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The Relationship of Vitamin D Deficiency in Type 2 Diabetes Patients: Dhaka, Bangladesh

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Abstract	Original Research Article

Introduction: Diabetes mellitus (DM) is a result of heterogeneous metabolic disorders, causes hyperglycemia due to deficiency in secretion and/or insulin action. The present retrospective cross-sectional study was done among 78 T2DM patients. Serum 25-hydroxyvitamin D [25(OH)D] levels reflect body stores of vitamin D which was measured in all and classified as normal ($\geq$30ng/mL), insufficient (>20 to 29.9ng/mL), and deficient ($\leq$20ng/mL). The mean serum 25(OH) D level was 27.91$\pm$2.58ng/mL (mean$\pm$SD). ***Aim of the Study***: Aim of the study was to find out the vitamin D status in type 2 diabetes mellitus patients. ***Methods***: This retrospective cross-sectional study was conducted in SMC Niltara Clinic, Dhaka, Bangladesh during the period from January 2020 to December 2020. All the results were statistically analysed by were taken by SPSS-20 version and MS-Excel-16. ***Result***: In total 78 patients divide into two groups. In Vitamin-D status was 24(41.38%) found normal in male and 8(40.00%) in female; insufficient found 22(37.93%) in male and 11(55.00%) in female; deficient found 12(20.69%) in male and 1(5.00%) in female. There was no statistical difference of 25(OH)D level between males and females (26.79$\pm$2.1 vs. 31.09$\pm$8.2ng/mL, mean$\pm$SEM; p=0.470); among smokers, non-smokers and ex-smokers (26.86$\pm$4.31, 27.10$\pm$2.49 and 42.62$\pm$1.71ng/mL respectively, mean$\pm$SEM; p=0.363); among normal weight, overweight and obese (30.61$\pm$6.16, 35.61$\pm$9.52 and 24.27$\pm$1.71ng/mL respectively, mean$\pm$SEM; p=0.191); and among normotensive, borderline hypertensive and hypertensive (25.29$\pm$2.46, 32.57$\pm$5.32 and 20.84$\pm$3.66ng/mL respectively, mean$\pm$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***: A large portion of Type-2 diabetes mellitus (DM) 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 sex and other veriables. However, wider scale studies are needed to properly understand the vitamin D status in Type-2 diabetes mellitus (DM) in our country.
Keywords: Diabetic mellitus, Vitamin D defficiency, Insulin.

INTRODUCTION

A common endocrine disease named diabetes mellitus (DM) as a result of heterogeneous metabolic disorders, causes hyperglycemia due to deficiency in secretion and/or insulin action. About 415 million people affecting worldwide by this [1]. In 2015, Bangladesh ranked 10 in the world with a total of 7 million diabetic people & it is estimated that 13.6 million people in around 2040 will have diabetes, will make 9th in the ranking at that time1. It includes two main types: type 1- destruction of insulin-producing pancreatic β-cells; type-2, the peripheral resistance of insulin hormone [2]. The prevalence of diabetes has

been increasing in epidemic proportions, with long-term complications [3]. DM have many complication, one of these complication is diabetic foot ulcer (DFU) has described as infection, ulceration and/or destruction of deep tissues associated with neurological abnormalities and various degrees of peripheral vascular disease [3, 4]. It is commonly caused by repetitive stress in patients with peripheral neuropathy [5], or initial injury (trauma) that is not detected by the patient [6], together with a peripheral vascular disease, plus contributes to the development of foot ulcers [7]. Vitamin D is steroid hormone fat-soluble [8, 9]. It discovered in 1922 by McCollum and mostly derived from sun exposure like

synthesized in the skin, and a small amount from the diet including fish milk, yogurt, orange juice, and cereals [10]. Its synthetizing mainly made on the skin with the effect of ultraviolet light [9] and activated by two hydroxylation reactions in the liver and kidneys [11]. In a word vitamin D status is an excellent marker of 'good health' (positive associations with young age, normal body weight, and a healthy lifestyle). It plays a vital role in bone metabolism and the regulation of intestinal absorption of minerals (calcium & phosphorus). Various studies suggest that vitamin D deficiency may play a major role in the causation of type 2 diabetes mellitus (T2DM) [12-14] Vitamin D may also play role in glycemic control in DM [15, 16]. Serum 25-hydroxyvitamin D [25(OH)D] levels reflect body stores of vitamin D [17] which 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±SD).Worldwide vitamin D deficiency is a common problem in the general population [18]. 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 [19-21]. 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 [22-24]. 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 T2DM patients in a tertiary care hospital.

