

## VITAMIN D SUPPLEMENTATION AND HBA1C LEVELS IN TYPE 2 DIABETIC PATIENTS

Dr. Mahesh Kumar Singh

Assistant Professor, Department of Biochemistry, Rama Medical College, Hospital and Research Center, Pilkhuwa Hapur.

**Article Info:** Received 04 January 2020; Accepted 27 January. 2020

**DOI:** <https://doi.org/10.32553/ijmbs.v4i1.911>

**Corresponding author:** Dr. Mahesh Kumar Singh

**Conflict of interest:** No conflict of interest.

### Abstract

**Introduction:** Type 2 diabetes mellitus (T2DM) is a major public health problem, with an estimated 65 million patients in India. Studies shown that low serum 25(OH) D concentrations are associated with an increased risk of type 2 diabetes and shown the beneficial effect of vitamin D supplementation on insulin sensitivity. Vitamin D is formed in humans by subcutaneous photosynthesis from its precursor, 7-dehydrocholesterol by exposing themselves to the sun. older age is associated with a decrease in 7-dehydrocholesterol concentration in the human skin. This lifestyle habit and their natural diet of low vitamin D consumption may cause poor glucose control in diabetic patients. The purpose of this study was to examine the association between serum 25(OH)D and glycosylated hemoglobin (HbA1c) levels.

**Material and Methods:** This was a prospective observational study of T2DM patients aged 18 and above who attended the outpatient clinics of a tertiary center. The following variables were collected from the cases: age, sex, type of diabetes, HbA1c result. Baseline HbA1c and vitamin D levels were recorded prior to supplementation and after a period of 6 months of supplementation with vitamin D, HbA1c and vitamin D levels were recorded once again.

**Results:** A total of 169 patients were included in the study and whose follow up was completed at the end of 6 months. Mean age of the study population was  $46.87 \pm 15.99$ . there were 74(43.79%) male and 95(56.21%) female. Mean HbA1c pre-supplementation (%) was  $9.58 \pm 2.41$  while post supplementation was  $7.21 \pm 1.08$ . There was a significant reduction of HbA1c of T2DM ( $P < 0.0001$ ). Vitamin D levels pre-supplementation (nmol/L) (mean  $\pm$  SD) was  $38.54 \pm 29.54$  while, Vitamin D levels post-supplementation (nmol/L) (mean  $\pm$  SD) was  $38.54 \pm 29.54$ . There was a significant increase of vitamin D levels of T2DM ( $P < 0.0001$ ).

**Conclusion:** Significant inverse association between vitamin levels D and HbA1c in T2DM patients was observed. Also there was significant reduction in HbA1c as vitamin D levels increased. Regular screening of vitamin levels D and HbA1c in T2DM patients is advised.

**Keywords:** Vitamin D, diabetes, T2DM, 25-hydroxyvitamin D

### Introduction

Type 2 diabetes mellitus (T2DM) is a major public health problem, with an estimated 65 million patients in India<sup>i</sup>. Low serum 25-hydroxyvitamin D [25(OH)D] concentrations and dietary calcium intake have been shown to be associated with impaired insulin sensitivity or secretion in people at high risk of type 2 diabetes<sup>ii</sup>. Studies shown that low serum 25(OH)D concentrations are associated with an increased risk of type 2 diabetes and also shown the beneficial effect of vitamin D supplementation on insulin sensitivity<sup>iii, iv</sup>.

Despite all the positive evidence showing the beneficial effect of vitamin D on many diseases and its need for optimal health status, still most of the people are vitamin D deficient and its deficiency can aggravate many diseases, commonly predisposition of diabetes and also play a role in the development of diabetes<sup>v</sup>. Vitamin D is formed in humans by subcutaneous photosynthesis from

its precursor, 7-dehydrocholesterol by exposing themselves to the sun<sup>vi</sup>. The association of low serum 25-hydroxyvitamin D<sub>3</sub> [25(OH)D<sub>3</sub>] concentrations with type 2 diabetes may be mediated through effects on glucose homeostasis and, in particular, a direct effect of vitamin D on the  $\beta$ -cell function, and thus insulin secretion<sup>vii</sup>. In countries at high latitude, very little pre-vitamin D is formed during the winter months. In addition, older age is associated with a decrease in 7-dehydrocholesterol concentration in the human skin<sup>viii</sup>. This lifestyle habit and their natural diet of low vitamin D consumption may cause poor glucose control in diabetic patients<sup>ix</sup>.

With this background the purpose of this study was to examine the association between serum 25(OH)D and glycosylated hemoglobin (HbA1c) levels

### Material and Methods:

This was a prospective observational study of T2DM patients aged 18 and above who attended the outpatient

clinics of a tertiary center \_\_\_\_\_. Patients were excluded if comorbid conditions like parathyroid disease is present, patients were also excluded if those currently using vitamin D or calcium and pregnancy or breastfeeding mothers. The following variables were collected from the cases: age, sex, type of diabetes, HbA1c result. Baseline HbA1c and vitamin D levels were recorded prior to supplementation and after a period of 6 months of supplementation with vitamin D, HbA1c and vitamin D levels were recorded once again.

