Correlation Between Vitamin D_3 and Fasting Blood Sugar in Type 2 Diabetes Mellitus Patients and Normal Individuals in A Bangladeshi Population

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Keywords: Type 2 diabetes mellitus, vitamin D_3, serum 25-hydroxycholecalciferol, fasting blood sugar, insulin resistance

Abstract

Background and Aims: Controversies prevail on association of vitamin D level and type 2 diabetes mellitus. The present study aims to compare serum 25-hydroxycholecalciferol (vitamin D_3) level and fasting blood glucose in type 2 diabetes mellitus patients and healthy subjects and evaluate their association in both groups.

Methods: This cross-sectional, observational study was done in Department of Biochemistry, Sylhet MAG Osmani Medical College, Bangladesh, between July 2015 and June 2016. The patients were selected from medicine out-patients departments (MOPD) of Sylhet MAG Osmani Medical College Hospital and Sylhet Diabetic Hospital, Bangladesh. A total of 135 study subjects were selected following convenient consecutive sampling technique. They grouped into case (Group A) i.e. 65 patients having type 2 diabetes mellitus, and control (Group B), i.e. 70 patients apparently healthy subjects (non-diabetic). Initial evaluation of the patients done by history and clinical examination was recorded in the preformed data collection sheet. Fasting blood glucose was measured by enzymatic method, while serum 25-hydroxycholecalciferol (vitamin D3) was measured by radioimmunoassay (RIA).

Results: The mean age of 42.02±3.29 years in case (Group A); while 41.35±3.97 years in control (Group B). There were 33 male (50.76%) and 32 (49.23%) female in group A, while 35 (50%) male and 35 (50%) female in group B. No significant age difference was observed between the groups (p=0.284). Serum 25-hydroxycholecalciferol in cases (Group A) was 55.73±9.02 ng/ml and in controls (Group B) 53.77±10.86 ng/ml (p=0.255). Fasting blood glucose was 161.98±62.47 mg/dl in cases (Group A) and 86.92±15.74 mg/dl in controls (Group B) (p<0.001). No correlation was found between serum 25-hydroxycholecalciferol and fasting blood glucose in any group: in type 2 diabetic patients (case group) (r=0.010, p=0.943), in healthy controls (r=0.186, p=0.122), and all study subjects together (r=0.095, p=0.268).

Conclusions: Our data suggest that serum 25-hydroxycholecalciferol (vitamin D3) was within optimum level in both type 2 diabetic patients and healthy individuals. However, no correlation was found between serum 25-hydroxycholecalciferol and fasting blood glucose in any group.

Introduction

Type 2 diabetes mellitus (T2DM) is a major global health problem. In 2013, there were 382 million people with diabetes; this number is estimated to grow to 592 million by 2035. The highest prevalence rates of T2DM are found in developing countries[1]. Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance and relative (or absolute) insulin deficiency[2]. In recent years, the influence of vitamin D on diabetes becomes a research interest – many studies paid attention to the relationship between vitamin D and insulin sensitivity and β-cell function. Some described that vitamin D is an important nutritional factor for type 2 diabetes mellitus pathogenesis by modulating insulin receptor gene expression and insulin secretion or through renin- angiotensin aldosterone system[3-6]. Other studies claimed that low vitamin D impairs insulin synthesis, secretion resulting in glucose intolerance especially in type 2 Diabetes Mellitus (T2DM)[7-10]. However, in other studies, any correlations between vitamin D and T2DM were denied[11,12]. Hence, controversies still prevail on association of vitamin D level

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and type 2 diabetes mellitus. To date there is no such reports available in our country in this issue. The question if vitamin D deficiency and type 2 diabetes mellitus are linked together in the country's workforce is still unanswered. 25-hydroxycholecalciferol (vitamin D_3) is the main circulating form of vitamin D in our body and because of its long half-life, it is used as a standard biomarker for the measurements of vitamin D status of any individual[13,14]. Therefore, we proposed this study that aims to assess and compare serum 25-hydroxycholecalciferol (vitamin D_3) level and fasting blood glucose in type 2 diabetes mellitus patients and healthy subjects as well as evaluate their association in both groups in a Bangladeshi population.

Methods

This cross-sectional, observational study was done in Department of Biochemistry, Sylhet MAG Osmani Medical College, Bangladesh, between July 2015 and June 2016. The patients were selected from medicine out-patients departments (MOPD) of Sylhet MAG Osmani Medical College Hospital and Sylhet Diabetic Hospital, Bangladesh. The patients were selected based on the following criteria:

Inclusion criteria:

1. Patients diagnosed with type 2 diabetes mellitus as cases, and
2. Normal adult healthy subjects (non-diabetic) as controls.