OBJECTIVES
* To identify the relationship of vitamin D deficiency in the diabetic patients.
* Investigate the vitamin-D status in T2DM.

METHODOLOGY & MATERIALS

This was a retrospective cross-sectional study and was conducted in SMC Niltara Clinic, Dhaka, Bangladesh during the period from January 2020 to December 2020. Purposive sampling study technique was used for this study. Patients taken diagnosed after the age of 20 years with central obesity, acanthosis nigricans, and other features of insulin resistance and having no ketosis were categorized as T2DM. Informed written consent was included for study. 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 excluded. 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. 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 [25]. Obesity status was determined by body mass index (BMI) categories applicable for the Asian Indians [26]. All the relevant data were analyzed by using SPSS version 20 software (SPSS Inc; Chicago, IL, USA). The categorical variables were represented as percentages and measurable variables as mean±SD. 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.

RESULT

Out of 78 patients we found 58(74.36%) male and 20(25.64%) female (Figure-1). Of the total sample size, the majority belonged to the obese category 48(61.54%), then 19(24.36%) were overweight and 11(14.10%) were of normal body weight (Figure-2). Looking at the clinical and laboratory characteristics of the patients, 56(71.82%) had a family history of type 2 DM and 22(28.21%) patients was absent. Of the 78 patients, 40(51.28%) were non-smoker, 5(6.41%) were ex-smoker, and the remaining 34(43.59%) were smokers. Categorizing them based on their blood pressure, 8(10%) were hypertensive, 31(39.74%) were borderline hypertensive, and the remaining 38(6.41%) were of normotensive category (Table-1). The correlation between 25(OH) D levels and other factors, divided between the male and female groups showed that significant inverse correlation with BMI only in male groups (r=-0.391, p=0.017), also showed that 25(OH) (r=0.334, p=0.044) FPG in males; but in females it had negative correlation (r=-0.537, p=0.058) with the same. Other factors (systolic blood pressure, and diastolic blood pressure) were not found to have any significant correlations with 25(OH) D levels There was no statistical difference of 25(OH)D level 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) 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 (Table-2). 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 value is not significant for all (Table-3). In Vitamin-D status was 24(41.38%) found normal in male and 8(40.00%) in female; insufficient found 22(37.93%) in male and 11(55.00%) in female; deficient found 12(20.69%) in male and 1(5.00%) in female (Table-4).
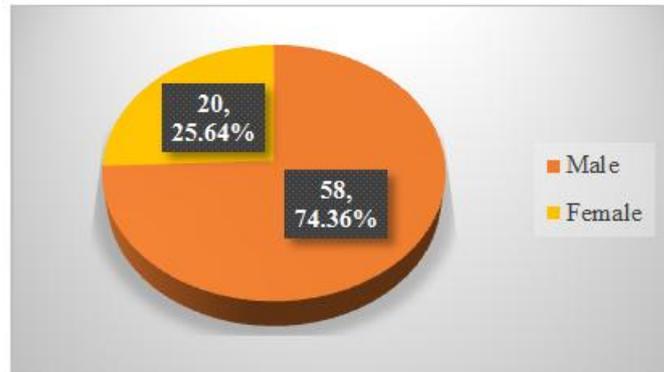

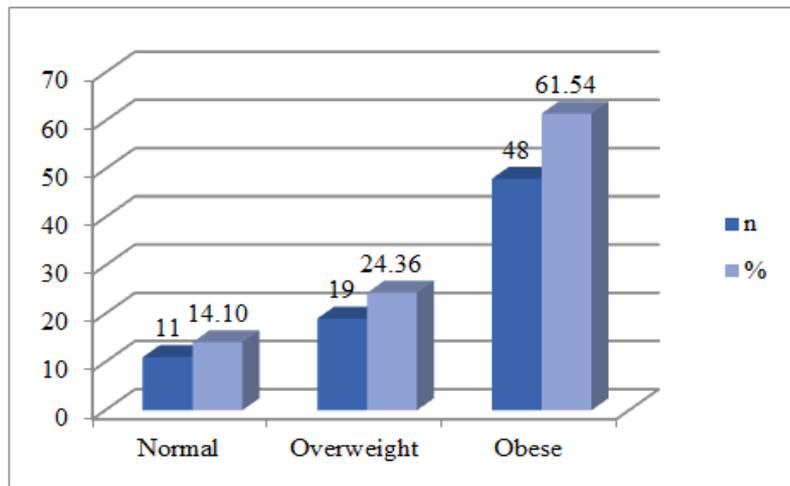**Fig-1: Distribute the study patients according to gender (N=78)**

