

Impact of Vitamin D on Calcium, Parathyroid Hormone and Lipid Profile Levels among Saudi-females with Type 2 Diabetes

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ABSTRACT

Aim: Evaluation of vitamin D levels in Saudi female patients with type 2 diabetes and its effect on the levels of serum calcium, parathyroid hormone (PTH) and lipid profiles of these patients.

Methodology: This study included 200 Saudi females with diabetes and 150 normal healthy females (non-diabetic). All of them were randomly selected based on study criteria and measurements were done in fasting blood samples. The amount of 25-hydroxy vitamin D (s-25 (OH) D), Ca, phosphorus, PTH, thyroid hormone, creatinine, albumin was estimated in the serum. The glycemetic and lipid profiles were also assessed

Results: Severe vitamin D deficiency (<25 nmol/ml) was observed in 60% of the participants, while mild vitamin D deficiency (=25-50 nmol/ml) was observed in 30% of the participant. Insufficient vitamin D (=50-75 nmol/ml) was observed in 10% of the participants. Serum 25 (OH) D correlated negatively with FBG, HbA1c, phosphorus, Atherogenic Index of Plasma, triglycerides, LDL and total cholesterol. There was a positive significant correlation between serums 25 (OH) D, PTH, and Calcium.

Conclusion: Low serum vitamin D, Ca and PTH levels was associated with impaired glucose metabolism and increased cardiovascular risk in type II diabetes.

Keywords: Calcium; Parathyroid hormone; Lipid profiles; Type 2 diabetes; Vitamin D deficiency

INTRODUCTION

Diabetes is one of the most common non-communicable diseases globally. At present, it is the fifth major cause of death in most high-income countries. Reports confirm that it has spread as an epidemic in many low and middle-income countries [1]. In the near future, this disease seems to remain as one of the most challenging health issues to be dealt with [1,2]. Surveys conducted in the Middle East have revealed that 24% of adult Saudis in the age group of 30-70 years suffer with diabetes, and 14% have impaired fasting blood glucose. It is worrying that the prevalence seems to be doubling every two decades, and in some countries like Saudi Arabia this could soon reach 50% in those over 50 years of age [3,4].

Vitamin D deficiency is defined as a decrease in the total serum concentration of 25-hydroxyvitamin D (25 (OH) D). The function of Vitamin D, a fat-soluble vitamin, is carried out through its binding to a specific receptor (VDR) located in the center of target cells [5,6]. Studies have shown that, Vitamin D deficiency is associated with increased risk of death and can lead to cardiovascular diseases

(CVD), different malignancies, infections, diabetes, autoimmune disorders, and kidney malfunctions [6]. It plays a key role in the regulation of calcium metabolism in the serum either directly or indirectly through the involvement of PTH. The vitamin D receptors can be seen in in different tissues that include the digestive tissue, the adipose tissue, the cardiac and skeletal muscle fiber, and the pancreatic β -cells [7]. Hence several studies have been done to investigate the role of vitamin D in the pathogenesis of metabolic diseases like diabetes [8,9]. *In vivo* studies done using animals have shown that vitamin D plays a significant role in secretion of insulin [10-11]. For example, Vitamin D deficient rabbits and mice have impaired insulin secretion, and supplementation with vitamin D corrects the defect by encouraging the biosynthesis of insulin in rabbits and mice pancreatic islet cells. In addition, mutations in the VDR (vitamin D receptors on pancreatic) in mice have reduced insulin secretion and lower glucose tolerance than those with efficient receptors [10-11]. Another explanation, the decreasing in the resistance of insulin to sugars maybe since it has an effect on the metabolism of calcium and phosphorus and also due to the

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up regulation of genes that express for insulin receptors [11-13]. Studies have informed significant enhancement in insulin secretion after variable doses and lengths of vitamin D3 supplementation in patients with T2DM [14]. In addition, improving vitamin D status in insulin resistant women resulted in reduced insulin resistance and sensitivity that may lead to control the T2DM complications [12].

