



Research Article

Association between Vitamin D, Fasting Blood Glucose, HbA1c and Fasting Lipid Profile in Euglycemic Individuals

Vijetha Shenoy, Priyanka Datta, Krishnananda Prabhu and Kriti Singh

Department of Biochemistry, Kasturba Medical College, Manipal University, Manipal, Karnataka, India

Correspondences should addressed to: Vijetha Shenoy; vijethashy@gmail.com

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Abstract

In addition to biological actions of vitamin D such as calcium absorption, regulation of bone and mineral metabolism, studies have shown that Vitamin D is necessary for normal insulin secretion. Vitamin D influences insulin production and secretion through its effect on calcium and phosphorous metabolism. Vitamin D modifies insulin response by acting on receptor gene. Vitamin D deficiency has been implicated in decreased insulin secretion and increased insulin resistance. **Objective:** To measure and correlate vitamin D with fasting plasma glucose, HbA1c and fasting lipid profile in euglycemic individuals. **Methods:** Ethics clearance was obtained prior to data collection. After an overnight fast, blood samples were collected for fasting plasma glucose, lipid profile, HbA1c and vitamin D from euglycemic individuals who consented to participate. Vitamin D assay was estimated in Elecsys 2010 by ECLIA method. Plasma glucose was estimated by Hexokinase method. Serum fasting lipid profile was estimated in Cobas 6000 (Roche), and HbA1c measured using ion exchange HPLC method using Biorad Variant II turbo. **Results:** There was an inverse correlation between vitamin D and fasting plasma glucose ($p < 0.001$); Vitamin D and HbA1c ($p < 0.001$) in groups 1 and 3. There was also a significant inverse correlation of Total cholesterol ($p = 0.05$), total cholesterol / HDL ratio ($p < 0.001$) with Vitamin D and significant direct correlation of HDL with vitamin D levels in groups 1 and 3. **Conclusion:** Deficiency of vitamin D can predispose to dysregulation of glucose and lipoprotein metabolism. There may be a role for vitamin D in better management of diabetes and dyslipidemia.

Key words: Vitamin D, Type 2 Diabetes mellitus, dyslipidemia

Introduction

The nature's own product, an ancient hormone produced in the skin by sun exposure, is Vitamin D. It is hydroxylated by liver to form 25-hydroxy vitamin D [25(OH) D], which is the predominant form of vitamin D in the circulation. (Ponda MP et al 2012) Vitamin D has many biological actions including calcium absorption, regulation of bone and mineral metabolism, muscle strengthening, cellular proliferation and differentiation, immune system modulation, inhibition of rennin synthesis and erythropoiesis etc. (De Luca HF 2004)

Animal studies have shown that Vitamin D is necessary for normal insulin secretion. Vitamin D reduces insulin resistance through regulation of the insulin receptor gene and its effects on calcium and phosphorous metabolism. (Nada AM 2013) Several studies have shown a role of vitamin D in insulin production, secretion and sensitivity. (Kositsawat JMDM et al 2010, Taheri E et al. 2012, Maxwell CS and Wood RJ 2011) Also, vitamin D deficiency has been implicated in decreased insulin secretion and increased insulin resistance which is the hallmark of type 2 diabetes mellitus. Further, type 2 diabetes mellitus and vitamin D deficiency have common predisposing factors such as obesity, less physical inactivity and ageing. (Rodriguez E et al. 2009) Studies have also shown vitamin D supplements in deficient individuals have resulted in improvement in insulin secretion and glucose tolerance. (Cade C and Norman AW. 1986, Bournalon PM, Billaudel B and Faure-Dussert A. 1999, Maestro B et al 2000, Talaei A, Mohamadi M and Adgi Z. 2013)

Cardiovascular disease (CVD) is the most common cause of death and disability in the world as well as in India. Efforts have been made to identify modifiable risk factors to prevent atherosclerosis. There is now increasing evidence through many epidemiological studies that vitamin D deficiency was closely associated with increased risk of major adverse CVD events. (Wang C 2013, Wang TJ et al 2008)

Vitamin D deficiency has been a global public health problem. The goal of this study was to measure and correlate total plasma vitamin D, fasting plasma glucose, glycated hemoglobin (HbA1c) and fasting lipid profile in euglycemic individuals.

