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Type 2 Diabetes: Vitamin D Status in Newly Diagnosed Patients, Dinajpur, Bangladesh

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Abstract **Original Research Article**

Introduction: Vitamin D deficiency is common in patients with type 2 diabetes mellitus (T2DM). Vitamin D status may have a causal role in the onset of T2DM and may influence glycemic control in these patients. The present cross-sectional study was done among newly diagnosed 110 T2DM patients. Serum 25(OH) D was measured in all and classified as normal (≥30ng/mL), insufficient (>20 to 29.9ng/mL), and deficient (≤20ng/mL). The mean serum 25(OH) D level was 27.91±2.58ng/mL (mean±SEM). ***Aim of the Study:*** Aim of the study was to find out the vitamin D status in newly diagnosed type 2 diabetes patients in. ***Material & Methods:*** This cross-sectional study comprising of 110 newly detected subjects with T2DM was conducted in the outpatient department of M Abdur Rahim Medical College, Dinajpur, Bangladesh during the period from January 2019 to December 2019. One hundred and ten (110) participants were selected maintaining an inclusion criteria. Obesity status was determined by body mass index (BMI) categories applicable for the Asian Indians. The relevant Data were analyzed by using Statistical Packages for Social Sciences (SPSS), version 23.0 software (SPSS Inc; Chicago, IL, USA). ***Results:*** Among the study subjects, 30% were Vit-D deficient, 36% were Vit-D insufficient and 34% had normal 25(OH) D. There was no statistical difference of 25(OH)D level between the younger (age <40 years) and older (≥40 years) patients (28.31±4.3 vs. 27.44±2.6ng/mL, mean±SEM; p=0.869); males and females (26.79±2.1 vs. 31.09±8.2ng/mL, mean±SEM; p=0.470); among smokers, non-smokers and ex-smokers (26.86±4.31, 27.10±2.49 and 42.62±1.71ng/mL respectively, mean±SEM; p=0.363); among normal weight, overweight and obese (30.61±6.16, 35.61±9.52 and 24.27±1.71ng/mL respectively, mean±SEM; p=0.191); and among normotensive, borderline hypertensive and hypertensive (25.29±2.46, 32.57±5.32 and 20.84±3.66ng/mL respectively, mean±SEM; p=0.277) patients. 25(OH) D level showed significant negative correlation with body mass index (r= -0.391, p=0.017) and positive correlation (r=0.334, p=0.044) with fasting plasma glucose in male subjects. ***Conclusion:*** Age, sex, smoking status, BMI, systolic BP, diastolic BP, family history of DM, and smoking status were not found to influence vitamin D level independently. Our study found a high frequency of subnormal vitamin D in newly diagnosed T2DM patients. Screening for vitamin D status may be beneficial in T2DM patients.

Keywords: Vitamin D deficiency, Type 2 Diabetes.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder affecting about 415 million people worldwide. In 2015, Bangladesh ranked 10 in the world with a total of 7 million diabetic people and it is estimated that in 2040 around 13.6 million of her people will have diabetes, making 9th in the ranking at that time [1]. Diabetes is multifactorial in origin and is caused by interplay of several environmental as well as genetic factors. Vitamin D, a fat-soluble vitamin discovered in 1922 by McCollum, is mostly derived from sun exposure (i.e., synthesized in the skin), and a small amount from the diet including fish milk, yogurt, orange juice, and cereals [2]. Vitamin D status is an excellent marker of 'good health', including positive associations with young age, normal body weight, and a healthy lifestyle. Vitamin D plays a vital role in bone metabolism and the regulation of intestinal absorption of minerals such as calcium and phosphorus. Various studies suggest that vitamin D deficiency may play a major role in the causation of type 2 diabetes mellitus (T2DM) [3-5], and some other chronic diseases like hypertension, cardiovascular disease [6, 7]. Vitamin D may also play

role in glycemic control in DM [8, 9]. Serum 25-hydroxyvitamin D [25(OH) D] levels reflect body stores of vitamin D [10]. Worldwide vitamin D deficiency is a common problem in the general population [11]. Although vitamin D deficiency is unexpected in tropical areas like the Indian subcontinent, several cross-sectional studies found a very high prevalence of vitamin D deficiency even among healthy individuals of various subsets of this population [12-14]. Recent studies have reported a very high prevalence of subnormal vitamin D in T2DM patients in this subcontinent, though some of those studies reported that the prevalence was not significantly higher when compared to normal individuals [15-17]. There is a lack of data on the prevalence of vitamin D deficiency among Bangladeshi T2DM patients. Hence, this study was undertaken to investigate the vitamin D status in newly diagnosed T2DM patients in this area.