Fig-2: Distribute the study patients according to BMI (N=78)

Table-1: Comparison of serum 25(OH)D level in different groups of study people (N=78)

Characteristics		Serum 25(OH)D level (ng/mL)		
		N (%)	Mean±SD	P-value
Family history of type 2 DM	Present (%)	56(71.79%)		
	Absent (%)	22(28.21%)		
Smoking status	Non-smoker	40(51.28%)	26.86±4.31	0.363
	Smoker	34(43.59%)	27.10±2.49	
	Ex-smoker	5(6.41%)	42.62±1.71	
Blood pressure	Normotensive	38(6.41%)	25.29±2.46	0.277
	Borderline hypertensive	31(39.74%)	32.57±5.32	
	Hypertensive	8(10.26%)	20.84±3.66	

Table-2: Correlations with other variables divide in two groups (n=78)

Variables	Male with Type-2 DM(n=58)		Female with Type-2 DM (n=20)	
	r	p	r	p
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

Table-3: Multiple regressions for serum 25(OH) D level in T2DM

Variables	B	SE	Beta	t	p
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

Table-4: Distribution of the study people according to the vitamin D status

Vitamin D deficiency	Male		Female	
	n	%	n	%
Normal	24	41.38	8	40.00
Insufficient	22	37.93	11	55.00
Deficient	12	20.69	1	5.00

DISCUSSION

The aim of the present study was to determine vitamin D status in Type-2 diabetes mellitus (DM) patients. Out of 78 patients we found 58(74.36%) male and 20(25.64%) female. From the total sample size, the majority belonged to the obese category 48(61.54%), then 19(24.36%) were overweight and 11(14.10%) were of normal body weight. Looking at the clinical and laboratory characteristics of the patients, 56(71.82%) had a family history of type 2 DM and 22(28.21%) patients was absent. Of the 78 patients, 40(51.28%) were non-smoker, 5(6.41%) were ex-smoker, and the remaining 34(43.59%) were smokers. Categorizing them based on their blood pressure, 8(10%) were hypertensive, 31(39.74%) were borderline hypertensive, and the remaining 38(6.41%) were of normotensive category. The mean serum 25(OH)D concentration in our study was 27.91±2.58ng/mL (mean±SD), which is higher than the findings. (18.81±15.18ng/ml, mean±SD) and (7.34±1.19ng/mL mean±SD) [26]. Our study observed no significant difference of 25(OH)D levels between males and females which is in agreement with the findings [27]. The correlation between 25(OH) D levels and other factors, divided between the male and female groups showed that significant inverse correlation with BMI only in male groups (r=-0.391, p=0.017), also showed that 25(OH) (r=0.334, p=0.044) FPG in males; but in females it had negative correlation (r=-0.537, p=0.058) with the same. 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 [28]. Sex was found to not have any significant effect to be an important confounder of 25(OH)D level in our study. 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 [29]. 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 lower 25(OH)D levels [30]. No direct correlations between BMI and 25(OH)D level was noticed during the study [28]. 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 [27]. 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 value is not significant for all. In Vitamin-D status was 24(41.38%) found normal in male and 8(40.00%) in female; insufficient found 22(37.93%) in male and 11(55.00%) in female; deficient found 12(20.69%) in male and 1(5.00%) in female. Recent studies done in India found a higher prevalence (81%) found that of Type-2 diabetes mellitus (DM) diabetes mellitus patients were Vit-D deficient or insufficient while around 67% of healthy control subjects were either deficient or insufficient as well [27]. In another study, D deficiency was found in 97.5% of the newly diagnosed Type-2 diabetes mellitus subject [28]. A large proportion of patients previously diagnosed as Type-2 diabetes mellitus 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 Type-2 diabetes mellitus (DM) diabetes mellitus patients were 71.4% and 15% respectively. This is higher than the frequency of Vit-D deficiency in the general population of India (70%). A recent Saudi Arabian study also found a higher frequency of subnormal vitamin D in T2DM patients (76.6% deficient and 22.2% insufficient) [31].

Limitations of the study

This was a single centered study with a small sized sample. 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. So the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION AND RECOMMENDATIONS

A large portion of Type-2 diabetes mellitus (DM) 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 sex and other veriables. However, wider scale studies are needed to properly understand the vitamin D status in Type-2 diabetes mellitus (DM) in our country. Vitamin D plays an important role in activating immune cells and enhancing their work in addition to regulating insulin secretion while reducing cell resistance to insulin.

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