10.5152/turkjnephrol.2023.23369

Original Article

Turkish Journal of Nephrology

Vitamin D Receptor Polymorphisms in Overweight/Obese Chronic Kidney Disease Patients on Dialysis

Gökhan Bağcı[1], Can Hüzmeli[2], Binnur Bağcı[3], Ferhan Candan[4]

[1]Department of Medical Biochemistry, Altinbaş University Faculty of Medicine, İstanbul, Türkiye
[2]Department of Nephrology, Hatay Training and Research Hospital, Hatay, Türkiye
[3]Department of Nutrition and Dietetics, Sivas Cumhuriyet University Faculty of Health Sciences, Sivas, Türkiye
[4]Division of Nephrology, Sivas Cumhuriyet University Faculty of Medicine, Sivas, Türkiye

ABSTRACT

Background: Little is known about the possible association of vitamin D receptor (VDR) gene polymorphisms in obese patients with chronic kidney disease on dialysis (CKD-G5D). Therefore, we aimed to investigate VDR gene TaqI, ApaI, and FokI single-nucleotide polymorphisms (SNPs) in overweight/obese CKD-G5D patients.
Methods: Seventy-one normal-weight and 68 overweight/obese CKD-G5D patients were included in the study. The polymerase chain reaction-restriction fragment length polymorphism method was used for genotyping. Demographic and laboratory data were obtained from the medical records of patients.
Results: For all 3 SNPs, no significant association was found between normal-weight and overweight/obese patients ($P > .05$). High-density lipoprotein (HDL) concentrations were lower, but triglyceride (TG) and glucose levels were higher in overweight/obese patients compared to normal-weight patients ($P < .001$ for HDL and TG and $P = .023$ for glucose). In overweight/obese patients, individuals with the TaqI CC genotype had higher (PTH) levels than those with TC and TT genotypes (CC = 717.1 ± 616.4, TC = 342.7 ± 360.8, and TT = 310.2 ± 323.4 pg/mL; $P = .028$). Similarly, patients with the ApaI genotype (627.3 ± 653.0 mg/dL) had higher TG levels than those with the AA and AC genotypes (CC = 627.3 ± 653.0, AA = 223.3 ± 156.6, AC = 193.1 ± 85.4; $P < .001$). Overweight/obese patients with the FokI TT genotype had higher glucose concentrations than those with the CC and CT genotypes (CC = 183.4 ± 128.4 mg/dL, TT = 151.9 ± 66.1 mg/dL, and CT = 107.6 ± 41.9 mg/dL; $P = .008$).
Conclusion: Our study suggests that VDR TaqI, ApaI, and FokI polymorphisms are not associated with obesity in CKD-G5D patients. However, they might increase the risk of secondary hyperparathyroidism, dyslipidemia, and hyperglycemia.
Keywords: CKD-G5D, hemodialysis, obesity, polymorphism, vitamin D receptor

Corresponding author: Gökhan Bağcı ✉ gokhanbagci@hotmail.com.tr **Received:** May 18, 2022 **Revision requested:** November 14, 2022
Last revision received: May 23, 2023 **Accepted:** August 17, 2023 **Publication Date:** November 03, 2023

Cite this article as: Bağcı G, Hüzmeli C, Bağcı B, Candan F. Vitamin D receptor polymorphisms in overweight/obese chronic kidney disease patients on dialysis. *Turk J Nephrol.* 2024;33(2):217-222.