Materials and Methods

Study Subjects

274 euglycemic individuals of 30- 75 years age, who visited hospital between March 2013 to July 2013 for general health check up, who satisfy our inclusion criteria were enrolled for this study.

Study Groups

Individuals were divided into three groups according to their plasma vitamin D levels: group 1 (<20 ng/ml), group 2 (20-30 ng/ml), and group 3 (>30 ng/ml)

Exclusion Criteria

Patients suffering from diabetes mellitus, mal-absorption, cancer, pregnant women, patients with cardiac, hepatic, renal, diseases and those on long term medications were excluded from this study.

Ethical Statement

Ethics clearance was obtained prior to data collection from the institutional ethics committee, Kasturba Hospital, Manipal University, Manipal, India. Informed consent was obtained from every participant before their participation.

Sample Collection

Using aseptic precautions, 4ml of fasting venous blood was collected in a syringe. It was equally aliquoted in red, grey and lavender vacutainers. Red capped vacutainers were used for estimation of lipid profile and total plasma vitamin D, grey capped vacutainers were used for estimation of blood sugar and lavender vacutainers were used for estimation of HbA1c.

Methods

Total vitamin D assay was estimated in Elecsys 2010 by ECLIA method. Glucose was estimated by Hexokinase method. Fasting lipid profile was estimated by kit method. All the above parameters were measured in auto analyzer Cobas 6000 (Roche Diagnostics), and HbA1c was measured in BIORAD variant II turbo using ion exchange High performance liquid chromatography method.

Statistical Analysis

Data was compiled and statistical analysis

was done using Statistical Package for the Social Sciences (SPSS) 16.0. Data were expressed as mean± standard deviation. Wherever appropriate, Independent student t test, ANOVA were used. *P* value <0.05 was considered as statistically significant.

Results

Total of 146 males and 128 females participated in this study. The mean age of subjects was 49.89±16.40 years. The general characteristics of the studied population are shown in Table 1.

Table 1: Demographic profile of the subjects

Age Groups (Mean Age)	Males	Females
30-40 (34.7±3.9)	48	32
41-50 (45.8±2.6)	25	29
51-60 (55.3±2.6)	30	35
61-75 (68.8±5.2)	30	45

Groups 1 and 3 showed an inverse correlation between vitamin D and fasting plasma glucose ($p < 0.001$), Vitamin D and HbA1c ($p < 0.001$). We also observed a significant inverse correlation of Total cholesterol ($p = 0.05$), and total cholesterol /

HDL ratio ($p < 0.01$) with vitamin D respectively, and significant direct correlation of HDL with vitamin D levels. Except for triglycerides, other biochemical parameters also showed significant correlation between groups 1 and 2.

Table 2: Correlation of Vitamin D with biochemical parameters

	Group 1 (n=122)	Group 2 (n=77)	Group 3 (n=75)
Name of the biochemical parameter	Mean± Standard Deviation	Mean± Standard Deviation	Mean± Standard Deviation
HbA1c	5.78±0.42	5.55±0.43	5.39±0.39
P value		<0.001*	<0.001*
Fasting Blood Glucose	98.51±11.05	95.54±9.01	91.72±8.64
P value		<0.001*	<0.001*
Total Cholesterol	194±45.90	178±36.99	167±33.83
P value		0.05*	0.001*
Triglycerides	149±56.92	134±60.95	114±38.27
P value		0.253 NS	0.001*
HDL- C	38.41±11.32	46.72±13.79	51.22±11.61
P value		0.001*	<0.001*
LDL-C	115±30.20	102±29.62	93±27.60
P value		0.042*	<0.001*
Total cholesterol/HDL -C ratio	5.25±3.25	3.64±1.21	2.94±1.20
P value		0.001*	<0.001*
Vitamin D	9.93±4.04	23.22±2.15	38.79±9.05
value		<0.001*	<0.001*

