Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Association between serum vitamin D levels and prostate cancer: A cross-sectional analysis

Ahmet Yuce[a,*], Erdal Benli[a], Ahmet Anil Acet[a], Abdullah Cirakoglu[a], Mevlut Keles[a], Ayhan Arslan[a]

[a] *Ordu University, Faculty of Medicine, Department of Urology, Ordu, Türkiye*

ARTICLE INFO

Keywords:
Prostate cancer
Vitamin D
Inflammation
Marker

Received: Nov 01, 2024
Accepted: Mar 04, 2025
Available Online: 25.03.2025

DOI:
10.5455/annalsmedres.2024.11.233

Abstract

Aim: This study aims to examine whether inflammatory parameters such as vitamin D, CRP, and sedimentation measured in the serum of patients diagnosed with prostate cancer are different from those of their healthy peers.

Materials and Methods: The results of 163 patients who applied to Ordu University Urology Clinic with a diagnosis of prostate cancer between December 2019 and December 2023 and 140 healthy men who applied for other reasons in the same period were examined. Vitamin D levels and inflammatory markers such as CRP and ESR were compared between groups.

Results: The age distribution of patients in the prostate cancer and control group was 66.9±8.6 and 61.8±7.6 years, respectively. The vitamin D levels were identified as 17.25 [9.18] (5.27 – 55) µg/L and 20.74 [7.98] (6.94 – 51.01) in the prostate cancer and control group, respectively (p=0.001). Additionally, inflammatory markers like CRP and ESR were identified to be high in the prostate cancer group (p<0.001).

Conclusion: The vitamin D levels measured in patients with prostate cancer diagnosis were reduced compared to the control group and inflammatory markers were found to be increased. There is insufficient evidence in the literature on vitamin D and cancer. Disruption of the oxidant-antioxidant balance due to the inflammatory microenvironment may lead to a decrease in compounds such as vitamin D and predisposition to prostate cancer.

Copyright © 2025 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Introduction

Prostate cancer (PCa) is the second most frequently diagnosed cancer in men worldwide [1]. 15–25% of men newly diagnosed with cancer are diagnosed with PCa [2]. The exact cause of this disease, other than age, genetic, and racial characteristics, is not fully known. PSA, discovered in the 1980s, and MRI, which has recently become available in the diagnosis of the disease, have revolutionized the diagnosis of the disease despite some shortcomings. However, the expected decrease in the mortality rate of PCa has not occurred and PCa-related mortality rates continue to increase [3]. As life expectancy increases worldwide, more men are expected to reach older in the coming days. The American Cancer Society reported that there will be 240 thousand new cases annually worldwide, and approximately 34 thousand newly diagnosed patients will die due to cancer [4]. In conclusion, PCa remains an important public health issue. For this reason, today, there is a great effort to reveal the causes responsible for the development of the disease or to detect some pathology that occurs during the development of the disease early. This is especially important in terms of monitoring risky patients and giving them recommendations for cancer prevention. Although the exact etiology of prostate cancer is unknown, important clues are accumulating on this subject. Significant evidence can be found in the literature indicating the involvement of an inflammatory process in the development or progression of the disease [5]. The most important evidence appears to come from pathological examination reports. In radical prostatectomy reports, there are often inflammatory findings accompanying cancer. The fact that this disease occurs especially in aging men indicates that a chronic process is effective. Some behaviors and habits that begin early in life, or the deficiency or excess of certain substances in the body, may contribute to this process. For example, the results of a previous study we conducted showed that a person's sexual behavior and the number of partners are associated with cancer, and inflammatory parameters are increased in cancer patients [6].

*Corresponding author:
Email address: ahmetyuce7@gmail.com (Ahmet Yuce)

One of the substances that attracts the most attention in recent studies is vitamin D. Vitamin D plays an important role in many essential cell functions in the human body, especially calcium and bone metabolism. In addition, it has been suggested that it may be associated with the development of some cancers, including PCa [7]. Studies have reported that vitamin D may be involved in the cancer development process through intracellular and extracellular pathways. Studies on this subject have reported that it may inhibit cancer development through its anti-angiogenesis, anti-inflammatory effects, and the immune system [8]. There are also study results to the contrary. For example, in the study conducted by Kim MH et al. in 2022, PCa patients had lower vitamin D levels, but no statistically significant difference was found [2]. Voutilainen et al. also confirmed the result of this study [9]. As a result, today, the relationship between vitamin D and PCa has not been clearly established. For this reason, no recommendations are made regarding vitamin D in the EAU or AUA guidelines, and studies on this subject are ongoing.

