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Vitamin D and its relation to metabolic profile in type 1 diabetic patients from Gaza Strip

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Abstract

Background: Recent research indicated the involvement of vitamin D in the pathophysiology of type 1 diabetes. In this study, we investigated serum vitamin D status and its relation to metabolic profile in type 1 diabetic patients from Gaza Strip.

Methods: This study was a case-control design and included 44 type 1 diabetic patients as well as 44 non-diabetic controls. Patients and controls were matched for age, gender and body mass index (BMI). Data were obtained from questionnaire interview, and biochemical analysis of blood samples.

Results: Serum vitamin D was significantly lower in diabetic patients compared to non-diabetic controls (34.1 ± 19.1 *versus* 43.9 ± 16.9 ng/dl, P=0.012). The number of patients having vitamin D deficient, insufficient and sufficient were 5 (11.4%), 20 (45.5%) and 19 (43.2%) compared to controls of 0 (0.0%), 13 (29.5%) and 31 (70.5%), respectively ($\chi^2_{(corrected)}$=6.711, P=0.035). Serum glucose, glycated hemoglobin (HbA1c), serum insulin, alkaline phosphatase (ALP), cholesterol, triglycerides and low-density lipoprotein cholesterol (LDL-C) were significantly higher in patients than in controls whereas serum calcium was significantly lower in patients. Serum vitamin D showed significant negative correlations with HbA1c (r=-0.258, P=0.015), insulin (r=-0.257, P=0.016) and LDL-C (r=- 0.281, P=0.008) whereas significant positive correlation was found with calcium (r=0.251, P=0.018).

Conclusion: The relationship of vitamin D with HbA1c, LDL-C and calcium suggests that vitamin D and/or calcium system may represent a future target for the design of novel therapeutic strategies for patients with type 1 Diabetes.

Background

Diabetes mellitus is a chronic and complex health condition characterized by hyperglycemia. Two main types of diabetes were identified: type 1 diabetes, associated with lack of or sever reduction in insulin secretion and type 2 diabetes where the cause is a result of both insulin resistance and insulin deficiency [1]. Type 1 diabetes is due to autoimmune or viral destructions of the pancreatic β-cells and usually strikes children and young adults, although disease onset can occur at any age [2]. Patients with type 1 diabetes accounts for 5-10% of diabetes and usually require insulin therapy [3].

In type 1 diabetes where insulin secretion is defective, the combination of increased hepatic glucose output and reduced peripheral tissues uptake leads to elevated blood glucose levels [4]. The increased availability of free fatty acids and ketone bodies exacerbates the reduced utilization of glucose, furthering the ensuing hyperglycemia. Production of ketone bodies in excess of the body's ability to utilize them leads to ketoacidosis [5]. Diabetic ketoacidosis is a state of severe insulin deficiency, with reduced lipoprotein lipase activity as a consequence, as insulin usually stimulates its activity. This reduced enzyme activity leads to profound decreases in triglyceride-rich lipoproteins (chylomicrons, very low-density lipoproteins) catabolism which is, by far, the main factor leading to hypertriglyceridemia [6]. In addition, disturbance in blood electrolytes was also reported in diabetic patients [7].

Vitamin D, a lipid-soluble vitamin, plays an essential role in maintaining skeletal integrity and function. Since foods containing natural vitamin D are rare, the primary source of vitamin D remains its nonenzymatic dermal synthesis through exposure to ultraviolet rays in sunlight [8]. Recently, extraskeletal effects of vitamin D have been recognized, and are now attracting interest of medical and nutritional communities as knowledge emerges of its association with many chronic diseases. Accumulating data showed that vitamin D status is positively correlated with health conditions such as cancer, immunity disorders, diabetes, muscle disorders and cardiovascular disease [9].

In the last decade, special interest has been paid to the involvement of vitamin D in type 1 diabetes. Epidemiologic studies showed that the population in countries with a high prevalence of type 1 diabetes is commonly vitamin D deficient, suggesting a strong relationship of vitamin D with type 1 diabetes [10,11]. Indeed, patients with type 1 diabetes are significantly more likely to have a lower serum vitamin D levels compared to non-diabetics [12]. In this context, global studies revealed a strong positive association of vitamin D with β-cell function [13]. It is hypothesized that vitamin D may have a therapeutic role in type 1 diabetes via its immune-modulatory properties [14]. In Gaza Strip, the published studies on vitamin D and diabetes are rare. To the best of our knowledge, only one study has recently been published on

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vitamin D status in type 2 diabetes [15]. Therefore, this study is the first to assess serum vitamin D and its relation to metabolic profile in type 1 diabetic patients from Gaza strip.

