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Polymorphism of Vitamin D Receptor Gene Taq1 (rs731236) and its Effect on Bone Turnover Markers in Iraqi Postmenopausal Osteoporotic Women After Vitamin D Supplementation

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Abstract

Vitamin D receptor gene polymorphism has been proposed as a risk factor for osteoporosis. This study aims to estimate the prevalence of genotypes of vitamin D receptor Taq1 (rs731236) gene polymorphism in postmenopausal women, with and without osteoporosis, and to study the association of VDR Taq1 polymorphism with the bone turnover markers (BTMs), procollagen-I, and deoxypyridinoline levels, before and after vitamin D supplementation. The patients' group consisted of forty women diagnosed with osteoporosis who were assigned to receive a dose of 50000 IU/week of Vitamin D for eight weeks. In addition, thirty postmenopausal women with no osteoporosis were assigned as the control group. Sequencing of vitamin D receptor Taq1 (rs731236) was studied, and three genotypes with different percentages were found. The A/G genotype had a higher percentage in the patients and the control groups (57.5% and 46.6%, respectively). The frequency of the A/G genotype compared to that of the remaining genotypes within a group showed no significant difference between the two study groups (p=0.36). Serum levels of vitamin D in osteoporotic women had increased significantly after vitamin D supplementation (from 17.4±15.4 to 41.4±20 mmole/L; p <0.001). However, serum levels of procollagen-I and deoxypyridinoline did not show significant change after vitamin D supplementation (p>0.05) with regarding to G/G and A/A genotypes. In contrast, for the A/G genotype, serum, deoxypyridinoline level was significantly elevated in the patients' group after supplementation compared to the baseline levels (p= 0.03). In conclusion, vitamin D supplementation does not significantly affect the serum levels of the bone turnover markers, procollagen-I and deoxypyridinoline, in postmenopausal women with osteoporosis. These markers are not appropriate for monitoring osteoporosis management by vitamin D supplementation.

Keywords: **Bone turnover markers; Deoxypyridinoline; Osteoporosis; Procollagen-I; Vitamin D receptor**

Introduction

Osteoporosis (OP) is a condition characterized by low bone mineral density (BMD), leading to deterioration in the fine meshwork of bone structure, making it more fragile and easily fractured. [1, 2]. Postmenopausal women can develop osteoporosis due to decreased estrogen levels after the menopause. Such a condition is associated with bone weakness due to overwhelming bone formation by enhanced bone resorption[3], and hence, osteoporosis is commonly developed[4]. During this period, the remodeling cycle will be inversed as compared with that in adult women because of reduced bone formation by osteoblasts and elevated bone resorption by osteoclasts, the main building units in bone tissue. The best indicators for monitoring the normal function of these units are by measuring bone turnover markers (BTMs)[5]. These markers are proteins in nature presented in blood circulation, reflecting the metabolic processes of the bone, and their level can indicate bone health and the dynamic remodeling process. [6, 7]. BTMs can help diagnose and follow up on osteoporosis treatment.[8].

Vitamin D (calcitriol), a steroid in nature[9], plays an essential role in maintaining the strength of bony structure besides other functions in different organs, and its deficiency could be the progenitor for various disease sequela[10-12]. It has been reported that there is a negative correlation between vitamin D serum levels and BTMs, which might help in diagnosing or monitoring some bone disorders[13]. Vitamin D level is affected by several factors besides low dietary intake [14], nowadays low sun exposure or getting elderly will make a resident lifestyle that can result in vitamin D deficiency in

these groups[15]. On the other hand, the vitamin D receptor (VDR) is a member of the nuclear receptor superfamily regulators and is necessary for calcitriol signaling. VDR can play a role in deficient of vitamin D and, therefore, altering the effect of vitamin D supplementation[16]. Polymorphism (Single Nucleotide Polymorphism SNPs) of vitamin D receptors can play a role in its function. It could be critical to alter the response to vitamin D supplements, which causes a lower response to vitamin D supplements, leading to a deficiency in vitamin D response.

