Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Prevalence of Vitamin D Deficiency and its Effect on the Glycemic Control and Lipid Profile among Type 2 Diabetes Mellitus Patients in a Tertiary Care Hospital

A Jegan, T Sudha Nanthini

Assistant Professor, Department of Pharmacology, Thanjavur Medical College, Thanjavur, Tamil Nadu, India

Abstract

Objective: The objective of the study was to find out the prevalence of Vitamin D deficiency among patients with type II diabetes mellitus (DM) and to assess the effect of Vitamin D in the control of blood sugar and lipid profile among patients with type 2 DM.

Material and Methods: Study setting: This study was conducted at diabetic clinic, Chennai Medical College Hospital and Research Centre, Irungalur, Tiruchirappalli. Study design: The present study was a hospital-based analytical cross-sectional design. Sample size: The sample size was taken as 90 (using the formula $4pq/l^2$). Analysis: The data collected were entered and analyzed using the SPSS software package (Version 21). Descriptive statistics (mean, standard deviation and 95% confidence interval) and appropriate tests of significance (ANOVA) were applied to establish the relationship between the study variables. $P < 0.05$ was considered to be statistically significant.

Results: We found that there was a significant reduction in all the glycemic indicators over the progressive weeks among the group of participants receiving Vitamin D supplements. We have also reported a uniform reduction in all the lipid profile values and glycemic indicators across all the three groups in the progressive weeks, with a significant reduction in the group receiving Vitamin D supplements.

Conclusions: Vitamin D supplementation improves glycemic control and can reduce or prevent the development of insulin resistance in type 2 diabetes mellitus patients. Considering the multitude of diseases associated with Vitamin D deficiency, increasing the population's awareness of the beneficial effect of Vitamin D on health will be an important strategy overall.

Key words: Vitamin D, Type 2 diabetes mellitus, Glycemic control, Lipid profile

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia as a result altered carbohydrate, fat, and protein metabolism. Type 2 DM counts the remaining 90–95% of world diabetic population. The World Health Organization estimated in 2000, 171 million people were suffered from this disease and this number is believed to double by the year 2030.[1]

Access this article online

www.ijss-sn.com

Month of Submission : 10-2019
Month of Peer Review : 11-2019
Month of Acceptance : 12-2019
Month of Publishing : 12-2019

Vitamin D deficiency is believed to affect not only skeletal but also extra skeletal organs leading to various diseases. Vitamin D deficiency has been found to be associated with increasing incidence of chronic illnesses such as DM, cardiovascular diseases, and malignancies.[2,3] The role of Vitamin D in glycemic control and lipid profile has a mixed documentation, while studies suggest that elevated Vitamin D levels are associated with improved glycemic control in type 2 DM (T2DM),[4] some studies have observed no such effect.[5] The effect of Vitamin D on serum lipids in T2DM is not exactly known.[6] Studies have also documented an inverse relationship between triglycerides, total cholesterol level Vitamin D.[7]

Vitamin D deficiency is prevalent all over the world, though Vitamin D can be synthesized in the skin by exposure to sunlight, this source alone is not enough. Vitamin D

Corresponding Author: T Sudha Nanthini, Department of Pharmacology, Thanjavur Medical College, Thanjavur, Tamil Nadu, India.

deficiency is the most left as an un-treated nutritional deficiency.[8] It affects people regardless of their age, sex, ethnicity, and topography. The dietary sources rich in Vitamin D are not affordable to most of the Indian population. Vitamin D supplements though available in the market are not consumed regularly due to their cost and decreased awareness regarding the supplements.[2] The present study was undertaken to assess the effect of Vitamin D in the control of blood sugar and lipid profile in the patients with T2DM.

MATERIALS AND METHODS

Study Setting

The study was conducted at the diabetic clinic, Chennai Medical College Hospital and Research Centre, Irungalur, Tiruchirappalli.

Study Design

The present study was a hospital-based analytical cross-sectional design.