There are several mechanisms that explain the role of vitamin D interference, for instance, a) occurrence of vitamin D receptors on pancreatic β cells, b) expression and activation of 1α hydroxylase in pancreatic β cells, c) existence of vitamin D response element in the insulin gene, d) occurrence of vitamin D receptors in the skeletal muscles, and e) increase in transcription of insulin receptor gene by 1, 25 (OH)D [15-17]. In addition, vitamin D diminishes the expression of pro-inflammatory cytokines such as interleukins, IL-1, IL-6, TNF- α , and also down regulate NF-K β (Nuclear factor) activity that are involved in the resistance of insulin [18, 19]. Also some studies proposed that vitamin D plays a vital role in the modulation of inflammatory responses, therefore, vitamin D may reduce insulin resistance and the risk of diabetes by reducing inflammatory responses [18-19].

Since low concentrations of 25 (OH) D and high concentrations of PTH are associated with an increased risk of MetS, and diabetes [20,21]. Numerous studies have recommended that low 25 (OH) D status is related to the development of the MetS and its individual components. There is also association found between PTH or 25 (OH) D and MetS in overweight or obese individuals from New Zealand or Spanish obese patients [20,21]. With increasing adiposity, the levels of PTH were observed to be higher while those of 25 (OH) D and calcium were lower [21]. The level of 25 (OH) D is deficient or insufficient with increase in obesity. It is less than 10% when BMI is less than 45 kg/m², and 26% when it is greater than 50 kg/m². The incidence of hyperparathyroidism was 12% in individuals that were not obese and it increased to 47.5% in morbidly obese individuals having a BMI greater than 50 kg/m². Hence, BMI, age and seasonality can predict levels of PTH and 25 (OH) D independently [22,23].

Some authors have reported that obesity, resistance to insulin and uncontrolled diabetes are positively associated with increased levels of PTH in type 2 diabetes patients. As PTH can contribute to the development of myocardial heart disease and dysfunction of systolic pressure, cardiovascular protection can be improved with treatment of hypovitaminosis D in type 2 diabetic patients. A positive correlation was also reported between PTH1-84 and β -cell function, suggesting that PTH1-84 plays a significant role in insulin secretion [24,25]. An association has been established between low levels of plasma 25 (OH) D and/or elevated levels of PTH with MetS and diabetes but has been controversial [26]. A recent study including systematic review and meta-analysis has shown that the occurrence of MetS was reduced to half when individuals had high concentrations of 25 (OH) D [27]. On the other hand, no relation has been reported between PTH and 25 (OH) D with the levels of calcium in Saudi females with type 2 DM. Therefore, the main objective of the current study was to examine the associations between the plasma levels of 25 (OH) D, calcium and PTH in type 2 diabetic patients and to explore the presence of MetS in diabetic females of the Saudi community.

SUBJECTS AND METHODS

Study population

Two hundred female diabetic patients, attending the diabetes clinic in Prince Maged Aben Abdel-Aziz Diabetic Center, Al Madinah

were selected for the present study along with corresponding 150 normal control subjects. The following data was collected: age, gender, present smoking habits (absent/present), presence of comorbidities associated with type 2 DM (obesity, hypertension, dyslipidemia), and patients under medication (triglyceride lowering agents like fibric acid derivatives and statins, oral anti-diabetic drugs, insulin and anti-hypertensive drugs).

Inclusion and exclusion criteria

The inclusion criteria were type 2 DM or patients with classical symptoms of diabetes (polyuria, polydipsia and polyphagia) with a random plasma glucose level of more than 200 mg/dl (aged 30-70 years); while controls were individuals with blood glucose within normal limits. The exclusion criteria for both was any subject with Type 1 DM, and had a history or evidence of parathyroid or calcium related diseases, history or evidence of endocrine diseases including hyperthyroidism, hypothyroidism, adrenal disease, and pituitary disease, or history of major renal, liver, heart or neurological disease, bone disease, malignancy and any history of use of drugs such as lipid-lowering drugs, antidiabetic drugs and calcium and vitamin D tablets.

Ethical considerations

This study was approved by the Medical Ethic Committee of Applied Medical Science Collage at Taibah University. All participants signed the written informed consent.

