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Original Article

Relationship of serum 25-hydroxyvitamin D [25(OH)D] concentration with diabetic patients attending BIRDEM Hospital, Dhaka

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Abstract

Background: Epidemiologic studies have shown that low vitamin D levels are associated with reduced insulin sensitivity and increased risk of developing type 2 diabetes mellitus. Many studies have been reported that serum concentration of vitamin D are lower in type 2 diabetic patient and non diabetic patient also in relation to age, sex, occupation, dietary intake and sun exposure.

Objectives: The present study was aimed to assess the serum 25-hydroxyvitamin D concentration [25(OH)D] among adult population attending BIRDEM hospital with and without type 2 diabetes mellitus and also find out the relationship between the deficiency of vitamin D and development of type 2 diabetes mellitus.

Materials and Methods: It was an analytical cross sectional study where around 250 subjects were taken purposively and among them, 200 were type 2 diabetic subjects and 50 were non diabetic. Study was conducted at BIRDEM hospital within the age group 18 to 65 years from January 2015 to December 2015. Data about socio-demographics were collected, blood pressure, height, weight were measured and BMI were calculated. Glycaemic status was assessed by HbA1c% and plasma glucose level. Vitamin D was measured by HPLC and SPSS (17) was used for t-test, chi-square test, ANOVA & Pearson's correlation coefficient test. Anthropometric and Biochemical parameters were collected by pre-questionnaire from the record book of the patient.

Results: The percentage of low serum 25-hydroxyvitamin D concentration [25(OH)D] was significantly higher in type 2 diabetics than non diabetics, that was 55.5% vs 20% (p value <.001). Patients with poor glycaemic control had a higher percentage of low 25(OH) D status (64.1%) where vitamin D level <20 ng/ml than those of vitamin D level >20ng/ml (35.9%).There was no significant difference of fasting blood glucose and serum 25-hydroxyvitamin D [25(OH)D] concentration. By using Pearson's correlation coefficient (r) result showed a significant inverse relationship between serum 25(OH)D concentration and 2 hours after breakfast and HbA1c in type 2 diabetic subjects (r = - 0.241, - 0.225; p = 0.071, 0.001 respectively). Patient with a diabetic duration more than or equal 5 years had low vitamin D level (p=.001). A statistically negative correlation of 25(OH) D level with HbA1c in type2 diabetic patient, (r = -.257, p= <.001). Moreover HbA1c was found as a significant predictor for vitamin D status in our body. There was no statistical significance was noticed in the mean value of [25(OH)D] with age, sex and BMI of type 2 diabetic subjects.

Conclusion: Vitamin D deficiency tends to increasing in type 2 diabetic patients. This may reflect the additive effect of glycaemic control on vitamin D status. Considering this higher percentage of low vitamin D level among T2DM patient, a strategy should develop in our health care facility for providing vitamin D to the population especially those with type 2 DM.

Keywords: 25-hydroxyvitamin D concentration, T2DM, HbA_{1c}

Introduction

Diabetes mellitus is a major global health problem, affecting 382 million people, accounting for 5.3 million deaths in 2013.[1-3] By 2035 the number of affected people is expected to increase to 592 million globally.[1,4] In the South Asian region, Bangladesh has the second largest number of adults with diabetes (5.1 million adults, 6.31%).[1] In Bangladesh a recent meta-analysis showed that the prevalence of Diabetes increased substantially, from 4% in 1995 to 2000 and 5% from 2001 to 2005 and 9% from 2006 to 2010. According to the International Diabetic Federation, the prevalence will be 13% by 2030.[1,5]