Thus, the role of vitamin D in bone metabolism could be affected by polymorphism in VDR that may play a role in developing osteoporosis through modulation of vitamin D activity [17].VDR *Taq1* (rs731236) polymorphism is one of the studied SNPs that affects the biological functioning of vitamin D the alteration in genetic sequences of VDR may have an impact on the activity of vitamin D with consequent disorders other than that related to bone disorders[18].According to our knowledge, there is no specific study in Iraq on VDR polymorphism and its role in osteoporosis. So, the present study aims to find the prevalence of specific genotypes for vitamin D receptor Taq1 (rs731236) by analyzing gene polymorphism in a sample of postmenopausal osteoporotic women and find their possible impact on serum levels of some bone turnover markers (procollagen-I and deoxypyridinoline) before and after taking a dose of vitamin D for eight weeks.

Materials and Methods

Patients' groups

The present case-control study was conducted in the Rheumatology Department in Basrah Teaching Hospital/ Basrah, Iraq. The study was approved by the Scientific Committee of the College of Pharmacy/ University of Baghdad (approval no. RECAUBCP24112021B). Every participant was informed about the nature of the survey, and verbal consent was obtained before enrollment. Seventy postmenopausal women were assigned to participate in this study; forty of them were diagnosed to have OP and were designated as the patients' group, and thirty women without OP served as the control group. The diagnosis of osteoporosis was based on the measurement of bone mineral density using a dual x-ray absorptiometry (DXA) scan. According to the World Health Organization (WHO) diagnostic criteria, a T-score $\leq -$ 2.5 in the lumbar spine, total hip, or femoral neck confirms OP[19]. The enrolled women have reported cessation of menstruation for at least two years. Women with endocrine disorders that may affect bone mineral density like thyroid and parathyroid disorders, Cushing syndrome, rheumatoid arthritis, systemic lupus erythematosus, renal or hepatic impairment, and those who received any treatment for osteoporosis, or were on vitamin D supplements for at least three months before the onset of the study were excluded.

Sampling and preservation

Five milliliters of venous blood specimens were obtained from each participant. Three milliliters of each blood sample were transferred to a gel tube, left at room temperature for at least 30 minutes to allow for clotting, and then centrifuged for 5–10 minutes at 3000 rpm to obtain the serum. The remaining two milliliters of blood samples were stored in tubes containing ethylene-diamine-tetra-acetic acid (EDTA) in a deep freeze at -40°C until DNA extraction. After eight weeks of vitamin D supplementation, a second blood sample was obtained from each postmenopausal woman with OP, and serum samples were extracted. The extracted serum samples at baseline and after vitamin D supplementation were frozen at -20 °C until the time of biochemical analysis.

Biochemical analysis

Serum levels of vitamin D were measured by electrochemiluminescence immunoassay; serum levels of some BTMs, deoxypyridinoline (DPD), and procollagen-I (PCI) by enzyme-linked immunosorbent assay (ELISA), according to the kits' manufacturer instructions. The kits used in the study for biochemical analysis, along with their suppliers, are listed in Table 1.

Table 1. Diagnostic Kits

Diagnostic kit	Supplier	Origin
Vitamin D	Cobas	Switzerland
Procollagen-I	MyBioSource	USA
Deoxypyridinoline	CUSABIO	China

DNA extraction

The ABIO pure Extraction procedure was used to extract genomic DNA from a blood sample according to the instructions of the DNA-extraction kit purchased from (Promega, USA).

Polymerase chain reaction

Primers

The primers (Forward and Reverse) of VDR Taq1 were designed and supplied by Macrogen

Company, Korea. The preparation of primers was according to the manufacturer's instructions. To establish the optimal primer annealing temperature, the annealing was assessed at 58, 59, and then 60 °C. The optimal annealing temperature was 60°C. The nucleotide sequence of the VDR Taq1 primers, their supplier, and the product DNA size are illustrated in Table 2.

Table 2. Primers and their suppliers

Primer Name	Sequencing	Supplier	Product Size (bp)
VDR TaqI	F:5´-AGAATGGGCTGGGTGGATA-3´ R:5´-ACGTGGTCTGGGCTACAGA-3´	Macrogen	859

PCR protocol

A total volume of 20µl comprising 10 µl GoTaq Green Master Mix (2X), 1 µl of each of the forward and reverse primers (10 pmol), 6 µl nuclease-free water, and 2µl of template DNA were used for PCR using a Thermal Cycler (Kyratec, Australia) according to the protocol presented in Table 3.

