Original Article JCMCTA 2024 ; 35 (1) : 161-166

Study of Serum Vitamin D Status in Type 2 Diabetic Patients in a Tertiary Care Hospital of Chattogram

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Abstract

Background: Hypovitaminosis D and Type 2 Diabetes Mellitus (T2DM) are public health concerns that have contributed to multiple adverse health outcomes. Recent studies linked Vitamin D Deficiency (VDD) and Insufficiency (VDI) with glycaemic control and diabetic complications in T2DM. The study assessed the association between vitamin D measured as serum 25-hydroxy vitamin D [25(OH)D] level and T2DM at a tertiary care hospital in Chattogram, Bangladesh.

Materials and methods: Sixty diagnosed T2DM patients (Case) attending Chittagong Medical College Hospital (CMCH) and 60 non-diabetics, apparently healthy individuals (Controls) were included in this study. Serum vitamin D levels were measured by chemiluminescent immunoassay and were categorized as Vitamin D Sufficiency (VDS) VDI and VDD with levels of ≥ 30.0, 20.0–29.9 and <20.0 ng/ml, respectively.

Results: The mean age of the T2DM patients was 47.8±8.8 years, with a mean duration of diabetes of 8.9±5.2 years, and 61.7% were male. The mean serum vitamin D levels were 24.3±7.9 and 31.7±7.6 ng/mL, respectively, in T2DM and control group (p<0.001). Taking a cut of 30 ng/ml, 70% of T2DM patients had either VDD or VDI compared to 31.3% of non-diabetic control subjects. In logistic regression analysis, participants with VDD were 7.486 times [Odds ratio (OR) 7.486, 95% confidence interval (CI) 2.78 to 13.80, p<0.001] increase odds of being T2DM. In comparison, those with VDI were 3.45 times [OR 3.45, 95% CI 1.32-to 8.957, p = 0.011)] increased odds of being T2DM. Duration of diabetes inversely correlated with serum 25(OH)D levels in T2DM patients (r=-0.54, p<0.001).

Conclusion: VDD is an independent predictor of T2DM. Future prospective interventional research should clarify vitamin D's crucial therapeutic role in prevention and management of T2DM.

Key words: Type 2 diabetes mellitus; Vitamin D deficiency; Vitamin D insufficiency; 25-hydroxy vitamin D.

Introduction

T2DM poses a severe threat to public health that considerably impacts human life and health expenditures. It is one of the world's leading causes of morbidity and mortality and its global incidence rates rose by over 100% between 1990 and 2017, reaching 22.94 million in 2017.[1,2] Currently, up to 8.4 million Bangladeshi adults have diabetes (8.1%). If the problem is not addressed with appropriate preventive measures, it is expected to increase to 15.0 million by 2045.[3,4] Emerging data from both animal and human studies indicates that vitamin D may have a function in altering the likelihood of developing diabetes.[5] There is increasing evidence that suggests a connection between the level of vitamin D in the body and the ability to produce and respond to insulin. The presence of both 1-α-hydroxylase and Vitamin D Receptor (VDR) in the pancreatic β–cells explains this phenomenon.[5-9] Furthermore, it has been reported that impaired insulin sensitivity is associated with low concentrations of vitamin D, whereas replacement with vitamin D in the deficient state shows improved insulin sensitivity.[10,11] Similarly VDR knockout or hypovitaminosis D impairs glucose-induced insulin secretion, whereas vitamin D supplementation improves insulin secretory response in both animals and humans.[9,11,12]

A recent systematic review pointed out that nearly seven out of ten adults in the South Asian region are suffering from VDD and another review from

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Submitted on : 13.03.2024
Accepted on : 20.04.2024

Bangladesh reported a prevalence of hypovitaminosis D ranging between 6% to 95.8 % in different age and sex groups.[13,14] Though VDD is highly prevalent in Bangladesh, vitamin-D estimation has rarely been done in diabetic patients in our country. In the face of the high T2DM among the Bangladeshi population, it could be hypothesized that Bangladeshi T2DM may present with a high prevalence of VDD. However, as there was a scarcity of studies among Bangladeshi diabetic population in this issue, it was difficult to generalize these results in our setting. In this context, the current study was conducted to provide a preliminary data on the vitamin D status among T2DM patients attended to a tertiary level hospital in Chattogram, Bangladesh.