METHODOLOGY AND MATERIALS

This cross-sectional study comprising of 110 newly detected subjects with T2DM was conducted in the outpatient department of M Abdur Rahim Medical College, Dinajpur, Bangladesh during the period from January 2019 to December 2019. Diabetes was diagnosed based on American Diabetes Association (ADA) 2017 criteria [18]. Patients diagnosed after the age of 25 years with central obesity and other features of insulin resistance and having no ketosis were categorized as T2DM. Informed written consent was taken from each subject. Patients having a history of poor sunlight exposure; liver, kidney, or thyroid dysfunction; malignancy, recent severe acute illness; strict vegans, and those taking vitamin D supplements were discarded. 5 ml venous blood was collected from each of the participants, serum separated by centrifugation and preserved until assay. Serum 25(OH)D was estimated by chemiluminescent immunoassay procedure (LIAISON DiaSorin Inc. 1951 Northwestern Ave, Stillwater, MN 55082-285 USA). 25(OH) D levels were considered as normal (≥30ng/mL), insufficient (>20 to ≤ 29.9ng/mL), and deficient (≤20ng/mL) as per Clinical Practice Guidelines (2011) of The Endocrine Society [19]. Obesity status was determined by body mass index (BMI) categories applicable for the Asian Indians [20]. All the relevant data were analyzed by using SPSS version 23.0 software (SPSS Inc; Chicago, IL, USA). The categorical variables were represented as percentages and measurable variables as mean±SD (or SEM). Independent sample t-test, Chi-square test, or one- way ANOVA was performed as applicable for comparing the variables between different groups. Pearson's correlation test was done to find out the association among different variables, and a regression model was applied to identify the confounding variables. P-value ≤0.05 was considered to be statistically significant.

RESULTS

The clinical and laboratory characteristics of the study subjects were shown in Table I. Their mean age was 40.64±10.6 years; 74% were male, 26% were female. 55.52% had a family history of type 2 diabetes and 66% of them were either overweight or obese. The mean serum 25(OH) D level was 27.91±2.58ng/mL. The frequency of subjects with different status of vitamin D made on the basis of recommended cut-off value is shown in Figure 2. The majority (66%) had subnormal (36% insufficient and 30% deficient) vitamin D.The mean values of vitamin D in various subgroups of study subjects are given in Table I. There was no statistical difference of 25(OH)D level between relatively younger (age <40 years) and older (≥40 years) patients (28.31±4.3 vs. 27.44±2.6ng/mL, mean±SEM; p=0.869); between males and females (26.79±2.1 vs. 31.09±8.2ng/mL, mean±SEM; p=0.470); among smokers, non-smokers and ex-smokers (26.86±4.31, 27.10±2.49 and 42.62±1.71ng/mL respectively, mean±SEM; p=0.363); among normal weight, overweight and obese (30.61±6.16, 35.61±9.52 and 24.27±1.71ng/mL respectively, mean±SEM; p=0.191); and among normotensive, borderline hypertensive and hypertensive (25.29±2.46, 32.57±5.32 and 20.84±3.66ng/mL respectively, mean±SEM; p=0.277) subjects. Relationships of 25(OH) D concentrations with other variables are shown in Table II. 25(OH) D level showed significant inverse correlation with BMI only in male subjects (r = -0.391, p = 0.017). Age, systolic blood pressure, and diastolic blood pressure were not found to have significant correlations with 25(OH) D levels. 25(OH) D level had significant positive correlation (r = 0.334, p = 0.044) with FPG in males; but in females it had negative correlation (r = -0.537, p = 0.058) with the same.As displayed in Table III, none among the variables of age, sex, smoking status, BMI, systolic BP, diastolic BP, family history of DM, and smoking status were found to influence 25(OH) D level independently (p = not significant for all).

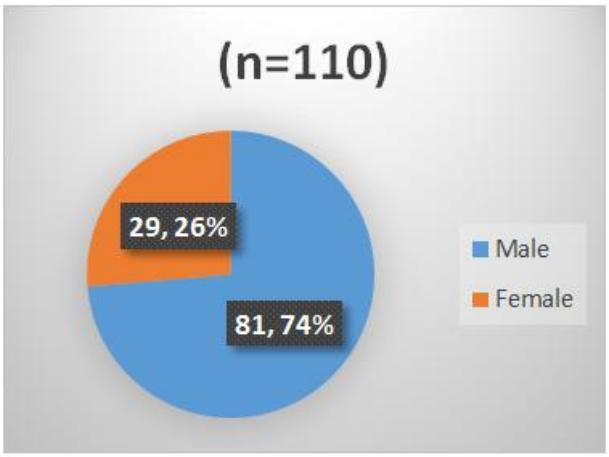

Fig-1: Gender ratio of sample size

Of the total sample size, more than one-third were male (n=81), and only 26% (n=29) were female.