Table 3. The PCR program temperature, duration, and number of rounds

Steps	Temperature (°C)	Duration	Rounds
Initial Denaturation	95	5 minutes	1
Denaturation	95	30 seconds	30
Annealing	55	30 seconds	
Extension	72	30 seconds	
Final extension	72	7 minutes	1
Hold	10	10minutes	

Detection of PCR products

The amplicons were assessed by Gel Electrophoresis System (Thermo Scientific, USA) using 1% agarose gel stained with GelGreen dye; 5µl of every sample was applied to the gel, and a 100-volt current for 1 hour was applied. A 100 bp ladder marker was used to assess the size of the amplicon (Figure. 1). Analysis of rs731236 SNP of VDR gene using Sanger sequencing as presented in (Figure. 2). If a single "A" appeared, indicate A homozygous allele. If a "G" peak appeared, it would mean a homozygous allele. The simultaneous presentation of "A" and "G" peaks indicates an A/G heterozygous allele.

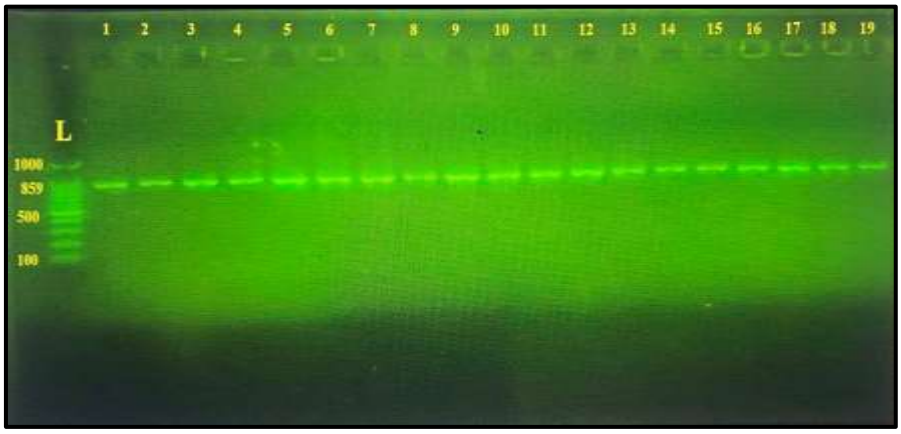

Figure 1. Gel electrophoresis of the PCR products using 1% agarose stained with Gel Green (M:100bp ladder marker. Lanes 1-19 resemble 859bp PCR products)

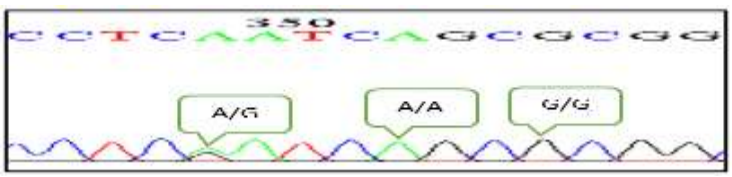

Figure 2. Analysis of vitamin D receptor Taq1 (rs731236) sequencing

Statistical analysis

The collected information was statistically analyzed using IBM SPSS Software (Version 26, IBM Corp., 2019). The uniformity of the data distribution was checked by using the Kolmogorov-Smirnov test. Continuous variables that were uniformly distributed were presented as mean ± standard deviation (SD), and the non-uniformly distributed variables were presented as median [interquartile range (IQR)]. Discrete variables were presented as counts and percentages. The difference between means was assayed by t-test, and the difference between medians was assayed by using Mann Whitney, Kruskal Wallis test was applied for assessing the independent variables, and the Wilcoxon test for a dependency of variables. A dependent t-test was applied to the normally distributed variable. A P-value is considered significant when its value is below 0.05.