Study Population

The participants included in the study were 36–60-year-old adults from both genders who had been previously diagnosed with T2DM and were all under treatment with metformin treatment.

Sample Size

The prevalence of T2DM is rural Tamil Nadu[9] 6% and, absolute error in estimated prevalence-5%, the sample size was taken as 90 (using the formula $4pq/l^2$).

Ethical Clearance

The study was approved by the Institutional Ethical Committee, Research Cell of Chennai Medical College Hospital and Research Centre.

Data Collection Tool

Data collection was done during working hours at a time feasible to the respondents. The study was conducted in the hospital premises after obtaining prior permissions from the concerned authorities. After obtaining informed consent from the participants, they were divided into three groups, based on their treatment schedules and observed. The first group consisted of T2DM on metformin therapy + normal serum vitamin 25(OH)D level and the second group included T2DM on metformin therapy + decreased serum 25(OH)D level and in the third group, T2DM on metformin therapy + decreased serum 25(OH)D level + Cholecalciferol 60000 IU weekly. The respondents were asked to fill a questionnaire which covered information on socio-demographic data. Biochemical parameters were measured by drawing 5 ml venous blood, the samples were collected from the subjects in all the three groups on 0^{th} day at the end of 4^{th}, 8^{th}, and 12^{th} weeks of the study period.

Statistical Analysis

The data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) (version 21.0) software package. Descriptive statistics were used to define the study population. Categorical and ordinal variables were expressed as frequency/percentages. Continuous variables were expressed as mean and standard deviation. Appropriate tests of significance (ANOVA) were applied to the study variables to establish the relationship between the study variables. $P < 0.05$ was considered to be statistically significant.

RESULTS

Majority of the sample population, 37 (41.1%) respondents were in the age group of 50–59 years. The mean age group of the respondents was 49.5 ± 7.44. Among the study participants, more than half were male 54 (60%) [Table 1].

Comparison of Mean Glycemic Values [Table 2]

Our results showed that among the study participants the mean fasting blood sugar for the first group (T2DM on metformin therapy + normal serum vitamin 25(OH)D level) at 0, 4, 8, and 12 weeks were 119.9 ± 8.4, 117.4 ± 7.4, 148.5± 5.4, and 112.5 ± 6.3, respectively. While in the second group (T2DM on metformin therapy + decreased serum 25(OH)D level), the values were 137.3 ± 6.2, 136.0 ± 7.1, 134.1 ± 4.2, and 131.9 ± 6.2. In the third group (T2DM on metformin therapy + decreased serum 25(OH) D level + Cholecalciferol 60000 IU weekly), the results were 139.2 ± 6.4, 134.9 ± 6.42, 130.7 ± 6.52, and 124.9 ± 8.07. We found that the reduction in fasting blood sugar was significantly more ($P = 0.032$) in the group receiving Vitamin D supplements [Table 2].

Table 1: Socio-demographic characteristics of the respondents (*n*=90)

Variable	Frequency (%)
Age	Mean age of respondents 49.5±7.44
30–39	14 (15.5)
40–49	32 (35.5)
50–59	37 (41.1)
>60	7 (7.9)
Gender	
Male	62 (68.8)
Female	38 (31.2)
Religion	
Hindu	76 (84.4)
Muslim	4 (4.5)
Christian	10 (11.1)
Marital status	
Single	7 (6.3)
Married	83 (93.7)

Table 2: Distribution and comparison of mean glycemic values among the respondents (*n*=90)

