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Study the association between prostate cancer and vitamin D receptor genetic polymorphism with relation to IL 6 (Cytokines) level

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Abstract

Background: Prostate cancer (PCA) is among the most common malignancies in men and it occurs under the influence of genetic, inflammatory, and nutritional factors. It has been suggested that the VDR rs1544410 polymorphism may regulate the activity of the vitamin D receptor and cancer risk, and interleukin-6 (IL-6) can be involved in the cancer-promoting inflammation. These factors should be looked at collectively.

Methods: The study design was a case-control study, which recruited 75 histologically proven PCA patients and 75 age matched healthy controls. ELISA was used to determine serum vitamin D3, vitamin A, and IL-6. Peripheral blood was used to extract genomic DNA and genotype the rs1544410 by TaqMan real-time PCR. Statistical analysis included Mann–Whitney U test, Fisher's exact test, one-way ANOVA with Games–Howell post hoc correction, and Pearson's correlation.

Results: PCA patients had significantly lower serum vitamin D3 (18.89 vs. 30.08 ng/mL; p=0.001) and vitamin A (0.96 vs. 5.08 µg/mL; p=0.001), and markedly elevated IL-6 (83.55 vs. 48.68 pg/mL; p=0.001). The TC genotype was strongly over-represented in patients (65.3% vs. 21.3%; OR=6.95; p<0.0001), while CC was protective (6.7% vs. 54.7%; OR=0.059; p<0.0001). Vitamin D3 and vitamin A were positively correlated (r=0.288; p<0.001) and both inversely correlated with IL-6.

Conclusion: The TC genotype of VDR rs1544410 has a significant relationship with the elevated risk of PCA. Vitamin D3 and vitamin A deficits and IL-6 increase are typical biochemical alterations of PCA patients irrespective of genotype, which underscores a combined immunonutritional model of PCA susceptibility.

Keywords: Prostate Cancer; VDR Gene Polymorphism; Rs1544410; Vitamin D3; IL-6; Genotyping

1. Introduction

Prostate cancer (PCA) is one of the most prevalent cancers in the male population that is diagnosed and has the first and the third highest incidence and mortality rates, respectively, among male cancers worldwide [1]. It has multifactorial aetiology as it includes hereditary predisposition, environmental exposures, and lifestyle determinants such as obesity, sedentary lifestyle, and smoking. Although progress has been made in early detection and multimodal treatment, the molecular mechanisms of PCA initiation and progression are not fully understood and thus there is need to discover tough genetic and biochemical risk factors [2].

Vitamin D has been revaluated as a calcium-regulating hormone to an immunomodulator that is pleiotropic, anti-proliferative, pro-differentiating, and pro-apoptotic. The major storage form, 25-hydroxyvitamin D [25(OH)D], which is the result of the hepatic hydroxylation process, is further hydroxylated by the renal 1,25(OH)2D3 as 1, 25-

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dihydroxyvitamin D3 [1,25(OH)2D3]. This metabolite interacts with Vitamin D Receptor (VDR), a nuclear transcription factor that is expressed in the prostate gland, to control genes that control the cell cycle progression and immune activities [3,4].

VDR gene SNPs alter receptor expression and ligand-binding affinity and hence the level of downstream vitamin D responses. Of special interest has been the rs1544410 (BsmI) intron 8 polymorphisms due to its postulated regulatory impact on VDR mRNA stability and tissue-specific levels of expression [5,6]. Inconsistent epidemiological findings on association of rs1544410 and PCa risk have been reported, possibly due to ethnic heterogeneity in patterns of linkage disequilibrium and vitamin D intake variation in study populations [7].

The microenvironment of inflammatory tumours is also an equally significant predictor of PCa aggressiveness. The multifunctional cytokine, interleukin-6 (IL-6), which is released by stromal and immune cells in the prostate, stimulates JAK/STAT3, PI3K/AKT, and MAPK signalling cascades that together support cell survival, treatment resistance, and metastatic dissemination [8,9,10]. The IL-6 also inhibits anti-tumour immunity by polarising macrophages and limiting cytotoxic T cell functions, which enhances its oncogenic effects [11].

