FULL LENGTH ARTICLE

Association of vitamin D receptor gene polymorphism (VDR) with vitamin D deficiency, metabolic and inflammatory markers in Egyptian obese women

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Abstract Vitamin D deficiency might contribute to the pathogenesis of metabolic syndrome and could cause immune disturbance. The aim of this study is to analyze the associations between Vitamin D receptor (VDR) gene polymorphism, serum 25-hydroxy vitamin D, metabolic and inflammatory biomarkers in Egyptian obese women. The study included 201 obese women with vitamin D deficiency and 249 obese matched age healthy controls with sufficient vitamin D levels. Their age ranged between 25 and 35 years. Inflammatory biomarkers (interleukin-6 and C-reactive protein) and serum 25(OH) D were measured by enzyme-linked immunosorbent assay. Insulin resistance (IR) was determined by the homeostasis model assessment of insulin resistance (HOMA-IR). Vitamin D receptor (VDR) gene polymorphisms of FokI, ApaI, and TaqI were studied by PCR using the restriction fragment length polymorphism (RFLP) technique. Obese women with vitamin D deficiency had significant higher values of inflammatory and metabolic parameters compared to controls. Multivariable-logistic regression showed associations between 25(OH) D deficiency and metabolic components when comparing cases with controls. Moreover, cases carrying polymorphic alleles showed significant lower levels of serum 25(OH) D and higher HOMA-IR, blood pressure levels and lipid parameters compared to those with the wild type homozygote in obese cases with vitamin D deficiency. Vitamin D deficiency in Egyptian obese women with vitamin D deficiency is associated with abnormal metabolic

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Introduction

A connection has been found between vitamin D deficiency and components of metabolic syndrome. The impact of the vitamin D on the development of metabolic syndrome has been proposed via gene transcription and hormonal modulation that affect the insulin metabolism. Vitamin D has a critical impact on lots of metabolic modulations including calcium-phosphate (Ca-P) homeostasis, and particularly the regulation of insulin secretion by the β-cells.[1]

An opposite relationship has been detected between serum 25(OH) D and metabolic disorders, diabetes, insulin resistance and beta cell function.[2,3] In the non-Hispanic white and Mexican American, the reverse relationship between 25(OH) D levels, diabetes and insulin resistance has been established by the National Health and Nutrition Examination Surveys (NHANES). However, the relationship has not found in the non-Hispanic black populations.[4,5]

It was suggested that Vitamin D might has a direct effect on the secretory function of the pancreatic cell through their nuclear VDRs[6] which could explain the association of lower serum vitamin D status and high risk of hypoglycemia and insulin resistance. Moreover, as the vitamin D-dependent calcium-binding protein, an effect or part of the vitamin D pathway, required for post insulin receptor effects in insulin-responsive tissues so, it affects the insulin sensitivity via stimulation of insulin receptor expression regulation of intracellular calcium. In addition to, indirect effects by means of inflammatory processes.[7]

Obesity is always accompanying by vitamin D deficiency. Some studies showed that vitamin D is significantly associated generally with obesity status and especially with waist circumference.[8] It was found that vitamin D, whether it is dietary ingested or acquired from sunlight exposure, is stored in the body fat cells in the form that is not bioavailable.[9] This is might explain why obese persons are chronically suffered from vitamin D deficiency.

It is observed that vitamin D deficiency raises the systemic inflammation as high levels of inflammatory markers such as C-reactive protein and interleukin-10 accompanies to Vitamin D deficiency. Furthermore, administration of 1,25(OH)2D to vitamin D-deficient individuals down regulated inflammatory markers.[10]

Many populations all over the world have been found to suffer from vitamin D deficiency where, 10–60% of adults showing values less than 20 ng/ml.[11] High prevalence of hypovitaminosis D is evident worldwide,[12] particularly in northern latitudes.[13]

Vitamin D receptor (VDR) as a member of steroid-hormone receptor super family, it has an essential role in modulating immune response and inflammation via binding with its counter ligand vitamin D. The complex of vitamin D and its receptor controls the B-cell insulin secretion.[1,14]