All patients were categorized in four groups according to their vitamin D level as follows: with severe Vitamin D deficiency (< 20 nmol/L), moderate Vitamin D deficiency (20 - 49.99 nmol/L), Vitamin D insufficiency (50 - 74.99 nmol/L) and Vitamin D sufficiency ( $\geq$  75 nmol/L). An association between vitamin D levels and HbA1c was tested. All participants were receiving their regular treatment with either insulin or oral hypoglycemic agents or both.

Statistical analysis was done. Continuous variables are represented as mean  $\pm$  SD and percentages. Unpaired t-test was used to analyze the difference between means. The Chi-square test was used for categorical data comparison. The data was statistically analyzed using SPSS version 21.0.  $P < 0.05$  was considered as statistically significant.

### Results:

A total of 169 patients were included in the study and whose follow up was completed at the end of 6 months.

**Table 1:** Baseline Characteristics of the Participants

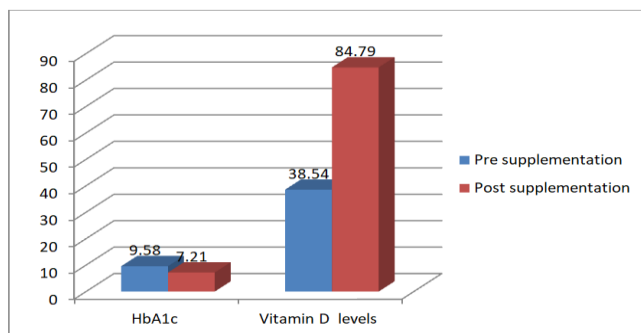
Age (years) (mean $\pm$ SD)	46.87 $\pm$ 15.99
Male	74 (43.79%)
Female	95 (56.21%)
HbA1c pre-supplementation (%) (mean $\pm$ SD)	9.58 $\pm$ 2.41
HbA1c post-supplementation (%) (mean $\pm$ SD)	7.21 $\pm$ 1.08
Vitamin D levels pre-supplementation (nmol/L) (mean $\pm$ SD)	38.54 $\pm$ 29.54
Vitamin D levels post-supplementation (nmol/L) (mean $\pm$ SD)	84.79 $\pm$ 19.47

**Table 2:** HbA1c pre-supplementation and post-supplementation statistics

HbA1c pre-supplementation and post-supplementation statistics	
Difference	-2.370
Standard error	0.207
95% CI	-2.7769 to -1.9631
t-statistic	-11.457
DF	324
Significance level	$P < 0.0001$

**Table 3:** Vitamin D pre-supplementation and post-supplementation statistics

Vitamin D pre-supplementation and post-supplementation statistics	
Difference	46.250
Standard error	2.771
95% CI	40.7983 to 51.7017
t-statistic	16.690
DF	324
Significance level	$P < 0.0001$



**Chart 1:** HbA1c and Vitamin D levels

Mean age of the study population was 46.87  $\pm$  15.99. there were 74(43.79%) male and 95(56.21%) female. Mean HbA1c pre-supplementation (%) was 9.58  $\pm$  2.41 while post supplementation was 7.21  $\pm$  1.08. There was a significant reduction of HbA1c of T2DM ( $P < 0.0001$ ). Vitamin D levels pre-supplementation (nmol/L) (mean  $\pm$  SD) was 38.54  $\pm$  29.54 while, Vitamin D levels post-supplementation (nmol/L) (mean  $\pm$  SD) was 38.54  $\pm$  29.54. There was a significant increase of vitamin D levels of T2DM ( $P < 0.0001$ ).

### Discussion:

Vitamin D deficiency is commonly encountered in all the population due to dietary habits and many studies reporting a deficiency in vitamin D levels among the population<sup>x</sup>. Vitamin D deficiency (25(OH)D < 50 nmol/L) and insufficiency (25(OH)D = 50 -74 nmol/L) were reported in 50% and 43.8% in a study sample of pregnant women in a tertiary care center<sup>xi</sup>.

Several studies suggest that vitamin D is a potential risk modifier for both types of diabetes<sup>xii</sup>. Also it has been shown that vitamin D has a direct effect in improved insulin secretion and insulin action, and subsequently, improved glucose homeostasis through activation of the vitamin D receptor on the  $\beta$ -cell of the pancreas islet of Langerhans<sup>xiii</sup>. Vitamin D also has an indirect role via regulation of calcium homeostasis on various mechanisms related to the pathophysiology of diabetes<sup>xiv</sup>. In a meta-analysis it has been suggested that combined supplementation of vitamin D and calcium may optimize glucose metabolism<sup>12</sup>. A study by Ordooei M et al they have shown that HbA1c may be reduced by

administration of vitamin D to children and adolescents with type 1 DM without changing the dose of insulin<sup>xv</sup>. Another study observed significant reduction in HbA1c levels from year 1 to year 2 and between year 1 and year 3 after supplementation of vitamin D in type 2 African American diabetic patients<sup>xvi</sup>.