The interaction between VDR-mediated signalling and IL-6-mediated inflammation is an unexplored aspect of PCa biology. Vitamin D3 suppresses the activation of NF- -B and cytokine gene expression which could suppress the production of IL-6 in the tumour environment [12]. Vitamin A also regulates immune activity through retinoic acid receptors and both micronutrients have been found to be low in PCa patients [13,14,15]. The biochemical architecture of PCa susceptibility may be elucidated by understanding how VDR genetic variation changes the association between these micronutrients and systemic inflammation. This study therefore investigated the association between VDR rs1544410 genotype, serum vitamin D3, vitamin A, and IL-6 levels in PCa patients versus healthy controls, with genotype-stratified post hoc analysis to disentangle genetic from disease-related contributions to observed biomarker differences.

2. Materials and Methods

2.1. Study Design and Participants

The study was a case-control case study involving 75 men diagnosed with prostate cancer that was confirmed in a histopathology lab and 75 healthy men who were controls. The case study took place in a tertiary medical centre located in Baghdad, Iraq. The criteria to diagnose SLE were not met; PCa was diagnosed with prostate biopsy. Controls did not have any controls that reported any current or past malignancy, autoimmune or chronic kidney disease or any vitamin D supplementation within three months before enrolment. Written informed consent was obtained from all participants and the study was approved by the institutional ethics committee.

2.2. Sample Collection

Aseptic collection of peripheral venous blood (10 mL) was done in EDTA anticoagulated tubes (to extract DNA) and plain serum separator tubes (to perform biochemical tests). Serum separated by centrifugation at 3,000 rpm for 10 min at 4°C and kept at −80°C till batched analysis.

2.3. Serum Biomarker Quantification

- **Vitamin D3 and Vitamin A:** Serum 25-hydroxyvitamin D3 and vitamin A concentrations were determined using commercial sandwich ELISA kits following manufacturer protocols. At 450 nm, absorbance was measured and four-parameter logistic standard curves used to determine concentrations.
- **IL-6:** Sandwich ELISA was used to measure serum interleukin-6. Each sample was tested twice; the results were in pg/mL.

2.4. DNA Extraction and rs1544410 Genotyping

Zymo-Spin IIC column-based kit was used to extract the genomic DNA. In short, blood was lysed using genomic lysis buffer, applied to the spin column, and washed using sequentially DNA Pre-Wash and g-DNA Wash Buffers, and eluted using nuclease-free water. Genotyping of rs1544410 was done by Taqman real time PCR using Custom SNP Genotyping Assay with Taqman Genotyping Master Mix at −20°C. Thermal cycling included initial enzyme activation, 40 denaturation-annealing/extension cycles, and automated allelic discrimination cluster analysis for genotype calling.

2.5. Statistical Analysis

All analyses were performed using IBMS SPSS statistics v26. Continuous variables are provided as mean ±SD, median and SE. Comparisons between groups were done using Mann-WHitney U tests. Fisher exact test was used to compare the frequencies of the genotypes with OR and 95% CI. One-way ANOVA was used to compare biomarker levels across genotype strata with GamesHowell post hoc correction. The correlation of Pearson was used to evaluate the relationship between the biomarkers. A two-tailed $p<0.05$ was considered to be statistically significant.

3. Results

3.1. Blood Group Distribution

Table 1 presents the frequencies of blood groups. The proportions of blood type A+ and AB+ were 20.0% and 17.3% respectively in patients and controls, which indicates that there are numerical tendencies to over-representation in PCa. The proportion of O- in patients (4.0%) was less than controls (13.3%). Groups O+ and AB- were well-balanced in each cohort (10.7% and 9.3%, respectively). Although there were these numerical differences, the chi-square test was not significant (χ^2=8.47; p=0.293) showing that there was no independent relationship between ABO blood group and PCa risk among this population.

Table 1 ABO blood group distribution in prostate cancer patients and healthy controls

Blood Group	Patients n (%)	Controls n (%)	χ^2 / p
B+	12 (16.0%)	10 (13.3%)	
B−	8 (10.7%)	11 (14.7%)	
O+	8 (10.7%)	8 (10.7%)	
O−	3 (4.0%)	10 (13.3%)	
A+	15 (20.0%)	8 (10.7%)	
AB+	13 (17.3%)	8 (10.7%)	
A−	9 (12.0%)	13 (17.3%)	
AB−	7 (9.3%)	7 (9.3%)	
Total	75 (100%)	75 (100%)	χ^2=8.47; p=0.293

Serum Vitamin D3, Vitamin A, and IL-6

All three biomarkers differed significantly between groups (Table 2). PCa patients had substantially lower mean vitamin D3 (18.89 ± 10.56 vs. 30.08 ± 10.36 ng/mL; p=0.001), confirming hypovitaminosis D as a characteristic of the PCa biochemical phenotype. Vitamin A was markedly reduced in patients (0.96 ± 0.89 vs. 5.08 ± 5.27 µg/mL; p=0.001), with less intra-group variability in patients than controls (SD 0.89 vs. 5.27). Conversely, mean IL-6 was nearly twofold higher in patients (83.55 ± 28.47 vs. 48.68 ± 23.10 pg/mL; p=0.001), indicating a pronounced pro-inflammatory state.

