CORRELATION BETWEEN VITAMIN D3 AND FASTING PLASMA GLUCOSE, A1C AND SERUM LIPIDS IN NON-DIABETIC SUBJECTS

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ABSTRACT

Objective: To study the correlation between vitamin D3 and fasting plasma glucose, haemoglobin A1c, and lipids in non diabetic persons .

Patients and methods: Eighty-eight healthy Saudi females; aged 18 to 50 years were recruited from an endocrine clinic in a tertiary care hospital in southern region of Saudi Arabia.

Exclusion Criteria: Diabetes mellitus, malabsorption, significant cardiac, hepatic, oncologic, renal or psychiatric disease. Use of medications known to affect serum vitamin D3, plasma glucose or lipid profile.

After an overnight fasting blood samples were collected for laboratory measurement of fasting plasma glucose, lipids, haemoglobin A1c (HbA1c) and vitamin D3 [25(OH)D3].

Results: Fasting plasma glucose inversely correlated to vitamin D3 level (*p=0.034)*. No significant correlation was found between vitamin D3 and HbA1c (*p=0.23)* or any of the components of lipid profile.

Conclusion: It seems that vitamin D3 affects glucose homeostasis. The lower the vitamin D3 level, the higher the blood sugar. Vitamin D3 level is not correlated to HbA1c in our study population of non-diabetic females. This may be attributed to age and ethnicity of the study group. Vitamin D3 level is not correlated to fasting lipid profile.

INTRODUCTION

There is an increasing epidemic of T2DM. Development of T2DM results from lack of insulin or inadequate insulin secretion following increases in insulin resistance. Management of the disease and its serious and disabling complications places huge costs upon sufferers and health providers. Thus, measures to reduce the diabetic burden are public health concerns (1).

Similarly, vitamin D deficiency is a highly prevalent condition. Low vitamin D levels have long been known to be associated with bone diseases, such as rickets in children and osteomalacia in adults. However, it has become apparent in recent years that adequate vitamin D levels are also important for optimal functioning of many organs and tissues throughout the body**.** Vitamin D receptors (VDR) exist in almost all tissues. They have been identified in heart and smooth muscles, liver, pancreatic islet β cells, immune cells (2, 3). Pancreatic β cells, and immune cells have been demonstrated to possess the 1 apha-hydroxylase enzyme (4-8), VDR and vitamin D-dependent calcium-binding proteins (CaBP) [9], suggesting a role for vitamin D in insulin secretion (10). Data are also rising about an association between vitamin D deficiency and an increased risk of cardiovascular disease (11).

It is not clear what levels of vitamin D are sufficient for prevention of T2DM. It may be that levels of vitamin D within the normal range for an effect on bone formation and calcium metabolism are too low to reduce the emergence of diabetes mellitus and to improve glucose homeostasis, but a clear minimum level of 25(OH)D_3 needed for slowing the development of diabetes mellitus has not been established.

PATIENTS AND METHODS

Eighty-eight healthy Saudi females were recruited from an endocrine clinic in a tertiary care hospital in southern region of Saudi Arabia. History taking and clinical examination were done for all participants. All were females within the age range of 18 to 50 years. Diabetes mellitus, Chronic renal impairment, chronic liver disease, other chronic illnesses, anemia, pregnancy, lactation and intake of medications that may affect vitamin D3 level, plasma glucose, HbA1c or lipid profile lead to exclusion from the study.

After an overnight fasting, blood samples were collected from all participants for the estimation of biochemical parameters. Vitamin D3, fasting plasma glucose, HbA1c, total cholesterol, low density lipoprotein (LDL-c), high density lipoprotein (HDL-c) and triglycerides were measured. Vitamin D3 was assayed by Cobas e 601 & Elecsys 2010 using liquid chromatograghytandem Mass Spectrometry (12).

Triglycerides, total cholesterol, LDL-c, HDL-c were measured using enzymatic colorimetric method on the Siemens Dimension RXL clinical chemistry system (13, 14). Fasting plasma glucose was determined on Siemens Dimension RXL chemistry analyser using bichromatic (340 and 383 nm) endpoint technique (15). Haemoglobin A1c assays based on the turbidimetric inhibition immunoassay (TINIA) [16].

