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Vitamin D status Association with newly diagnosed Type2 Diabetes Mellitus: A Case Control Study

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Abstract

Diabetes mellitus is one of the most common metabolic diseases in the world that can affect nearly every organ system in the body. Vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes. The aim of study; to investigate vitamin D level in type 2 diabetes and controls. A retrospective case control study with 47 newly diagnosed diabetic patients aged (35-70 years) and 54 controls matching age±5years and gender. Measuring HbA1c, FBG, assay serum 25(OH) D level were done for patients and/or controls. Results of current study, showed a more severe vitamin D deficiency in newly diagnosed diabetes than controls (46.8% vs.33.3%) and difference between vitamin D level in newly diagnosed diabetes compare to controls was not statistical significant (p=0.108). Conclusion: no statistical significant difference between newly diagnosed diabetes and controls concerning to vitamin D level.

Key words: Diabetes mellitus. Type 2 Diabetes mellitus, Vitamin D, Vitamin D deficiency

Introduction:

Diabetes mellitus is the most common metabolic diseases characterized by hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism; due to the impairment of insulin secretion, insulin action and /or both [1].

Egypt is one of the countries with highest prevalence of diabetes mellitus; it was ranked number Eight globally, as it had over 7.8 million cases diabetes in 2015 [2] and moreover type 2 diabetes mellitus (T2DM) was estimated to increase from 4.4 million in 2007 to 7.5 million in 2013, and it is expected that it will jump to 13.1 by 2035 in Egypt [3-6].

Pathophysiology of T2DM is developed by insulin resistance and impaired pancreatic β-cell function; and it is associated with systemic inflammation [7-13]. Vitamin D deficiency is a global health problem, it was estimated that one billion individuals had vitamin D deficiency in 2008 [14]. 25(OH)D normal level is more than 30 ng/mL (>75 nmol/L),25(OH)D deficiency is < 20 ng / mL (<50 nmol/ L), and insufficiency level of 25(OH)D is ranged between 21 to 29 ng/ mL (51 to 74 nmol / L) [15,16].

Vitamin D deficiency and T2DM have shared the same risk factors, such as obesity, aging, and sedentary lifestyle [17] and vitamin D has non skeletal role through vitamin D receptors are present in many tissues specially in the pancreas [11,17-20]. So that some studies showed that vitamin D deficiency is associated with incidence of diabetes [21].

Vitamin D stimulus of insulin synthesizing directly by its interaction with 1,25 (OH)2D3-RXR-VDR complex which binds to vitamin D responsive elements found in the insulin gene promoter region to enhance the transcriptional activity of the insulin and insulin secretion [22-24], and indirectly it has regulatory role in the calcium flux through the cell membrane for the secretion of insulin [20, 25, 26] .

Vitamin D improves insulin sensitivity and glucose haemostasis, directly, by it action on vitamin D receptors in both skeletal and adipose tissue, which is peripheral insulin responsive tissue [26, 27], and indirectly, by its inhibited rennin formation and local pancreatic Renin Angiotensin Aldosterone System, whereby Angiotensin II helps the insulin resistance by inhibiting the action of insulin in vascular and skeletal muscle tissue leading to hyperglycaemia [28, 29].

Moreover, vitamin D preserves pancreatic cell function and down regulates inflammation by it having antiapoptotic action is mediated by down-regulating Fas-related pathways (Fas/Fas-L) and modulates the generation and effects of cytokines [26,30], it up regulates the expression of calbindin-D28K found in many tissues including pancreatic β -cell [13,31,32],whereby calbindin-D28K interferes with cytokines generation and inactivates pro-apoptotic-3 [33].

Patients and methods:

Study design and setting:

A Hospital based case - control study was done during the period from December, 2015 to June, 2016. Forty seven newly diagnose type 2 diabetic cases were recruited from family medicine and internal medicine clinics at Fayoum University Hospital

Study population:

Cases definiation:

Inclusion criteria ,Type2 diabetes mellitus in age group (35-70yeasr) were recruited according to criteria of diabetes: HbA1c (≥6.5%), FBG ≥126mg/dL (7.0mmol/L), 2hpp ≥ 200 mg/dL (11.1 mmol/L), a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, and random blood glucose is ≥ 200 mg/dL (11.1 mmol/L) [34].