Table 2 Serum vitamin D3, vitamin A, and IL-6 levels in prostate cancer patients and controls

Parameter	Group	n	Mean	Median	SD	SE	p-value
Vitamin D3 (ng/mL)	Patients	75	18.89	15.33	10.56	1.22	0.001
	Controls	75	30.08	29.52	10.36	1.20	—
Vitamin A (µg/mL)	Patients	75	0.96	0.78	0.89	0.10	0.001
	Controls	75	5.08	3.15	5.27	0.61	—
IL-6 (pg/mL)	Patients	75	83.55	80.23	28.47	3.29	0.001
	Controls	75	48.68	48.50	23.10	2.67	—

3.2. VDR rs1544410 Genotype Frequencies and Prostate Cancer Risk

Table 3 shows the genotype distribution and odds ratios. TC heterozygous genotype was significantly higher in PCa patients (65.3%) as compared to controls (21.3%), with an OR of 6.949 (95% CI: 3.352-14.405; p<0.0001), showing that there was a nearly sevenfold risk of PCa development in TC carriers. A moderate numerical over-representation in the patients was observed in the TT genotype (28.0% vs. 24.0; OR=1.231; p=0.576), which was not statistically significant. The CC homozygous genotype on the other hand was significantly under-represented in patients (6.7% vs. 54.7; OR=0.059; 95% CI: 0.022-0.163; p<0.0001) which is also in line with a strong protective effect of CC homozygosity against PCa.

Table 3 Association of VDR rs1544410 genotype with prostate cancer risk

Genotype	Patients n (%)	Controls n (%)	OR	Fisher p	95% CI
TT	21 (28.0%)	18 (24.0%)	1.231	0.576	0.59–2.56
TC	49 (65.3%)	16 (21.3%)	6.949	<0.0001	3.35–14.41
CC	5 (6.7%)	41 (54.7%)	0.059	<0.0001	0.022–0.163

3.3. Genotype-Stratified Biomarker Levels and Post Hoc Analysis

Table 4 summarizes biomarker concentrations stratified by each group of the genotype of rs1544410. CC patients had the lowest levels of vitamin D3 (mean 13.81 ng/mL), and all patient subgroups were significantly lower than their control counterparts (p=0.001). The same thing happened with Vitamin A: TT patients 0.74 µg/mL, TC patients 1.10 µg/mL, and CC patients 0.60 µg/mL, were significantly lower than the control levels (~5.05.3 µg/mL; p=0.001). IL-6 was elevated across all patient genotype subgroups (TT: 87.55; TC: 82.44; CC: 77.69 pg/mL) relative to controls (TT: 51.87; TC: 47.42; CC: 47.77 pg/mL; p=0.001). Post hoc pairwise comparisons revealed that patient-control differences in all three biomarkers were statistically significant in virtually all genotypic pairings (p<0.001 in most), but intra-patient genotype differences (TT vs. TC, TT vs. CC, TC vs. CC patients) were uniformly non-significant (p>0.05). This genotype-independent trend is a solid-state confirmation that the changes in biomarkers in PCa are a reflection of disease biology as opposed to a direct effect of genotype.

Table 4 Serum vitamin D3, vitamin A, and IL-6 levels stratified by rs1544410 genotype in prostate cancer patients and healthy controls, with post hoc significance summary

Parameter	Genotype/Group	n	Mean	SD	SE	p-value	Post hoc*
Vitamin D3 (ng/mL)	TT Patients	21	19.68	10.40	2.27	0.001	Sig vs ctrl
	TC Patients	49	19.08	11.03	1.58	—	Sig vs ctrl
	CC Patients	5	13.81	5.21	2.33	—	p=0.014
	TT Controls	18	28.03	11.36	2.68	—	—
	TC Controls	16	31.52	10.59	2.65	—	—
	CC Controls	41	30.41	9.94	1.55	—	—
Vitamin A (µg/mL)	TT Patients	21	0.74	0.71	0.15	0.001	p=0.006
	TC Patients	49	1.10	0.97	0.14	—	p=0.003
	CC Patients	5	0.60	0.27	0.12	—	NS
	TT Controls	18	5.16	4.89	1.15	—	—
	TC Controls	16	5.27	6.59	1.65	—	—
	CC Controls	41	4.97	5.00	0.78	—	—
IL-6 (pg/mL)	TT Patients	21	87.55	37.39	8.16	0.001	p<0.001
	TC Patients	49	82.44	25.00	3.57	—	p<0.001
	CC Patients	5	77.69	19.15	8.56	—	NS