NS- not significant *- significant

Table 3: Age wise distribution of biochemical parameters

Groups	Group 1 (30-40 Years)	Group 2 (41-50 years)	Group 3 (51-60 years)	Group 4 (61-75 years)
	Mean±S.D.	Mean±S.D.	Mean±S.D.	Mean±S.D.
Vitamin D	26.14±10.2	22.15±10.8	20.25±9.1	18.5±8.2
Total cholesterol	174.3±31.2	180±25.53	194.9±44.3	180.2±34.6
Triglycerides	123.8±60.0	120.8±49.28	149.6±66.1	127.8±60.8
HDL- Cholesterol	50.1±10.2	48.1±12	45.8±12	48.6±11.2
LDL- Cholesterol	112.6±31.4	120.7±40	114.3±31	103.8±36.58
HbA1c	5.5±0.4	5.6±0.43	5.61±0.41	5.7±0.48
Fasting Blood Sugar	94.24±10.6	94.7±7.5	97.71±12	96.52±8.68

There is no statistically significant difference in biochemical parameters according to different age groups.

Table 4: Correlation of vitamin D with lipid parameters in Males and Females

	male	female
Total cholesterol	r = -0.2	r = 0.03
Triglycerides	r = -0.2	r = -0.1
HDL- Cholesterol	r = 0.2	r = 0.3
LDL- Cholesterol	r = -0.2	r = -0.01
HbA1c	r = -0.3	r = -0.3

In males and females, there was inverse correlation between vitamin D and HbA1c, triglycerides and LDL, and significant direct

correlation of HDL with vitamin D levels. We observed negative correlation in males between vitamin D and total cholesterol but not in females.

Discussion

In this study, vitamin D3 level showed a significant negative correlation to fasting plasma glucose (FPG). This is in agreement with several studies which found the same association (Ken C C et al 2004, Ashraf AP et al 2011, Jessica A A and Ambika A 2010). Such negative correlation was also demonstrated in Middle Eastern population. (Marie-H. G et al 2009). 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. (McGill AT et al 2008) Whereas another study of 7,198 British Caucasians showed a nonlinear inverse relationship between vitamin D and HbA1C (Hyppönen E and Power C 2006). Alemzadeh et al. found a significant relationship between 25(OH) and HbA1c in Caucasians, but not in African Americans (Alemzadeh R et al 2008). From these studies, it is evident that the association between vitamin D status and HbA1c is age dependent. These studies may also reflect a role for ethnicity in this relationship. 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. (Guasch. A et al 2012)

Vitamin D has been shown to have a role in insulin production, secretion and insulin resistance. In recent years, it has become apparent that for optimal functioning of many organs and tissues throughout the body adequate levels of Vitamin D is also important. Vitamin D receptors are identified in heart, smooth muscle, islets cells of pancreas which secrete insulin and immune cells. (Nagpal S and Rathnachalam R 2005, Bikle DD 2003) It has been also demonstrated that Islets cells of pancreas and immune cells possess 1 alpha hydroxylase enzyme required for synthesis of vitamin D, vitamin D receptor and vitamin D dependent calcium binding proteins, suggesting an important role of vitamin D in insulin secretion. (Kajikawa M et al 1999, Bland R et al 2004) Vitamin D circulates in

the bloodstream with its complex proteins particularly lipoproteins. Hormonal form of vitamin D i.e. calcitriol is able to increase the lipoprotein lipase activity in adipocytes resulting in removal of triglyceride enriched with lipoproteins from the blood. Previous studies also showed similar results in diabetic individuals when compared with the non-diabetic individuals. (Potolitsyna NN et al 2011)

Non diabetic individuals with deficient status of vitamin D levels might have greater risk of developing type 2 diabetes mellitus in near future, than individuals with normal vitamin D levels.

Limitation of Study

BMI adjustments for parameters are not done because medical records about height and weight are not available for all patients.

Conclusion

Deficient levels of vitamin D may predispose euglycemic person for diabetes and dyslipidemia. Vitamin D supplements in euglycemic individuals may play an important role in reducing the risk, which requires more studies.

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