Variable	Group I	Group II	Group III	Test of significance* (ANOVA)
Fasting blood sugar (weeks)				
0	119.9±8.4	137.3±6.2	139.2±6.4	*P*=0.032
4	117.4±7.4	136.0±7.1	134.9±6.42	
8	148.5±5.4	134.1±4.2	130.7±6.52	
12	112.5±6.3	131.9±6.2	124.9±8.07	
Postprandial blood sugar				
0	159.9±7.4	177.6±6.7	177.9±8.2	*P*=0.024
4	157.5±5.3	177±6.8	175.0±6.8	
8	154.6±6.6	174.6±5.4	170.7±6.6	
12	147.7±4.4	171.8±4.8	163.6±10.7	
Insulin resistance levels				
0	2.19±0.6	3.49±0.3	3.6±0.5	*P*=0.037
4	2.1±0.2	3.4±0.3	3.3±0.5	
8	1.95±0.2	3.22±0.2	2.9±0.4	
12	1.83±0.3	3.1±0.3	2.6±0.4	
HbA_1c levels				
0	6.44±0.4	7.36±0.4	7.46±0.31	*P*=0.046
4	6.35±0.5	7.27±0.3	7.24±0.32	
8	6.21±0.3	7.17±0.5	7.03±0.32	
12	6.15±0.2	6.81±0.3	6.77±0.32	

*$P<0.05$ was taken to be statistically significant. HbA_1c: Hemoglobin A1c

The postprandial blood sugar values for the first group at 0, 4, 8, and 12 weeks were 159.9 ± 7.4, 157.5 ± 5.3, 154.6 ± 6.6, and 147.7 ± 4.4, respectively, while in the second group, the values were 177.6 ± 6.7, 177 ± 6.8, 174.6 ± 5.4, and 171.8 ± 4.8, respectively. In the third group, the results were 177.9 ± 8.2, 175.0 ± 6.8, 170.7 ± 6.6, and 163.6 ± 10.7. We found that the reduction in postprandial blood sugar was significantly more (P =0.024) in the group receiving Vitamin D supplements.

The insulin resistance levels for the first group at 0, 4, 8, and 12 weeks were 2.19 ± 0.6, 2.1 ± 0.2, 1.95 ± 0.2, and 1.83 ± 0.3, respectively, while in the second group, the values were 3.49 ± 0.3, 3.4 ± 0.3, 3.22 ± 0.2, and 3.1 ± 0.3, respectively. In the third group, the results were 3.6 ± 0.5, 3.3 ± 0.5, 2.9 ± 0.4, and 2.6 ± 0.4, respectively. We found that there was a significant reduction in insulin resistance levels (P = 0.037) in the group receiving Vitamin D supplements.

The HbA1C levels for the first group at 0, 4, 8, and 12 weeks were 6.44 ± 0.4, 6.35 ± 0.5, 6.21 ± 0.3, and 6.15 ± 0.2, respectively, while in the second group, the values were 7.36 ± 0.4, 7.27 ± 0.3, 7.17 ± 0.5, and 6.81 ± 0.3, respectively. In the third group, the results were 7.46 ± 0.31, 7.24 ± 0.32, 7.03 ± 0.32, and 6.77 ± 0.32, respectively. We found that there was a significant reduction in HbA1C levels (P = 0.029) in the group receiving Vitamin D supplements.

Comparison of Mean Lipid Profile Values

Our results showed a uniform reduction in all the lipid profile values across all the three groups in the progressive weeks, except for high-density lipoproteins (HDLs) which showed a significant increase. There was a significant reduction in triglyceride (TGL) levels in all three groups in the progressive weeks. The Vitamin D levels were also significantly higher in the third group, as shown in Table 3.

Weekly Comparison of Vitamin D Levels in Group Receiving Supplements

In the group receiving Vitamin D supplements, we found that there was a significant reduction in all the glycemic indicators over the progressive weeks, as shown in Table 4. We also noted that with regular Supplementation of vitamin D there was a significant reduction in the lipid profile values [Table 4].

DISCUSSION

The increased prevalence of DM is attributed to low serum Vitamin D status.[10] Vitamin D supplementation to T2DM patients increases serurm 25(OH)D level.[11] Studies in humans have shown that Vitamin D supplementation in infancy reduces the risk of type 1 DM during early adulthood. As Vitamin D modulates insulin receptor (INS-R) gene expression and insulin secretion, Vitamin D deficiency is an environmental etiological factor for T2DM.