Methods

Study design and study population

The present study is a case-control design. The study population comprised type 1 diabetic patients aged 18-35 years who were referred to various diabetic care units in Gaza Strip (the representative clinics for diabetic patients in Gaza Strip). Patients with type 2 diabetes, pregnant women and patients who take hormone replacement therapy or corticosteroid therapy were excluded. Control group included non-diabetic apparently healthy persons.

Sampling and sample size

Non-probability accidental sample of type 1 diabetic patients, previously diagnosed according to the World Health Organization diagnostic criteria for diabetes [16], were selected as cases from diabetic care units at El-Shifa hospital, Al-Aqsa hospital, the Palestinian medical relief center and Al-Nusairat clinic in Gaza strip. Controls were selected from the general population. Cases and controls were matched for age, gender and BMI. There were no family relationship between cases and controls. The sample size calculations were based on the formula for case-control studies. EPI-INFO statistical package version 3.5.1 was used with 95% CI, 80% power and 50% proportion as conservative and OR > 2. The sample size in case of 1:1 ratio of case control was found to be 41:41. For a no-response expectation, the sample size was increased to 44 patients (22 males and 22 females). The controls also consisted of 44 non-diabetic individuals (22 males and 22 females).

Questionnaire interview and patients' records

A meeting interview was used for filling in the questionnaire which was designed for matching the study requirement for both patients and controls. All interviews were conducted *face to face* by only one investigator. The questionnaire was based on diabetic clinic questions of the Palestinian Ministry of Health with some modifications [17]. Most questions were the yes/no type, which offer a dichotomous choice [18]. The questionnaire was validated, and piloted with 8 individuals not included in the population sample, and modified as necessary. The questionnaire included questions on age, education, employment, family income, family history of diabetes, diet, physical activity, frequent testing of blood glucose level, and insulin injection among the cases (frequency of insulin injection/day and insulin dose). Duration of diabetes and diabetic complications were obtained from the patients' records.

Body mass index

The body weight and height of each individual dressed in light clothing without shoes were measured using a carefully calibrated balance (Detecto, CAP-180 Kg, USA) for weight and a vertical measuring rod for height and the BMI was calculated as Kilogram (kg) body mass/height in meter squared [19].

Blood sampling and processing

Fasting blood samples (about 8 ml each) were collected from patients and controls. About 2 ml blood was placed into EDTA vacutainer tube to perform HbA1c. The remainder quantity of blood (about 6 ml) was placed into a plastic tube and was left for a while without anticoagulant to allow blood to clot. Then, serum samples were obtained by centrifugation at 4000 rpm/10 min using a Rotina 46 Hettich Centrifuge, Japan.

Biochemical analysis

Serum vitamin D was determined by enzyme-linked immunosorbent assay which is designed by Calbiotech, Inc for the quantitation of total vitamin D in human serum and plasma [20]. Anti-vitamin D antibody coated wells were incubated with vitamin D standards, controls, samples, and vitamin D-biotin conjugate at room temperature for 90 min. During the incubation, a fixed amount of biotin-labeled vitamin D competes with the endogenous vitamin D in the sample, standard, or quality control serum for a fixed number of binding sites on the anti-vitamin D antibody. Following a wash step, bound vitamin D-biotin was detected with streptavidin- horseradish peroxidase enzyme (SA-HRP). SA-HRP conjugate immunologically bound to the well progressively decreases as the concentration of vitamin D in the specimen increases. Unbound SA-HRP conjugate was then removed and the wells were washed. Next, a solution of 3,3′,5,5′-Tetramethylbenzidine (TMB) reagent was added and incubated at room temperature for 30 minutes, resulting in the development of blue color. The color development was stopped with the addition of stop solution, and the absorbance was measured spectrophotometrically at 450 nm. A standard curve was obtained by plotting the concentration of the standard versus the absorbance. The glucose oxidase/glucose peroxidase (POD) method was used to measure serum glucose using Labkit Kits, Spain [21]. HbA1C was determined by the colorimetric determination of glycated hemoglobin in whole blood using Stanbio Kit, Texas-USA [22]. Serum insulin was measured by microparticle enzyme immunoassay, using Abbott IMx Insulin assay [23]. Serum cholesterol and triglycerides were measured by the cholesterol oxidase/POD method and by the glycerol phosphate oxidase/POD method, respectively, using the BioSystems kit, Spain [24,25]. High-density lipoprotein cholesterol was determined by the precipitating method using Labkit kit, Spain [26]. Low-density lipoprotein cholesterol was calculated using the empirical relationship of Friedewald [27]. Serum ALP was measured by kinetic photometric test, according to the international federation of clinical chemistry and laboratory medicine, using DiaSys reagent kits [28]. Serum calcium was assayed following instructions of Randox reagent kit manual [29]. Serum phosphorus was determined by phosphomolybdate UV end point, using Amonium Molybdate Diagnostic kit [30].