	TT Controls	18	51.87	27.18	6.41	—	—
	TC Controls	16	47.42	22.78	5.70	—	—
	CC Controls	41	47.77	21.74	3.40	—	—

*Games–Howell post hoc test. Sig = significant; NS = not significant. All patient–control pairings significant at p<0.001 unless noted. Intra-patient genotype comparisons non-significant throughout.

3.4. Biomarker Interrelationships and Correlation with Age

The Pearson's correlation matrix is presented in Table 5. There was a significant positive correlation between vitamin D3 and vitamin A in the entire cohort (r=0.288; df=148; p<0.001) indicating that there may have been common regulatory activity or co-deficiency patterns in PCa. Both vitamins had an inverse relationship with IL-6: vitamin D3 vs. IL-6 (r=−0.198; p=0.015) and vitamin A vs. IL-6 (r=−0.209; p=0.010): this is expected as these vitamins have anti-inflammatory effects. The age was not found to have any significant relationship with vitamin D3 (r= -0.007; p=0.932), vitamin A (r=0.066; p= 0.422), or IL-6 (r=0.020; p= 0.813), which indicating that the observed changes in biomarkers are disease-driven rather than age-related phenomena.

Table 5 Pearson's correlation matrix for serum vitamin D3, vitamin A, IL-6, and age in the full study cohort (n=150)

Parameter	Stat.	Vitamin D3	Vitamin A	IL-6	Age
Vitamin D3	r	—	0.288***	−0.198*	−0.007
	p	—	<0.001	0.015	0.932
Vitamin A	r	0.288***	—	−0.209**	0.066
	p	<0.001	—	0.010	0.422
IL-6	r	−0.198*	−0.209**	—	0.020
	p	0.015	0.010	—	0.813
Age	r	−0.007	0.066	0.020	—
	p	0.932	0.422	0.813	—

DF=148 for all pairwise correlations. *p<0.05; **p<0.01; ***p<0.001.

4. Discussion

The current study offers a combined genetic and biochemical analysis of prostate cancer risk in terms of VDR polymorphism of the VDR rs1544410 and immunonutritional biomarkers. The results define an exciting risk profile that is typified by TC heterozygosity, vitamin shortage, and systemic IL-6 elevation, providing translational understanding of the pathogenesis and possible prevention targets in PCA.

4.1. VDR rs1544410 and PCa Risk

One of the most clinically important results of the current study is the near sevenfold higher PCA odds in TC carriers (OR=6.95; p<0.0001). BsmI rs1544410 polymorphism can affect the VDR mRNA stability and tissue-specific expression; heterozygosity can produce intermediate receptor activity inadequate to sustain the anti-proliferative vitamin D signalling in the prostate epithelium [5,6]. Close protective relationship of CC homozygosity (OR=0.059) further indicates that complete transcriptional competence of VDR suppresses prostate carcinogenesis. These results are consistent with the published literature that reports on the enrichment of the B allele (T allele) in PCa cohorts [16,18], but the effect sizes differ across populations, probably because linkage disequilibrium structure and environmental levels of vitamin D differ. Our non-significant TT association might be due to intermediate receptor activity or population-specific LD with other functional VDR variants [7].

4.2. Vitamin D3 Deficiency in PCa

The overall reduction of the vitamin D3 levels in all PCa genotype subgroups is consistent with abundant evidence indicating the relationship between hypovitaminosis D and increased PCa risk and aggressive disease phenotypes [3,14]. VDR-based vitamin D signalling triggers cell cycle arrest at the G1/S phase, induces differentiation, and triggers apoptosis in prostate cells; its dysfunction due to both receptor polymorphisms and substrate depletion generates a

laissez-faire oncogenic environment [4,19]. Interestingly, the mean vitamin D3 (13.81 ng/mL) of CC patients was lowest despite their protective genotype, indicating that nutritional supplementation can also be effective in genetically privileged persons. This finding has direct clinical implications on the role of vitamin D optimisation on PCa prevention programmes.

