

A CROSS-SECTIONAL STUDY ON VITAMIN D3 LEVEL IN TYPE 2 DIABETES MELLITUS PATIENTS FROM CHENNAI, INDIA

P.J.Parameaswari¹, Carnagarin Revathy², Balasubramanian Shanthi³

ABSTRACT

The present study highlights the importance of Vitamin D3 and its significance in Diabetes. We have recruited 34 type2 diabetes patients cross sectionally who were on regular treatment between 0-5 years from a Community HealthCare Center in Chennai, after obtaining the informed consent in vernacular language. Blood Investigations on Fasting, Post Prandial & Glycosylated Haemoglobin, Vit D3 levels were measured. Our main aim of this study was to elicit the relationship between Vit D3 and HBA₁C. Among those participants 15(44.1%) were females and 19(55.9%) males. Data was analysed using SPSS 16.0, and the mean±SE (mean) of 8 patients who had "Good control" (i.e. HBA₁C < 7%) was 16.5±0.82. Among them 3(37.5%) were females & 5(62.5%) were males. For 26 patients who were under 'Bad Control' (HBA₁C ≥ 7%), Pearson's coefficient of correlation between HBA₁C and Vit D3 was observed to be negative 'r = - 0.369' (P = 0.044), which is yet to be perused with larger sample size.

Keywords: Vit D3, HBA₁C, type2 diabetes, Correlation

INTRODUCTION

Diabetes is a major threat to global public health that is rapidly getting worse and the biggest impact is on adults of working age. In developing countries at least one in ten deaths among adults aged 35 to 64 is attributable to diabetes¹, and in some, the figure is as high as one in five. Simple lifestyle adjustments such as a healthy diet and physical activity², often combined with medication, have been shown to be effective in promoting a full and healthy life with diabetes.

Various factors play a role in the etiopathogenesis and the glycemc control among type 2 diabetes

mellitus(t2DM) patients. Vitamin D is derived from 7 dehydro cholesterol or ergosterol by UV radiation³. Chole calciferol is hydroxylated at the 25th position in the liver to form 25 hydroxy cholecalciferol. This is the major transport form of the vitamin. It then gets hydroxylated at the first position to form calcitriol which is the active form of vitamin D.

Interestingly, many studies reveal that Vitamin D3, (calcitriol) has a role in the synthesis and secretion of insulin⁴. Previous studies reveal that Vitamin D3 receptors are found in β cells of pancreatic islets promoting insulin secretion and decreasing insulin resistance by receptor mediated molecular mechanisms⁵ Various definitions for vitamin D insufficiency have appeared in the literature; the best established one pertains to serum levels below 30 ng/mL⁶. A recent meta-analysis has demonstrated that low vitamin D levels in middle-aged and elderly populations represent a risk factor for t2DM, cardiovascular disease and metabolic syndrome⁷. Deficiency of Vitamin D is associated with impairment of insulin synthesis and secretion and increase in insulin resistance. This study is done to find out the correlation between vitamin D3 levels and blood glucose levels as well as glycemc control in already diagnosed t2DM patients.

In many cases, t2DM – accounting for over 90% of all cases of diabetes – can be prevented through lifestyle interventions alone. The aim of this study was to examine the correlation between HBA₁C and vit D3 and to test for clinical and statistical significance. This study was ethically approved by the institutional research committee (IEC/54/2011-12).

MATERIALS & METHODOLOGY

Study Design: Cross-Sectional Study⁸

Study Area: A Community HealthCare Center in a metropolitan City, Chennai

Study Period: July 2011 to Feb 2012

Study Population: Type2 diabetes patients who were on regular treatment between

0-5 years who didn't have any other comorbid illness and who had given informed consent.

Study Material: The structured form with informations on Age, Sex, FBS, PPBS, HBA1C & Vit D3 along with the duration of regular treatment collected on first hand.

RESULTS

The data was analysed using SPSS 16.0 and were presented as descriptive statistics⁷ like frequency, percentage, mean, standard error, and the inferential statistics - student-t-test for two independent samples, 95% confidence interval, ANOVA and correlation coefficient. The data were segregated according to the glycaemic control and tested for its significance at 5% level. Values within parantheses represent percentage.