Statistical analysis

Data were analyzed using the Statistical Package for Social Science Inc., Chicago, IL (SPSS) computer program version 23 for windows. A Simple distribution of the study variables and cross tabulation was applied. Chi-square (χ^2) was used to identify the difference between variables. Yates's continuity correction test, $\chi^2_{(corrected)}$, was used when not more than 20% of the cells had an expected frequency of less than five and when the expected numbers were small. The independent sample t-test procedure was used to compare means of quantitative variables by the separated cases into two qualitative groups such as the relationship between vitamin D levels of controls and patients. The one-way ANOVA test was used for analysis of variance. Pearson's correlation test was applied. The results were accepted as statistically significant when $P<0.05$. The percentage difference was calculated according to the formula: Percentage difference equals the absolute value of the change in value, divided by the average of the 2 numbers, all multiplied by 100.

$$\text{Percentage difference} = (|(V1-V2)| / ((V1+V2)/2)) \times 100.$$

Results

Clinical and socio-demographic aspects

Table 1 showed no significant differences between diabetic patients and controls in terms of age, BMI, education, employment, family income/month and physical activity (P > 0.05). However, family history of diabetes, diet and frequent testing of blood glucose were significantly higher among patients than controls (χ^2=14.012, P<0.001; χ^2=13.477, P=< 0.001 and χ^2=40.994, P<0.001, respectively).

Duration of diabetes, diabetic complications and insulin therapy

As depicted from Table 2, the mean diabetes duration was 9.1 ± 7.0 years; distributed as follows: patients with diabetes<7 years were 25 (56.8%), whereas those with diabetic duration of 7-14 years were 11 (25.0%). The rest of patients 8 (18.2%) had diabetes for more than 14 years. Retinopathy was the only complication found in patients 2 (4.5%). Six (13.6%), 28 (63.6) and 10 (22.7%) patients received one, two and three insulin doses/day, respectively with the mean of 49.4 ± 20.5 UL.cc/ml.

Serum vitamin D and its categories in controls and diabetic patients

Table 3 revealed significant decrease of serum vitamin D in diabetic patients compared to controls (34.1 ± 19.1 *versus* 43.9 ± 16.9 ng/dl, P=0.012). The number of patients having vitamin D deficient, insufficient and sufficient were 5 (11.4%), 20 (45.5%) and 19 (43.2%) with respect to controls of 0 (0.0%), 13 (29.5%) and 31 (70.5%), respectively ($\chi^2_{(corrected)}$=6.711 and P=0.035).

Metabolic profile of controls and diabetic patients

Serum glucose (P<0.001), HbA1c (P<0.001), serum insulin (P=0.001), ALP (P=0.023), cholesterol (P<0.001), triglycerides (P<0.001) and LDL-C (P<0.001) were significantly higher, whereas calcium was significantly lower (P=0.024) in patients than in controls (Table 4). Stratification of vitamin D levels according to glycemic control as judged by HbA1c levels in patients is presented in Table 5. Vitamin D deficient group has the highest levels of HbA1c (F=12.626, P<0.001).

Serum vitamin D in relation to the metabolic profile

As indicated in Table 6, Pearson correlation test displayed significant negative correlations of serum vitamin D with HbA1c (r=-0.258, P=0.015), insulin (r=-0.257, P=0.016) and LDL-C (r=-0.281, P=0.008), while significant positive correlation was found with calcium (r=0.251, P=0.018).

Discussion

Diabetes mellitus is one of the most dangerous and well-recognized chronic disease worldwide as it is a gateway to other diseases. In Gaza Strip, the incidence and mortality rates of diabetes are high: 224.1/100,000 population and 2.71/1000 patients, respectively [31]. Despite that, there is a lack of a proper hospital and clinic recording system of the disease. In addition, research on diabetes has been focused on type 2 and only one recent study suggested a therapeutic value of vitamin D in clinical settings for controlling of type 2 diabetes [15]. Although type 1 diabetes strikes an important segment of society represented by children and young adults, there was no previous study linked such metabolic disorder with vitamin D in Gaza Strip.