Biochemical assays

Fasting samples needs to be collected after a minimum 12-14 hour overnight fasting status. The blood samples were subjected to estimation of serum glucose, calcium, phosphate, alkaline phosphatase, total cholesterol, HDL, LDL, triglycerides, serum albumin, and creatinine. The concentrations were determined according to routine biochemical laboratory methods and the assays were performed using the automated machine Dimension XP and Siemens (Healthcare Diagnostics Ltd. Frimley, Camberley). The calcium concentrations were calculated based on the serum albumin concentrations as follows: Corrected calcium (mmol/L) = total calcium (mmol/L) measured + 0.02 (40 - serum albumin [g/L]), where 40 g/L is the average albumin level. Serum 25 (OH) D was measured by the electro-chemiluminescence immunoassay using Cobas auto-analyzer (Roche Diagnostics, West Sussex, UK) whereby the normal, insufficient and deficient vitamin D status was defined as 25 (OH) D serum concentration of 75.00 nmol/L, 25.00-75.00 nmol/L, and less than 25.00 nmol/L, respectively [22,23]. The Parathyroid and Thyroid hormones (T3, T4) were determined by the chemiluminescent enzyme-labeled immunometric assay using an IMMULITE 2000 Systems analyzer (Siemens, Gwyneth, UK) according to the manufacture's instruction. Glycated hemoglobin (HbA1c) was also determined using whole blood in EDTA tube by the boronic acid conjugate affinity chromatography methods using Nycocard HbA1c reader according to manufacturer's instructions.

Other measurements

For each participant, a physical examination was done that included the measurement of height, weight and Body mass index BMI (kg/m²). BMI was calculated dividing weight by square of the height. The prevalence of MetS in the diabetic patients was determined by using the guidelines recommended by the National Cholesterol Education Program, Adult Treatment Panel III (2002 panel) [28]. It was defined by the presence of three or more of the

following conditions: fasting blood glucose level ≥ 5.6 mmol/L, blood pressure $\geq 130/85$ mmHg, triglycerides ≥ 1.7 mmol/L, HDL cholesterol <1.29 mmol/L, waist circumference >88 cm for women and BMI $>30\%$ [28]. Atherogenic dyslipidemia is defined as a condition when there is concomitant presence of high concentrations of plasma triglycerides and low concentrations of HDL and was calculated as an Atherogenic Index of Plasma (AIP)= $\log(TG/HDL-C)$. An AIP value that is less than 0.11 is associated with lower risk of CVD while the values that lie in the range 0.11-0.21 and above 0.21 are associated with intermediate and increased risks, respectively [28].

Statistical analysis

Data were analyzed using Graph Pad Prism 7 (GraphPad Software, CA, USA). Quantitative data were normally distributed and expressed as mean \pm SD. Correlations between variables were calculated using Spearman correlation analysis. The independent-samples T test was used for comparing the variables and controls. A $p < 0.05$, 0.01 indicated statistical significance.

RESULTS

Serum biochemical markers of the study population

The levels of the various serum biochemical markers in the two groups are shown in Table 1. In diabetic groups, elevation in LDL, cholesterol and triglyceride levels were observed, whereas the levels of vitamin D were lower than the reference value ($p=0.004$). The levels of calcium, albumin and PTH in the T2DM group were lower than that in control ($p=0.002$, $p=0.03$ and $p=0.01$, respectively). While higher levels of creatinine and phosphate were observed in the T2DM group, there were no significant differences in the thyroid hormone levels between the two groups. The prevalence of MetS in the current study samples was present in 150 (75%) diabetic patients based on the diagnostic criteria. In addition, the AIP, was considerably higher in the T2DM group than in the

control group ($p=0.002$) and 55% of study samples with high risk of CVD ($AIP > 0.21$).

