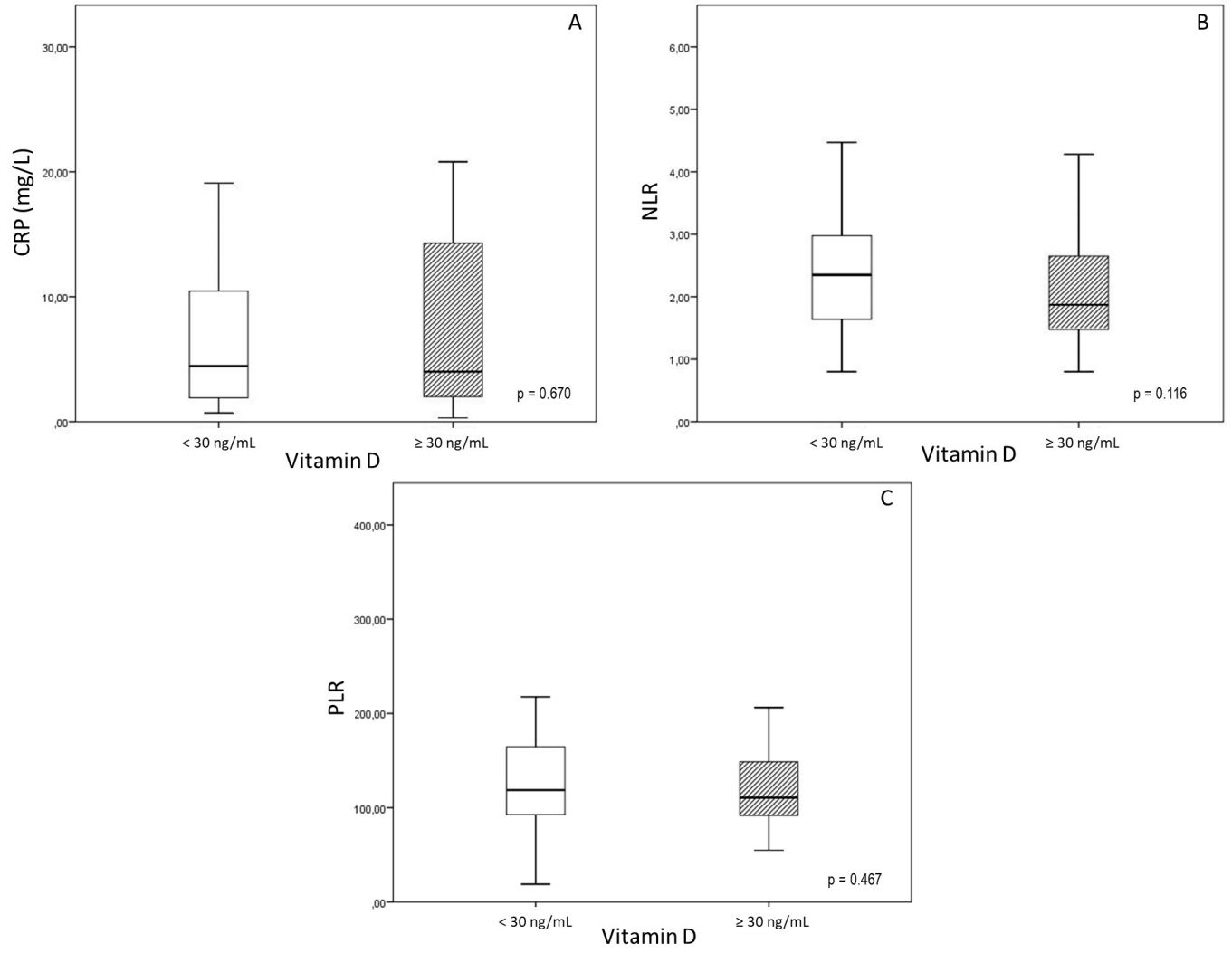

FIGURE 1 - Inflammatory markers according to the presence and absence of hypovitaminosis D of the elderly assessed in the study. CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio.