Exclusion criteria:

1. Known case of any acute or chronic liver and kidney disease;
2. Known case of any malignancy;
3. Pregnant women;
4. Patients who use any drugs containing vitamin D or interfere with vitamin D metabolism, e.g. carbamazepine, sodium valproate, isoniazid, calcitonin etc.

A total of 135 study subjects were selected following convenient consecutive sampling technique. They grouped into case (Group A) i.e. 65 patients having type 2 diabetes mellitus, and control (Group B), i.e. 70 patients apparently healthy subjects (non-diabetic). Cases are type 2 diabetic patients as per criteria of the American Diabetes Association[2]. Initial evaluation of the patients done by history and clinical examination was recorded in the preformed data collection sheet. Demographic profile, pulse, blood pressure, height, body weight, waist circumference - all were recorded. History of hypertension, smoking, previous illness and obesity were noted. Detailed drug history was also taken. After 10-12 hours overnight fasting, venous blood samples were collected to measure fasting blood glucose and vitamin D levels. Fasting blood glucose was measured by conventional glucose hexokinase enzymatic method. Serum 25-hydroxycholecalciferol (vitamin D_3) was measured by radioimmunoassay (RIA) in a two-step procedure, with coefficient variation of intra-assay <8% and interassay <10%. The first step involved rapid extraction of vitamin D_3 and other hydroxylated metabolites from serum or plasma with acetonitrile. Following extraction, the treated samples were assayed by competitive RIA using an antibody with specificity to vitamin D_3. The sample, antibody and tracer were incubated for 90 min at 20-25°C. We used widely accepted cut-off values for levels of D_3, as stratified according to the classification of the Endocrine Society's Clinical Guidelines[14]: deficiency (<20 ng/ml), insufficiency (20–29 ng/ml) and sufficiency (≥30 ng/ml).

Quantitative data expressed as mean and standard deviation. Comparison between groups was done by unpaired Student 't' test, while correlation was done by Pearson's correlation test. A probability value (p) of <0.05 was considered statistically significant. Data was analyzed using 'R' Statistical Package version 2.7.

The research was approved by the Ethical Committee of Sylhet MAG Osmani Medical College, Bangladesh.

Results

In the present study, age of the participants ranged from 35 to 50 years, with the mean age of 42.02±3.29 years in case (Group A or diabetic group); while 41.35±3.97 years in control (Group B or non-diabetic group). No significant difference was observed between the groups (p=0.284). There were 33 male (50.76%) and 32 (49.23%) female in group A, while 35 (50%) male and 35 (50%) female in group B (Table 1). Serum 25-hydroxycholecalciferol in cases (Group A) was 55.73±9.02 ng/ml and in controls (Group B) 53.77±10.86 ng/ml. No significant difference was found between the groups (p=0.255) (Table 2). Fasting blood glucose was 161.98±62.47 mg/dl in cases (Group A) and 86.92±15.74 mg/dl in controls (Group B). Significant difference was found between the groups (p<0.001) (Table 2). There was no significant correlation of serum 25-hydroxycholecalciferol with fasting blood glucose in any group: as found in type 2 diabetic patients (case group) (r=0.010, p=0.943), in healthy controls (r=0.186, p=0.122), and as per all study subjects together (r=0.095, p=0.268) (Table 3, Fig. 1).

Table 1. Distribution of study subjects based on age and sex (n=135)

Parameters	Study group		
	Group A (Cases) (n=65)	Group B (Controls) (n=70)	p value
Age (in years) Mean±SD	42.02±3.29	41.35±3.97	0.284
Male	33 (50.76%)	35 (50%)	
Female	32 (49.23%)	35 (50%)	

Figures in the parentheses indicate percentage. Unpaired Student 't' test was applied to reach the p value.

Table 2. Biochemical parameters in study subjects

Parameters	Cases or Diabetic group	Controls or Non-diabetic group (n = 70) (Mean ± SD)	p value
25-hydroxycholecalciferol (ng/ml)	55.73±9.02 (33.1-79.5)	53.77±10.86 (31.5-74.5)	0.255
Fasting blood glucose (mg/dl)	161.98±62.47 (80-371)	86.92±15.74 (64-115)	<0.001

Figures in the parentheses indicate range. Unpaired Student 't' test was applied to reach the p value.