Materials and methods

A comparative cross-sectional study was conducted in CMCH, Chattogram, Bangladesh from November 2021 to October 2022. The study proposal was approved by the ethical review committee of Chittagong Medical College. The participants were provided with information regarding the nature, goal, and process of the study, and written informed consent was obtained from them.

T2DM patients aged between 30-50 years attending the Department of Endocrinology, CMCH, were included in the study. An equal number of age-matched non-diabetic, apparently healthy individuals were included as a comparison group. Assuming the mean difference of serum vitamin D levels of 3.33 ng/dl and standard deviation of serum vitamin D level in the case and control group of 6.85 and 6.25 ng/dl with 80% power and 95% confidence level, a total of 60 samples were required in each group to test the hypothesis.[15] Individuals on vitamin D supplements, pregnant and lactating women, mentally unstable patients, patients who had metabolic bone disease, malabsorption syndrome, liver, thyroid and kidney dysfunction and individuals having a history of poor sunlight exposure were excluded from the study.

Data were collected by using a structured case record form. After overnight fasting (8-12 hours), 7 ml of blood was collected between 8.00 and 9.00 am. Serum 25(OH) level was estimated by chemiluminescent immunoassay procedure in (Siemens advia centaur XP).

Any patients having a previous diagnosis of T2DM by a registered physician and were on treatment with anti-diabetic drugs were considered diabetic cases in this study. Participants in the control group had fasting glucose, 2 hours plasma glucose after 75 gm and HbA1c levels <7 mmol/L, <11.1 mmol/L, and <6.5%, respectively.

The vitamin D status of the participants was assessed by measuring 25(OH)D levels in serum, which reflects vitamin D produced endogenously and that obtained from foods and supplements. In serum, 25(OH)D has a relatively long circulating half-life of 15 days.[16,17] Endocrine Society clinical practice guideline, 2011 defined vitamin D status into vitamin D sufficiency, insufficiency and deficiency with the cut-off values of 30, 20 - 29.9 and <20 ng/ml respectively.[18] The socioeconomic class of the participants were categorized as per the Modified Kuppuswamy socioeconomic status scale.[19]

Data were analyzed using SPSS-23. Data were expressed as count (Percentage) or mean (±Standard Deviation (SD). The chi-square test compared categorical variables between groups, and an unpaired t-test was used to test the mean difference of quantitative variables between the two groups. A multivariate binary logistic regression analysis was used to determine the independent association between odds of vitamin D status in predicting T2DM. The Pearson correlation coefficient determined the correlation between the duration of diabetes and serum vitamin D levels. p value <0.05 was considered statistically significant.

Results

The mean age of the T2DM patients was 47.8±8.8 years and ranged between 30-60 years. There was male preponderance among the diabetic patients with 61.7% male. Most of the T2DM patients were service holder, followed by homemakers. More than half (56.7%) of the T2DM patients were from middle socioeconomic status. Table I shows that, both the groups were comparable in terms of the distribution of sociodemographic characteristics.

Table I Sociodemographic characteristics of the diabetic and non-diabetic participants

Variables	T2DM (n=60)	Non-T2DM (n=60)	p value
Age, Years			
Mean ±SD	47.8±8.8	44.4±9.4	0.050* NS
Range	30-60	30-60	
Sex			
Male	37 (61.7)	41 (68.3)	0.444†NS
Female	23 (38.3)	19 (31.7)	
Occupation			
Service	25 (41.7)	26 (43.3)	0.381†NS
House makers	18 (30.0)	15 (25.0)	
Business	8 (13.3)	14 (23.3)	
Others	9 (15.0)	5 (8.3)	
Socioeconomic status			
Lower	26 (43.3)	25 (41.7)	0.853†NS
Middle	34 (56.7)	35 (58.3)	

*Independent sample t-test, †Chi-square test. SD: Standard Deviation, NS: Statistically Not Significant.