Vitamin D supplementation significantly reduces fasting blood glucose, postprandial blood glucose, and HbA1c levels ($P < 0.05$) in Group III T2DM patients. Further, an inverse relationship between serum 25(OH) D and HbA1c level was observed.[12] Vitamin D exerts this

Table 3: Distribution and comparison of mean lipid profile values and Vitamin D values among the respondents (*n*=90)

Variable	Group I	Group II	Group III	Test of significance* (ANOVA)
Total cholesterol levels (weeks)				
0	192.4±7.3	194.9±8.1	196.03±7.1	*P*=0.14
4	191.2±5.6	194.1±6.2	191.64±9.9	
8	189.9±8.4	193.3±7.8	188.58±7.7	
12	189±6.8	192.6±5.7	185.30±6.4	
TGL levels (weeks)				
0	234.7±8.3	238.7±7.8	238.6±9.6	*P*=0.045
4	233.3±6.9	238.09±6.5	235.1±9.9	
8	231.8±5.6	237.6±5.2	227.25±7.7	
12	230.5±7.4	236.7±8.3	226.01±6.7	
LDL levels (weeks)				
0	104.6±5.9	109.9±6.1	114.2±5.3	*P*=0.98
4	103.5±7.4	111.9±8.3	111.03±4.7	
8	102.5±6.2	109.4±5.4	109.4±5.5	
12	101.5±8.1	108.5±7.8	109.8±11.4	
HDL levels (weeks)				
0	40±2.1	38.5±7.3	38.5±2.1	*P*=0.046
4	40.7±1.7	39.1±6.8	40.1±1.4	
8	41.5±3.4	39.7±8.5	39.9±6.8	
12	42±1.6	40.3±5.6	42.2±2.0	
Vitamin D levels (weeks)				
0	30.9±6.2	14.33±6.3	12.8±4.1	*P*=0.037
4	31.3±7.8	14.88±8.4	17±6.0	
8	31.9±5.7	16.05±5.8	21.9±7.1	
12	32.4±8.5	17.13±7.6	28.1±7.6	

*$P<0.05$ was taken to be statistically significant. TGL: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

Table 4: Effect of Vitamin D levels on glycemic indicators and lipid profile values among the respondents (Group III) receiving Vitamin D therapeutic supplements (*n*=30)

Variable	0 weeks	4 weeks	8 weeks	12 weeks	Test of significance* (ANOVA)
	Mean±SD (CI)				
Fasting blood sugar	139.2±6.4 (136.8–141.6)	134.9±6.42 (132.5–137.3)	130.7±6.52 (128.2–133.1)	124.9±8.07 (121.8–127.9)	0.017
Postprandial blood sugar	177.9±8.2 (174.8–181)	175.0±6.8 (172.5–177)	170.7±6.6 (168.2–173.1)	163.6±10.7 (159.6–167.9)	0.009
Insulin resistance levels	3.6±0.5 (3.4–3.8)	3.3±0.5 (3.1–3.4)	2.9±0.4 (2.8–3.1)	2.6±0.4 (2.4–2.8)	0.025
HbA_1c levels	7.4±0.31 (7.34–7.57)	7.2±0.32 (7.12–7.36)	7.0±0.32 (6.9–7.15)	6.7±0.32 (6.6–6.8)	0.029
Total cholesterol levels	196.0±7.1 (193.3–198.5)	191.6±9.9 (188.9–194.3)	188.5±7.7 (185.7–191.4)	185.3±6.7 (182.7–187.8)	0.041
TGL levels	238.6±9.6 (234.9–242.2)	235.1±9.9 (231.4–238.8)	227.6±12.3 (222.6–231.8)	226.0±11.2 (221.8–230.2)	0.033
LDL levels	114.2±5.3 (112–116)	111.0±4.7 (109–112)	109.4±5.5 (107–111)	109.8±11.4 (105–114)	0.09
HDL levels	38.5±2.1 (37.7–39)	40.0±1.4 (39.5–40.5)	39.9±6.8 (37.3–42.4)	42.2±2.0 (41.5–43)	0.07
Vitamin D levels	12.8±4.1 (11.3–14.4)	17.0±6.0 (14.7–19.3)	21.9±7.1 (19.2–24.5)	28.1±7.6 (25.2–30.9)	0.016