This study aims to examine whether inflammatory parameters such as vitamin D, CRP, and sedimentation measured in the serum of patients diagnosed with prostate cancer are different from those of their healthy peers.

Materials and Methods

Study design and patients

This study was conducted at Ordu University Faculty of Medicine Urology Clinic. Permission for the study was obtained from the local ethics committee (No: 2023/278). Between December 2019 and December 2023, 163 patients with elevated PSA and diagnosed with prostate cancer as a result of prostate biopsy and 140 healthy people who applied for other reasons in the same period were included in the study. Study data were recorded prospectively by an expert in this field. The serum samples of the patients were taken in the morning at the first admission, after a 10-hour fast. In patients with a PSA value of ≥4 ng/mL, the elevation in PSA values was confirmed 2 - 4 weeks after benign causes were excluded. Patients with a PSA value of ≥4 ng/mL were subjected to a 12-quadrant systemic biopsy under transrectal ultrasound guidance after necessary information and written consent. Male patients with serum total PSA value <2.5 ng/mL were recorded for the control group.

Male patients diagnosed with prostate cancer, not receiving vitamin D or calcium treatment, and without any known bone disease were included in the study. Patients for whom pathology results could not be obtained, patients whose pathology results did not clearly indicate malignancy such as PIN, ASAP, prostatitis, patients with a known bone disease, those taking vitamin D externally, or those using medications that could affect vitamin D metabolism were excluded from the study. Demographic characteristics of the patients, such as age, BMI, and comorbidities, were recorded. In addition, accessible data such as serum total PSA, vitamin D, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), which could be determined at the time of admission to the clinic, were recorded.

Statistical analysis

The SPSS 20.0 package (Statistical Package for the Social Sciences, Version 20.0 SPSS Inc. Illinois, USA) was used to analyze the data. For the simplest within-group and between-group comparisons, approximately n=220 (110+110) was needed at alpha=0.05 and the effect size was determined for statistical power of 0.95 (Sample size was obtained using GPower 3.1 software). Arithmetic mean ± standard deviation, median (1st Quarter-3rd Quarter), minimum and maximum values were used to summarize numerical data, and numbers and percentages were used to summarize categorical data. The suitability of the data for normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogrorov-Smirnov/Shapiro-Wilk tests). Relationships between categorical data were evaluated with the Chi-square test. To evaluate the relationship between numerical data determined to be not normally distributed and categorical data, the Mann-Whitney U test was used if the categorical data was in two categories. Correlation between values was done using Spearman's rank correlation coefficient. Situations with $p<0.05$ were considered statistically significant.

Results

A total of 303 patients, 163 diagnosed with prostate cancer and 140 patients as the control group, were enrolled in this study. The mean age (mean ± Std) of prostate cancer patients was 66.92±8.67 years, and the control group was 61.8±7.68 years ($p<0.001$). The BMI distribution of the groups was 27.27±12.89 and 27.73±6.56, respectively ($p<0.001$) (Table 1). Laboratory parameters are shown as mean ± Std for normal distribution and median [IQR] (min–max) for non-normal distribution. The PSA value was 9.09 [67.76] (4.12 – 706.7) ng/mL in the PCa group and 0.895 [1.04] (0.13 – 2.49) ng/mL in the control group ($p<0.001$). The median values of the groups in terms of

Table 1. PCa and Control Group characteristics and serum values.

	Groups		
	PCa Group	Control Group	p
Age[a]	66.92±8.67	61.80±7.68	<0.001***
BMI[a]	27.27±12.89	27.73±6.56	<0.001***
PSA (ng/mL)[b]	9.09 [67.76]	0.895 [1.04]	<0.001***
Testosterone (ng/dL)[b]	4.79 [2.59]	5.865 [3.17]	0.012*
Sedimentation (min)[b]	19.7 [19]	16.2 [11.25]	<0.001***
CRP (mg/L)[b]	0.27 [0.48]	0.135 [0.24]	<0.001***
Calcium (mg/dL)[b]	9.5 [0.7]	9.6 [0.8]	0.024*

[a]: mean ± SD, [b]: median [IQR]. *:<0.05, ***:<0.001

Table 2. Vitamin D Mann-Whitney U Test with groups.