As vitamin D receptors (VDR) are widely distributed along several body tissues, their gene polymorphisms may affect the risk of vitamin D-related metabolic disorders, and could adjust the receptor effectiveness according to vitamin D status.[15] A number of polymorphisms in the VDR genes that capable of changing the activity of VDR protein have been identified.[16] The main functional loci of VDR gene are FokI (rs2228570), BsmI (rs1544410), ApaI (rs7975232) and TaqI (rs731236) and all of them are located between exons 8 and 9 apart from FokI is in exon.[17]

Some of these polymorphisms have been linked to diseases such as type 2 diabetes mellitus.[18] An association has been reported between VDR gene polymorphism and metabolic changes connected to obesity.[16] Some studies have investigated the association between VDR gene polymorphisms and the risk for metabolic syndrome disorder.

The aim of this study is to evaluate the associations of vitamin D receptor (VDR) gene polymorphism, 25 hydroxy vitamin D levels, clinical, anthropometric and biochemical parameters in Egyptian obese women and assess its potential risk for metabolic components and inflammatory markers.

Methods

The study investigated 201 obese women (BMI $\geq$ 30 kg/m^2) with vitamin D deficiency, (25(OH) D $<$ 20 nmol/l) and 249 obese age-matched healthy women controls with sufficient vitamin D levels. Obese women between the ages of 25 and 30 years were recruited from the obesity clinic, National Research Centre, Egypt. Exclusion criteria were: the presence of chronic illnesses that potentially alter vitamin D metabolism, the use of medications, pregnant or breast-feeding women, the use of vitamin D supplements and another diseases (e.g., hyper/hypothyroidism, hyper-prolactinemia, Cushing's syndrome, congenital adrenal hyperplasia (CAH) or hormonal secreting tumor). Controls had sufficient levels of vitamin D (25(OH) D $>$ 75 nmol/l). HOMA-IR value $>$3 was used for the diagnosis of insulin resistance (IR).[19]

Genotyping

Peripheral venous blood samples were collected on EDTA. Genomic DNA was extracted from peripheral white blood cells using salting out procedure.[20] DNA was amplified by polymerase chain reaction (PCR) and examined (by specific restriction enzymes) using the restriction fragment length polymorphism (RFLP) technique. The VDR genotype of each subject was identified according to the digestion pattern

and alleles according to the presence (f, t, and a) or the absence (F, T, and A) of the FokI, TaqI, and ApaI, restriction enzyme cleavage sites, respectively. Each VDR markers were amplified as following:

FokI polymorphism of patients and controls DNA was amplified by PCR reaction in 25 μl total volume for FokI containing 10 mM trisHCl, 200 μM dNTPs, 20 pmol from the primer sequences F: 5′-AGC TGG CCCTGG CAC TGACTC GCT CT-3′ and R: 5′- ATGGAA ACA CCT TGC TTC TTC TCC CTC-3′, 1.5 mM MgCl₂, 0.5 u taq polymerase (fenzyme), and using 50–100 ng of DNA as template. The temperature sittings were as follows; 5 min at 94 °C, followed by 35 cycles of 95 °C for 60 s, 68 °C for 60 s and 72 °C for 2 min followed by 72 °C for 7 min as a final extension step. The PCR product was electrophoresed on 2% agarose gel stained with ethidium bromide. PCR product 265 bp were visualized on UV trans-illuminator with using molecular weight marker to determine the quality of PCR products. Then conduct 10 μl of PCR product to 1 unite restriction enzyme (FastDigestFok-I, Fermentas) at 37 °C for 15 min, followed by 65 °C for 3 min for digestion. After digestion were loaded the products on 2% agarose gel stained with ethidium bromide to identify the digestion pattern. The FF genotype, homozygote of common allele its meaning absence of restriction site and showed one band at 265 bp. The ff genotype (homozygote of infrequent allele) generated two fragments at 196 bp and 69 bp. Presence of three fragments at 265 bp, 196 bp and 69 bp was appearance as Ff.