Reference ranges, total cholesterol: 50-200 milli-gram per deciliter (mg/dl), triglycerides: 30-150 mg/dl, HDL-c: 35-55mg/dl, LDL-c: 100-130mg/dl, HbA1c: 4.5-6%, Vitamin D3: 11-42 nanogram per milliliter (ng/ml).

Statistical analysis:

Collected data were analyzed using the Statistical Package for Social Sciences (SPSS ver. 19). Descriptive statistics (i.e., mean and standard deviation) were applied. Pearson's Correlation Coefficients (r) between study variables were calculated. Significant p-values were considered at <0.05.

RESULTS

The mean age for participants was 35.7±10.7 years, with a mean BMI 33.2±8.3 kg/m^2. Their mean serum vitamin D3 level was 8.8±4.5 ng/ml. Their mean lipid profile values, fasting plasma glucose as well as HbA1c were within normal ranges, as shown in table (1).

Vitamin D3 level was significantly inversely correlated with fasting plama glucose (r=-0.234, p=0.034), while correlations with other biochemical variables were not statistically significant, as shown in table (2).

Table (1) Means and standard deviations (Mean± SD) of different variables

Variable	Number of cases	Mean± SD
Age	88	35.7±10.7
BMI	88	33.2±8.3
Vitamin D3	88	8.8±4.5
Total cholesterol	70	185.3±42.9
HDL-c	44	48.4±15.4
LDL-c	44	117±39.8
Triglycerides	68	118.5±66.6
Fasting plasma glucose	83	96.8±18.9
HbA1c	53	6.1±0.56

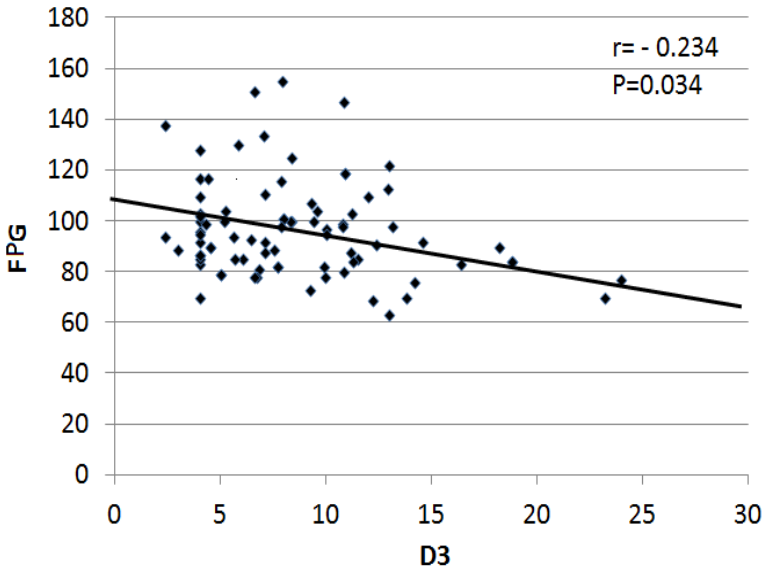
D3: vitamin D3, BMI: body mass index, FPG: fasting plasma glucose, HbA1c: hemoglobin A1c, T-cholesterol: total cholesterol, HDL-c: high density lipoprotein cholesterol, LDL-c: low density lipoprotein cholesterol.

Table (2) Correlation between vitamin D3 and different variables

variable		FPG	HbA1c	T-cholesterol	HDL-c	LDL-c	Triglycerides
D3	r	-0.234	-0.168	-0.123	-0.089	-0.158	-0.009
	p	0.034	0.23	0.311	0.566	0.307	0.94
	n	83	53	70	44	44	68

D3: vitamin D3, FPG: fasting plasma glucose, HbA1c: hemoglobin A1c, T-cholesterol: total cholesterol, HDL-c: high density lipoprotein cholesterol, LDL-c: low density lipoprotein cholesterol, n: number of patients.