INTRODUCTION

Obesity is a chronic multifactorial disease in which genetic and environmental factors play a role. It is a major public health problem affecting a significant number of people worldwide and associated with many diseases with high morbidity and mortality, such as type 2 diabetes, cardiovascular disease, hypertension, and some cancer types.[1] Obesity is one of the important risk factors for chronic kidney disease (CKD) and is also a strong risk factor that increases the risk of kidney function loss, especially after dialysis treatment is started.[2]

Vitamin D receptor (VDR) is a nuclear receptor that binds to 1,25-dihydroxyvitamin D 1,25$(OH)_2$D with high affinity.[3] Vitamin D receptor expression was detected in the majority of human tissues, including osteoblasts, smooth muscle cells, macrophages, epithelial cells, and pancreatic beta cells, and its expression is also highly found in adipocytes. Adipose tissues express both the VDR and the enzymes involved in vitamin D metabolism.[4]

Vitamin D deficiency is common in CKD patients. Because of the complex role of vitamin D in CKD, some variants

in the VDR gene have been considered as a way of improving the management of the disease since they are thought to affect response to therapeutic approaches.[5,6]

We aimed to evaluate VDR gene polymorphisms in overweight/obese and non-overweight/obese dialysis (CKD-G5D) patients. A secondary objective was to investigate whether there is a relationship between VDR polymorphisms and demographic and biochemical data in overweight/obese CKD-G5D patients.

METHODS

Subjects

Local ethics committee approval was obtained from Sivas Cumhuriyet University (Approval no: 2013-07/03; Date: July 27, 2013). All patients gave a written informed consent to participate in the current study. For this cross-sectional study, a total of 139 CKD-G5D patients, who presented to the clinic in Sivas Cumhuriyet University and were monitored in hemodialysis (HD) centers in Sivas City, were screened. According to the body mass index (BMI) classification, patients with BMIs ≥25 and <30 were considered overweight, and patients with BMI ≥30 were considered obese. Patients with BMI ≥18 and <25 were considered normal weight. According to this classification, 68 patients were considered obese or overweight, and 71 patients were considered normal weight.

Demographic characteristics and routinely available laboratory data were obtained from the medical records of patients. Patients with a BMI less than 18 and patients with active infection or malignancy were excluded from the study.

Fasting blood specimens were collected to measure blood chemistry parameters. 25(OH)D, triglyceride (TG), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), C-reactive protein (CRP), creatinine, calcium, phosphate, potassium, sodium, blood urea nitrogen (BUN), PTH, protein, albumin, and glucose concentrations were measured by routine laboratory methods.

MAIN POINTS

- Compared to normal-weight patients, vitamin D receptor gene TaqI, ApaI, and FokI genotypes and allele frequencies are not different in overweight/obese dialysis (CKD-G5D) patients.
- Overweight/obese CKD-G5D patients with the TaqI CC genotype had higher PTH levels.
- Overweight/obese CKD-G5D individuals with the ApaI CC genotype had higher triglyceride levels.
- Overweight/obese CKD-G5D individuals with the FokI TT genotype had higher glucose levels.
- Vitamin D receptor polymorphisms have been suggested to increase the risk of secondary hyperparathyroidism, dyslipidemia, and hyperglycemia.

Genotyping

After sampling 5 mL of blood from the patients with K_3DTA tubes, the samples were stored at –20 °C. The sampling was done using the Genomic DNA QIAamp DNA Blood Mini Kit (QIAGEN, Hilden, Germany). Polymerase chain reaction (PCR)-restriction fragment length polymorphism method was used for genotyping. Primers used for PCR were as follows: TaqI (rs731236) F: 5′-CAG AGC ATG GAC AGG GAG CAA G-3′ and R: 5′-GCA ACTC CTC ATG GCT GAG GTC TCA-3′, ApaI (rs7975232) F: 5′ CAG AGC ATG GAC AGG GAG CAA G-3′ and R: 5′-GCA ACT CCT CAT GGC TGA GGT CTC A-3′, and FokI (rs2228570) F: 5′-AGC TGG CCC TGG CAC TGA CTC TTG CTC T-3′ and R: 5′-ATG GAA ACA CCT TGC TTC TTC TCC CTC-3′. The PCR conditions were as follows: denaturation at 94 °C for 15 s, annealing at 63°C for TaqI and ApaI and 65°C for FokI for 30 s, extension at 72°C for 30 s for 35 cycles, and final extension at 72°C for 7 minutes. Polymerase chain reaction products were digested separately with restriction enzymes TaqI, ApaI, and FokI (Thermo Fisher Scientific, Waltham, Mass, USA). The digested products were analyzed by electrophoresis in a 2% agarose gel stained with ethidium bromide and then evaluated under ultraviolet light.