Table II shows that, the mean serum vitamin D levels in the T2DM group were 24.3±7.9 ng/mL as compared healthy non-diabetic group having 31.7±7.6 ng/mL, indicating a mean difference of 7.5 (95% CI: 4.7-10.3) ng/ml between the two groups. The difference was highly significant statistically (p<0.001). In diabetic patient vitamin D level was deficient in 21 (35%), insufficient in 21 (35%) and sufficient in 18 (30%) patients. In the non-diabetic healthy group, these parameters were seen in 3 (5%), in 17 (28.3%) and in 40 (66.7%) patients.

Table II Comparison of the serum vitamin D between diabetic and non-diabetic participants

Serum vitamin D	T2DM (n=60)	Non-T2DM (n=60)	p value
Vitamin D level, ng/ml			
Mean ±SD	24.3±7.9	31.7±7.6	<0.001*S
Range	9.8-36.8	9.8-47.8	
Vitamin D status			
Vitamin D deficiency	21 (35.0)	3 (5.0)	
Vitamin D insufficiency	21 (35.0)	17 (28.3)	<0.001†S
Vitamin D sufficiency	18 (30.0)	40 (66.7)	

*Independent sample t-test, †Chi-square test. SD: Standard Deviation; NS: Statistically Not Significant, S: Statistically significant.

Logistic regression analysis indicated that participants with deficient vitamin D were 7.486 times [OR=7.486, 95% CI (2.78 to 13.80), p<0.001)] increase odds of being T2DM while those with insufficiency were 3.45 times [OR = 3.45, 95% CI (1.32- to 8.957) p = 0.011)] increase odds of being T2DM (Table III).

Table III Binary logistic regression analysis showing independent association between T2DM and other variables

Variables	B	OR	95% CI for OR		p value
			Lower	Upper	
Vitamin D status					
Sufficient	Reference category				
Insufficient	1.238	3.450	1.329	8.957	0.011
Deficient	2.013	7.486	2.781	13.802	<0.001
Age	0.010	1.010	0.960	1.062	0.709
Sex	0.470	1.601	0.614	4.170	0.336
SES	-0.269	.764	0.327	1.785	0.534

OR: Odds Ratio, CI: Confidence Interval, SES: Socioeconomic Status. Significant values are in bold face.

Duration of diabetes was ranged between 1.0-20.0 years with a mean duration of 8.9±5.2 years. Pearson correlation coefficient test shows that duration of diabetes was moderate negative correlation with serum vitamin D levels in T2DM patients (Figure 1).

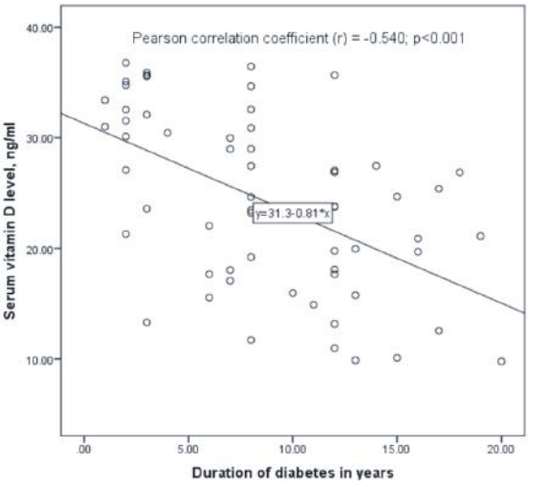

Figure 1 Scatter-dot diagram showing relation between duration of diabetes and serum vitamin D level in type 2 diabetic patients