Results and Discussion

Demographic data

In Table 4, the demographic data of the participants are presented. There is a non-significant difference in the age between the patients' and the control groups (p=0.11). Regarding body mass index, there is a significant difference between the study groups (p<0.001). Participants in the control group were obese, and patients were overweight. The increments in BMD and osteoporotic are lower when compared with the underweight population. Several studies explained the link between BMI and BMD with the possibility of osteoporosis and fracture risk. One of these studies related to the lowered levels of sex hormone-binding globulin in obese patients, which can promote bone strength. [20-22]. Also, the duration of menopause is significantly higher for the patients' group (p=0.04). Deficient vitamin D is associated with early menopause and can reduce the age of reproduction in women.[23], but this study revealed that menopause is a multifactorial-dependent process besides vitamin D deficiency. Although the vitamin D serum levels were low for all the study participants, however, serum vitamin D levels were significantly lower in OP women (p<0.001). The osteoporotic women showed a lower value in BMD when they measured by T-score. The primary action of 1,25(OH)2D, an active vitamin D metabolite, is to increase the intestinal absorption of calcium. A lack of vitamin D can result in bone loss, osteoporosis, fractures, and mineralization abnormalities, which can eventually cause muscle weakness, which can lead to falls and fractures. Bone turnover and bone mineral density are related to vitamin D levels.[24, 25].

Serum levels of DPD and PCI for the two study groups showed non-significant differences (p= 0.65, p=0.13), respectively, at baseline between patients and control. Bone turnover markers (BTMs) level is affected by various factors, which could be diurnal, body weight, and menopausal state[8]. BMI of participants of this study ranges from being overweight (patients' group) to obese (control group) and previous studies had related lowered BTM levels in obese patients. Thus, the results of the present study of lowered BTM levels for the overweight patients compared to the obese control group are mostly attributed to differences in mean BMI.

Bone mineral density, the leading indicator for diagnosis, showed a significant difference between patients and controls, as the selection of the participants was based on its values; the patients, T-score values were lower than -2.5, while values higher than -2.5 for participants with osteopenia, according to WHO characterization.[19]

Table 4. Demographic, clinical, and biochemical characteristics of participants

Variable	Control (n=30)	Patients (n=40)	P-Value
Age (years)	58.4±5.9	60.2±6.4	0.11
BMI (kg/m^2)	31.67±5.6	27.12±5.4	<0.001*
Duration of menopause (years)	8±4.2	9.97±4.9	0.04*
Vitamin D level (nmole/L)	28.8±24.3	17.4±15.4	<0.001*
DPD (ng/L)	1.80 (1.06-2.6)	1.49 (0.89-2.96)	0.65$
PCI (ng/L)	2.25 (1.22-4.44)	3.35(1.93-6.98)	0.13$
T-score	-1.11±0.85	-2.6±0.03	<0.001*

***=significance when p value <0.05. An independent t-test measured the difference. DPD=deoxypyridinoline, BMI: body mass index. PCI= procollagen-I, Data are presented as Median (IQR1-IQR3), $=P-value measured by Mann Whitney**

Genotype distribution of VDR Taq1 gene in participants

In Table 5, the genotype frequency of VDR is presented. The percentage of wild genotype (A/G) is higher (57.5%) in the patients' group than that of the control group (46.6%), but with a non-significant difference (p=0.36). The A/A genotype in the control group is found to be higher (36.6%) than that of the patients' group (30%), but the difference is non-significant (p=0.55). The G/G genotype had lower percentages (12.5% in patients and 16.6% in control) and non-significant differences (p=0.7). Allele frequency showed a higher prevalence of the A allele, with 58.75% in patients and 60% in control. In comparison, the G allele was presented with 41.25% in patients and 40% in control, with a non-

significant difference between the two alleles (p=0.8). An observational study about the prevalent of TaqI genotypes in osteoporotic women found the predominant A/G genotype and a relation between TaqI VDR rs731236 gene polymorphism and risk of osteoporosis, that could plays a role in vitamin D level and osteoporosis development[18]. Further studies were applied to osteoporotic women in Saudi Arabia, revealing the predominant A/G genotype, which is associated with osteoporotic risk and a higher percentage of the A allele. [18, 26], similar to the findings of the present study.

Table 5. Genotype and allele frequency of VDR Taq1 polymorphism of participants

rs731236				
Genotype	**Patients (n=40)**		**Control (n=30)**	
	No.	**percentage**	**No.**	**Percentage**
A/A	12	30	11	36.67
A/G	23	57.5	14	46.67
G/G	5	12.5	5	16.66
A	47	58.75	36	60
G	33	41.25	24	40

Data is presented in numbers and %. The chi-square test measured the difference. The wild genotype is presented in bold line

Pharmacogenetics is important to study drug resistance and response to minimize suspected side effects and get the best management results[27]. Genetic factors play an essential role in developing osteoporosis. Polymorphism of the related genes can prognose for disease or reduce response to the prescribed therapy. In osteoporosis, polymorphism in the VDR gene causes a reduction in response to vitamin D therapy , and that will result in reducing the activity of the active form of vitamin D at VDR, which will result in lowering BMD, leading to a reduction in bone strength and increasing rates of fractures.[1, 26]. For the participants' demographic data, there were non-significant differences for the age between patients and controls. However, the menopausal period showed a significant difference. Deficient vitamin D is associated with early menopause and can reduce the age of reproduction in women.[23]. In the present study, a significant BMI difference between patients and control BMI indicates overweight and obese, respectively.