Statistical Analysis

All statistical analyses of the study were performed by the Statistical Package for the Social Sciences (SPSS), version 22.0 (IBM SPSS Corp.; Armonk, NY, USA). Continuous variables were first tested for normal distribution with 1-sample Kolmogorov–Smirnov and Shapiro–Wilk tests. The homogeneity of the variances was tested with the Levene test. Normally distributed continuous variables were expressed as mean ± SD and non-normally distributed variables as medians and interquartile ranges (25-75th percentiles). The Student's *t*-test or Mann–Whitney *U*-test was used for group comparisons. The chi-square test or Fisher's exact test was used for the evaluation of categorical values, including genotype and allele frequencies of VDR single-nucleotide polymorphisms (SNPs). Analysis of variance with a Bonferroni correction (Bonferroni post hoc test) was used to compare selected parameters in overweight/obese patients according to genotypes of TaqI, ApaI, and FokI SNPs. Odds ratios were calculated using MedCalc Odds Ratio Calculator (MedCalc Software, Ostend, Belgium; https://www.medcalc.org). Statistical significance was defined as *P* value less than .05. Results were expressed with a 95% confidence interval.

RESULTS

Demographic and biochemical data of patients are shown in Table 1. Theheight, weight, and BMI were significantly different in the 2 groups ($P = .028$ for height and $P < .001$ for weight and BMI). The female frequency in overweight/obese patients was higher than normal-weight patients (67.6%-43.7%, $P = .004$). Diabetes mellitus was 52.9% in overweight/obese patients and

Table 1. Baseline Characteristics of Overweight/Obese and Normal-Weight CKD-G5D Patients

Characteristic	Overall (N = 139)	Overweight/Obese (N = 68)	Normal Weight (N = 71)	*P*
Age (years)	58.6 ± 14.1	60.5 ± 10.3	56.8 ± 16.8	.125
Sex (male/female) %	44.6 / 55.4	32.4 / 67.6	56.3 / 43.7	**.004**
Height (cm)	165 (160-170)	163 (159-167)	168 (160-170)	**.028**
Weight (kg)	68.8 ± 13.2	78.3 ± 11.1	59.6 ± 7.2	**<.001**
Body mass index (kg/m^2)	24.8 (21.3-28.3)	28.4 (26.8-31.5)	21.5 (20.4-23.5)	**<.001**
Smoking (%)	15 (10.8)	5 (9.1)	10 (16.7)	.177
Duration of dialysis (months)	48 (27-96)	54 (24-94)	42 (27-96)	.657
Diabetes mellitus (n, %)	52 (37.4)	36 (52.9)	16 (22.5)	**<.001**
Hypertension (n, %)	25 (18)	13 (19.1)	12 (16.9)	.733
25(OH)D (ng/mL)	10.4 (7.9-13.7)	10.3 (7.8-14.9)	10.8 (8.1-12.9)	.757
Triglycerides (mg/dL)	156 (109-239)	191 (133-274)	133 (87-184)	**<.001**
Cholesterol (mg/dL)	165 (139-206)	183 (139-213)	160 (139-200)	.114
High-density lipoprotein (mg/dL)	34 (27-40)	31 (25-37)	37 (29-46)	**<.001**
Low-density lipoprotein (mg/dL)	99 (73-136)	110.5 (77-145)	96 (72-125)	.112
C-reactive protein (mg/L)	9.8 (2.8-29)	10.5 (3.9-40)	6.7 (2.1-21)	.119
Creatinine (mg/dL)	7.2 (6.0-9.6)	7.5 (6.3-9.7)	6.9 (5.6-9.6)	.454
Calcium (mg/dL)	8.7 (8.2-9.1)	8.6 (8.3-9.1)	8.7 (8.2-9.2)	.939
Phosphate (mg/dL)	4.4 (3.6-5.4)	4.6 (3.7-5.4)	4.2 (3.6-5.5)	.499
Potassium (mEq/L)	5.2 (4.4-5.7)	5.2 (4.5-5.7)	5.1 (4.4-5.9)	.938
Sodium (mEq/L)	138 (135-140)	138 (137-140)	138 (136-140)	.314
Blood urea nitrogen (mg/dL)	64.5 ± 18.3	63.7 ± 16.8	65.2 ± 19.8	.647
Parathormone (pg/mL)	255 (120-488)	238 (127-470)	262 (109-513)	.583
Protein (g/dL)	6.8 (6.5-7.2)	6.9 (6.5-7.3)	6.8 (6.4-7.0)	.066
Albumin (g/dL)	3.9 (3.6-4.2)	3.8 (3.6-4.2)	3.9 (3.7-4.2)	.299
Glucose (mg/dL)	105 (86-147)	116 (90-155)	100 (84-121)	**.023**
Erythropoietin use (n, %)	92 (66.2)	46 (67.6)	46 (64.8)	.858
Vitamin D use (n, %)	49 (35.3)	24 (35.3)	25 (35.2)	.992
Calcium use (n, %)	85 (61.2)	42 (61.8)	43 (60.6)	.885