4.3. Vitamin A Deficiency and Retinoid Signalling

The markedly reduced vitamin A in PCa patients (0.96 vs. 5.08 μg/mL; p=0.001) builds upon previous studies of vitamin A deficiency in urological cancers [13]. Vitamin A, acting mostly via its active metabolite retinoic acid, is an activator of RAR/RXR-mediated transcriptional programmes that overlap VDR signalling, such as those that regulate cellular differentiation and proliferation. RXR is a heterodimeric partner of VDR and vitamin A deficiency can thus interact with the functional effects of VDR polymorphisms to reduce the availability of RXR to form productive VDRRXR complexes [12]. The fact that vitamin D3-vitamin A is positively correlated (r=0.288; p<0.001) is in line with this overlapping regulatory axis and justifies the inclusion of both micronutrients in PCa risk evaluation.

4.4. IL-6 as a Disease-Invariant Inflammatory Biomarker

The genotype-independent increase of IL-6 in PCa patients in all genotypic subgroups (p<0.001 in all patient- vs. control comparisons) supports the use of IL-6 as a strong biomarker of PCa-related inflammation [8,9]. The negative correlations with vitamin D3 (r=−0.198) and vitamin A (r=−0.209) are indications that these micronutrients have a quantifiable suppression on systemic IL-6 production, as is supported by data that 1,25(OH)2D3 inhibits NF-kB-driven IL-6 transcription in immune and stromal cells [10,12,21]. Targeted therapeutic approaches to replenish vitamin D3 and vitamin A to physiological levels could thus help to suppress the pro-inflammatory IL-6 axis, which mediates PCa progression and resistance to therapy.

4.5. Age Independence and Clinical Implications

The absence of meaningful age associations with any of the measured biomarkers undermines the belief that the measured metabolic differences can be attributed to the ageing process. Rather, the vitamin depletion and the increase of IL-6 in PCa seem to be controlled by disease-specific biological processes [20]. This age-independence reinforces the possible usefulness of these biomarkers in identifying at-risk patients across the adult age range and justifies their consideration as screening adjuncts with PSA. The next round of studies that include Gleason score, PSA level, and data on disease staging will be necessary to determine whether the level of vitamin deficiency and IL-6 increase are associated with pathological severity, which will enable clinical staging and prognostication [15].

4.6. Limitations

Limitations are the cross-sectional design that does not allow drawing a causal conclusion and the single-centre population that restricts the possibility of generalising the results to other ethnic groups. Lack of PSA and Gleason scoring, as well as treatment data, prevents disease-severity stratification. To generalize and further develop these results, longitudinal studies using larger multicentre cohorts, a longer analysis of the VDR haplotype, and in vitro mechanistic studies of the impacts of rs1544410 on VDR function are required [22].

5. Conclusion

The current case-control study determines that TC genotype of VDR rs1544410 is associated with an almost sevenfold risk of prostate cancer (OR=6.95; p<0.0001), whereas the CC homozygosity is protective (OR=0.059; p<0.0001). Genotype-independently, PCa patients have a very low serum vitamin D3 and vitamin A and a very high IL-6, which typifies an immunonutritional deficit and pro-inflammatory biochemical phenotype. The negative relationships between the two vitamins and IL-6 confirm the existence of a mechanistic anti-inflammatory effect of these micronutrients. The fact that these biomarkers are independent of age further highlights their disease-specific implication. Collectively, these results serve as strong arguments in favor of the incorporation of VDR genotyping into PCa risk stratification models alongside the vitamin D3, vitamin A, and IL-6 measurements, and in favor of investigating the opportunities of micronutrient-based interventions as the auxiliary approach to PCa prevention and management.

Compliance with ethical standards

Disclosure of conflict of interest

Approved by the Ethics Committee of ibn Sina University of Medical and Pharmaceutical Sciences. Informed consent was obtained from all participants.

Statement of informed consent

"Informed consent was obtained from all individual participants included in the study."

References

[1] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33.

[2] Rawla P. Epidemiology of prostate cancer. World J Oncol. 2019;10(2):63–89.

[3] Bouillon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, et al. Skeletal and extraskeletal actions of vitamin D: current evidence and outstanding questions. Endocr Rev. 2019;40(4):1109–1151.