Regarding CRP, average values of 4.5 mg/L (1.9 – 10.5) and 4.0 mg/L (2.0 – 14.5) were found in the Vitamin D groups <30 ng/mL and vitamin D ≥30 ng/mL, respectively (Figure 1 A). There was no statistical difference between the two groups ($p > 0.05$).

The average CRP value in healthy people is up to 0.8 mg/L. Approximately 99.0% of the healthy population have CRP values below 10 mg/L and, in most cases, levels do not reach 2 mg/L. Values above 10 mg/L indicate active inflammatory process (Collares, Paulino, 2006).

It is known that CRP values vary according to the individual's age and their increase occurs in the process of healthy and pathological physiological aging, with significant pro-inflammatory action (Tang *et al*., 2017). However, there are few studies performed in the elderly population and, therefore, reference values for this age group are not yet defined.

A study carried out with elderlies (over 65 years old), proposed values of CRP (ultra-sensitive method) <6.6 mg/dL for women and <6.8 mg/dL for men (Herbeth, Siest, Henny, 2001). These values were higher than those found in this study.

Studies on the association between vitamin D levels and CRP in the elderly are also scarce. Thus, further studies are needed to establish parameters between

hypovitaminosis D and inflammatory markers in this population.

However, some studies carried out on individuals of other age groups found an association between hypovitaminosis D and increased CRP.

In a cross-sectional study with 15,167 patients of different age groups, a statistically significant inverse relationship was observed between vitamin D and CRP at levels <21 ng/mL. However, it was found that vitamin D at levels ≥21 ng/mL is associated with an increase in serum CRP. The authors concluded that the role of vitamin D supplementation in reducing inflammation can be beneficial only among those individuals with vitamin D levels <21 ng/mL (Amer, Qayyum, 2012).

Another cross-sectional study covering 5,870 English people over 50 years old observed an independent and inverse association between hypovitaminosis D (≤30 ng/mL) and CRP (Oliveira *et al*., 2017).

Timms *et al.* (2002) analyzed a non-diabetic population without severe diseases and concluded that vitamin D insufficiency was associated with increased CRP.

Correlations between vitamin D levels and inflammatory markers were analyzed using Spearman's correlation coefficient. The result for CRP was r = – 0.007; p = 0.949, for NLR and PLR ratios were r = – 0.159; p = 0.141 and r = – 0.105; p = 0.354, respectively. Therefore, vitamin D showed no correlation with the other parameters of the study.

However, similar to this study, other authors have found no significant association between vitamin D and inflammatory markers.

Azizieh *et al.* (2016), analyzed a group of 118 women aged 19 to 47 years and found no significant correlations between serum vitamin D levels and CRP levels.

A survey that evaluated a population with and without chronic kidney disease did not find a significant relationship between inflammatory markers and vitamin D levels (Yildirim, Hur, Kokturk, 2013).

The difficulties encountered when comparing studies that analyze the association between vitamin D and CRP levels derive from the lack of uniformity between the research designs, the age of the studied group and the CRP dosing techniques. Thus, some use a method less sensitive while others use a more sensitive one for PCR research, making the comparative analysis of this inflammatory marker more difficult.

In addition to CRP, used as an inflammatory biomarker, hematological changes were also assessed. These changes, arising from the development and progression of immunological, inflammatory or infectious diseases, reflect the patient's clinical condition. They can be qualitative or quantitative and are easily seen in the complete blood count, which is a low-invasive and inexpensive test. Thus, the NLR and PLR values, obtained from the blood count data, have helped in the diagnosis and monitoring of different types of diseases (Zhang *et al.*, 2017).

In this study, the mean NLR values found were 2.35 (1.64 – 2.99) and 1.87 (1.47 – 2.76), in the groups Vitamin D <30 ng/mL and vitamin D ≥30 ng/mL respectively (Figure 1 B) and for PLR the values were 119 (92 - 165) and 111 (89 - 149), respectively (Figure 1C). There was no statistical difference between these groups for the studied parameters (all p> 0.05).

It is necessary to consider that the levels of NLR and PLR increase with age (Akbas *et al.*, 2016; Li *et al.*, 2015). However, there are still no standardized reference values for these parameters for the elderly population.

