Original article

Evaluation of vitamin D level in Sudanese diabetic patients at Shendi locality, Sudan

Suha Elrayah E. **Alaraky**[1], Mosab O. **Khalid**[1], Haghamad **Allzain**[2,*], Khaled H. **Bakheit**[3]

1. Department of Clinical Chemistry, Faculty of Laboratory Sciences, Shendi University, Shendi, Sudan
2. Department of Biochemistry, Faculty of Medicine, Shendi University, Shendi, Sudan, *hajhamad@ush.sd*
3. Department of Biochemistry, Faculty of Medicine, King Abudaziz University, Jeddah, KSA

Abstract

Vitamin D is a steroid pro-hormone that enhances bone calcification and reduces the risk of cancer, especially of colon, prostate and breast. It is also considered as the environment and genetic risk-modulating factor for diabetes especially in young people and in those living in high altitude near earth poles. This study was conducted at Shendi Locality, Sudan; from April to August 2018, to evaluate the level of vitamin D among diabetic patients. Sixty males and females were enrolled in the study. Forty were diabetics as cases and 20 healthy non-diabetics as a control group. Findings showed a significant decrease in mean vitamin D levels in diabetic patients compared to the control group, 73.4 ± 22.9 and 19.9 ± 9.7nmol/L respectively. A positive impact of sun light exposure on vitamin D level (P = 0.001) and the negative effect of age and duration of the disease, P = 0.001 and 0.030 respectively, were found. In conclusion, vitamin D level is decreased in diabetic patients, with significant variation between vitamin D level with age, duration of the disease and sun light exposure, and insignificant variation with hypertension and glycemic status of diabetic patients.

Keywords: Vitamin D, diabetes mellitus.

Introduction

Vitamin D (Calciferol) is a steroid compound that can be obtained from food, but most people achieve their vitamin D needs by endogenous synthesis through direct ultraviolet B-mediated synthesis in the skin. Vitamin D is converted to the active form (1,25(OH) 2D) by two hydroxylation steps in the liver and kidney [1,2]. Most vitamin D compounds are protein-bound, mostly to vitamin D binding protein (DBP), although albumin and lipoproteins contribute to lesser degrees [3]. The 1,25(OH)2D, is transported by the DBP to nuclear vitamin D receptor (VDR) and exerts its effects mainly by activating it, and leads to the transcription and regulation of over 200 genes. The discovery that VDR's are widely expressed in the immune system led to the recognition of the central immune-modulatory role for 1,25(OH)2D and the discovery of VDR in the pancreatic cells led to the recognition of the role of vitamin D in insulin production and secretion [4]. Vitamin D insufficiency is suspected as a potential environmental and genetic risk factor for type 1 diabetes mellitus (T1DM). Serum 25(OH)D is considered to be the best biochemical marker of vitamin D status as it reflects both the amount taken in the diet and that produced in the skin in response to UVB radiation exposure. Most agree that a 25(OH)D concentration <50nmol/L is an indication of vitamin D deficiency, whereas a 25(OH) D

concentration of 51-74nmol/L, is considered to indicate insufficiency and concentration of 75nmol/L is considered to be sufficient.

Healthy adults and children can obtain enough vitamin D by being exposed to sunlight in the face and hands for 2 hours per week. However elderly, dark-skinned, pregnant women, breastfeeding women and early childhood are more at risk of becoming vitamin D deficient, therefore, they may need extra food supplementation to keep normal serum levels of 25(OH)D [5]. The lack of sun exposure is known to be the primary cause of low serum 25(OH)D. However, as stated earlier even with adequate sun exposure low serum 25(OH)D levels can be found [6].

Vitamin D deficiency often runs in families, VDR polymorphisms have been associated with an increase in the susceptibility to T1DM in Caucasians, in Bangladeshi Indians, and Japanese. T1DM is a chronic progressive autoimmune disease that affects genetically prone individuals. The autoimmune process is an inflammatory response targeted specifically the B-cells in the islets of Langerhans, causing their mass reduction and dysfunction [7]. Progression of T1DM has been shown to involve infiltration into pancreatic islet cells by several types of immune cells including antigen-presenting cells, CD4+, and CD8+ T cells, and B cells.

There is suggestion of possible physiological role for 1,25(OH)2D in the immune system, with a tightly regulated secretion of 1,25(OH)2D by macrophages and dendritic cells upon immune stimulation on the one hand and a direct inhibitory effect of the molecule on antigen presentation and T cell proliferation and cytokine secretion on the other hand. These immune effects are typically mediated through the binding of 1,25(OH)2D to VDR since these receptors are present in all of these immune cells [1,8].

Recent evidence has shown that vitamin D could also be an environmental or genetic factor that may play a role in the pathogenesis of T2DM [9,10].

Polymorphismson DBP and 1α-hidroxylase genes have been suggested to affect the availability of active vitamin D forms in β-cells and insulin secretion [11]. For glucose intolerance and T2DM to develop, defects in pancreatic B-cells function, insulin sensitivity, and systematic inflammation are often present. Evidence has been found that vitamin D has a role in all of these mechanisms.

Vitamin D may affect insulin sensitivity either, by stimulating the expression of insulin receptor or via its role in regulating extracellular calcium and ensuring normal calcium influx through cell membranes and adequate intracellular cytosolic calcium pool, which is essential for optimal insulin-mediated functions in insulin-responsive

tissues such as skeletal muscle and adipose tissue. Vitamin D is also essential for normal insulin release in response to glucose. when 1,25(OH)2D binds to the nuclear VDR, which is found in a variety of tissues, including the pancreatic islet β-cells. It is a master regulator of transcription and is shown to activate the protein biosynthesis in pancreatic islets, therefore, increasing the insulin secretion. Vitamin D through regulating extracellular calcium and its flux through the β-cell affects insulin secretion in response to glucose. Vitamin D may improve insulin sensitivity and promote β-cell survival by directly modulating the generation and effects of cytokines. Vitamin D is reported to down-regulate the production of several cytokines [11].