[4] Siddappa M, Hussain S, Wani SA, Tang H, Gray JS, Jafari H, et al. Vitamin D receptor cistrome-transcriptome analyses establish quantitatively distinct receptor genomic interactions in African American prostate cancer regulated by BAZ1A. bioRxiv. 2022. doi:10.1101/2022.01.31.478573.

[5] Agliardi C, Guerini FR, Bolognesi E, Zanzottera M, Clerici M. VDR gene single nucleotide polymorphisms and autoimmunity: a narrative review. Biology (Basel). 2023;12(7):916.

[6] Latini A, De Benedittis G, Perricone C, Colafrancesco S, Conigliaro P, Ceccarelli F, et al. VDR polymorphisms in autoimmune connective tissue diseases: focus on Italian population. J Immunol Res. 2021;2021:8277560.

[7] Magiełda-Stola J, Kurzawińska G, Ożarowski M, Karpiński TM, Drews K, Seremak-Mrozikiewicz A. The significance of VDR genetic polymorphisms in the etiology of preeclampsia in pregnant Polish women. Diagnostics. 2021;11(9):1718.

[8] Hirano T. IL-6 in inflammation, autoimmunity and cancer. Int Immunol. 2021;33(3):127–148.

[9] Guo Y, Wang B, Wang T, Gao L, Yang ZJ, Wang FF, et al. Biological characteristics of IL-6 and related intestinal diseases. Int J Biol Sci. 2021;17(1):204–219.

[10] Wang Y, Chen X, Chen Y. Interleukin-6 gene −572G/C polymorphism and prostate cancer risk. Afr Health Sci. 2018;18(2):267–274.

[11] Al-Mualm M, Salih S, Shahla S. Genetic polymorphism of IL-22 and IL-27 genes in Iraqi patients with urinary bladder carcinoma. Biochem Cell Arch. 2020;20(2):4451–4456.

[12] Liu W, Zhang L, Xu HJ, Li Y, Hu CM, Yang JY, et al. The anti-inflammatory effects of vitamin D in tumorigenesis. Int J Mol Sci. 2018;19(9):2773.

[13] Fleet JC, Kovalenko PL, Li Y, Smolinski J, Spees C, Yu JG, et al. Vitamin D signaling suppresses early prostate carcinogenesis in TgAPT121 mice. Cancer Prev Res (Phila). 2019;12(6):343–355.

[14] Mohseni H, Amani R, Hosseini SA, Ekrami A, Ahmadzadeh A, Latifi SM. Genetic variations in VDR could modulate the efficacy of vitamin D3 supplementation on inflammatory markers and total antioxidant capacity among breast cancer women: a randomized double-blind controlled trial. Asian Pac J Cancer Prev. 2019;20(7):2065–2072.

[15] Sekhoacha M, Riet K, Motloung P, Gumenku L, Adegoke A, Mashele S. Prostate cancer review: genetics, diagnosis, treatment options, and alternative approaches. Molecules. 2022;27(17):5730.

[16] Shaat N, Katsarou A, Shahida B, Prasad RB, Kristensen K, Planck T. Association between the rs1544410 polymorphism in the vitamin D receptor (VDR) gene and insulin secretion after gestational diabetes mellitus. PLoS One. 2020;15(5):e0232536.

[17] Kumie G, Melak T, Baynes HW. The association of serum lipid levels with breast cancer risks among women at Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia. Breast Cancer (Dove Med Press). 2020;12:279–287.

[18] Li W, Middha M, Bicak M, Sjoberg DD, Vertosick E, Dahlin A, et al. Genome-wide scan identifies role for AOX1 in prostate cancer survival. Eur Urol. 2018;74(6):710–719.

[19] Sìrbe C, Rednic S, Grama A, Pop TL. An update on the effects of vitamin D on the immune system and autoimmune diseases. Int J Mol Sci. 2022;23(17):9784.

[20] Mohammed AM, Sarmad Zayni FM, AL-Anni MM, Faiq Corial FI, Adnan Al-Rubaee F. Diagnostic and predictive values of IL-6 in a group of Iraqi patients with rheumatoid arthritis. J Fac Med Baghdad. 2023;65:2023.

[21] Bilal M, Ashraf S, Zhao X. Dietary component-induced inflammation and its amelioration by prebiotics, probiotics, and synbiotics. Front Nutr. 2022;9:931458.

[22] Yeh JH, Chou CT, Chen IS, Lu T, Lin KL, Yu CC, et al. Effect of thymol on Ca2+ homeostasis and viability in PC3 human prostate cancer cells. Chin J Physiol. 2017;60(1):32–40.