Associations between serum biochemical markers and glucose status in type 2 DM patients

Correlations between the serum biochemical markers in patients with T2DM were presented in Table 2. Total vitamin D was negatively correlated with FBG level, and HbA1c ($r=-0.751$, $p=0.001$, $r=-0.642$, $p=0.002$, respectively). Calcium, albumin and PTH were negatively correlated with FBG ($r=-0.531$, $p=0.003$, $r=-0.512$, $p=0.03$, $r=-0.522$, $p=0.02$, respectively), whereas no significant correlation could be observed with HbA1c. Significant positive correlations were also found between FBG levels cholesterol, TAG and LDL-cholesterol (Table 2), but correlation with HDL-cholesterol ($r=-0.521$, $p=0.02$) was negative. Similarly, significant positive correlations were seen between FBG and creatinine and phosphate ($r=0.543$, $p=0.02$, $r=0.493$, $p=0.05$, respectively). A significant positive correlation also found between FBG levels and BMI ($r=0.671$, $p=0.002$). The result indicated a significant positive correlation between FBG level and AIP.

Characteristics of participants by vitamin D status

This study aims to examine whether different vitamin D status could affect metabolic variables in T2DM cases. Patients were divided into three groups based on vitamin D level as the normal, insufficient and deficient vitamin D status on the basis of their serum concentrations as $25(OH)D > 75.00$ nmol/L, between 25.00 and 75.00 nmol/L, and < 25.00 nmol/L, respectively. Significant differences were observed between vitamin D status and some metabolic variables among the three groups (Table 3).

Correlations between metabolic syndrome and its components and levels of vitamin D

As depicted in Table 4, based on correlation coefficient, there was a significant inverse correlation between vitamin D deficiency

Table 1: The biochemical characteristics and other parameters in diabetic Saudi's-females and non-diabetic.

Parameters	Non-diabetic N=150	Diabetic N=200	p-value
Age (years)	39.50 \pm 8.54	50.00 \pm 9.55	-
Duration of diabetes (years)	-	13.2 \pm 9.7	-
FBG (mmol/L)	5 \pm 0.50	12.25 \pm 3.34	<0.001**
HbA1c (%)	3.5 \pm 0.73	9.65 \pm 1.52	<0.001**
LDL-cholesterol (mmol/L)	1.15 \pm 1.3	3.79 \pm 0.85	0.03*
HDL-cholesterol (mmol/L)	1.59 \pm 0.71	0.9 \pm 0.17	0.01*
Total cholesterol (mmol/L)	2.40 \pm 1.10	6.597 \pm 0.97	0.02*
Triglycerides (mmol/L)	1.06 \pm 0.52	2.89 \pm 1.82	0.03*
Weight (kg)	70.05 \pm 10.4	71.80 \pm 10.98	0.15
Length (cm)	155.45 \pm 4.79	155.67 \pm 5.55	0.06
BMI (kg/m ²)	22.4 \pm 3.4	25.35 \pm 6.5	0.06
PTH (ng/L)	37.5 \pm 13.7	10.5 \pm 5.3	0.01**
Ca (mmol/L)	2.30 \pm 0.16	1.5 \pm 0.32	0.002**
Vit D (nmol/L)	13.5 \pm 1.6	10.5 \pm 2.21	0.004**
T4 (mmol/L)	12.5 \pm 0.44	12.4 \pm 0.52	0.08
T3 (mmol/L)	5.8 \pm 1.05	5.5 \pm 1.25	0.07
Creatinine (umol/L)	55.54 \pm 13.11	88.67 \pm 20.14	<0.001**
Phosphorus (mmol/L)	0.90 \pm 0.05	1.78 \pm 1.10	0.002**
Albumin (g/L)	40.14 \pm 1.16	30.14 \pm 2.61	0.03*
AIP	0.11 \pm 0.21	0.21 \pm 0.20	0.002**

Table 2: Correlations between the serum biochemical markers in patients with T2DM.