It has been reported that vitamin D deficiency may predispose to glucose intolerance, altered insulin secretion and type 2 diabetes mellitus. Vitamin D replenishment improves glycaemia and insulin secretion in patients with type 2 diabetes with established hypovitaminosis D, thereby suggesting a role for vitamin D in the pathogenesis of type 2 diabetes mellitus. Vitamin D deficiency may influence its effects on insulin secretion and sensitivity via its effects on intracellular calcium.[6] Vitamin D deficiency has been shown to alter insulin synthesis and secretion in both humans and animal models. It has been reported that vitamin D deficiency may predispose to glucose intolerance, altered insulin secretion and type 2 diabetes mellitus. The presence of vitamin D receptors (VDR) and vitamin D-binding proteins (DBP) in pancreatic tissue and the relationship between certain allelic variations in the VDR and DBP genes with glucose tolerance and insulin secretion have further supported this hypothesis. The mechanism of action of vitamin D in type 2 diabetes is thought to be mediated not only through regulation of plasma calcium levels, which regulate insulin synthesis and secretion, but also through a direct action on pancreatic β-cell function.[7] T2DM and vitamin D deficiency have risk factors in common such as African-American, Asian, or Hispanic ethnicity, obesity, aging and low physical activity.[8] Most experts defined vitamin D deficiency as 25(OH) D below 20 ng/ml whereas insufficiency as 25 (OH)D of 21– 29 ng/ml, and sufficiency as 25 (OH)D of 30 –100 ng/ml (to convert to nanomoles per liter, multiply by 2.496).[9] Various studies support the hypothesis that low vitamin D status (as assessed by circulating [25(OH) D] levels), is associated with insulin resistance, impaired glucose intolerance and thereby vitamin D deficiency may be associated with higher risk of development of Type 2 DM.[8] Vitamin D may also contribute to survival of the pancreatic cells and inhibit inflammatory processes. Moreover, vitamin D modulates insulin receptor, gene expression and insulin secretion, thus it is an important factor for T2DM.[8]

Vitamin D deficiency is common worldwide irrespective of its occurrence in both high and low-latitude countries. In addition to the European countries, vitamin D deficiency has been reported in many countries in the Middle East, Africa and Asia.[10] Despite the abundant sunlight, vitamin D deficiency is prevalent in South Asian countries as well as other neighboring countries such as Turkey, China, Japan and Thailand. Prevalence of hypovitaminosis D was 80% in South Asian adult population. Vitamin D deficiency may cause the bone-deforming disease like rickets in children, while it may cause osteomalacia in adult and disturbed muscle metabolism owing to impairment in calcium balance. These effects have also been observed in patients with T2DM, who may exhibit abnormalities in mineral and vitamin D metabolism that can eventually produce osteopenia. A number of mechanisms linking vitamin D deficiency and T2DM have been postulated, however, still not established.

There are little information regarding the interrelationship between the T2DM, vitamin D concentration, dietary intake of vitamin D and other riskfactors of serum vitamin D concentration. So, the present study was aimed to assess the serum concentration of vitamin D in T2DM subjects and healthy counterpart and also find out the relationship between the deficiency of vitamin D and development of T2DM.

Materials and Methods

This was an analytical cross sectional study and was carried out in Biochemistry Department, BIRDEM, Dhaka. The study period was from January 2015 to December 2015. About 250 patients aged 18-65 years with and without diabetes and both sexes were selected from the Outpatient Department of BIRDEM General hospital, Dhaka where patients from different parts of the country visited for their routine diabetic checkup. Subjects were taken 250 and they were divided into two groups. Out of them 200 were in T2DM group and 50 were in Non-DM group. For the study, subjects were under physical and routine examination followed by required biochemical assay. Here study variables were fasting blood glucose, 2 hours postprandial glucose, HbA1c and Serum 25-hydroxyvitamin D concentration [25(OH)D]. The following laboratory investigations were done for each of the study subjects in BIRDEM general hospital. Plasma glucose by Enzymatic Glucose-Oxidase (GOD-PAP) method, HbA_{1c} by BIO-RAD Variant (modified HPLC method), Serum 25-hydroxyvitamin D concentration [25(OH)D] by HPLC method. Ethical Review Committee of Bangladesh Diabetic Samity (BADAS) approved the study. Statistical analysis was done for unpaired t-test , ANOVA test and chi-square test and pearson's correlation coefficient test. $P \leq 0.05$ was taken as a level of significance. All statistical analysis was performed with the help of software SPSS for Windows (statistical package for social science), 17 version.

Results

Among all type 2 diabetic subjects, 25-hydroxyvitamin D concentration [25(OH)D] levels in type 2 diabetic subjects was around 55.5% (111out of 200) as compared to that of 20% of non diabetics (10 out of 50) ,where total vitamin D levels were less than 20 ng/ml (Table 1). There was statistically significant difference was found among Type 2 diabetic & non diabetic group ($p<0.001$) & serum total vitamin D deficiency was more in Type 2 diabetic group.

Table I: Distribution of study participants on the basis of vitamin D status

Serum Vitamin D Total (ng/ml)	Group		p value
	Type 2 diabetes (n =200)	Without diabetes (n = 50)	
< 20	111 (55.5%)	10 (20%)	<0.001
≥ 20	89 (44.5%)	40 (80%)	

Statistical analysis was done by t-test. P≤ 0.05 was taken as a level of significance.