*$P<0.05$ was taken to be statistically significant. CI: Confidence interval, TGL: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: Standard deviation, HbA_1c: Hemoglobin A1c

beneficial effect by direct and indirect mechanisms. Vitamin D promotes pancreatic β-cell function and increases insulin secretion in numerous ways.[13] The presence of Vitamin D receptors (VDR) and binding of

25(OH) D with Vitamin D binding proteins in β cells of pancreas[12] leads to the transcription of genes regulated by 25(OH)D and facilitates the secretion of insulin from pancreatic β cells activation of Vitamin D occurs in pancreatic β-cells by intracellular 1-α-hydroxylase enzyme.[13] Vitamin D, by its direct action, enhances insulin secretion by forming $1,25(OH)_2D_3$-RXR-VDR complex, which binds to Vitamin D responsive elements found in the insulin gene promoter region, enhancing the transcriptional activation of the insulin gene, and increase insulin synthesis.[14] Insulin secretion is a calcium-dependent process and is influenced by calcium influx through the cell membrane.

Vitamin D indirectly promotes calcium influx into the β-cells of the pancreas by regulating calbindin, a cytosolic calcium-binding protein found in β-cells resulting in increased insulin synthesis.[15] Vitamin D supplementation along with metformin in Group III T2DM patients also significantly reduces insulin resistance as compared to Group II T2DM patients with metformin monotherapy. The mechanism by which Vitamin D reduces insulin resistance is a complex one. Vitamin D enhances insulin sensitivity by stimulating the transcription of INS-R gene[14] and thereby reduces insulin resistance.[16] Further Vitamin D exerts anti-apoptotic effect by attenuating the expression of pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha, and nuclear factor kappa-beta involved in insulin resistance Vitamin D also suppresses the renin gene reducing hyperglycemic induced increase in renin levels in pancreatic β cells and blockade of renin-angiotensin activity. This has been proposed as a novel target for the management of diabetes and metabolic syndrome.[17]

Regarding the analysis of the lipid profile, *post hoc* test reveals a significant reduction in TGL level in Group III T2DM patients as compared to Group II T2DM subjects. Vitamin D also reduces total cholesterol levels and increases HDL levels but insignificantly. Vitamin D exerts its action on lipid metabolism by activating transcriptional factor, peroxisome proliferator-activated receptor-δ. It is implicated in the regulation of fatty acid metabolism in skeletal muscles and adipose tissue.[18,19] The inhibitory effect of Vitamin D on lipids facilitates a reduction in insulin resistance.

The highlight of the present study is the identification of a higher prevalence of Vitamin D deficiency and insufficiency among T2DM study population. Vitamin D supplementation significantly increases serum 25(OH)D level in Group III T2DM subjects.

CONCLUSIONS AND RECOMMENDATIONS

Vitamin D improves glycemic control in T2DM patients by lowering fasting blood glucose and HbA1c levels. An inverse relationship between serum 25(OH)D and HbA1c levels in T2DM patients has been observed. Vitamin D also reduces TGL level and improves HDL level in T2DM patients. Further, Vitamin D promotes insulin synthesis and improves insulin sensitivity in T2DM patients. Hence, Vitamin D supplementation improves glycemic control and can reduce or prevent the development of insulin resistance in T2DM patients. Considering the multitude of diseases associated with Vitamin D deficiency, increasing the population's awareness of the beneficial effect of Vitamin D on health will be an important strategy overall.