Parameters	FBG		HbA1c	
	r	p	r	p
LDL-cholesterol (mmol/L)	0.541	0.04*	0.012	0.09
HDL-cholesterol (mmol/L)	-0.521	0.02*	0.321	0.84
Total cholesterol (mmol/L)	0.431	0.05*	0.321	0.1
Triglycerides (mmol/L)	0.573	0.03*	0.364	0.24
BMI (kg/m ²)	0.671	0.002**	0.652	0.03*
PTH (ng/L)	-0.522	0.02*	-0.333	0.07
Ca (mmol/L)	-0.531	0.003**	-0.232	0.1
Vit D (nmol/L)	-0.751	0.001**	-0.642	0.002**
T4 (mmol/L)	0.214	0.67	0.232	0.68
T3 (mmol/L)	0.321	0.43	0.326	0.33
Creatinine (umol/L)	0.543	0.02*	0.122	0.74
Phosphorus (mmol/L)	0.493	0.05*	0.221	0.81
Albumin (g/L)	-0.512	0.03*	0.121	0.66
AIP	0.487	0.02*	0.213	0.75

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table 3: Characteristics of participants by vitamin D status.

Parameters	Severe vitamin DD	Mild vitamin DD	Insufficient vitamin D	p value
Percentage of samples with vitamin D deficiency	60%	30%	10%	-
FBG (mmol/L)	11.12 ± 5.34	9.2 ± 3.34	9.87 ± 3.34	0.04*
HbA1c (%)	9.89% ± 1.53	7.68% ± 1.57	6.9% ± 1.2	0.03*
BMI (kg/m ²)	24.8 ± 6.52	22.6 ± 5.52	21.9 ± 5.5	0.04*
PTH (ng/L)	10.5 ± 5.3	10 ± 4.2	9.5 ± 4.3	0.06
Ca (mmol/L)	1.5 ± 0.32	1.4 ± 0.30	1.4 ± 0.31	0.08
AIP	0.22 ± 0.20	0.20 ± 0.20	0.18 ± 0.20	0.03*

*Correlation is significant at the 0.05 level (2-tailed). Severe vitamin D deficiency <25 nmol/ml, Mild vitamin D deficiency=25-50 nmol/ml, Insufficient vitamin D=50-75 nmol/ml and Normal >75 nmol/ml

(vitamin DD) levels with FBS ($r=-0.534$). BMI and TAG also have a significant inverse correlation with vitamin D deficiency levels ($r=-0.563$, $r=-0.61$). However, there was no correlation with other parameters ($p>0.05$).

Correlation of the biochemical markers based on total vitamin D in type 2 DM

The results of the correlation based on total vitamins D have been illustrated in Table 5. In the T2DM patients, as the level of total vitamin D decreased, the levels of calcium and PTH also decreased, whereas, the levels of cholesterol, TAG and LDL-cholesterol increased. In this study, there was a significant positive correlation between calcium and vitamin D ($r=0.834$, $p=0.002$). Similarly, a significant positive correlation was observed between PTH and vitamin D ($r=0.821$, $p=0.003$). On the contrary, significant inverse correlations of serum vitamin D were seen with the level of cholesterol, TAG, LDL-cholesterol, BMI and phosphate (Table 5). However, there were no correlations of vitamin D with albumin and creatinine levels in T2DM. The results indicate that the prevalence of severe vitamin D deficiency was 60% in diabetic patients with MetS and that there is a significant negative correlation between vitamin D level and AIP for diabetic patients.

Correlation of the biochemical markers based on total Calcium levels in type 2 DM

The associations of Calcium levels (Ca) with different metabolic parameters are shown in Table 6. Serum Ca was negatively associated with triglycerides, cholesterol and BMI, whereas a positive significant association was observed with PTH (Table 6). The Pearson correlation showed a significant and direct association between Ca level and serum albumin level in T2DM group ($r=0.654$, $p=0.003$). However, no correlations were found between PTH and other markers (Table 6).

DISCUSSION

The high prevalence of diabetes in Saudi Arabia has raised concern about vitamin D status, as a number of studies have reported increased vitamin D deficiency in patients with type 2 diabetes mellitus (T2DM) compared to healthy controls [29]. The present study showcases similar findings showing a reduction in vitamin D, Calcium and PTH levels in female diabetic patients in Saudi Arabia. Some studies have suggested that vitamin D normally induces insulin synthesis, protects the pancreatic islets, reduces insulin resistance and hunger and hence controls the progression of T2DM [30]. Moreover, diabetic patients with vitamin D deficiency have hypocalcemia and an increased prevalence of hypoparathyroidism, which was also highlighted in the present study.