This study intended to evaluate the vitamin D level in Sudanese diabetic patients in Shendi Locality according to sun light exposure, age, gender, duration of diabetes, and glycemic status, to fill existence gap in the knowledge and to foster the present one to enhance prevention and treatment of the disease.

Materials and methods

This study was conducted in Shendi Locality, Sudan, from April to August 2018. Included 40 diabetic patients and 20 healthy individuals as control. Those on vitamin D supplementation and with any disease that affects vitamin D levels were excluded.

After consent was obtained, data was collected using a structured questionnaire. Venous blood samples of 6ml were collected from each participant through venipuncture technique then 2ml were placed into fluoride oxalate container for glucose estimation, 2 ml in a plain container for vit D measured by Ichroma and 2ml in EDTA container for HbA1c.

Informed consent was attached to each questionnaire to be declared verbally to each patient. Blood specimens were centrifuged at 3000 rounds per minute for five minutes to obtain the serum which was gently collected into a plain container and stored at -20 ºC until the analysis. Glucose measurement was done using Reagent kit glucose hexokinase (COD 11656) from Biosystem reagents & industries (C/Costa Brava 30 08030 Barcelona (Spain) by Spectrophotometer. Ichroma™ HbA1c is a fluorescence immunoassay (FIA) for the quantitative determination of HbA1c (Hemoglobin A1c) in human whole blood. The instrument for Ichroma™ tests displays the content of glycated hemoglobin in terms of percent of the total hemoglobin in the blood. Vitamin (D) was measured using Ichroma™ vitamin D; it is a fluorescence immunoassay (FIA) for the quantitative determination of total 25(OH) D2\D3 level in human serum\plasma.

The study was approved by the Research Ethical Committee of the Faculty of Medical Laboratory Science, Shendi University.

Data was analyzed using the statistical package for social sciences (SPSS) for Windows, version 21. Pearson Chi-Square test was used for categorical data with *P*-value ≤ 0.05 as significant. Analysis of variance (ANOVA) was used for continuous data and the statistical results were displayed as means ± SD.

Results and discussion

This study showed that Vitamin D level decreases in diabetic patients compared to non-diabetics. The mean vitamin D level in the case and the control groups was 73.4 ± 22.9 and 19.9 ± 7.9 respectively, which was statistically significant (*P* = 0.000). This finding is in line with a previous report from Bahrain that low vitamin D level, mean 38.5 found in 101 of diabetic patients [12], likewise, a result from India that low vitamin D, mean 16.9 found in 48 cases [13].

When the relationship between vitamin D levels in diabetic patients concerning the duration (in years) of diabetes was evaluated (Table 1), vitamin D decreases with increasing duration of diabetes, which was statistically significant (*P* = 0.030). Regarding the level of vitamin D with the three age groups of diabetic patients (Table 2), a significant decrease level with increasing age was found (*P* = 0.010). There was age-related changes that affect vitamin D metabolisms such as declined renal function and consequence increase in the requirement for vitamin D in the elderly, but there was no proof evidence for the causative role yet established [14].

Table 1. Duration of diabetes in years with a mean of vitamin D levels

Duration of diabetes	No.	Mean	*P*-value
> 8 yr	16	23.7 ± 10.0	
8 – 16 yr	16	17.9 ± 5.0	0.030
< 16 yr	8	16.4 ± 4.7	

Table 2. Diabetics age groups with a mean of vitamin D levels

Age groups	No.	Mean	*P*-value
> 35 yr	14	24.8 ± 10.3	
35-45 yr	3	17.9 ± 4.9	0.010
< 45 yr	23	17.2 ± 4.7	

Considering the gender variation, a significantly higher level of vitamin D was found in females compared with males (*P* = 0.010), with a mean of 22.8 ± 5.0 and 16.8 ± 10.0) respectively. This finding contradicts other findings as females might generally have decreased cutaneous synthesis due to being homebound, having darker skin pigmentation, or due to covering their skin [15]. The explanation for this difference might be due to more sun exposure of excellent quality as the area is less polluted, especially in rural areas as women were less homebound. This gender difference requires more research in the future to identify possible underlying factors. The study demonstrated a positive impact of sun exposure on vitamin D level with mean

levels of 13.5 and 22.8 for short and long time of sun exposure respectively ($P = 0.001$).

Concerning glycemic status, hypertension and compliance with diabetic medication, the study showed no significant difference in vitamin D level (Table 3), which did not agree with a previous finding that a significant association of vitamin D and glycemic control as regards to HbA1c and fasting plasma glucose [13].

Table 3. $HbA1_C$ % with a mean of vitamin D levels

$HbA1_C$%	No.	Mean	*P*-value
7 – 10	19	19.7 ± 6.3	0.870
11 – 13	21	20.1 ± 9.3	

In conclusion, vitamin D level differs in diabetics compared to non-diabetics with a positive effect of longer sun exposure and negative effect of increasing age and duration of the disease. Vitamin D intake should be encouraged for diabetics in the form of vitamin D rich food items or nutritional supplements. Besides, exposure to sun light, especially for elderly and chronic patients should be advised.

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