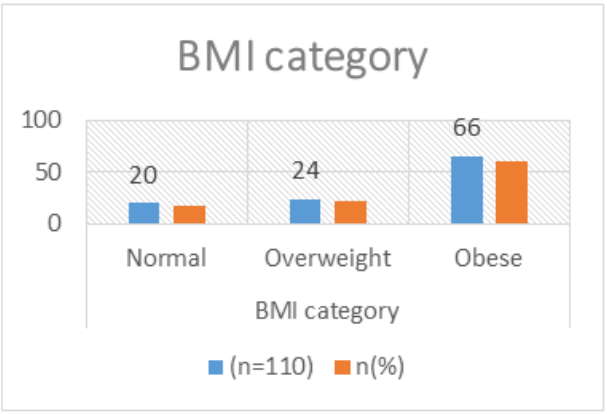

Chart-I: Weight diagram based on BMI

Of the total sample size, the majority belonged to the obese category (n=66). Of the remaining 44 patients, 20 were of normal body weight and 24 belonged to the overweight category.

Table-I: Comparison of serum 25(OH) D level in different groups of study subject

Characteristics		Serum 25(OH)D level (ng/mL)			
		N	%	Mean±SEM	P
Family history of type 2 DM	Present (%)	61	55.52		
	Absent (%)	49	44.48		
Smoking status	Non-smoker	57	51.81	26.86±4.31	
	Smoker	46	41.81	27.10±2.49	0.363†
	Ex-smoker	7	6.363	42.62±1.71	
Blood pressure	Normotensive	53	48.18	25.29±2.46	
	Borderline hypertensive	46	41.81	32.57±5.32	0.277†
	Hypertensive	11	10	20.84±3.66	

*by independent sample t-test; †by one-way ANOVA

Looking at the clinical and laboratory characteristics of the patients, 71.82% had a family history of type 2 DM, which was absent in the remaining 31 patients. Of the 110 patients, 51 were non-smoker, 7 were ex-smoker, and the remaining 46 were smokers. Categorizing them based on their blood pressure, 10% were hypertensive, 41.82% were borderline hypertensive, and the remaining 48.18% were of normotensive category.

Table-II: Correlations with other variables

Variables	Male with Type 2 DM (n=81)		Female with Type 2 DM (n=29)	
	r	p	r	p
Age and 25(OH)D level	0.134	0.429	0.16	0.602
BMI and 25(OH)D level	-0.391	0.017	-0.08	0.794
SBP and 25(OH)D level	-0.059	0.728	-0.229	0.451
DBP and 25(OH)D level	0.146	0.388	0.23	0.45
FPG and 25(OH)D level	0.334	0.044	-0.537	0.058

BMI= Body Mass Index; SBP= Systolic Blood Pressure; DBP= Diastolic Blood Pressure by Pearson's correlation.

The above table shows the correlation between 25 (OH) D levels and other factors, divided between the male and female groups. 25(OH) D level showed significant inverse correlation with BMI only in male subjects (r = -0.391, p = 0.017). It also showed that 25(OH) D level had significant positive correlation (r = 0.334, p = 0.044) with FPG in males; but in females it had negative correlation (r = -0.537, p = 0.058) with the same. Other factors such as age, systolic blood pressure, and diastolic blood pressure were not found to have any significant correlations with 25(OH) D levels.

Table-III: Multiple regressions for serum 25(OH) D level in T2DM

Variables	B	SE	Beta	t	p
(Constant)	8.174	46.05	-	0.177	0.86
Age	0.206	0.318	0.119	0.647	0.521
Sex	13.114	8.719	0.318	1.504	0.14
BMI	-1.24	0.798	-0.267	-1.533	0.128
Systolic BP	-0.405	0.244	-0.308	-1.657	0.105
Diastolic BP	0.958	0.653	0.293	1.468	0.15
Family H/O T2DM	2.252	6.426	0.056	0.35	0.728
Smoking status	4.329	6.66	0.145	0.65	0.519
FPG	-0.914	0.859	-0.166	-1.065	0.293

As shown in the table above, none among the variables of age, sex, smoking status, BMI, systolic BP, diastolic BP, family history of DM, and smoking status were found to influence 25(OH)D level independently (p = not significant for all).