Groups	n	Median	Mean Rank	u	p
PCa	163	17.25	164.14	8.321	0.001*
Control	140	20.74	131.53		

The median value of serum 25-Hydroxy Vitamin D level was 20.74 µg/L in the control group and 17.25 µg/L in the PCa group (p=0.001). *:<0.05, ***:<0.001.

Table 3. PSA Level and Vitamin D Level Spearman Correlation test.

Groups	n	r	p
Vitamin D Level PSA Level	303	-0.166	0.005*

According to the results to determine the relationship between the patients' serum 25-Hydroxy Vitamin D levels and serum total PSA levels, there is a negative linear relationship between 25-Hydroxy Vitamin D levels and serum total PSA levels (r = -0.166, p = 0.005).

r-value	Linear Relationship Size
Up to 0.30	Small (weak correlation)
Between 0.30 -0.70	Moderate (moderate correlation)
Greater than 0.70	Large (strong correlation)

*:<0.05, ***:<0.001.

total testosterone were determined as 4.79 [2.59] (0.23 – 10.47) ng/dL in PCa patients and 5.865 [3.17] (1.53 – 13.9) ng/dL in the control group (p = 0.012). The distribution of calcium value according to groups was determined as 9.5 [0.7] (5.5 – 10.6) mg/dL and 9.6 [0.8] (8.8 – 11.9) mg/dL for the PCa and control groups, respectively (p = 0.024) (Table 1).

When the groups were compared in terms of inflammatory markers measured in serum, the sedimentation rate was 19.7 [19] (1 – 78) min and 16.2 [11.25] (1 – 49) min for the prostate cancer and control groups, respectively (p<0.001). Likewise, the distribution of the groups for CRP was determined as 0.27 [0.48] (0.00 – 21) mg/L and 0.135 [0.24] (0.00 – 3.78) mg/L, respectively (p<0.001) (Table 1).

The median value of serum 25-Hydroxy Vitamin D level was 20.74 [7.98] (6.94 – 51.01) µg/L in the control group and 17.25 [9.18] (5.27 – 55) µg/L in the PCa group (p=0.001) (Table 2). A negative linear relationship exists between the groups' vitamin D levels and serum total PSA levels (r = -166, p = 0.005) (Table 3).

Discussion

Despite advances in the diagnosis and surgical treatment of prostate cancer, the expected improvements in morbidity and mortality have not occurred. Today, many patients and their families continue to be affected by this disease. There are intense efforts to identify the factors that cause the onset and development of this disease or to detect the markers that appear in the early stages of the disease. This issue is important in terms of preventing the disease and making recommendations to patients at risk. This study was designed by retrospectively examining prospectively recorded data to investigate the relationship between vitamin D and inflammatory parameters and prostate cancer. As a result of the study, it was determined that the vitamin D value measured in the serum of patients diagnosed with PCa was decreased compared to their healthy peers. In addition, the increase in CRP and sedimentation values measured in serum detected the presence of an inflammatory background in cancer patients. When these results are evaluated together, it appears that there may be a relationship between vitamin D and cancer. The reason for the decrease in vitamin D in prostate cancer patients may be its use as an antioxidant substance consumed in the inflammatory environment. It is thought that there is an increased inflammatory response in cancer patients, in which the oxidant-antioxidant balance is disrupted in favor of the oxidant and vitamin D decreases in this environment.

The number of men reaching older ages is increasing in developed countries. This means more men are diagnosed with prostate cancer [10]. In our study, the average age of the cancer group was 66.92 years, and the age of the cancer patients was approximately five years older than the control group. This cancer remains a significant public health problem affecting all societies. There is a great effort to prevent this disease in developed countries. Studies have provided important evidence, such as age, genetics, and racial characteristics related to PCa, but the exact cause of the disease has not been understood [11]. Today, diagnosis and surgical techniques have recorded the greatest successes regarding this disease. There is no recommendation to be given, especially to patients at risk for PCa, and the guidelines are silent on this issue.