A study by Lee C J et al showed relationship between vitamin D supplementation and change in HbA1c and fasting blood glucose among patients with T2DM found there was a modest reduction in HbA1c (-0.32% (-0.53 to -0.10),  $I^2 = 91.9\%$ ) compared to placebo after vitamin D supplementation<sup>xvii</sup>. The meta-analysis by Mirhosseini N et al<sup>xviii</sup>. Observed a significant reduction in HbA1c levels and following vitamin D supplementation and significant increase in serum 25(OH)D levels which was comparable with our study.

#### Conclusion:

To conclude we found that there is a significant inverse association between vitamin levels D and HbA1c in T2DM patients. Also there was significant reduction in HbA1c as vitamin D levels increased. Regular screening of vitamin levels D and HbA1c in T2DM patients is advised.

#### References:

1. Indian Council for Medical Research. Assessment of Burden of Non-communicable Diseases. New Delhi: Indian Council of Medical Research, 2018.
2. Kayaniyl S, Vieth R, Retnakaran R, Knight JA, Qi Y, Gerstein HC, Perkins BA, Harris SB, Zinman B, Hanley AJ. Association of vitamin D with insulin resistance and beta-cell dysfunction in subjects at risk for type 2 diabetes. *Diabetes Care*. 2010 Jun; 33(6):1379-81.
3. Shab-Bidar S, Neyestani TR, Djazayeri A, Eshraghian MR, Houshiarrad A, Gharavi A, Kalayi A, Shariatzadeh N, Zahedirad M, Khalaji N, Haidari H Regular consumption of vitamin D-fortified yogurt drink (Doogh) improved endothelial biomarkers in subjects with type 2 diabetes: a randomized double-blind clinical trial. *BMC Med*. 2011 Nov 24; 9 (0):125.
4. Nagpal J, Pande JN, Bhartia A. A double-blind, randomized, placebo-controlled trial of the short-term effect of vitamin D3 supplementation on insulin sensitivity in apparently healthy, middle-aged, centrally obese men. *Diabet Med*. 2009 Jan; 26(1):19-27.
5. Pittas AG, Nelson J, Mitri J, Hillmann W, Garganta C, Nathan DM, Hu FB, Dawson-Hughes B, Diabetes Prevention Program Research Group. Plasma 25-hydroxyvitamin D and progression to diabetes in patients at risk for diabetes: an ancillary analysis in the Diabetes Prevention Program. *Diabetes Care*. 2012 Mar; 35(3):565-73.
6. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007;**357**:266–281
7. Alvarez JA, Ashraf A. Role of vitamin D in insulin secretion and insulin sensitivity for glucose homeostasis. *Int J Endocrinol* 2010;2010:351–385
8. MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. *J Clin Invest* 1985;76:1536.
9. Buhary BM, Almohareb O, Aljohani N, et al. Association of Glycosylated Hemoglobin Levels With Vitamin D Status. *J Clin Med Res*. 2017;9(12):1013–1018.
10. AlBuhairan FS, Tamim H, Al Dubayee M, AlDhukair S, Al Shehri S, Tamimi W, El Bcheraoui C, Magzoub ME, de Vries N, Al Alwan I. Time for an Adolescent Health Surveillance System in Saudi Arabia: Findings From "Jeeluna". *J Adolesc Health*. 2015 Sep; 57(3):263-9.
11. Al-Faris NA High Prevalence of Vitamin D Deficiency among Pregnant Saudi Women. *Nutrients*. 2016 Feb 4; 8(2):77.
12. Pittas AG, Dawson-Hughes B. Vitamin D and diabetes. *J Steroid Biochem Mol Biol*. 2010 Jul; 121(1-2):425-9.
13. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2007 Jun; 92(6):2017-29.
14. Al-Shoumer KA, Al-Essa TM. Is there a relationship between vitamin D with insulin resistance and diabetes mellitus? *World J Diabetes*. 2015 Jul 25; 6(8):1057-64.
15. Ordoeie M, Shojaoddiny-Ardekani A, Hoseinipoor SH, Miroliai M, Zare-Zardini H. Effect of vitamin D on HbA1c levels of children and adolescents with diabetes mellitus type 1. *Minerva Pediatr*. 2017 Oct; 69(5):391-395.
16. Green RT, Gambhir KK, Nunlee-Bland G, Odonkor WA, Ganta VA. Maintenance of long-term adequate levels of vitamin d lowers HbA1c in African American patients with type 2 diabetes. *Ethn Dis*. 2014 Summer; 24(3):335-41.
17. Lee CJ, Iyer G, Liu Y, Kalyani RR, Bamba N, Ligon CB, Varma S, Mathioudakis N. The effect of vitamin D supplementation on glucose metabolism in type 2 diabetes mellitus: A systematic review and meta-analysis of intervention studies. *J Diabetes Complications*. 2017 Jul; 31(7):1115-1126.
18. Mirhosseini N, Vatanparast H, Mazidi M, Kimball SM. The Effect of Improved Serum 25-Hydroxyvitamin D Status on Glycemic Control in Diabetic Patients: A Meta-Analysis. *J Clin Endocrinol Metab*. 2017 Sep 1; 102(9):3097-3110.