Exclusion Criteria: patients with type 1 diabetes , pregnant women, patients receiving vitamin D therapeutic dose , comorbid conditions, such as end-stage renal disease or dialysis, which is based on patient history and clinical examinations [35,36].

Controls group:

Fifty four non diabetic controls comparable to cases in age ± 5years and matching in gender were recruited from other clinics (ENT, dermatology, ophthalmology and surgery clinic) at Fayoum University Hospital were recruited according to the following criteria: HbA1c (<5.7%), FBG <110 mg/dl (<6.1 mmol/l), 2hpp <140 mg/dl (<7.8 mmol/L) [34] .

Study tools

An interview questionnaire was used, it contained: sociodemographic data: age, sex, marital status and education level).

Anthropometric measurements: weight and height were assessed by using light clothing and without shoes, and then body mass index [BMI] was calculated by dividing weight in kilograms by the square of height in meters.

Sample collection and processing

All blood samples collected from cases and controls were tested at the clinical pathology laboratory in Fayoum University Hospital. Cases and controls were informed that they should fast at least 8 hours without any caloric intake and blood samples were collected by a well-trained nurse following aseptic precautions using disposal syringe at the family medicine clinic.

Collected 4ml of fasting blood sample were divided to (1ml of blood) evacuated in ETDA vacuum tube for HbA1c assay and the rest 3ml of blood is collected in SSGT vacuum tube then, it is allowed to clot at room temperature (15-25c) and centrifuge for 15 minutes to obtain free serum then (1ml of free serum) is taken to measure FPG and the rest 2ml of serum is collected in separate plastic tubes and stored at (-20c) to assay total 25-OH Vitamin D .

HbA1c was measured by immune- turbidimetry enhanced by latex particles. End point by kites was manufactured by ELITech Clinical Systems SAS-Zone Industrielle-61500SEES, France.

Assay of Total 25-OH Vitamin D by an enzyme link immunosorbent which assays ELISA by Kites manufactured by DRG International, Inc., USA.2014.

FBG was measured by Glucose oxidase (GOD), which catalyses the oxidation of glucose to gluconic acid. The formed hydrogen peroxide (H2O2) is detected by a chromogenic oxygen acceptor, phenol, 4-aminophenazone (4-AP), in the presence of peroxidase (POD) by kites manufactured by SPINREACT, S.A. /S.A.U .

Ethical consideration

Study Approval from the Ethical Review Committee at Ain Sham University was obtained prior of the study (FMASU MD 110/2015), and take written informed Consent was obtained from all participants after the explanation nature of the study and assuring that confidentiality will be maintained throughout the work.

Data Management and Analysis

Data was collected, revised, coded and introduced to a PC. Statistical analysis using the Statistical Package for Social Science(SPSS) ,version 15 was performed.

Chi- Square statistic and fisher's exact test were used to compare nominal and ordinal variable. A "P" value of 0.05 was chosen as the level of statistical significance

Results

As shown in table1, no statistical significant difference was observed between cases and controls as regards age (p=0.279), sex (p=0.727), education (p=0.129) and marital status (p=0.825). Similarly in table 3, there was not statistical significant difference between both groups as regard to BMI (p=0.425)

Table 2 shows that, vitamin D deficiency was higher in newly diagnosed diabetic patient than controls (46.8 vs. 33.3%). No statistical significant difference between vitamin D level in newly diagnosed diabetes compare to controls (p=0.108).

Table1. Sociodemographic data among diabetic patient and healthy controls

Items		Newly diagnosed Diabetes (N=47)		Healthy controls (N=54)		P value
		N	%	N	%	
Age	<40	9	19.1	16	29.6	0.295*
	40-60	32	68.1	35	64.8	
	>60	6	12.8	3	5.6	
Sex	Male	21	44.7%	26	48.1%	0.727**
	Female	26	55.3%	28	51.9%	
Education	Illiterate	23	48.9%	16	29.6%	0.129*
	Prim./Second.	21	44.7%	32	59.3%	
	University	3	6.4%	6	11.1%	
Marital status	Married	38	80.9%	46	85.2%	0.825*
	Divorced	1	2.1%	2	3.7%	
	Widow	7	14.9%	5	9.3%	
	Single	1	2.1%	1	1.9%	