TaqI polymorphism. The PCR cycle conditions were initially denaturized at 94 °C for 4 min, followed by 35 cycles at 94 °C for 60 s, 68 °C for 60 s and 72 °C for 2 min followed by 72 °C for 7 min as a final extension step. In total volume 25 μl were containing 10 mM trisHCl, 200 μM dNTPs, 20 pmol from the primer sequences F: 5′- CAG AGC ATG GAC AGG GAGCAA-3′ and R: 5′-CAC TTC GAG CAC AAG GGGCGT TAG C-3′, 1.5 mM MgCl₂, 0.5 u taq polymerase(fenzyme), and using 50–100 ng of DNA as template. The PCR product was electrophoresed on 2% agarose gel stained with ethidium bromide. PCR product 600 bp were visualized on UV trans-illuminator with using molecular weight marker to determine the quality of PCR product. The PCR product was digested with the restriction enzyme Taq-I (FastDigest-Taq-I, Fermentas) 10 unit for 15 min at 37 °C and followed by 65 °C for 3 min according to manufacturer's instructions. The digested samples were added to loading dye and size fractionated by electrophoresis in a 1.5% agarose gel. Visualization after ethidium bromide staining was accomplished by UV trans-illuminator. Taq-I digestion revealed one obligatory restriction site, the homozygous TT (absence of the specific Taq-I restriction site) yielded bands of 500 bp and 210 bp. The homozygous tt exhibited 210 bp and the heterozygous Tt 290 bp fragments.

ApaI polymorphism. The PCR cycle conditions were initially denaturized at 94 °C for 4 min, followed by 35 cycles at 94 °C for 30 s, 65 °C for 30 s, and 72 °C for 2 min and final extension at 72 °C for 4 min. In total volume 25 μl were containing 10 mM trisHCl, 200 μM dNTPs, 20 pmol from the primer sequences F: 5′-CAA CCA AGA CTA CAA GTA CCG CGT CAGTGA-3′ and R: 5′- CAC TTC GAG CAC AAG GGGCGT TAG C-3′, 1.5 mM MgCl₂, 0.5 u taq polymerase (Fenzyme), and using 50–100 ng of DNA as template. The PCR product was electrophoresed on 1.5% agarose gel stained with ethidium bromide to check the quality of reaction. The amplified 2000 bp PCR product was subjected to Apa-I restriction enzyme (Fast Digest, Fermentas) for digestion. 10 μl of PCR product was digested with 10 units of Apa-I restriction enzyme in a 20 μl total volume using green buffer at 37 °C for 15 min and followed by 65 °C for 3 min. The Apa-I enzyme digested product was loaded on a 1.5% agarose gel stained with ethidium bromide. The 2000 bp was digested as a common allele A (wild type) and presence of restriction site resulting in 1700 bp and 300 bp was assigned as infrequent allele (mutant allele). Genotypes were exhibited as homozygotes for common allele AA and homozygotes for mutant allele aa. Presence of 2000 bp, 1700 bp and 300 bp fragments was exhibited as heterozygotes Aa.

All patients and controls were subjected to full medical history and clinical examination. Anthropometric measurements included body weight, height, waist and hip circumferences.

This study was approved by local ethics committee of the National Research Centre (No: 16361); the purpose of the protocol was explained to both the patients and control women, and written informed consent was obtained from them before beginning the study.

Anthropometric measurements were obtained according to standardized equipment and following the recommendations of the International Biological Program. All measurements were taken 3 times on the left side of the body and the mean of the 3 values was used. Body weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1 cm. Height was measured with the patients standing with their backs leaning against the stadiometer of the same scale. BMI was calculated as weight in kilograms divided by height in meters square (kg/m²). Waist circumference (WC) and hip circumference (HC) were measured in cm using a plastic, non-stretchable tailors tape. WC was measured with light clothing at a level midway between the lower rib margin and the iliac crest standing and breathing normally. HC was measured at the level at the widest circumference over the buttocks (at the greater trochanter). Subsequently the waist hip ratio (WHR) was calculated as WC divided by HC.