The difference in BMI can be considered a risk factor for osteoporotic patients to get fractures. It was found that lumber bone density in obese patients was higher than that of non-obese or underweight, which can explain a higher risk of fracture rate in non-obese patients, and this risk is increased if associated with vitamin D deficiency. [28-30].

Bone turnover markers in studied groups

Serum levels of BTMs and vitamin D in both the patients' and the control groups are all illustrated in Table 6. Here, serum BTMs and vitamin D levels in the patients' group were measured at baseline and after eight weeks of vitamin D supplementation. There is a change in serum levels of these bone turnover markers, but it was non-significant (p=0.17 for DPD and p=0.79 for PCI).

Table 6. Serum levels of bone turnover markers and vitamin D before and after vitamin D supplementation in postmenopausal women with OP

Variables	**At baseline**	**After vitamin D supplementation**	**p-value**
DPD (ng/L)	1.49 (0.89-2.96)	1.91 (1.64-4.36)	0.17#
PCI (ng/L)	3.35 (1.93-6.98)	2.74 (1.06-7.09)	0.79#
Vitamin D (nmole/L)	17.4±15.4	41.4±20	<0.001*

Data presented as median with (IQR1-IQR3), Vitamin D as mean ± SD #=p-value measured by Wilcoxon test, *=p-value calculated by dependent t-test. *=P-value is significant when being lower than 0.05

Bone turnover markers are considered the indicator of bone health and are easily measured to assess the degree of osteoclast and osteoblast functions[8]. In the present study, two BTMs were studied. The BTM related to osteoblast function and bone formation is pro-collagen I, and the second marker related to osteoclast function and bone resorption is deoxypyridinoline (DPD)[10]. The level at baseline and before vitamin D supplementation was higher in an osteoporotic group than that of the control non-osteoporotic group for PCI, with a non-significant difference (p=0.13). Meanwhile, DPD's level in the control group was slightly higher than that of the patients' group, with a non-significant difference (p=0.65). Generally, serum level of bone turnover markers revealed higher bone degradation over bone formation, which is the characterization of osteoporosis [31]. In the present study, the serum level of PCI in OP patients was higher than in the control group. Serum levels of BTM during the

postmenopausal period are usually in higher concentrations; this could relate to a higher bone formation rate in women in the first ten years of postmenopausal to overcome the degeneration in skeletal meshwork [31]. After supplementation with vitamin D, there is a slight reduction in serum procollagen-I and a slight elevation in DPD level with a non-significant difference for both (p=0.79 and 0.17, respectively). Such results are seen in *Jorde R. et al.*, 2019[25]. Also, other studies showed non-significant changes in BTMs.

The first one was illustrated by Lerch Baum, Elisabeth, et al., 2019, who studied the effect of a vitamin D supplement of 20000 IU/week for 12 weeks duration on the serum level of BTMs and showed a non-significant change in BTMs (57). Another study was conducted on osteoporotic women who were administered 2800IU of vitamin D daily for three months. This study also showed a non-significant increase in BTM, but there was an increase in trabecular BMD [32]. In the present study, vitamin D supplementation may be insufficient to significantly lower serum levels of BTMs, or the duration of supplementation may not be enough.