Akbas *et al.* (2016) conducted a study with 4,120 individuals and among those over the age of 65 the average value found was 2.77 for NLR and 138.7 for PLR. These values are higher when compared to those found in this study.

The values of NLR and PLR were also analyzed according to gender, in the presence and absence of hypovitaminosis D. The group with hypovitaminosis presented mean values for NLR of 2.44 (1.60 – 3.05) for women and 2.33 (1.64 – 2.95) in men, p = 0.861 (Figure 2A). For PLR the values found where 119 (96 - 187) and 116 (90 - 156), for women and men respectively, with p = 0.429 (Figure 2B).

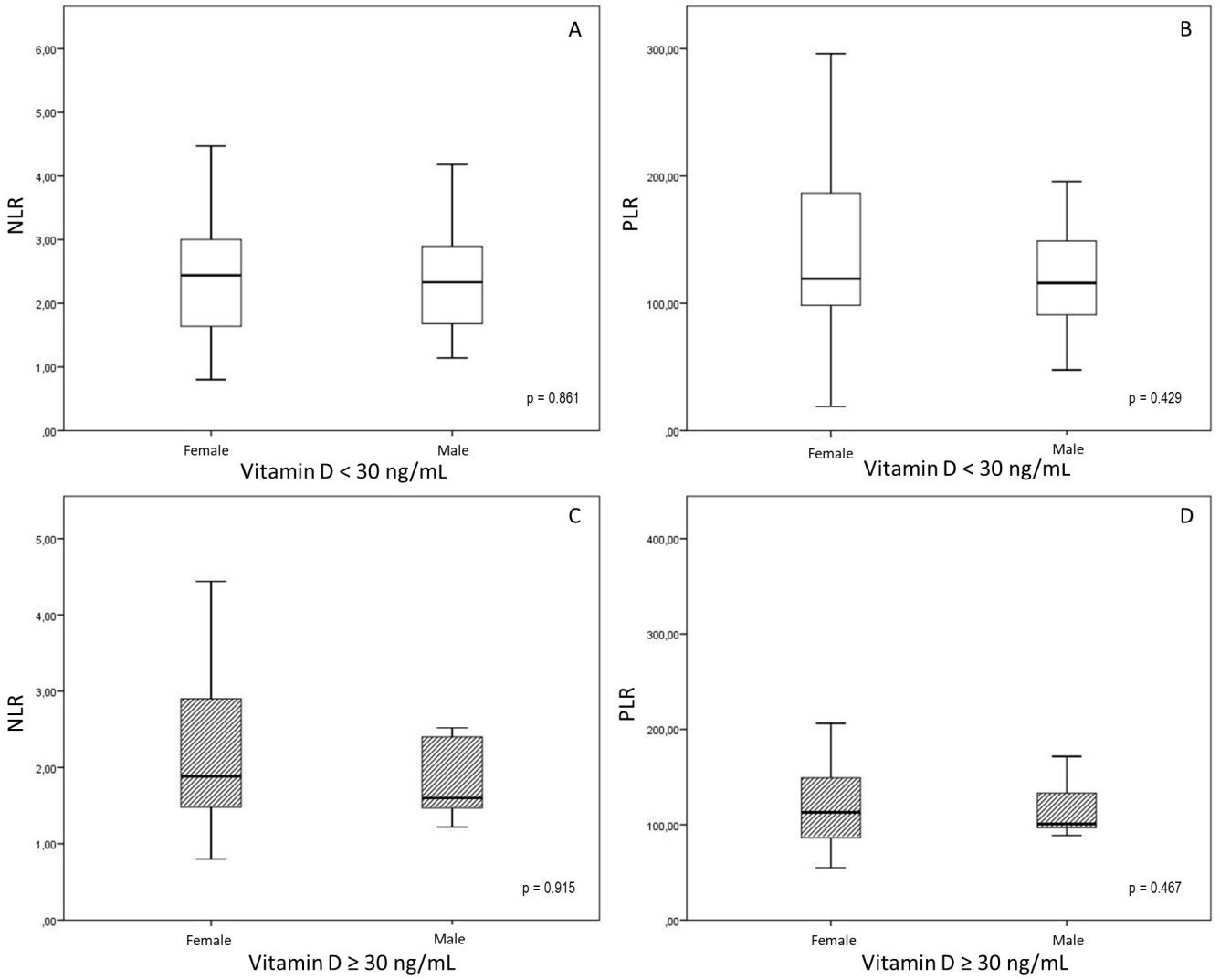

FIGURE 2 - Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio; distributed by gender in individuals in the presence and absence of hypovitaminosis D. NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio.