Systolic and diastolic blood pressures (SBP and DBP) were measured twice in the right arm in a sitting position after a 10 min rest period; using a mercury sphygmomanometer the average of the two measurements was used for analysis. Blood pressure was measured according to a standardized operating procedure using a calibrated sphygmomanometer and brachial inflation cuff (HEM-7200 M3, Omron Healthcare, Kyoto, Japan).

Serum analysis

Blood samples were collected after a 12-h overnight fast and stored at <80 °C until analyzed. An Olympus AU400 automatic analyzer (Olympus Corporation, Tokyo, Japan) was used to measure serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglycerides (TG) and fasting blood glucose(FBG); fasting blood insulin (FBI) were measured with commercial kits (Roche Diagnostics, Indianapolis, IN, USA). Low density lipoprotein cholesterol (LDL-C) was calculated according to certain equation (LDL-

C = Total cholesterol − Triglycerides/5 + HDL-C). The insulin sensitivity was then calculated using Homeostasis Model Assessment (HOMA-IR) according to the following formula: HOMA-IR = FBG (mmol/l) × FBI (μU/ml)/22.5.

The cut-off level of HOMA-IR was >3.0 to specify insulin resistance.[21]

Serum 25(OH) D levels were measured by immunoassay (DiaSorin 25-OH D assay, Still water, Minnesota, USA). Serum IL-6 and high-sensitive C-reactive protein (hs-CRP) levels were measured by commercially available sandwich enzyme-linked immunosorbent assay ELISA kits.

Statistics

SPSS version 16 statistical package was used to perform the analyses. Student's T-test for continuous variables to compare mean values between two independent groups and Chi square test for categorical variables were used. Univariate regression was performed to identify significant predictor's risk factors of obese in the deficient and sufficient vitamin D groups.

Statistical analysis
Pearson's Chi square test (2 df) was applied to test for deviation from Hardy−Weinberg equilibrium in both the case and control group.

Results

Table 1 shows the means of various biochemical and inflammatory parameters in the two studied groups, cases and controls. Results shows significant higher systolic blood pressure, diastolic blood pressure, BMI, FBG, FBI, HOMA-IR, LDL-C, triglycerides, LDL-C, IL-6 and CRP and lower HDL-C in cases than the controls.

Table 2 shows the risk factors for the metabolic parameters in obese cases with vitamin D deficiency and obese controls with vitamin D sufficiency, the risk variables that were significantly associated with metabolic parameters were WC, WHR, dyslipidemia, acanthosis nigricans and

HOMA-IR. Women with WC > 80 higher odds of low vitamin D (OR = 2.4, p = 0.01), WHR > 0.85 (OR = 2.15, p = 0.02), dyslipidemia (OR = 2.22, p = 0.01), with acanthosis nigricans (OR = 2.16, p = 0.01) and with elevated HOMA-IR (OR = 1.98, p = 0.04).

The allele and genotype frequency distribution and carriage rate of VDR (ApaI, FokI and TaqI) genes among obese cases and controls were shown in Table 3. The results showed significant differences in the distribution of VDR polymorphisms in cases compared to controls. Obese deficient cases showed higher frequencies of mutant alleles a, f, t and VDR (ApaI, FokI and TaqI) genotype carriers. The allele and genotype frequency distribution of VDR of, FokI, ApaI and TaqI polymorphisms frequencies did not deviate from Hardy−Weinberg equilibrium expectations in cases and controls.

Table 4 shows means of metabolic and inflammatory parameters according VDR gene polymorphisms at ApaI, FokI and TaqI in obese cases with vitamin D deficiency. Women carrying mutant alleles for the VDR for ApaI (Aa+aa), for FokI (Ff+ff) and for TaqI (Tt+tt) showed significant lower values of serum 25(OH) D and higher HOMA-IR, BP than those with the wild genotypes for the VDR (AA), (FF) and (TT), respectively.