Student's *t*-test or Mann–Whitney *U*-test was used for group comparisons.
Data were expressed as mean ± SD, median, and interquartile range or as frequency and percent, as appropriate.

22.5% in normal-weight patients. Lower HDL concentrations and higher levels of TG and glucose were detected in the overweight/obese patients ($P < .001$ for HDL and TG and $P = .023$ for glucose). Other demographic parameters and laboratory findings were not statistically different between the groups.

Table 2 shows the genotype and allele frequencies of VDR gene SNPs in overweight/obese and normal-weight patients. There was no significant difference between normal and overweight/obese patients for all 3 SNPs ($P > .05$). Table 3 demonstrates the comparisons of some selected parameters according to TaqI, ApaI, and FokI genotypes of VDR gene in overweight/obese patients. The genotypes of TaqI SNP did not show any significant differences in all selected parameters except PTH level. The CC genotype of the TaqI showed a higher PTH level (717.1 ± 616.4 pg/mL) than the TC genotype (342.7 ± 360.8 pg/mL) and the TT genotype (310.2 ± 323.4 pg/mL) ($P = .028$). The genotypes of ApaI did not show any statistically significant differences in all selected parameters except TG level. However, a higher TG level was found in the CC genotype of the ApaI (627.3 ± 653.0 mg/dL) compared to AA (223.3 ± 156.6) and AC genotypes (193.1 ± 85.4) ($P < .001$). There were no significant differences in the selected parameters between the 3 genotypes of the FokI SNP other than glucose level. Overweight/obese patients carrying

Table 2. Genotype and Allele Frequencies of VDR Gene SNPs in Overweight/Obese and Normal-Weight CKD-G5D Patients

SNP genotype/ allele	Overweight/ Obese (N = 68)	Normal Weight (N = 71)	OR (95% CI)	*P*
TaqI TT	32 (47.1)	30 (42.3)	Reference	—
TC	28 (41.2)	25 (35.2)	1.05 (0.50-2.18)	.89
CC	8 (11.8)	16 (22.5)	0.46 (0.17-1.25)	.13
T	0.676	0.598	Reference	—
C	0.324	0.402	0.71 (0.43-1.16)	.17
ApaI AA	31 (45.6)	35 (49.3)	Reference	—
AC	34 (50.0)	31 (43.7)	1.19 (0.60-2.37)	.60
CC	3 (4.4)	5 (7.0)	0.67 (0.14-3.06)	.61
A	0.695	0.709	Reference	—
C	0.305	0.291	1.01 (0.60-1.70)	.95
FokI CC	34 (50.0)	30 (42.3)	Reference	—
CT	27 (39.7)	35 (49.3)	0.68 (0.33-1.37)	.28
TT	7 (10.3)	6 (8.5)	1.02 (0.31-3.40)	.96
C	0.698	0.669	Reference	—
T	0.302	0.331	0.87 (0.52-1.44)	.59