A careful review of the literature reveals an important relationship between PCa and a chronic inflammatory process. The fact that the prostate is open to the outside world through the urethra makes it a particularly vulnerable target for infectious agents. For example, a sexually transmitted microorganism can settle in the prostate tissue and initiate a chronic inflammatory process. In a study on this subject, Cohen and his colleagues demonstrated the presence of P. Acne in the pathological specimens of prostate cancer patients. Additionally, the presence of significant inflammation along with cancer has been reported in patients carrying this agent [12]. The results of a previous study we conducted also support these data. In this study, we found that there is a relationship between sexual behaviors and prostate cancer. It has been shown that inflammatory parameters such as CRP and NLR measured in the serum of patients with PCa are increased compared to the control group [6]. There may be many reasons for the development of cancer in a chronic inflammatory environment. For example, the oxidative environment resulting from the arrival of many immune system cells, such as macrophages and lymphocytes, in this environment and the secretion of many pro-inflammatory substances, such as cytokines, may be the reason for this. This oxidative environment is unsuitable for normal cell physiology, resulting in cell death and apoptosis. Cell proliferation increases to replace destroyed cells. This accelerated cell regeneration may cause some cells to get out of control and gain immortality [13]. Additionally, oxidative stress resulting from this inflammatory process may initiate or affect the oncogenic process by causing DNA damage [14]. Studies have shown that inflammatory cells such as macrophages accompany cancerous tissue in cancers seen in humans and rats [15]. It has been shown that PSA values decrease in some PCa patients using acetylsalicylic acid and NSAID [16]. The results of this study presented also support these data. Compared to the control group, inflammatory markers such as CRP and ESR measured in the serum of prostate cancer patients were

observed to increase. When these results and the data in the literature are considered together, it is understood that an inflammatory environment is effective in the development of PCa. There are other cancers that develop on a chronic inflammatory basis, such as thyroid cancer, cervical cancer, and urothelial cancer. Some authors even thought that cancer could be prevented by eliminating this inflammatory environment. NSAIDs have been used to reduce the incidence of cancer [17]. In conclusion, there is serious evidence showing that there is a close relationship between an inflammatory environment that occurs for various reasons and the development of many cancers, such as prostate cancer.

Vitamin D, which plays an important role in many cellular functions such as calcium and bone metabolism, has recently been extensively studied in the literature, especially regarding cancer. Its association with many cancers, such as breast, colon, rectum, stomach, and esophagus, has been reported [18]. Likewise, its relationship with prostate cancer was also examined. One of the first studies on this subject examined the effect of vitamin D on normal, benign, and cancerous prostate cell cultures. As a result of the study, it was reported that vitamin D irreversibly inhibited epithelial cells and that the prostate cell inhibition effect of vitamin D could be used for treatment purposes [19]. Although the relationship between vitamin D and cancer has not been definitively established, significant evidence exists on this subject. This effect is thought to occur through many different pathways, such as cell differentiation inhibition, apoptosis induction, cellular proliferation, and angiogenesis [20]. What most studies have in common is its inhibitory effect on the inflammatory process. In a study on this subject, Gupta reported that vitamin D is effective in prostate cancer by inhibiting some pathways that play a role in inflammation, such as the production of inflammatory cytokines and inhibition of nuclear factor κB (NF-κB) signaling [21]. Selective COX-2 inhibitor NSAIDs, such as celecoxib, have been shown to suppress PCa in the TRAMP PCa model [22]. In another study, Kim et al. showed in a multivariate analysis that the incidence of clinically significant prostate cancer was significantly increased in people with low vitamin D levels [2]. The effect of vitamin D on some precancerous lesions known for prostate cancer was also examined. In an interesting study on this subject, the effect of vitamin D on PIN, considered a precancerous lesion, was examined. In this experimental model, vitamin D slowed or prevented the progression of PIN to cancer [23]. Some studies examined the effect of vitamin D on PSA in patients diagnosed with cancer. In one of these studies, Campbell et al. started vitamin D in patients with PCa who were followed up with active surveillance. Compared to the baseline, as the vitamin D levels of the patients increased, their PSA values decreased [24]. Our study found a negative relationship between vitamin D value and PSA. This decrease is significant, considering the importance of PSA in the follow-up and prognosis of cancer patients.

There are also some studies reporting that there is no relationship between vitamin D and prostate cancer. In a study on this subject, Voutilainen et al. examined the relationship between vitamin D and lung and prostate cancer. As a result of the study, they did not find any relationship [9]. However, there are not enough studies in the literature to support these results. This may be related to the shortcomings of the studies.