Table 1. Clinical and socio-demographic characters of controls and diabetic patients

Character	Controls (n=44)	Patients (n=44)	Test	P-value
Age (year)	28.4 ± 5.4	29.1 ± 6.6	t=0.481	0.632
BMI (kg/m^2)	24.3 ± 3.4	24.8 ± 3.1	t=0.314	0.758
Education University Secondary school Preparatory school Primary school	 26 (59.1) 16 (36.4) 1 (2.3) 1 (2.3)	 23 (52.3) 13 (29.5) 7 (15.9) 1 (2.3)	χ^2=3.845	0.279*
Employment Yes No	 12 (27.3) 32 (72.7)	 18 (40.9) 26 (59.1)	χ^2=1.821	0.177
Family income/month (NIS) < 1000 1000-2000 > 2000	 5 (11.4) 4 (9.1) 35 (79.5)	 6 (13.6) 9 (20.5) 29 (65.9)	χ^2=1.621	0.445*
Family history of diabetes Yes No	 19 (43.2) 25 (56.8)	 36 (81.8) 8 (18.2)	χ^2=14.012	< 0.001
Diet Yes No	 10 (22.7) 34 (77.3)	 27 (61.4) 17 (38.6)	χ^2=13.477	< 0.001
Physical activity Yes No	 21 (47.7) 23 (52.3)	 14 (31.8) 30 (68.2)	χ^2=2.325	0.127
Frequent testing of blood glucose Yes No	 8 (18.2) 36 (81.8)	 38 (86.4) 6 (13.6)	χ^2=40.994	< 0.001

kg: kilogram, m: meter, BMI: body mass index: People with BMI=18.5-24.9 were considered to have normal weight [19].
NIS: new Israeli Shekel (~ 0.27 $US).
Values are n (%) except age and BMI where values are expressed as means ± SD.
*P-value of $\chi^2_{(corrected)}$ test, P < 0.05: Significant, P > 0.05: not significant.

Table 2. Duration of diabetes, diabetic complications and insulin therapy in patients (n=44)

Item	No.	%
Diabetes duration (year) < 7 7-14 >14	 25 11 8	 56.8 25.0 18.2
Mean duration ± SD (year)	9.1±7.0	
Retinopathy Yes No	 2 42	 4.5 95.5
Insulin injection/day One dose Two doses Three doses	 6 28 10	 13.6 63.6 22.7
Dose /day ± SD (UL.cc/ml)	49.4 ± 20.5	

Table 3. Serum vitamin D and its categories in controls and diabetic patients

Category	Controls (n=44)	Patients (n=44)	Test	P-value
Vitamin D (ng/dl) *(min-max)*	43.9 ± 16.9 *(19-82)*	34.1 ± 19.1*(7.2-72)*	t=2.584	0.012
Deficient (< 10 ng/dl)	0 (0.0)	5 (11.4)	χ^2=6.711	0.035
Insufficient (10-30 ng/dl)	13 (29.5)	20 (45.5)		
Sufficient (>30 ng/dl)	31 (70.5)	19 (43.2)		

Values are n (%) except vitamin D where values are expressed as means ± SD.
P-value of $\chi^2_{(corrected)}$ test.
P < 0.05: Significant.

Family history of diabetes, diet and testing of blood glucose were more frequent in patients than controls. It is well-accepted that family history is associated with type 1 diabetes [32,33]. In this regard, Alhonen and his colleagues concluded that type 1 diabetes not only cluster in the nuclear families of children with type 1 diabetes but is