Table 4: Correlation between metabolic syndrome components and levels of vitamin D.

Parameters	Severe vitamin DD		Mild vitamin DD		Insufficient vitamin D	
	r	p	r	p	r	p
Number of patients	120		60		20	
FBG(mmol/L)	-0.534	0.021*	-0.521	0.023*	-0.511	0.02*
HDL-cholesterol (mmol/L)	0.212	>0.05	0.231	>0.05	0.251	>0.05
Triglycerides (mmol/L)	-0.61	0.014*	-0.62	0.012*	0.66	0.01*
BMI (kg/m ²)	-0.563	0.031*	-0.543	0.034*	-0.523	0.03*

Table 5: Correlation between different variables and vitamin D levels in diabetic Saudi females.

Parameters	Vitamin D	
	p	r
FBG (mmol/L)	0.001**	-0.751
HbA1c (%)	0.002**	-0.642
LDL-cholesterol (mmol/L)	0.03*	-0.532
HDL-cholesterol (mmol/L)	0.71	0.023
Total cholesterol (mmol/L)	0.021*	-0.543
Triglycerides (mmol/L)	0.031*	-0.565
BMI (kg/m ²)	0.04*	-0.612
PTH (ng/L)	0.003**	0.821
Ca (mmol/L)	0.002**	0.834
T4 (mmol/L)	0.06	0.111
T3 (mmol/L)	0.063	0.212
Creatinine (umol/L)	0.07	0.223
Phosphorus (mmol/L)	0.03*	-0.675
Albumin (g/L)	0.06	0.342
AIP	0.03*	-0.453

**Correlation is significant at the 0.01 level (2-tailed) *Correlation is significant at the 0.05 level (2-tailed)

Table 6: Correlation of different variables with Ca and PTH levels in diabetic Saudi-females.

Parameters	Ca		PTH	
	p	r	p	r
FBG (mmol/L)	0.003	-0.531	0.07	0.421
HbA1c (%)	0.1	-0.232	0.06	0.454
LDL-cholesterol (mmol/L)	0.98	0.011	0.88	0.014
HDL-cholesterol (mmol/L)	0.95	0.021	0.84	0.019
Total cholesterol (mmol/L)	0.024*	-0.545	0.03*	0.645
Triglycerides (mmol/L)	0.032*	-0.531	0.04*	0.753
BMI (kg/m ²)	0.021*	-0.543	0.02*	0.673
PTH (ng/L)	0.003**	0.853		
Vit D (mmol/L)	0.002**	0.834	0.003**	0.821
T4 (mmol/L)	0.81	0.032	0.05*	0.545
T3 (mmol/L)	0.78	0.034	0.05*	0.532
Creatinine (umol/L)	0.05*	-0.532	0.07	0.333
Phosphorus (mmol/L)	0.004**	-0.547	0.02*	-0.632
Albumin (g/L)	0.003**	0.654	0.08	0.342
Ca (mmol/L)			0.003**	0.853

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).

A large number of studies are available that focus on the incidence of diabetes and vitamin D status, while only a few studies have assessed the association of vitamin D status with various pathophysiological, cardio-metabolic, calcium homeostatic and

PTH parameters in diabetic patients [31,32]. Low concentrations of plasma vitamin D have been associated with the progression of diabetes, MetS, obesity, osteoporosis and cardiovascular disease [31,32]. Vitamin D has a negative relationship with glycaemia and