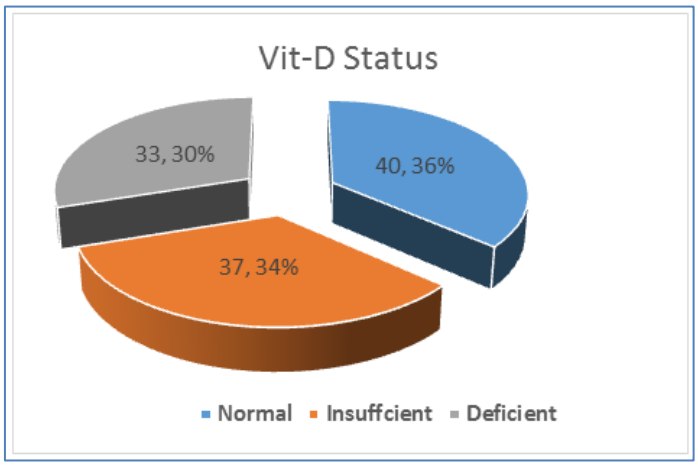

Fig-2: Vitamin D status in the study subjects

From the graph, we can see that Vit-D status was normal at 36% (n=40). Of the remaining 70 patients, 33 were Vit-D deficient, and the remaining 34% (n=37) had an insufficient amount of Vit-D

DISCUSSION

The aim of the present study was to determine vitamin D status in newly diagnosed T2DM patients. Our study observed that the frequency of subnormal vitamin D is high (66%) in newly detected T2DM. 30% were deficient and 36% were insufficient, and only 34% of the study subjects had sufficient levels of vitamin D. Recent studies done in India found a higher prevalence of vitamin D deficiency in T2DM patients. In their study, it was found that 81% of newly diagnosed T2DM patients were Vit-D deficient or insufficient while around 67% of healthy control subjects were either deficient or insufficient as well [21]. In another study, D deficiency was found in 97.5% of the newly diagnosed T2DM subject [22]. A large proportion of patients previously diagnosed as T2DM taking anti-diabetic drugs have also been found to have subnormal levels of vitamin D. Their study found that the frequency of D-deficient and D-insufficient T2DM patients were 71.4% and 15% respectively [16]. This is higher than the frequency of Vit-D deficiency in the general population of India (70%) [14]. Another study found a higher frequency (81.5%) of D-deficiency in Indian T2DM subjects but the frequency was not higher than non-diabetic controls in the study [15]. A recent Saudi Arabian study also found a higher frequency of subnormal vitamin D in T2DM patients (76.6% deficient and 22.2% insufficient) [23]. The mean serum 25(OH) D concentration in our study was 27.91±2.58ng/mL (mean±SEM), which is higher than the findings. (18.81±15.18ng/ml, mean±SD) and (7.34±1.19ng/mL mean±SD) [21, 22].Our study observed no significant difference of 25(OH) D levels between males and females which is in agreement with the findings [22,16, 23]. On the contrary, in an Indian study in the general population, women were found to have a higher prevalence of vitamin D deficiency compared with men [24]. Sex was found to not have any significant effect to be an important confounder of 25 (OH) D level in our study. Age was an important factor affecting 25(OH) D levels, and a decline in 25(OH) D levels has been reported with advancing age [25]. Our study found no significant difference of 25(OH) D levels between age groups <40 years and ≥40 years. On the contrary, we found 25(OH) D levels to be increased with increasing age [16]. In this study there were no significant differences of 25(OH) D levels among normal weight, overweight and obese T2DM

subjects; but 25(OH) D levels had a significant negative correlation with BMI only male subjects. The study had demonstrated an inverse relationship between 25(OH) D levels and BMI in subjects with metabolic syndrome or diabetes; those with high BMI had lowered 25(OH) D levels [21, 26]. No direct correlations between BMI and 25 (OH) D levels were noticed during the study [16, 22]. Our study found a significant positive correlation of 25(OH) D level and FPG in males, but in females, D level had a negative correlation with FPG though it was non-significant. The study also found a significant negative correlation of D level with FPG [21].

Limitations of the study

This study had several limitations. The sample size was small and no healthy control group was taken, so the causal role of vitamin D levels on type 2 DM could not be determined. Seasonal variation, the extent of sunlight exposure, and dietary vitamin D intake were also not quantified.

CONCLUSION AND RECOMMENDATIONS

A large portion of newly diagnosed T2DM subjects in Bangladesh has subnormal vitamin D as revealed by our study. Vitamin D level had a significant negative correlation with BMI only male subjects and showed no correlation with age and sex. However, wider scale studies are needed to properly understand the vitamin D status in T2DM in our country.

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