The chi-square test or Fisher's exact test was used for the evaluation of categorical values including genotype and allele frequencies of VDR SNPs.
CI, confidence interval; OR, odds ratio; SNP, single-nucleotide polymorphism; VDR, vitamin D receptor.

FokI TT genotype had higher glucose concentration compared to CC and CT genotypes (CC: 183.4 ± 128.4; TT: 151.9 ± 66.1; CT: 107.6 ± 41.9, *P* = .008).

DISCUSSION

Our study showed that VDR gene TaqI, ApaI, and FokI genotype and allele frequencies are not different in overweight/obese CKD-G5D patients compared to normal-weight patients.

Obesity and diabetes mellitus are very common in CKD-G5D patients. Adipose tissue is also known as the main storage source for vitamin D.[8] Furthermore, there are many studies reporting that vitamin D deficiency is associated with obesity[2] and dyslipidemia.[9]

Vitamin D receptor is present on adipocytes, and many studies have been carried out to examine the relationship between VDR gene polymorphisms and obesity. In a study with obese women, vitamin D deficiency and insufficiency were detected in 80.3% of the subjects. Moreover, it was reported that ApaI polymorphism was not significantly different between the 2 groups.[10] Furthermore, in the Chinese population, the TT genotype and the T allele of TaqI SNP are found to be associated with obesity.[11] Similar to this study, the TaqI T allele was shown

Table 3. Comparison of some selected parameters according to VDR gene TaqI, ApaI, and FokI genotypes in overweight/obese CKD-G5D patients.