Table 4. Metabolic profile of controls and diabetic patients

Category	Controls (n=44)	Patients (n=44)	% Difference	*t*-test	P-value
Glucose (mg/dl)	75.0 ± 14.4	212.2 ± 101.2	95.5	7.097	< 0.001
HbA1c (%)	5.9 ± 1.2	7.7 ± 1.8	26.5	5.863	< 0.001
Insulin (µIU/ml)	13.0 ± 12.9	23.4 ± 16.4	-57.1	3.311	0.001
ALP (U/L)	116.6 ± 42.5	164.2 ± 129.6	33.9	2.317	0.023
Cholesterol (mg/dl)	152.9 ± 30.7	197.0 ± 45.6	25.2	5.318	< 0.001
Triglycerides (mg/dl)	94.0 ± 51.3	142.1 ± 63.5	40.7	3.916	< 0.001
HDL-C (mg/dl)	57.7 ± 12.8	57.1 ± 23.0	-1.1	0.149	0.882
LDL-C (mg/dl)	56.5 ± 24.6	88.5 ± 50.6	44.1	3.770	< 0.001
Calcium (mg/dl)	9.38 ± 0.56	9.04 ± 0.41	-3.7	2.293	0.024
Phosphorus (mg/dl)	4.21 ± 0.91	4.32 ± 0.1.14	2.6	0.441	0.659

HbA1c: Glycated hemoglobin, ALP: Alkaline phosphatase, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol.
Values are expressed as means ± SD.
P < 0.05: Significant, P > 0.05: not significant.

Table 5. Stratification of vitamin D levels according to glycemic control as judged by HbA1c levels in patients

Category of vitamin D	Patients No.	HbA1c mean±SD (min-max)	F	P-value
Deficient (< 10 ng/dl)	5	10.6 ± 3.1 (5.5-13.3)	12.626	< 0.001
Insufficient (10-30 ng/dl)	20	7.0 ± 1.1 (5.4-9.8)		
Sufficient (>30 ng/dl)	19	7.8 ± 1.1 (6.0-9.5)		
Total	44	7.7 ± 1.8 (5.4-13.3)		

HbA1c: Glycated hemoglobin.
Values are expressed as means ± SD.
P < 0.05: Significant.

Table 6. Serum vitamin D in relation to the metabolic profile

Parameter	Serum vitamin D (ng/dl)	P-value
	Pearson's correlation (r)	
Glucose (mg/dl)	-0.155	0.149
HbA1c (%)	-0.258	0.015
Insulin (µIU/ml)	-0.257	0.016
ALP (U/L)	-0.145	0.177
Cholesterol (mg/dl)	-0.178	0.097
Triglycerides (mg/dl)	-0.114	0.289
HDL-C (mg/dl)	0.128	0.234
LDL-C (mg/dl)	-0.281	0.008
Calcium (mg/dl)	0.251	0.018
Phosphorus (mg/dl)	-0.153	0.322

HbA1c: Glycated hemoglobin, ALP: Alkaline phosphatase, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol.
The correlation was analyzed using Pearson's correlation coefficient (normally distributed data).
P < 0.05: Significant, P > 0.05: not significant.

also overrepresented in their extended families [34]. Diet and testing of blood glucose are important in the management of people living with diabetes. However, the specific types of diet were not assessed. A beneficial relationship exists between frequency of blood glucose monitoring and lower HbA1c in pediatric patients with type 1 diabetes [35].

The result that more than half of patients (56.8%) had diabetes for 7 years or less may imply that type 1 diabetes affects young individuals. It is well-known that type 1 diabetes usually strikes children and young adults, although disease onset can occur at any age [36]. Retinopathy as a diabetic complication found in this study was previously reported in the literature [37]. About two-thirds of the patients received two insulin doses/day. Such a relatively intense insulin therapy was observed in type 1 diabetic patients [38]. Irrespective of this finding, intense insulin therapy is aimed at improving metabolic control in patients with type 1 diabetes [39]. The mean insulin dose treatment/day in this study (49.4 ± 20.5 UI.cc/ml) was around the treatment dose of 43.2 ± 12.8 UI.cc/ml in type 1 diabetic Japanese patients [40].

Serum vitamin D was significantly lower in patients than controls. When categorized, the number of patients having vitamin D deficient and insufficient was significantly higher with respect to controls. The possibility of vitamin D deficiency/insufficiency has been explored before in larger cohorts of patients with type 1 diabetes of different ethnic origins. Whereas some of these studies do find a higher prevalence of vitamin D deficiency/insufficiency among type 1 diabetic patients from China and Saudi Arabia [12,41], others from Italy and Turkey do not [42,43]. Such discrepancy may be explained in that few if any of these studies analyze data taking into consideration the occupation of the patients, which could be important given the effect of sun exposure. However, this point was beyond the scope of the present study. Nevertheless, Tomasello and his colleagues concluded that vitamin D supplementation in early childhood may offer protection against the development of type 1 diabetes [44]. This suggests that hypovitaminosis D may play a critical role in the development of autoimmune diseases such as type 1 diabetes. The underlying proposed pathogenesis is that vitamin D deficiency promotes β-cells destruction by immune

system attacks, directly by its action on β-cells or indirectly by acting on different immune cells [45]. The detection of vitamin D receptors (VDR) in most cells of the immune system as well as in pancreatic cells may support this idea and led to the suggestion of a potential role for vitamin D as an immuno-and/or β-cell modulator [46]. Vitamin D may also promote morphological improvement in pancreatic islet cells, decrease apoptosis, reduce inflammation, and have nongenomic effects mediated by messenger VDR [47,48].