There is confusion about vitamin D in the literature, and there may be many reasons for this. Especially the retrospective planning of the studies and the lack of data on inflammatory parameters feed this problem. Our study provides important information to the literature in this field by prospectively recording the data and including inflammatory parameters such as CRP and ESR. As a result of the study, it was shown that the vitamin D value measured in the serum of prostate cancer patients decreased compared to the control group, and inflammatory markers such as CRP and ESR increased. In conclusion, vitamin D seems to be related to cancer with its anti-inflammatory effect on the immune system [25]. The increased inflammatory environment in patients with prostate cancer may cause the oxidant-antioxidant balance to deteriorate and antioxidant compounds to decrease. It is known that some antioxidant compounds are reduced in the increased inflammatory environment in patients with PCa [26]. Vitamin D may also be an anti-inflammatory or antioxidant substance consumed in this environment.

Limitations

The study has some problems, such as not being double-blind and reflecting the results of a single center. According to our study results, although a correlation with vitamin D was found, it was found to be quite weak. For this reason, randomized and multicenter studies are needed on this subject. However, there are features that make the study strong, such as its prospective design and the study of inflammatory parameters, unlike many previous studies. We think it will shed light on the confusion about vitamin D in the literature.

Conclusion

There are major efforts to discover various markers that occur during the development of prostate cancer. These studies are very important in terms of recommendations or treatments for patients. In our study results, it was determined that vitamin D levels decreased compared to the control group. In addition, the presence of an inflammatory environment in prostate cancer patients was demonstrated by CRP and ESR measured in serum. When the study results are evaluated together, vitamin D may be reduced as a protector against cancer development and as an antioxidant substance in the inflammatory environment created by cancer cells. As a result, it was determined that low vitamin D level may be a risk factor for prostate cancer. We think that risky people should be followed up early and the deficiency should be replaced.

Ethics Committee Approval

This study was conducted at Ordu University Faculty of Medicine Urology Clinic. Permission for the study was obtained from the local ethics committee (No: 2023/278).