	TaqI				ApaI				FokI			
Parameter	**TT**	**TC**	**CC**	***P***	**AA**	**AC**	**CC**	***P***	**CC**	**CT**	**TT**	***P***
Body mass index (kg/m^2)	29.1 (3.4)	30.0 (4.6)	29.7 (4.1)	.70	29.3 (3.4)	29.9 (4.6)	27.8 (1.8)	.62	29.4 (4.5)	29.5 (3.6)	30.6 (3.2)	.74
25(OH)D (ng/mL)	11.3 (4.3)	11.4 (6.0)	11.8 (5.0)	.47	10.9 (3.9)	11.4 (4.5)	16.8 (4.4)	.08	11.3 (4.2)	11.7 (4.5)	11.3 (4.9)	.93
Triglycerides (mg/dL)	210.2 (195.8)	183.4 (103.8)	166.9 (86.8)	.81	223.3 (156.6)	193.1 (85.4)	627.3 (653.0)	**< .001**	224.4 (138.6)	246.7 (252.9)	198.1 (78.3)	.80
Cholesterol (mg/dL)	176.9 (55.1)	181.3 (44.2)	154.6 (53.4)	.17	182.6 (56.2)	187.3 (64.8)	137.7 (33.0)	.39	188.6 (61.7)	174.9 (63.8)	185.7 (39.0)	.69
High-density lipoprotein (mg/dL)	33.9 (10.2)	36.7 (14.0)	34.8 (12.4)	.67	32.3 (10.4)	31.3 (9.1)	25.3 (3.5)	.48	31.7 (10.3)	30.7 (8.4)	33.1 (11.0)	.82
Low-density lipoprotein (mg/dL)	138.0 (137.6)	112.5 (48.7)	108.1 (38.4)	.56	134.6 (137.3)	116.7 (51.9)	96.7 (65.2)	.69	142.0 (130.5)	103.0 (54.5)	117.7 (37.7)	.32
Creatinine (mg/dL)	7.8 (2.5)	8.0 (2.9)	8.4 (1.6)	.83	7.8 (2.6)	8.1 (2.6)	7.3 (2.8)	.79	7.4 (2.5)	8.4 (2.5)	8.5 (2.8)	.29
Calcium (mg/dL)	8.7 (0.8)	8.5 (0.7)	8.6 (0.5)	.52	8.7 (0.8)	8.5 (0.7)	9.3 (0.8)	.18	8.4 (0.9)	8.8 (0.8)	8.6 (1.3)	.85
Phosphate (mg/dL)	4.8 (1.3)	4.3 (1.4)	4.8 (1.1)	.34	4.6 (1.3)	4.6 (1.4)	4.3 (1.2)	.90	4.6 (1.2)	4.6 (1.6)	4.3 (1.0)	.79
Blood urea nitrogen (mg/dL)	67.0 (14.0)	61.7 (19.0)	58.1 (18.4)	.29	67.0 (18.2)	60.8 (15.6)	64 (14.8)	.34	60.3 (15.9)	65.4 (17.0)	74.3 (17.2)	.11
Parathormone (pg/mL)	310.2 (323.4)	342.7 (360.8)	717.1 (616.4)	**.028**	480.0 (481.0)	286.2 (298.3)	261.7 (22.7)	.13	258.9 (221.3)	489.3 (534.7)	484.7 (350.6)	.06
Glucose (mg/dL)	133.8 (54.9)	138.6 (78.8)	148.8 (101.5)	.86	133.2 (83.8)	139.2 (60.0)	163.7 (33.6)	.76	151.9 (66.1)	107.6 (41.9)	183.4 (128.4)	**.008**

Analysis of variance with a Bonferroni correction (Bonferroni post hoc test) was used to compare the parameters in overweight/obese patients according to genotypes of TaqI, ApaI, and FokI SNPs. VDR, vitamin D receptor.

to be associated with higher BMI in the Greek population.[12] In contrast, in the 1958 British birth cohort study (1958BC) of 5224 participants, VDR SNPs were not associated with obesity traits.[13] In a cross-sectional study of 198 adult Arabs with metabolic syndrome, TT carriers of the FokI SNP had higher total cholesterol than CC and CT carriers.[14] Furthermore, in a recent study conducted with 402 obese and 489 non-obese Saudis, VDR TaqI minor allele polymorphisms were found to be more frequent in obese individuals.[15] However we found no association between VDR polymorphism and overweight/obesity. According to the results of the studies included in a recent systematic review, it has been reported that no definite conclusion can be reached between VDR polymorphisms and obesity.[16]

In the current study, lower HDL and higher TG concentrations were detected in overweight/obese CKD-G5D patients compared to normal patients. In a study of 1534 individuals, a positive correlation was found between vitamin D, HDL, and age. A negative correlation was found between vitamin D and BMI, LDL, total cholesterol, and TG.[17] Another study shows that serum 25(OH)D levels are correlated with serum lipids and atherogenic plasma index. Furthermore, it is suggested that vitamin D deficiency may be associated with an increased risk of dyslipidemia, especially in men.[18] Recent randomized clinical trials evaluating the effect of vitamin D supplementation on blood lipids have reported conflicting evidence. It has been found that vitamin D supplementation has no significant effect on blood lipids compared to placebo.[19] These new findings make it difficult to understand whether there is a causal relationship between vitamin D deficiency and a negative blood lipid profile.