Table II shows serum 25-hydroxyvitamin D concentration (ng/ml) levels in diabetic subjects according to glycaemic control.The mean serum 25-hydroxyvitamin D concentration [25(OH)D] level was significantly lower ($p<0.001$) for patient with poor glycemic control as compared to that for fair and good glycemic control type 2 diabetic patients respectively (Table II).

Table II: Serum 25-hydroxyvitamin D concentration (ng/ml) levels in diabetic subjects according to glycaemic control.

		Serum 25-hydroxyvitamin D concentration (ng/ml)	
Clinical variables		Total	
	N		p-value
Glycemic control			
Good (<6.5)	48	32.74±7.17	
Fair (6.5–7.4)	48	24.39±7.46	<0.001
Poor (≥7.5)	103	19.92±7.38	

Statistical analysis was done by ANOVA test. p≤0.05 was taken as a level of significance

A significant difference was also observed between mean±SD values for serum 25-hydroxyvitamin D concentration [25(OH)D] level of patient with diabetic duration more than or equal to five (5) years and of those with duration less than 5 years respectively (26.14±9.59 vs 20.44±8.50). No statistically significant difference was noticed in the mean value of serum 25-hydroxyvitamin D concentration [25(OH)D] level for age, sex and BMI of type 2 diabetic subjects (Table III).

Table III: Serum vitamin D levels in diabetic subjects according to different clinical variables.

		Serum 25-hydroxyvitamin D concentration (ng/ml)	
Clinical variables		Total	
	N		p value
Age (years)			
< 50	97	19.91±8.29	0.401
≥ 50	103	18.98±7.37	
Gender			
Male	57	20.44±6.86	0.249
Female	143	19.02±8.17	
BMI (kg/m^2)			
Normal weight (<25)	61	18.94±9.01	0.758
Over weight (25–29.9)	102	19.83±7.44	
Obese (≥30)	37	19.13±6.87	
Diabetes duration (years)			
< 5	97	26.14 ± 9.59	0.001
≥ 5	103	20.44 ± 8.50	

Statistical analysis was done by unpaired t-test , ANOVA test and chi-square test. P≤ 0.05 was taken as a level of significance.

Table IV shows the distribution of diabetic subjects on the basis of Serum 25-hydroxyvitamin D concentration (ng/ml)levels according Glycaemic control (HbA_{1c}%). When there was 25-hydroxyvitamin D concentration [25(OH)D] level less than 20 ng/mL, then poor glycemic control was 64.1 % where p < 0 .001 (Table IV).

Table IV: Distribution of diabetic subjects on the basis of Serum 25-hydroxyvitamin D concentration (ng/ml)levels according Glycaemic control (HbA_{1c}%)

Serum 25-hydroxyvitamin D concentration level (ng/ml)	Glycaemic control (HbA_{1c}%)			p value
	Good	Fair	Poor	
	(n=48)	(n=49)	(n=103)	
< 20	13(27.1%)	32(65.3%)	66(64.1%)	<0.001
≥20	35(72.9%)	17(34.7%)	37(35.9%)	
Total	48(100%)	49(100%)	103(100%)	

Statistical analysis was done by Chi -square test. p≤ 0.05 was taken as a level of significance.

By using Pearson's correlation coefficient (r) result showed (Table V) a significant inverse relationship between serum 25-hydroxyvitamin D concentration and 2 hours after breakfast and HbA_{1c} in type 2 diabetic subjects (r = - 0.241, - 0.225; p = 0.071, 0.001respectively).

Table V: Correlation of 25-hydroxyvitamin D with other parameters in diabetics and non diabetics

Parameter	Group			
	Type 2diabetes (n =200)		Without diabetes (n = 50)	
	r value	p value	r value	p value
Fasting blood glucose (mmol/L)	- 0.138	0.052	- 0.327	0.080
2 hrs after blood glucose (mmol/L)	- 0.241*	0.071	- 0.141	0.328
HbA_{1c} (%)	- 0.225*	0.001	- 0.204	0.156