References

1. Al-Ghazawi M, Salameh H, Amo-Afful S, et al. An In-Depth Look Into the Epidemiological and Etiological Aspects of Prostate Cancer: A Literature Review. *Cureus.* 2023;15(11):e48252. DOI: 10.7759/cureus.48252.
2. Kim MH, Yoo S, Choo MS, et al. The role of the serum 25-OH vitamin D level on detecting prostate cancer in men with elevated prostate-specific antigen levels. *Sci Rep.* 2022;12(1):14089. DOI: 10.1038/s41598-022-17563-8.
3. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin.* 2024;74(1):12-49. DOI: 10.3322/caac.21820.
4. Creighton CJ, Zhang F, Zhang Y, et al. Comparative and integrative analysis of transcriptomic and epigenomic-wide DNA methylation changes in African American prostate cancer. *Epigenetics.* 2023;18(1):2180585. DOI: 10.1080/15592294.2023.2180585.
5. Benli E, Cirakoglu A, Ayyıldız SN, Yüce A. Comparison of serum uric acid levels between prostate cancer patients and a control group. *Cent European J Urol.* 2018;71(2):242-47. DOI: 10.5173/ceju.2018.1619.
6. Benli E, Yuce A, Cirakoglu A, et al. Comparison of Sexual Behavior and Inflammatory Parameters in Prostate Cancer Patients with Control Group: Prospective Controlled Study. *Urol J.* 2021;19(2):101-05. DOI: 10.22037/uj.v18i.6464.
7. Stroomberg HV, Vojdeman FJ, Madsen CM, et al. Vitamin D levels and the risk of prostate cancer and prostate cancer mortality. *Acta Oncol.* 2021;60(3):316-22. DOI: 10.1080/0284186X.2020.1837391.
8. Wang L, Wang C, Wang J, et al. Longitudinal, observational study on associations between postoperative nutritional vitamin D supplementation and clinical outcomes in esophageal cancer patients undergoing esophagectomy. *Sci Rep.* 2016;6:38962. DOI: 10.1038/srep38962.
9. Voutilainen A, Virtanen JK, Hantunen S, et al. Multiplicative, additive, and interactive associations of 25-hydroxyvitamin D with lung and prostate cancer. *Int J Vitam Nutr Res.* 2024;94(2):133-42. DOI: 10.1024/0300-9831/a000780.
10. Schwartz SM. Epidemiology of Cancer. Clin Chem. 2024;70(1):140-49. DOI: 10.1093/clinchem/hvad202.
11. Cui H, Zhang W, Zhang L, et al. Risk factors for prostate cancer: An umbrella review of prospective observational studies and mendelian randomization analyses. *PLoS Med.* 2024;21(3):e1004362. DOI: 10.1371/journal.pmed.1004362.
12. Cohen RJ, Shannon BA, McNeal JE, et al. Propionibacterium acnes associated with inflammation in radical prostatectomy specimens: a possible link to cancer evolution? *J Urol.* 2005;173(6):1969-74. DOI: 10.1097/01.ju.0000158161.15277.78.
13. Ge M, Papagiannakopoulos T, Bar-Peled L. Reductive stress in cancer: coming out of the shadows. *Trends Cancer.* 2024;10(2):103-12. DOI: 10.1016/j.trecan.2023.10.002.
14. Iqbal MJ, Kabeer A, Abbas Z, et al. Interplay of oxidative stress, cellular communication and signaling pathways in cancer. *Cell Commun Signal.* 2024;22(1):7. DOI: 10.1186/s12964-023-01398-5.
15. Rasheed RA, Sadek AS, Khattab RT, et al. Diacerein provokes apoptosis, improves redox balance, and downregulates PCNA and TNF-α in a rat model of testosterone-induced benign prostatic hyperplasia: A new non-invasive approach. *PLoS One.* 2023;18(11):e0293682. DOI: 10.1371/journal.pone.0293682.
16. Fowke JH, Motley SS, Smith JA Jr, et al. Association of nonsteroidal anti-inflammatory drugs, prostate specific antigen and prostate volume. *J Urol.* 2009;181(5):2064-70. DOI: 10.1016/j.juro.2009.01.031.
17. Kolawole OR, Kashfi K. NSAIDs and Cancer Resolution: New Paradigms beyond Cyclooxygenase. *Int J Mol Sci.* 2022;23(3):1432. DOI: 10.3390/ijms23031432.
18. Sobhi P, Bahrami M, Mahdizadeh F, et al. Vitamin D and potential effects on cancers: a review. *Mol Biol Rep.* 2024;51:190. DOI: 10.1007/s11033-023-09111-y.
19. Erzurumlu Y, Aydogdu E, Dogan HK, et al. 1,25(OH)2 D3 induced vitamin D receptor signaling negatively regulates endoplasmic reticulum-associated degradation (ERAD) and androgen receptor signaling in human prostate cancer cells. *Cell Signal.* 2023;103:110577. DOI: 10.1016/j.cellsig.2022.110577.
20. Hendrickson WK, Flavin R, Kasperzyk JL, et al. Vitamin D receptor protein expression in tumor tissue and prostate cancer progression. J Clin Oncol. 2011;29(17):2378-85. DOI: 10.1200/JCO.2010.30.9880.
21. Gupta S. Prostate cancer chemoprevention: current status and future prospects. *Toxicol Appl Pharmacol.* 2007;224(3):369-76. DOI: 10.1016/j.taap.2006.11.008.
22. Kido LA, Montico F, Sauce R, et al. Anti-inflammatory therapies in TRAMP mice: delay in PCa progression. *Endocr Relat Cancer.* 2016;23(4):235-50. DOI: 10.1530/ERC-15-0540.
23. Abu El Maaty MA, Grelet E, Keime C, et al. Single-cell analyses unravel cell type-specific responses to a vitamin D analog in prostatic precancerous lesions. *Sci Adv.* 2021;7(31):eabg5982. DOI: 10.1126/sciadv.abg5982.
24. Campbell RA, Li J, Malone L, Levy DA. Correlative Analysis of Vitamin D and Omega-3 Fatty Acid Intake in Men on Active Surveillance for Prostate Cancer. *Urology.* 2021;155:110-16. DOI: 10.1016/j.urology.2021.04.050.
25. Ao T, Kikuta J, Ishii M. The Effects of Vitamin D on Immune System and Inflammatory Diseases. *Biomolecules.* 2021;11(11):1624. DOI: 10.3390/biom11111624.
26. Jiang J, Chen B, Tang B, Wei Q. Selenium in Prostate Cancer: Prevention, Progression, and Treatment. *Pharmaceuticals (Basel).* 2023;16(9):1250. DOI: 10.3390/ph16091250.