In the present study, glucose concentration was higher in the overweight/obese group. This may be due to the high number of patients with diabetes mellitus in the overweight/obese group. In a study involving 120 non-diabetic CKD patients, obese patients treated with $1,25(OH)_2D$ had similar insulin concentrations compared to non-obese patients, whereas untreated obese patients had a higher insulin concentration.[20] In our study, overweight/obese patients with the FokI homozygous mutant TT genotype had higher glucose concentrations than those with CC and CT genotypes. In another study, individuals with the FokI TT genotype were associated with higher homeostatic model assessment for insulin resistance (HOMA-IR) values than individuals with CT genotype. Thus, VDR FokI polymorphism has been suggested to be associated with diabetes mellitus.[21]

It has been suggested that there is a potential association between parathyroid function and VDR polymorphisms in CKD patients.[6] In the current study, significantly higher PTH levels were found in overweight/obese patients carrying TaqI CC genotype compared to those carrying TT and TC genotypes. Similar findings were found for TaqI variants in Iranian HD patients.[22] In contrast, Ozdemir et al[6] suggested that the TaqI TT genotype increases the risk of development of hyperparathyroidism in Turkish HD patients. Given that the demographics of their patient populations differ from those of our patients, their results are likely to be different from ours.

The main limitation of the current study is the relatively small sample size. Further, we only calculated BMI for the evaluation of obesity. We did not measure the waist-to-hip ratio and waist circumference for the evaluation of obesity. Another limitation is that BsmI, one of the most studied SNPs in the VDR gene, was not included in our study. Therefore, potential associations of BsmI with obesity susceptibility and CKD comorbidities could not be demonstrated in the current study. In addition, due to the lack of information regarding patients' drug use, such as glucose-lowering drugs, antihyperlipidemic drugs, and drugs used for the treatment of secondary hyperparathyroidism, potential differences that may arise from the reducing effects of these drugs were not considered in our study.

In conclusion, although this study has shown that VDR polymorphisms are not related to obesity susceptibility, in overweight/obese CKD-G5D patients, VDR polymorphisms have been suggested to increase the risk of secondary hyperparathyroidism, dyslipidemia, and hyperglycemia, which are among the most common obesity-related comorbidities of CKD The VDR gene polymorphisms may play a role in the pathogenesis of obesity, hence more comprehensive and larger studies are needed to reveal the relationship between VDR polymorphisms and obesity in CKD-G5D patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Sivas Cumhuriyet University (Approval No: 2013-07/03, Date: July 2 2023).

Informed Consent: Written informed consent was obtained from patients and healthy controls who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – G.B., C.H., B.B., F.C.; Design – G.B., CH., F.F.; Supervision – G.B., C.H.; Resources – C.H., F.F.; Materials – C.H., F.C.; Data Collection and/or Processing – G.B., B.B.; Analysis and/or Interpretation – G.B.; Literature Search – G.B., F.C.; Writing Manuscript – G.B.; Critical Review – G.B., C.H., F.C.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143(21):e984-e1010. [CrossRef]
2. Yim HE, Yoo KH. Obesity and chronic kidney disease: prevalence, mechanism, and management. *Clin Exp Pediatr*. 2021;64(10):511-518. [CrossRef]