REFERENCES

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, *et al*. Global Vitamin D status and determinants of hypovitaminosis D. Osteoporos Int 2009;20:1807-20.
3. Forrest KY, Stuhldreher WL. Prevalence and correlates of Vitamin D deficiency in US adults. Nutr Res 2011;31:48-54.
4. Athanassiou IK, Athanassiou P, Anastasios G, Philippos K. Vitamin D and glycemic control in diabetes mellitus Type 2. Ther Adv Endocrinol Metab 2013;4:122-8.
5. Breslavsky A, Frand J, Matas Z, Boaz M, Barnea Z, Shargorodsky M. Effect of high doses of Vitamin D on arterial properties, adiponectin, leptin and glucose homeostasis in Type 2 diabetic patients. Clin Nutr 2013;32:970-5.
6. Jorde R, Sneve M, Torjesenand P, Figenschau Y. No improvement in cardiovascular risk factors in overweight and obese subjects after supplementation with Vitamin D3 for one year. J Int Med 2010;267:462-72.
7. Saedisomeolia A, Taheri E, Djalali M, Moghadam M, Qorbani M. Association between serum level of Vitamin D and lipid profiles in Type 2 diabetic patients in Iran. J Diabetes Metab Disord 2014;13:1-7.
8. Van Schoor NM, Lips P. Worldwide Vitamin D Status. Best Pract Res Clin Endocrinol Metab 2011;25:671-80.
9. Gupta SK, Singh Z, Purty AJ, Kar M, Vedapriya DR, Mahajan P, *et al*. Diabetes prevalence and its risk factors in rural area of Tamil Nadu. Indian J Community Med 2010;35:396-9.
10. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81.
11. Alkharfy KM, Daghri NM, Sabico SB, Othman AA, Moharram O, Alokail MS, *et al*. Vitamin D supplementation in patients with diabetes mellitus Type 2 on different therapeutic regimens: A one-year prospective study. Cardiovasc Diabetol 2013;12:113.
12. Zittermann A. Vitamin D and disease prevention with special reference to cardiovascular disease. Prog Biophys Mol Biol 2006;92:39-48.
13. Harinarayan CV, Sachan A, Reddy PA, Satish KM, Prasad UV, Srivani P. Vitamin D status and bone mineral density in women of reproductive and postmenopausal age groups: A cross-sectional study from south India. J Assoc Phys India 2011;59:698-704.
14. Bland R, Markovic D, Hills CE, Hughes SV, Chan SL, Squires PE, *et al*. Expression of 25-hydroxyvitamin D3-1alpha-hydroxylase in pancreatic islets. J Steroid Biochem Mol Biol 2004;89:121-5.
15. Maestro B, Davila N, Carranza MC, Calle C. Identification of a Vitamin D response element in the human insulin receptor gene promoter. J Steroid Biochem Mol Biol 2003;84:223-30.

16. Cohen-Lahav M, Douvdevani A, Chaimovitz C, Shany S. The antiinflammatory activity of 1,25 dihydroxy vitamin D3 in macrophages. J Steroid Biochem Mol Biol 2007;103:558-62.
17. Cheng Q, Li YC, Boucher BJ, Leung PS. A novel role for Vitamin D: Modulation of expression and function of the local renin angiotensin system in mouse pancreatic islets. Diabetologia 2011;54:2077-81.
18. Dunlop TW, Vaisanen S, Frank C, Molnar F, Sinkkonen L, Carlberg C, *et al*. The human peroxisome proliferator-activated receptor δ gene is a primary target of 1α, 25-dihydroxyvitamin D3 and its nuclear receptor. J Mol Biol 2005;349:248-60.
19. Al-Daghri NM, Alkharfy KM, Al-Othman A, El-Kholie E, Moharram O, Alokail MS, *et al*. Vitamin D supplementation as an adjuvant therapy for patients with T2DM: An 18-month prospective interventional study. Cardiovasc Diabetol 2012;11:85.

How to cite this article: Jegan A, Nanthini TS. Prevalence of Vitamin D Deficiency and its Effect on the Glycemic Control and Lipid Profile among Type 2 Diabetes Mellitus Patients in a Tertiary Care Hospital. Int J Sci Stud 2019;7(9):35-40.

Source of Support: Nil, **Conflicts of Interest:** None declared.