Discussions

This is a cross sectional study that aim to evaluate 25-hydroxyvitamin D concentration [25(OH)D] status among type 2 diabetic patient. A total of 250 subjects were enrolled for study of which 200 were type 2 diabetic patients and 50 were healthy individuals without diabetes. In this study the mean plasma 25-hydroxyvitamin D concentration [25(OH)D] level was significantly low in type 2 diabetics than non diabetics ($p<0.001$). This findings were similar with other studies.[11, 12] Moreover, it was found that 200 of the T2DM subjects had low vitamin D concentration <20 ng/ml). Such a high prevalence of low vitamin D status is worth mentioning. It is favorably comparable to values from the developing countries[13] but it is markedly higher than values of diabetic and normal populations in western countries.[14] In this study, subjects with T2DM, up to 55.5% of the subjects had 25-hydroxyvitamin D [25(OH)D] deficiency. This result also supports with another report of Korean patients with T2DM,[15] where 25(OH)D in patient with T2DM vitamin D deficiency, prevalence was 85.9%. Another study showed that prevalence of 25(OH)D deficiency was higher in Turkish adult with T2DM (88.8%) and healthy subjects (79.9%).[16] These variations in the results of different studies might be explained by differences in dietary intake, sun avoidance behaviors, geographical environment, skin color, or genetic predisposition. Mean value of 25-hydroxyvitamin D concentration [25(OH)D] levels were found significantly lower in type 2 diabetes mellitus patients than the non diabetics in this present study. Similar findings were also observed where it was found that 25(OH) D and 1, 25(OH) D levels were not significantly different in diabetic patients when compared with that of controls.[17] Moreover, there was no inverse association between vitamin D status and Type 2 DM in non-Hispanic blacks was present, despite their poor vitamin D status.[18] However, in some ethnic populations (non-Hispanic whites and Mexican Americans), the inverse association was very much evident.

There was an trend inverse relationship between vitamin D and HbA_{1c} in our study. Patients with poor glycaemic control (as was assessed by HbA_{1c}%) had lower mean 25-hydroxyvitamin D concentration [25(OH)D] concentrations and a higher prevalence of low vitamin D status as compared to those with fair and good glycaemic control. Similar consistent result was found where vitamin D levels were found to be negatively correlated with HbA_{1c}.[19] Furthermore, another study supports these findings where HbA_{1c} level were higher in vitamin D deficient patient compared to that of patients with optimum level.[20] Moreover, other studies supports our results concerning the relationship between HbA_{1c} and vitamin D.[21, 22] It was a surprising fact that Vitamin-D supplementation was not found to be effective in reducing HbA_{1c}.[23] Another study showed that within T2DM subjects, regardless of a common finding of vitamin D deficiency, low vitamin D is associated neither with increased prevalence of the metabolic syndrome, nor is there any association with glycaemic control which disagrees to the findings of our results.[24] In our study there was no significant difference between fasting blood glucose and different vitamin D levels but there was significant difference between different vitamin D level and 2 hours after breakfast.

An alternative aspect was ruled out, as age, sex and BMI, the impacts of these factors on vitamin D status, were not found statistically significant in our study. The reason for this is not clear enough, although there were a high number of patients with low vitamin D levels and these were females and they were older and obese. Similar studies showed that the majority of female patients 73.6% were vitamin D deficient (<25 nmol/L) compared to 46.9% of male patients.[25] In a large cohort study of older adults involving 7791 subjects, initially diabetes-free, serum 25(OH)D levels were inversely associated with incident diabetes in women but not in men.[26] Results of above study were consistent with our findings.[25, 26] Another study showed that no significant difference in distribution of 25(OH)D level among age and sex was found which support our study result.[27]

However, the finding of low levels of vitamin D in individuals with and without diabetes could then be explained by the insufficient synthesis in the skin and inadequate intake or absorption of vitamin D. In addition limited exposure to sun light and low sea food intake may affect vitamin D status in these groups. Despite this high prevalence, no studies had been carried previously on vitamin D status in our population. Furthermore, this study has considerable strength as up to our knowledge, this one is first study in our population to estimate the assessment of 25-hydroxyvitamin D concentration 25(OH)D in T2DM patients. In addition to this measurement of 25-hydroxyvitamin D concentration 25(OH)D D was performed in one laboratory, so comparison of vitamin D level among the groups was considered as valid. Our study suggests that a longitudinal study among T2DM patients can present the purposeful insight about the implications of 25(OH)D concentration in T2DM.

Conclusions

Finally it can be concluded that, type 2 diabetic subjects have low 25-hydroxyvitamin D [25(OH)D] concentration when compared with non diabetic subjects. Patients with poor glycaemic control have a higher prevalence of low 25-hydroxyvitamin D concentration [25(OH)D] level.

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