Table 5 shows correlation of 25(OH) vitamin D levels with clinical and biochemical parameters in obese with vitamin D deficiency and controls. Serum concentrations of 25(OH) D were inversely correlated with metabolic features in cases such as blood pressure, BMI, FBG, FBI, HOMA-IR, LDL-C, triglycerides and inflammatory markers (IL-6, and hs-CRP) positively correlated with HDL-C. On the other hand, obese controls with sufficient vitamin D levels showed no correlations with metabolic parameters and inflammatory markers.

Discussion

Vitamin D is a hormone precursor and its D deficiency has been found to be associated with various metabolic disorders such as obesity, diabetes, cardiovascular disease (CVD) risk factors and inflammatory diseases.[22] There is general agreement that

Table 1 Clinical and biochemical profiles in obese cases with vitamin D deficiency and controls.

Characteristics	Obese cases with vitamin D deficiency Mean ± SD	Obese controls with vitamin D sufficiency Mean ± SD	p
SBP (mmHg)	158.71 ± 9.59	142.71 ± 8.44	<0.001
DBP (mmHg)	94.54 ± 6.87	73.83 ± 10.43	<0.001
FBG (mg/dl)	142.52 ± 8. 22	90.52 ± 5.22	<0.001
FBI (μU/ml)	18.20 ± 0.85	8.20 ± 0.65	<0.001
HOMA-IR	6.88 ± 1.29	2.3 ± 0.99	<0.001
Triglycerides (mg/dl)	145.65 ± 50.61	100.41 ± 43.29	<0.001
LDL-C (mg/dl)	173.71 ± 35.890	112.61 ± 29.381	<0.001
HDL-C (mg/dl)	40.44 ± 10.217	49.86 ± 10.560	<0.001
hs-CRP(mg/ml)	18.88 ± 5.31	5.20 ± 2.52	<0.001
IL-6 (pg/ml)	2.49 ± 0.20	0.92 ± 0.13	<0.001

SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL-C: low-density lipoprotein, HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma glucose; FBI: fasting plasma insulin; HOMA-IR: homeostasis model assessment of insulin resistance, hs-CRP: high-sensitive C-reactive protein; BP: blood pressure; IL-6: interleukin 6.

Table 2 Multivariable-logistic regression of metabolic risk factors.

Variables	Obese cases with vitamin D deficiency 25(OH) D (<20 nmol/l)%	Obese controls with vitamin D sufficiency 25(OH) D (≥75 nmol/l)%	OR (CI 95%)	p value
Waist circumference (cm)				
<80	33.33%	72.22%	1 (Reference)	0.01
>80	66.66%	27.77%	2.40 (2.28−6.72)	
waist-to-hip ratios (WHR)				
≤0.85	36.66%	71.11%	1 (Reference)	0.02
>0.85	62.33%	28.88%	2.15	
Dyslipidemia				
No	26.66%	74.44%	1 (Reference)	0.01
Yes	73.34%	25.55%	2.22	
Acanthosis nigricans				
Absent	40.00%	72.22%	1 (Reference)	0.01
Present	60.00%	27.77%	2.16	
HOMA-IR				
<3	31.66%	65.55%	1 (Reference)	0.04
>3	68.33%	34.44%	1.98	

HOMA-IR: homeostasis model assessment-insulin resistance.

Table 3 Distribution of the VDR of genotypes and alleles in cases and controls.