Serum glucose, HbA1c, serum insulin, ALP, cholesterol, triglycerides and LDL-C were significantly higher in patients than in controls whereas serum calcium was significantly lower in patients. Similar results were documented in the literature including Arab countries such as Egyptian and Algerian population [49-51]. The levels of HbA1c in the blood reflect the glucose levels to which the erythrocyte has been exposed during its lifespan [52]. Therefore, the HbA1c test is attractive as it measures chronic glycaemia, rather than instantaneous blood glucose levels and is relied on for initiation of insulin therapy [53]. Hyperinsulinemia could be a consequence of intense insulin therapy accompanied with insulin resistance which is a prominent feature of patients with type 1 diabetes and involves hepatic, peripheral and adipose tissues [54]. In such condition, alteration in ALP activity and disturbance of lipid metabolism would be expected. A defect in LDL-C uptake by cells was reported in low levels of vitamin D [55]. The observed hypocalcaemia in diabetic patients may be associated to renal impairment and/or low levels of blood vitamin D, an enhancer of intestinal calcium absorption [56,57].

When related to serum vitamin D, HbA1C, insulin and LDL-C showed significant negative correlations with vitamin D. Conversely, a significant positive correlation was found with calcium. In this context, vitamin D-deficient diabetic group has the highest levels of HbA1c. These findings are in agreement with that obtained by other authors [58,59]. A poor glycemic control may affect directly on vitamin D metabolism and activity [60] and/ or vitamin D has an indirect role via regulation of calcium homeostasis on various mechanisms (like pancreatic beta-cell dysfunction, impaired insulin action and systemic inflammation) related to the pathophysiology of type 1 diabetes [61]. However, this needs further investigation as . The inverse relationship of vitamin D with HbA1c and LDL-C may indicate that it is the long-term abnormal carbohydrate and lipid metabolism of type 1 diabetes that may be associated with hypovitaminosis D. Therefore, supplementation of vitamin D may be useful in the improvement of glycemic control and dyslipidemia in type 1 diabetes. Hence, one can say that vitamin D could be of clinical relevance in glucometabolic control in type 1 diabetes [62]. In another study, vitamin D supplementation did not improve glycemic control in type 2 diabetes [63]. Irrespective of this controversial outcomes, public health message on the importance of vitamin D status; especially in diabetic children and adolescents, should be disseminated to the public. The direct relationship of vitamin D deficiency with hypocalcaemia suggests the inseparable involvement of both metabolic alterations in the pathogenesis of type 1 diabetes and implies the efficient role of vitamin D in intestinal calcium absorption. Consequently in addition to vitamin D implications in the control of type 1 diabetes, the strategy of calcium therapy should not be ruled out. In this regard, further research is required on the status of calcium and its relation to the metabolic profile in type 1 diabetes.

Conclusions

Serum vitamin D was significantly lower in diabetic patients compared to non-diabetic controls. Serum glucose, HbA1c, serum insulin, ALP, cholesterol, triglycerides and LDL-C were significantly higher in patients than in controls whereas serum calcium was significantly lower in patients. Serum vitamin D showed significant negative correlations with HbA1c, insulin and LDL-C whereas a significant positive correlation was found with calcium.

Declarations

Acknowledgments

Not applicable.

Authors' contributions

This work was carried out in collaboration between all authors. Maged Yassin designed the study, wrote the protocol, helped in the statistical analysis and wrote the first draft of the manuscript. Said Alghora managed the analyses of the study and revised the final draft of the manuscript. Inass Elhamalawi performed the experimental work. Mohammed Yasin managed the literature searches. All authors read and approved the final manuscript, and they have taken due care to ensure the integrity of the work.

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Availability of data and materials

All data and materials are fully available and are shown within the manuscript.

Ethical Consideration

The research was undertaken according to the Declaration of Helsinki and after the Local Research Ethics Committee had approved the study (No. 14/991). All participants provided written informed consent prior to the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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