For the group with vitamin D ≥30 ng/mL, the mean NLR values were 1.88 (1.46 – 2.93) and 1.60 (1.46 – 2.46) for women and men, respectively; $p = 0.915$ (Figure 2C). And for PLR the values found were 113 (84 - 155) and 101 (97 - 151), for women and men, respectively, $p = 0.467$ (Figure 2D). Therefore, there was no statistical difference between the groups studied.

Li *et al.* (2015) analyzed samples from 1,568 females and 1,694 males. In healthy individuals over 70 years of age, the mean NLR values were 1.85 ± 0.58 for women and 2.05 ± 0.61 for men. These values were close to those found in this study, especially in women whose mean values found were 1.88.

The increase in NLR and PLR can be partially explained by the presence of chronic noncommunicable diseases and comorbidities present in the sample and are common in elderly people. The increase in NLR and PLR in the presence of comorbidities such as diabetes and hypertension was reported in another study (Mendes, Oliveira, Alcântara, 2019).

PLR and NLR have been used to determine inflammation in different types of neoplasia, metabolic syndrome, infectious diseases, cardiovascular diseases, end-stage renal disease, surgical stress, systemic inflammation and chronic conditions (Akbas *et al.*, 2016). However, the use of these measures to determine

the association between inflammation and vitamin D deficiency needs further studies to understand the pathophysiological processes involved.

A study by Koseoglu (2017) on 211 postmenopausal women found a significantly high NLR in women with low bone mineral density. He also observed an association between PLR and bone loss that could reflect the negative effect of chronic systemic inflammation on vitamin D metabolism, leading to osteoporosis and bone fractures.

Akbas *et al*. (2016) found an inverse association between vitamin D levels and NLR and PLR inflammatory markers. That is, NLR and PLR were significantly higher in patients with lower levels of vitamin D and PLR was considered an independent predictor of vitamin D levels.

Discrepancies in the literature points to the need for further studies on the possible association between vitamin D and inflammation. The joint evaluation of NLR, PLR and other inflammatory markers can facilitate the understanding of the inflammatory process and its infectious, thrombotic or neoplastic complications.

In this sense, this work sought to analyze the status of total 25 hydroxyvitamin D and its association with the levels of the inflammatory markers CRP, NLR and PLR. Another relevant point refers to the demographic characteristics of the studied population, since few studies have evaluated this association in patients over 60 years old and institutionalized.

Nevertheless, this study showed limitations, including the cross-sectional design, the use of a convenience sample (not probabilistic) with a small number of participants which can restrict the extensive application of the results regarding the elderly in general. Another limitation refers to the fact that the individuals in the sample have a high prevalence of chronic non-transmissible diseases, comorbidities and consequently make use of a large number of medications. Also, other important inflammatory markers, such as cytokines, had not been evaluated.

Even so, this work opened new perspectives for carrying out prospective studies, with the selection of more numerous groups involving healthy elderly individuals who may contribute to the understanding of the association of vitamin D and inflammatory markers.

The results of this study point to a predominant profile of vitamin D deficiency (<30 ng/mL) in the individuals evaluated, although no association was found between vitamin D values and the inflammatory markers analyzed.

These markers have shown potential in many studies reported in the literature. However, its association with vitamin D levels in the elderly needs to be elucidated in prospective studies designed specifically with repeated measurements of laboratory parameters and information on morbidity and mortality in the follow-up reports. Hypovitaminosis D is a serious condition that compromises the quality of life of the elderly because it is closely associated with immunity and maintenance of daily activities. Thus, it is necessary to create strategies to mitigate the health problems of the elderly and promote healthy aging process.

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