	Genotypes	Obese cases with vitamin D deficiency N = 201 n (%)	Obese controls with vitamin D sufficiency N = 249 n (%)	p value
ApaI	AA	97 (48.25)	179 (71.88)	0.04
	Aa	84 (41.79)	50 (20.08)	
	aa	20 (9.95)	20 (8.03)	
	A	278 (69.15)	408 (81.92)	0.03
	a	124 (30.84)	90 (18.07)	
FokI	FF	93 (42.26)	175 (70.28)	0.03
	Ff	84 (41.79)	50 (20.08)	
	ff	24 (11.94)	24 (9.63)	
	F	270 (47.16)	400 (80.32)	0.02
	f	132 (64.70)	98 (19.67)	
TaqI	TT	100 (57.71)	184 (73.89)	0.02
	Tt	80 (39.80)	45 (18.07)	
	tt	21 (10.44)	20 (8.32)	
	T	280 (69.51)	413 (82.93)	0.3
	t	122 (59.80)	85 (17.06)	

Table 4 Metabolic and inflammatory parameters according VDR gene polymorphisms for ApaI, FokI and TaqI in obese cases with vitamin D deficiency.

VDR genotype	25(OH) D (nmol/l)	SBP	DBP	FBG	FBI	HOMA-IR	CRP (mg/L)	IL-6 (pg/ml)
ApaI								
AA	17.4 ± 1.5	138.7 ± 7.5	81.5 ± 6.8	112.5 ± 6. 2	12.2 ± 0.8	2.8 ± 0.9	10.8 ± 4.2	2.4 ± 0.2
Aa+aa	13.5 ± 1.4*	156.7 ± 8.5**	94.5 ± 5.8*	142.5 ± 5. 3**	17.2 ± 0.8**	6.8 ± 1.2**	18.8 ± 5.3**	5.4 ± 0.2*
FokI								
FF	18.7 ± 1.5	129.6 ± 7.6	84.4 ± 6.5	120.5 ± 7.2	10.2 ± 0.6	3.1 ± 1.2	10.9 ± 5.11	2.7 ± 0.8
ff+Ff	13.5 ± 2.1**	158.7 ± 8.5**	95.9 ± 7.8	152.52 ± 6.4**	19.2 ± 0.9	6.9 ± 1.2**	17.4 ± 0.2**	4.9 ± 0.9**
TaqI								
TT	19.5 ± 2.7	134.7 ± 9.2	83.4 ± 7.8	123.52 ± 4.5	11.2 ± 0.5	2.8 ± 1.2	11.1 ± 0.2	2.1 ± 0.6
tt+Tt	14.7 ± 1.1**	155.6 ± 9.9**	94.8 ± 6.8**	132.52 ± 6.5*	20.2 ± 0.8*	5.8 ± 1.2**	16.4 ± 0.6**	5.5 ± 0.7*

SBP: systolic blood pressure; DBP: diastolic blood pressure; fasting plasma glucose; FBI: fasting plasma insulin; HOMA-IR: homeostasis model assessment of insulin resistance; hs-CRP: high-sensitive C-reactive protein; IL-6: interleukin 6 Statistical significance; *$p < 0.05$; **$p < 0.01$.

Table 5 Correlation of 25-(OH) vitamin D levels with metabolic parameters in cases and controls.

Serum 25(OH) vitamin D	SBP	DBP	FBG	FBI	HOMA-IR	Triglycerides	HDL-C	LDL-C	IL-6	hs-CRP
Obese controls with vitamin D sufficiency	0.10	0.20	0.12	0.45	0.12	0.10	0.45	0.18	0.15	0.12
Obese cases with vitamin D deficiency	−0.46**	−0.45**	−0.34*	−0.35*	−0.47**	−0.38*	0.34*	−0.33*	−0..35*	−0.35*

Statistical significance: $*p < 0.05$, $**p < 0.01$.

serum 25(OH) D concentrations best reflect vitamin D status current definitions being suggested to be sufficient (>75 nmol/l) and classical deficiency (<20 nmol/l).[23]

Although the deficiency in the vitamin D level has been observed in the general population, women and children seem to be the most affected groups. Particularly, girls and women from the Middle East.[24] Causes that might contribute to the observed high prevalence of vitamin D deficiency include; skin color as dark skin contain high melanin that might affect the vitamin D photosynthesis. And little exposure to sunlight as in aging and using of extensive body coverage. In addition, obesity and low dietary vitamin D intake could also worsen the problem.[24,25]