Figure (1): shows the inverse correlation between vitamin D3 and FPG



FPG: fasting plasma glucose, D3: vitamin D3

DISCUSSION

In our study vitamin D3 level showed significant negative correlation to fasting plasma glucose (FPG). This is in agreement with several studies which found the same association (17-19). Such negative correlation was also demonstrated in Middle Eastern population by Marie et al (20).

We could not detect a significant correlation between 25(OH)D3 and HbA1c (*p=0.23*). Several reports are available about the correlation between vitamin D3 and HbA1c with variable findings. Jatupol et al found an inverse correlation between vitamin D3 and HbA1c but this was age related as it was evident in the age group of 35-74 years but not in the 18-34 years age group (21). Micah et al did not find significant correlation between vitamin D3 level and HbA1c in obese children (22). Similarly, Earl et al, 2011 found that the concentrations of vitamin D were inversely correlated to concentrations of glucose among Mexican American male adolescents aged 12-17 years (P = 0.007). But, no significant association between vitamin D and HbA1c was detected (23). This is similar to our finding in our study population.

The association between vitamin D3 and HbA1c was weakly observed in a New Zealand study of 250 overweight and obese adults aged more than 18 years (24) where as in another study of 7,198 British Caucasians showed a nonlinear inverse relationship between vitamin D and HbA1C (25). Alemzadeh et al found a significant relationship between 25(OH) and HbA1c in Caucasians but not in African Americans (26). We may conclude from these studies that the association between vitamin D status and HbA1c is age dependent. These studies may also reflect a role of ethnicity in this relationship.

Effect of vitamin D3 on glucose homeostasis may be mediated through its direct action on VDR present in various tissues including the pancreatic islets, or through changes in calcium, or parathyroid hormone (27, 28).

Vitamin D may also reduce insulin resistance by its immunomodulatory and anti-inflammatory effects (29), hence the association between vitamin D deficiency and obesity as well as T2DM (30). Since both DM and obesity, are conditions of increased inflammatory reaction which by its turn increases insulin resistance (31).

Vitamin D reduces apoptosis of ß cells by inhibiting inflammatory reactions (27) and increasing calbindin, a cytosolic calcium binding protein (32).

Vitamin D was also demonstrated to be linked to cardiovascular disease (33, 34). Depending on this, several reports are available about the association between vitamin D and plasma lipids in a trial to approach the mechanism by which vitamin D affects cardiovascular health.

In our study, we did not find a significant association between vitamin D3 level and triglycerides, total cholesterol, LDL-c or HDL-c. In consistence with our report, a cross-sectional study that was conducted by Diana et al who found no significant association between 25(OH)D3 and lipid levels in the studied population (35).

On the other hand, in a study carried out by Guasch et al, there was an association between 25(OH)D3 concentrations and hypertriglyceridemia component of the metabolic syndrome. But, this association could be mediated by inflammation, because it disappeared when highly sensitive c-reactive protein was introduced as a co-variable in the analysis (36).

Presence of variations among several studies may be due to small sample size, different age groups of the studied populations, different ethnicity. Moreover, the analysis derives from only a single measurement of the studied parameters.

Contribution of Vitamin D deficiency to CVD may be explained by the hyperproduction of parathyroid hormone and consequently secondary hyperparathyroidism, cardiomyocyte hypertrophy, ventricular hypertrophy and vascular remodelling. Also, release of cytokines from smooth muscle vascular cells (37). Vitamin D may inhibit vascular calcification by blocking the release of inflammatory cytokines and adhesion molecules and preventing abnormal changes in smooth muscle cells in vessel walls (38). Accordingly, low vitamin D levels may be associated with increased risk for development of the coronary arterial calcifications seen in atherosclerosis (39).

CONCLUSION

Vitamin D3 is inversely correlated to fasting plasma glucose in non-diabetic females. No correlation was detected between vitamin D3 and HbA1c in the studied population. No association between vitamin D3 and serum lipid levels, so effect of vitamin D3 on cardiovascular health as detected in some studies may be due to other mechanisms rather than its effect on lipid profile.

RECOMMENDATIONS

Further studies are highly recommended to investigate the effect of vitamin D3 replacement on prevention of the development of T2DM and cardiovascular disease and to define the effective cut off values for prevention of these extra-bone diseases.

DECLARATION OF INTEREST

The author has no conflict of interest.

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