Table 3. Correlation of Serum 25-hydroxycholecalciferol (vit D_3) with Fasting Blood Glucose

Group	Independent Variable	Dependent Variable	r	p
Group A Cases or Diabetic group (n=65)	Serum 25-hydroxy cholecalciferol	Fasting blood sugar	0.010	0.943
Group B Controls or Non-diabetic group (n=70)			0.186	0.122
All study subjects (n=135)			0.095	0.268

Pearsons's correlation test was done. Correlation was significant at the 0.05 level.

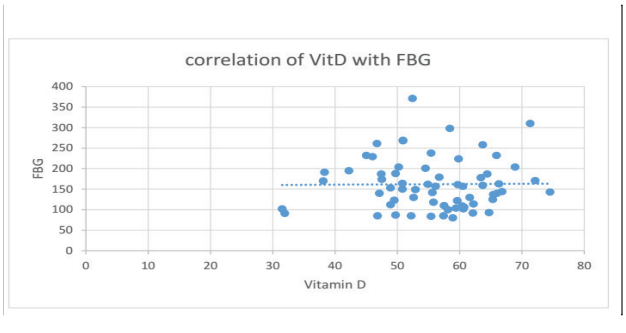

Fig. 1. Correlation of vitamin D3 with fasting blood glucose (n = 135)

Discussion

This study evaluated serum 25-hydroxycholecalciferol (vitamin D3) and fasting blood glucose status in Type 2 Diabetes Mellitus (T2DM) patients. In this study, the mean age of T2DM patients (Group A or diabetic) was 42.02±3.29 years and age of the healthy controls (Group B or non-diabetic) was 41.35±3.99 years. There was no significant age difference between two groups. However, this result is similar to the study of Al-Timimi & Ali[15], and Alhumaidi, Agha & Dewish et al.[16].

Fasting blood glucose was found 161.98±62.47 mg/dl in cases (Group A) and 86.92 ±15.74 mg/dl in controls (Group B). Significant difference between the groups was observed in the study. Our findings are similar to the results of Al-Timimi & Ali[15], Alhumaidi et al.[16], and Hidayat et al.[17]. Higher fasting blood glucose of the T2DM patients despite treatment indicates uncontrolled diabetes.

Serum 25-hydroxycholecalciferol in cases (Group A) was 55.73±9.02 ng/ml and in controls (Group B) 53.77±10.86 ng/ml. Nonetheless, the difference was not statistically significant. Similarly, Hidayat et al.[17] showed insufficiency in both cases and controls with statistically non-significant difference of vitamin D status. Nevertheless, statistically significant difference of vitamin D level in diabetic patient and non-diabetic subjects were reported by Bachali et al.[9], Afzal, Bojesen & Nordestgaard[10], Al-Timimi & Ali[15], Subramanian et al.[18], Bayani et al.[19], and Ozder, Eker & Bilginc[20].

In this study, vitamin D level in both groups were high. Firstly, slightly higher vitamin D level in cases, (T2DM patients in group A) may be due to body's attempt to synthesis more vitamin D to produce more insulin to overcome diabetes. Secondly, the high vitamin D value may be due to seasonal effect, physical activity, increased amount of sun exposure during the study period. Thirdly, physically active group may be exposed to sunlight in similar proportion; hence, their vitamin D level was sufficient, as found in both diabetic and non-diabetic subjects. Finally, we collected our data mainly during the summer season (from March to June of 2016) that may cause high level of serum 25-hydroxycholecalciferol (vitamin D_3) in situ.

Most importantly, in the present study, vitamin D level had no correlation with fasting blood glucose in cases or controls or combined perspective. Though theoretically hypovitaminosis D might be associated with uncontrolled DM, in our study population hypovitaminosis D was absent, and therefore, probably not associated with causation or maintenance of T2DM. Our results are supported by Gulseth et al.[11], and Marques-Vidal et al.[12].

Limitations of our study include smaller sample size and short study period during summer season when UV exposure was sufficient. Our study was a cross-sectional study; hence, we could not affirm the causal relationship between vitamin D and insulin sensitivity and β-cell function. Moreover, the subjects in this study were all from a single region (Sylhet division, the north-east zone of the country), the geographic and seasonal distribution of vitamin D level in the population was minimized in our study.

As there are geographical, genetic and ethnic variations in vitamin D level, we recommend further prospective and multi-centric studies with larger samples and longer duration in different parts of the country to explore the association of vitamin D with T2DM.

Conclusion

Our data suggest that serum 25-hydroxycholecalciferol (vitamin D3) was within optimum level in both type 2 diabetic patients and healthy individuals. However, no correlation was found between serum 25-hydroxycholecalciferol (vitamin D) and fasting blood glucose in any group.

Conflict Of Interest

None to disclose

SOURCES OF FUNDING

None

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