*Fisher exact test ** Chi- Square test

Table 2. Vitamin D level in diabetic patients and healthy controls:

Items		Newly diagnosed Diabetes (N=47)		Healthy controls (N=54)		P value
		N	%	N	%	
Vitamin D status	Normal	13	27.7	26	48.1	0.108*
	Insufficiency	12	25.5	10	18.5	
	Deficiency	22	46.8	18	33.3	

*Fisher exact test

Table 3. Comparison body mass index (BMI) among newly diagnosed diabetic patients and healthy controls

Items		Newly diagnosed Diabetes (N=47)		Health Controls (N=54)		p value
		N	%	N	%	
BMI	Normal	6	35.3	11	64.7	0.425*
	Over weight / obesity	41	48.8	43	51.2	

*Fisher exact test

Discussion

In the current study vitamin D deficiency was observed among 46.8% and 33.3% of cases and controls respectively (p=0.108).

Similarly , kumar et al., 2017 study showed that vitamin D deficiency was higher in type2 diabetic patients than controls (32.1%vs.24.6%) with no statistical significant difference (p=0.31) [37].

The current study results agree with Al-Shoumer et al., 2013 study carried out in Kuwait showed that mean of vitamin D deficiency in diabetic cases higher than controls (25.4±2.1 vs. 21.6±2) and there was not statistical significant difference [38].

In Another study carried out among Saudi women, vitamin D deficiency was higher in diabetic patients subject than healthy controls (83% vs.76%) with no statistical significant difference (p= 0.708)[39].

Additionally, a study conduct in a tertiary referral center in the UK among Asian patients showed that percentage vitamin D deficiency was low among cases as control (13% vs. 19%) moreover there was not statistical significant difference (p=0.336). [40]

Another study carried in Iran showed that prevalence of vitamin D deficiency was higher T2DM patients than controls (82.1% vs.75.6%) but there was no statistical significant difference between both groups as regards to vitamin D level (p=0.75). [41

Also no statistical significant difference between mean level of vitamin D was observed in retrospective study that evaluated the medical records of patients with T2DM and healthy controls in Turkey, 25(OH) vitamin D mean± SD was (21.1±8.6 vs.21.4±11.8) among diabetes patients and controls respectively (p=0.302). [42]

However, several studies have demonstrated statistical significant lower vitamin D level among type2 diabetic patient. In a study conducted at tertiary care hospital in North India 81% of T2DM and 67% of healthy control subjects (p=0.002). [44]

Also in another study carried out in Pakistan among 97 diabetic patient and 93 healthy subjects ,vitamin D insufficiency and deficiency were found among 78% of cases and 29% of controls (p=<0.005). [45]

Similarly A case control studies conducted at the diabetic clinic of the Nkawie Government Hospital in Kumasi, Ghana in 2015 showed that vitamin D deficiency was observed among 92.4% of T2DM cases versus 60.2% of non-diabetic controls (p=<0.0001). [46]

The current study showed that, there was no statistical significant difference between newly diagnosed diabetic subjects and controls group regards to classification of BMI (P=0.425).

Similar results are reported in other studies as Usluogullari et al.,2015 study and Daga et al.,2012 study reported no statistical significant difference concerning to BMI (p = 0.38 vs. 0.518) [42,43]. And another study conducts Saudi Arabian showed no statistical significant difference as regarding BMI [39].

Several explanations of the observed low level of vitamin D among T2DM patients and control group. Could be suggested in the current study although , Egypt is a sunny country decreased sun exposure due to sedentary life and trying to avoid direct contact to sunlight at most of the times ,in additional to inadequate diet may contributed to low vitamin D level among cases and controls.

In addition to high prevalence of overweight and obesity among both groups which may leads to lower level of vitamin D.

Conclusion

There is a discrepancy in the literature regarding the association between low serum vitamin D level and T2DM .the current study showed non statistically significant of vitamin D deficiency level among T2DM subjects than healthy controls (48.8% vs.33.3%). Whether vitamin D status in patient having T2DM has role in the pathogenesis of the diseases needs to be seen in future studies.

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