Serum vitamin D levels showed a highly significant difference (p<0.001). The increment in vitamin D level is related to the supplementation of vitamin D with a relatively high dose (50000 IU/ week). Besides, the highly deficient level in the patient group will help and aid for more elevation and good increments in its level after supplementation with vitamin D

Serum level of the studied bone turnover per VDR Taq1 genotypes:

In Table 7, serum levels of studied BTMs in different genotypes of the VDR TaqI gene were expressed. Serum levels of DPD showed non-significant differences in A/A and G/G genotypes (p=0.37, p=0.67) while significant for A/G genotype (p=0.67) between baseline and post supplementation. Also, non-significant difference in DPD serum level regarding genotypes at baseline (p=0.79) and after supplementation with vitamin D (p=0.6). For PCI, a non-significant difference in A/A, A/G, and G/G genotypes (p=58, p=072, and p=0.83, respectively) after supplementation of vitamin D. Also, the difference at baseline among genotypes and after supplementation were non-significant (p=0.66 and p=0,81, respectively). The non-significant reduction in serum level of BTMs can be related to the low level of vitamin D in patients (lower than 30nmol/L), such results found in R. Jorde, et al, 2019 [33]. It is possible to increase the percent of decrement of BTMs if it is longer duration in supplementation[34].

Table 7. Serum level of the studied bone turnover per VDR Taq1 genotypes

SNP	Genotype	No.	Serum Vitamin D level (nmole/L)		p-value
			At baseline	After vitamin D supplementation	
rs731236	AA	12	12.5 (8.2-20)	39 (29.2-62.7)	0.001*
	AG	23	17 (9-27)	37 (28-45)	<0.001*
	GG	5	8 (4-15)	35 (31-41)	0.01*
p-value			0.22$	0.62$	

DPD=deoxypyridinoline, PCI=procollagen I. $=p-value measured by Kruskal Wallis, α =p-value measured by Mann Whitney, *= significant when p-value <0.05.

In Table 8, serum levels of vitamin D according to genotypes of VDR SNP were illustrated. Serum vitamin D level was significantly elevated in postmenopausal women with OP after vitamin D supplementation regarding the VDR Taq1 genotype for A/A, A/G, and G/G genotypes (p=0.001, p<0.001, and p=0.01, respectively). At the same time, there was a non-significant difference in serum vitamin D levels among patients with the three genotypes of VDR Taq1, whether at baseline (p=0.22) or after vitamin D supplementation (p=0.62). As mentioned, the significant difference is due to vitamin D supplementation with a high dose (50000IU/ week). Besides, the participants all were deficient in vitamin D levels, and this is considered one of the factors for good response to vitamin D supplementation.

Table 8. Serum level of the studied Vitamin per VDR Taq1 genotypes

SNP	genotype	No. (%)	DPD level (ng/ml)			PCI level (ng/ml)		
			At baseline	After vitamin D supplementation	p-value	At baseline	After vitamin D supplementation	p-value
rs731236	A/A	12 (30)	1.49 (0.64-7.09)	1.85(1.6-6.7)	0.37 ᵅ	3.5 (2.6-10.4)	2.85(1.11-11.59)	0.58 ᵅ
	A/G	23(57.5)	1.1(0.95-2.2)	2.02(1.68-4.51)	0.03 α *	3.28 (1.07-.35)	2.64(1.06-6.4)	0.72 ᵅ
	G/G	5 (12.5)	1.88 (1-4.3)	1.81(0.54-3.3)	0.67 α	2.8 (1.9-2.11)	2.33(0.81-47.9)	0.83ᵅ
			0.79$	0.6$		0.66$	0.81$	

$=p-value measured by Kruskal Wallis, *=p-value measured by Mann Whitney

Bone turnover markers, DPD serum level had increased after complete vitamin D supplementation while Pro-Collagen I showed reduction in serum level, with regarding to genotypes of studied SNP but were non-significant for both. The reduction can reflect the responsiveness of OP women to vitamin D supplement by reduction in their serum levels post complete supplementation with vitamin D. For DPD, the supplements could be insufficient for reduction its level. A previous study illustrated that changes in BTMs serum levels showed non-significant difference after vitamin D supplements [25], that involving supplementation of vitamin D with calcium and non-significant differences were reported on BTM serum levels. Supplementation with vitamin D had corrected the baseline deficient serum level of vitamin D and this correction was different among the studied VDR Taq1 genotypes. Where A/G heterozygote showed the highest significant difference compared to the others, although all the genotypes exert significant elevation in vitamin D levels after 8 weeks of supplementation.