the glycemic component of MetS. This result is in agreement with many group studies and recent meta-analysis showed that there is an inverse relationship of the 25 (OH) D levels with increased threat of type 2 diabetes [33]. Recently, vitamin D deficiency has been associated with the development of diseases like insulin resistance and type 2 diabetes [34]. Diverse studies have confirmed that vitamin D plays a functional role in glucose tolerance by affecting insulin secretion and insulin sensitivity. Our results showed that there is high prevalence of MetS in diabetic females with severe reduction of vitamin D level. Our data suggested that the 25 (OH) D levels are negatively associated with triglyceride levels and BMI, but positively associated with HDL- Cholesterol (a component of MetS). Our work suggests that MetS and AIP are inversely associated with 25(OH) D levels. This result corroborates well with a recent meta-analysis study that displayed that the predominance of MetS decreased with increasing concentrations of 25 (OH) D [34,35]. In addition, some studies have indicated that the predominance of hypovitaminosis D commonly increases in adults suffering with coronary heart disease and heart failure collectively called CVD [36,37]. In the current study, AIP measurement have shown that low 25 (OH) D levels display a negative relation with increased risk of CVD in diabetic females. Furthermore, results from our study indicated that the key features of diabetes dyslipidemia were higher levels of plasma triglycerides, lower levels of HDL cholesterol (HDL-c), and higher levels of LDL in Saudi females with T2DM, suggesting that vitamin D deficiency may be the cause of higher levels of bloodstream lipids. However, another study indicated that obesity may be the cause of low levels of vitamin D [29].

An observational study conducted in 2016 suggested that an association exists between Vitamin D and calcium in type 2 diabetes [26]. It was reported that patients with vitamin D and calcium deficiency, had high levels of blood glucose [26]. However, there are limited and unproven reports suggesting a role of PTH in insulin sensitivity by increasing the release of vitamin D. In addition, a study on patients with type 2 diabetes mellitus showed that vitamin D, calcium and parathyroid hormone levels were reduced in diabetic patients [33]. We found a significant inverse correlation between serum calcium and levels of glucose in T2DM. In our study, individuals with diabetes develop hypocalcemia and hyperphosphatemia with low levels of blood vitamin D that may lead to an increased risk of acute renal failure. This was in agreement with a study done by Fry et al. [38] and reported patients with DM have an increased risk of developing acute renal failure due to hypocalcemia, hyperphosphatemia and hypoalbuminemia [38]. In the present study, it was also revealed that albumin level was statistically decreased significantly in diabetic female patients in comparison to the control group. Abnormalities that relate to calcium and vitamin D homeostasis are widespread in diabetic patients and may be the cause of high morbidity and mortality. Besides, it was observed that T2DM patients have a higher incidence of hypoparathyroidism. This result was similar to the studies done by Takiishi et al. [34] and Sadiya et al. [30] who reported that patients had a reduction in blood PTH levels leading to hypocalcemia in DM patients [26-34]. One possible explanation for this hypocalcemia, hyperphosphatemia and hypoalbuminemia may be the increased urinary excretion of these biomarkers as a result of diabetic nephropathy. Malawadi et al., [39] reported that the glomerular filtration rate was significantly lower in diabetics, suggesting associated nephropathy. It is a well-known fact that diabetic nephropathy is associated with albuminuria; micro albuminuria being the earliest indicator of development of

diabetic nephropathy [38]. Recent study in Saudi Arabia indicated that Blood glucose level, age, and cholesterol level were the most important factors related to vitamin D status. Also, the study population with normal blood glucose and cholesterol level had higher serum vitamin D levels compared to patients with diabetes and hypercholesterolemia. However, Vitamin D deficiency is still chronic issue in Saudi Arabia particularly for patients with diabetes and hypercholesterolemia [40-42].

CONCLUSION

Only a few studies have been published regarding the association of serum vitamin D, calcium and PTH in diabetic patients, and to the best of our knowledge, this is the first study correlating levels of calcium, PTH and vitamin D in T2DM Saudi female patients. We found a significant inverse correlation of serum vitamin D, PTH and calcium with levels of blood glucose in T2DM. Thus, we propose that greater attention is given to serum vitamin D, calcium and PTH during the treatment of diabetic patients, which may reduce the increase the risk of developing diabetes and its complication such as cardiovascular disease.

The major concern is to whether estimate the levels of serum vitamin D and Calcium routinely in all type 2 diabetes patients. Also, whether a cut off value be assigned to serum vitamin D and Calcium so that a good glycemic control is established. The present study is an attempt on the same lines but further studies have to be performed in order to establish specific guidelines in this area.

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