Discussion

In the present study the mean difference in serum vitamin D levels was 7.5 ng/ml between T2DM patients and healthy non-diabetic group. The present study findings were similar to the other case-control studies conducted on different population.[20-25] In contrast, one study in Japanese population having as high as 70% prevalence of VDD, has not shown any difference in vitamin D levels between patients with diabetes compared to normal population.[26] Another study from India, there was no statistically significant difference in the mean values of vitamin D levels among T2DM cases and controls (19.05±9.77ng/ml vs. 18.48±9.84ng/ml, p=0.658).[27] These differing reports suggest that, vitamin D levels in patients with T2DM vary widely according to ethnicity or some other unknown reasons. Moreover, sunlight exposure, diet and health status play major contributing roles to vitamin D status.[18,28]

Present study demonstrated that, among the T2DM patients' serum vitamin D levels were either deficient or insufficient in most (70%) of the cases and o 30% had sufficient level of serum vitamin D. In the non-diabetic healthy group, two third of the participants had sufficient vitamin D level, and only 33.3% had hypovitaminosis D. The link between VDD and T2DM were explained by several theories. VDR are found in the β-cells of the pancreas and in adipose tissue and skeletal muscle. Another assumption has suggested that through its membranous receptors expressed on the β-cells, vitamin D increases calcium influx into -cells. The changes in the levels of intracellular calcium concentration in beta cells represent an essential step that leads to glucose-induced insulin secretion. Thus, the net result is the enhancement of beta-cell functions, synthesis, and secretion of insulin.[29-31]

Present study determined the independent association between vitamin D status and T2DM after adjusting other variables. In the present study, VDD participants were 7.486 times increase odds of being type 2 diabetic while those with insufficiency were 3.45 times increase odds of being type 2 diabetic. The present study findings confirmed the findings of Fondjo et al.[24] who found similar higher odds of T2DM among the patients with VDI and VDD compared to the T2DM patients with VDS.

Nasr et al. observed that, duration of DM was the only factor, found to be positively correlated with VDD in T2DM patients in their logistic regression analysis. The correlation between duration of diabetes and serum vitamin D level was assessed in the present study and a moderate negative correlation (r= -0.54) was observed which was similar to the findings of Nasr et al.[23]

To the best of our knowledge, this present study was the first study that studied the differences in the prevalence of VDD between T2DM patients and non-diabetics in Chattogram, Bangladesh. The link between VDD and T2DM has attracted the attention of the medical society. The present study opened the window for the future interventional study to prove the hypothesis of adding vitamin D for individuals with high-risk features for diabetes, i.e., with prediabetes to aid in preventing the incidence of the disease. The study results would be imperative for the policy-makers in planning primary prevention programs and for the researcher to conduct future studies to confirm the causal association between vitamin D and T2DM.

Limitations

Present study findings should be considered in the light of few limitations. Firstly, T2DM patients were selected from a single center, and it is only generalizable to those who present to a public tertiary level hospital for care. Secondly, cross sectional type of the study design was not suitable to determine the temporal association between VDD and incidence of T2DM. Lastly, ELISA method was used to measure vitamin D levels, which is less sensitive to Liquid Chromatography Mass Spectrometry method.

Conclusion

In conclusion, present study demonstrated that, vitamin D concentration was significantly lower in T2DM patients than the non-diabetic healthy individuals. VDD was significantly higher in T2DM patients than the non-diabetic individuals, and duration of diabetes inversely correlated with serum vitamin D level.

Recommendations

Physicians should be aware of the prevalent hypovitaminosis D during the management of patietns with T2DM. Correcting VDD may present a beneficial role in patient with T2 DM.

Well-designed interventional study could show whether dietary or supplementary vitamin D might reduce the development and progression of T2DM.

Acknowledgement
Authors acknowledged all the respondents.

Contribution of authors
SS-Conception, data collection, analysis, manuscript drafting & final approval.
MHI-Design, interpretation of data, critical revision & final approval.
SSU-Interpretation of data, drafting & final approval.
IUR-Analysis, critical revision & final approval.

Disclosure
All the authors declared no competing interest.

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