Conclusion

Although vitamin D receptor *Taq 1*(rs731236) gene polymorphism of heterozygote A/G genotype exhibits a higher percentage compared to the other genotypes, still, with non-significant variation between osteoporotic and non-osteoporotic (control) postmenopausal women, which gives an impact of lacking the association between osteoporosis and VDR Taq I gene polymorphism. Furthermore, vitamin D supplementation was not associated with significant alteration in serum levels of the measured BTMs, which makes them not suitable for the follow-up or monitoring osteoporosis after vitamin D supplementation.

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Conflicts of Interest

There is no conflict of interest

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Ethics Statements

This study got approval from the ethical committee at the University of Baghdad/ College of Pharmacy/ Baghdad and carries approval No.: **RECAUBCP24112021B**

Author Contribution

Study conception and design: N.M. and Sh. H.; data collection: N.M.; analysis and interpretation of results: N.M. and Sh.H.; draft manuscript preparation: N.M. All authors reviewed the results and approved the final version of the manuscript.

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تعدد الاشكال الجينية للجين المسؤول عن مستقبلات فيتامين د (rs731236) Taq1 وتأثيراته على علامات استقلاب العظم في عينة من النساء العراقيات المصابات بهشاشة العظام في مرحلة ما بعد سن اليأس بعد تناول مكملات فيتامين د

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الخلاصة

ان تعدد الاشكال الجينية لمستقبلات فيتامين د يفترض انها قد تؤدي الى الهشاشة. تهدف هذه الدراسة الى معرفة مدى تواجد الشكل الجيني لمستقبل فيتامين د (rs731236) Taq1) لدى النساء في فترة ما بعد سن اليأس سواء كُنَّ مصابات بهشاشة العظام او لا, وأيضا دراسة الارتباط بين مستقبل فيتامين د (rs731236) Taq1) مع علامات استقلاب العظم (بروكولاجين-١ و دي اوكسيبايريدينولين) لدى النساء المصابات بالهشاشة في فترة ما بعد انقطاع الطمث بعد تناولهن لجرعة من فيتامين د ولفترة معينة وأيضا لدى النساء غير المصابات بهشاشة العظام. مجموعة المرضى مكونة من أربعين امرأة تم تشخيصهن بالهشاشة بعدها تم البدء بأخذ ٥٠٠٠٠ وحدة دولية من فيتامين د/أسبوع لمدة ثمان أسابيع، بالإضافة الى ثلاثين امرأة في فترة ما بعد انقطاع الطمث غير مصابات بالهشاشة باعتبارهن كمجموعة ضابطة. تمت دراسة تسلسل جين مستقبل فيتامين د (rs731236) Taq1), وتم إيجاد ثلاث أنماط جينية بنسب مختلفة. النمط الجيني A/G كان الأعلى نسبة في مجموعتي المرضى والمجموعة الضابطة (٥٧,٥ %,٤٦,٦٪), على الترتيب. نسبة تكرار النمط الجيني A/G لم تكن ذات دلالة إحصائية (P= ٠,٣٥) حين تمت مقارنته ما بين مجموعة المريضات والمجموعة الضابطة. مستوى فيتامين د لدى النساء المصابات بالهشاشة قد ازداد وبمؤشر إحصائي مجدي (من ١٥,٤±١٧,٤ الى ٢٠±٤١,٤ ملي مول/لتر) بعد تناولهن لفيتامين د. على أي حال, لم تظهر علامات استقلاب العظام (بروكولاجين-١ و دي اوكسي بايريدينولين) فرقًا مهما بعد تناول فيتامين د(p<٠,٠٥) ما عدا مستوى دي اوكسي بايريدينولين حيث كان ارتفع بدرجة محسوسة بعد تناول فيتامين د مقارنة بمستواه عند بدء الدراسة لدى النساء ممن لديهن A/G النمط الجيني (p =٠,٠٣). كخلاصة، لقد اظهرت النتائج ان فيتامين د لم يغير بدرجة فعالة مستويات عوامل استقلاب العظم, بروكولاجين-١ و دي اوكسي بايريدينولين لدى النساء المصابات بالهشاشة في مرحلة ما بعد سن اليأس. و ان هذه العوامل غير ملائمة لمتابعة مرضى الهشاشة مع اخذ مكملات فيتامين د.

الكلمات الرئيسية: علامات دوران العظم، دي اوكسي بايريدينولين، هشاشة العظام، بروكولاجين-١, مستقبل فيتامين د.