3. Zmijewski MA, Carlberg C. Vitamin D receptor (s): in the nucleus but also at membranes? *Exp Dermatol*. 2020;29(9):876-884. [CrossRef]
4. Abbas MA. Physiological functions of vitamin D in adipose tissue. *J Steroid Biochem Mol Biol*. 2017;165(B):369-381. [CrossRef]
5. Yang S, Li A, Wang J, et al. Vitamin D receptor: a novel therapeutic target for kidney diseases. *Curr Med Chem*. 2018;25(27):3256-3271. [CrossRef]
6. Ozdemir FN, Sezer S, Atac B, et al. Vitamin D receptor BsmI and TaqI gene polymorphisms in a Turkish ESRD population: influences on parathyroid hormone response. *Transplant Proc*. 2005;37(7):2922-2924. [CrossRef]
7. Lucisano S, Buemi M, Passantino A, Aloisi C, Cernaro V, Santoro D. New insights on the role of vitamin D in the progression of renal damage. *Kidney Blood Press Res*. 2013;37(6):667-678.
8. Wamberg L, Christiansen T, Paulsen SK, et al. Expression of vitamin D-metabolizing enzymes in human adipose tissue -- the effect of obesity and diet-induced weight loss. *Int J Obes (Lond)*. 2013;37(5):651-657. [CrossRef]
9. Jiang X, Peng M, Chen S, Wu S, Zhang W. Vitamin D deficiency is associated with dyslipidemia: a cross-sectional study in 3788 subjects. *Curr Med Res Opin*. 2019;35(6):1059-1063. [CrossRef]
10. Sharif E, Swaidan N, Shurbaji S, Rizk NM. Associations of vitamin D receptor polymorphism rs1544410 with adiposity phenotypes. *Endocrinol Metab Int J*. 2016;3(6);00069.
11. Fan HR, Lin LQ, Ma H, Li Y, Sun CH. Association between vitamin D receptor gene polymorphism (TaqI) and obesity in Chinese population. *J Genet*. 2015;94(3):473-478. [CrossRef]
12. Vasilopoulos Y, Sarafidou T, Kotsa K, et al. VDR TaqI is associated with obesity in the Greek population. *Gene*. 2013;512(2):237-239. [CrossRef]
13. Vimaleswaran KS, Cavadino A, Berry DJ, et al. Genetic association analysis of vitamin D pathway with obesity traits. *Int J Obes (Lond)*. 2013;37(10):1399-1406. [CrossRef]
14. Hasan HA, AbuOdeh RO, Muda WAMBW, Mohamed HJBJ, Samsudin AR. Association of vitamin D receptor gene polymorphisms with metabolic syndrome and its components among adult Arabs from the United Arab Emirates. *Diabetes Metab Syndr*. 2017;11(suppl 2):S531-S537. [CrossRef]
15. Al-Daghri NM, Guerini FR, Al-Attas OS, et al. Vitamin D receptor gene polymorphisms are associated with obesity and inflammosome activity. *PLOS ONE*. 2014;9(7):e102141. [CrossRef]
16. Faghfouri AH, Faghfuri E, Maleki V, Payahoo L, Balmoral A, Khaje Bishak Y. A comprehensive insight into the potential roles of VDR gene polymorphism in obesity: A systematic review. *Arch Physiol Biochem*. 2022;128(6):1645-1657. [CrossRef]
17. Glueck CJ, Jetty V, Rothschild M, et al. Associations between Serum 25-hydroxyvitamin D and Lipids, lipoprotein Cholesterols, and homocysteine. *N Am J Med Sci*. 2016;8(7):284-290. [CrossRef]
18. Wang Y, Si S, Liu J, et al. The associations of serum lipids with vitamin D status. *PLoS One*. 2016;11(10):e0165157. [CrossRef]
19. Ponda MP, Huang X, Odeh MA, Breslow JL, Kaufman HW. Vitamin D may not improve lipid levels: a serial clinical laboratory data study. *Circulation*. 2012;126(3):270-277. [CrossRef]
20. Friedman DJ, Bhatt N, Hayman NS, et al. Impact of activated vitamin D on insulin resistance in nondiabetic chronic kidney disease patients. *Clin Endocrinol (Oxf)*. 2012;77(1):56-61. [CrossRef]
21. Angel B, Lera L, Sánchez H, Oyarzún A, Albala C. FokI polymorphism in vitamin D receptor gene: differential expression of TNFα in peripheral mononuclear cells of type 2 diabetic subjects. *Meta Gene*. 2016;7:1-6. [CrossRef]
22. Pourfarzam M, Nia KM, Atapour A, Sadeghi HM. The influence of BsmI and TaqI vitamin D receptor gene polymorphisms on the intensity of hyperparathyroidism in Iranian hemodialysis patients. *Adv Biomed Res*. 2014;3:213. [CrossRef]