It is well known that vitamin D and calcium are essential for good musculoskeletal status. Vitamin D has been linked basically to bone health, and its deficiency causes rickets in children and osteomalacia and osteoporosis in adults.[26] However, recently it is become clear that many other organs in the body are required adequate vitamin D level in order to maintain optimal function of those organs.[27] Thus, bad effects of vitamin D deficiency extend beyond the skeletal system condition. It appears that vitamin D deficiency is linked to higher susceptibility of hypertension, diabetes and the metabolic syndrome, and chronic vascular inflammation. Epidemiologic studies have also recently linked vitamin D deficiency with increased risk of major adverse CV events.

In the present case control study, inflammatory and metabolic parameters were significantly adverse in the deficient vitamin D levels. In addition, link between obesity indices and low vitamin D has been found. Some studies have reported that vitamin D stores in the adipose tissue and its deficiency disturbs action of insulin.[26,28]

A probably essential pathophysiological mechanism that connects metabolic syndrome and its accompanying metabolic disruption is the insulin resistance and its subsequent developed hyperinsulinemia. Vitamin D controls gene transcription via nuclear vitamin D receptors (VDR) which are spread across various tissues. The pathogenesis of obesity has been connected to the effects of VDR. Models, both in vivo and in vitro, showed that vitamin D is playing an essential role in maintaining normal insulin level in accordance to glucose and keep glucose tolerance.

In the present study, significant differences in the VDR gene polymorphism have been observed between obese and control cases. Where, women carrying alleles (Aa, aa) for ApaI, (Ff, ff) for FokI and (Tt, tt) for TaqI showed significant lower values of serum 25(OH) D, higher HOMA-IR, BP compared to those with common homozygous alleles (AA), (FF) and (TT), for the VDR respectively. A study conducted on Egyptian diabetic patients[29] suggested the presence of

association between VDR polymorphisms, particularly FokI, and essential components of metabolic syndrome that might affect its severity. Where the ff allele has been correlated with higher waist circumference, HOMA-IR plasma IL-6, with lower HDL-C and lower vitamin D levels compared to FF genotypes in those diabetic patients with metabolic syndrome. FokI VDR has been found to be significantly related to lipid profiles and pro-inflammatory cytokines IL-6 in diabetic patients without metabolic syndrome.[29] In investigation of the connection between the VDR gene polymorphism and obesity in T2DM French Caucasians patients, an association has been observed at those group of patients with early-onset T2DM.[30] A probable association between ff genotypes and obesity has been reported in a preliminary study on obese Pakistins.[31] In PCO Egyptian women, a connection between the VDR Taq-I gene polymorphism and higher risk of PCO has been observed. The recessive homozygous and the heterozygous alleles of VDR Taq-I polymorphism has found to be linked to the anthropometric, metabolic disturbances in those PCOS patients plus significantly lower levels of 25(OH) D.[32] In Saudi individuals, an association has been reported between the TaqI polymorphism and the BMI where (t) allele was positively associated with higher BMI and obesity irrespective to age and sex.[33] Other studies have reported opposite results found no association between VDR gene polymorphism and diabetes risk.[34,35] Moreover, other study[35] reported significant association of age and waist-hip ratio with Taq-I genotypes of VDR gene polymorphism. Other study conducted on a group of Poland men[16] has found association between the FokI VDR polymorphism and insulin sensitivity and serum HDL level. However, it was shown that individuals carry the FF and Ff alleles had higher fasting insulin levels and lower HDL levels compared to ff genotypes, results that contradict ours. It was suggested that, disagreement between studies might be caused by genetic differences between populations or different environmental circumstances.[29]

The present study concludes that VDR Polymorphism is associated with metabolic and abnormal inflammatory profiles in our obese cases with vitamin D deficiency.

Conflicts of interest

No conflict of interests.

Acknowledgments

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