Table 1 describes the distribution of patients according to the glycemc control of t2dM patients over a period of 3 months. 8(23.5) of them had a good control with a Mean±SE of 16.5±0.82, 7(20.6) had a fair control with 20.1±1.03 , majority 16(47.1) had unsatisfactory control with 20.0±0.91 and 3(8.8) were on poor control over HBA1C with 20.6±0.66 respectively. The 95% CI for the 'good control'(HBA1C ≤ 7.0) group was observed to be narrow while comparing with the 'bad control' (HBA1C >7.0)group.

HBA1C (%)	N (N%)	Mean±SE	95% CI
Good (5.6% - 7.0%)	8 (23.5)	16.5± 0.82	14.5 to 18.4
Fair (7.01% - 8.0%)	7 (20.6)	20.1±1.03	17.6 to 22.6
Unsatisfactory (8.01% - 10.0%)	16 (47.1)	20.0±0.91	18.0 to 21.9
Poor (>10.01%)	3 (8.8)	20.6±0.66	17.8 to 23.5

TABLE I : DESCRIPTIVE STATISTICS FOR HBA1C (%)

Among Thirty Four t2dM patients 15 (44.1) were females and 19(55.9) were males. Table 2 provides the descriptive statistics for their Glycemic⁸ parameters based on the HBA1C control. The age of our participants were ranging from 38 to 56 years. The Mean±SE age for those 8 patients on good control was 40.3±0.49 with a FBS of 112.8±6.72 ,

PPBS of 184.6 ± 16.88 and Vit D3 of 16.5±0.82. The age of majority 16 participants on unsatisfactory control was 43.8±2.18 with a FBS of 155.2±10.05 , PPBS of 306.5±13.20 and Vit D3 of 20.0±0.91 respectively. While observing the Vit D3 values for patients on 'good control' (HBA1C ≤ 7.0) ranged from 14 to 20 when compared to patients on 'bad control' (HBA1C >7.0) ranging between 12 to 26.

Parameters	HBAC ₁			
	Good Control N=8	Fair Control N=7	Unsatisfactory Control N=16	Poor Control N=3
Age(years) Range Mean±SE 95% CI	38 - 42 40.3 ± 0.49 39.2 to 41.5	38 - 63 43.1 ± 3.32 35.0 to 51.2	38 - 67 43.8 ± 2.18 39.1 to 48.4	41 - 56 46.3 ± 4.84 25.5 to 67.1
FBS (g%) Range Mean±SE 95% CI	77 - 134 112.8 ± 6.72 96.9 to 128.7	63-198 124.4 ± 17.23 82.2 to 166.5	98-257 155.2 ± 10.05 133.8 to 176.6	131-290 190.0 ± 50.26 26.2 to 406.2
PPBS(g%) Range Mean±SE 95% CI	140 - 283 184.6 ± 16.88 144.7 to 224.5	203-326 260.5 ± 16.8 219.4 to 301.7	194-414 306.5 ± 13.2 278.3 to 334.7	237-412 322.3 ± 50.56 104.7 to 539.9
Vit D3() Range Mean±SE 95% CI	14 - 20 16.5 ± 0.82 14.5 to 18.4	16-24 20.1 ± 1.03 17.6 to 22.6	12-26 20.0 ± 0.91 18.0 to 21.9	20-22 20.6 ± 0.66 17.8 to 23.5

Table II: DESCRIPTIVE STATISTICS FOR THE GLYCEMIC PARAMETERS

The test of difference in means of Vit D3 between HBA1C(%) control groups are presented in Table 3. when Mean±SE of Vit D3 of patients under 'Good control' is 16.5±0.82 compared to 7 patients on 'Fair control' with 20.0±1.03 issued a t-value = 2.78 (P= 0.01).

HBA1C	N	Mean±SE	t-value (P-value)
Good Control Fair Control	8 7	16.5±0.82 20.0±1.03	2.78 (0.01)*
Good Control Unsatisfactory Control	8 16	16.5±0.82 20.0±0.91	2.45 (0.02)*
Good Control Poor Control	8 3	16.5±0.82 20.6±0.66	2.89 (0.01)*

Table III: STUDENT -TTEST FOR VIT D3

*Significant at 5% level

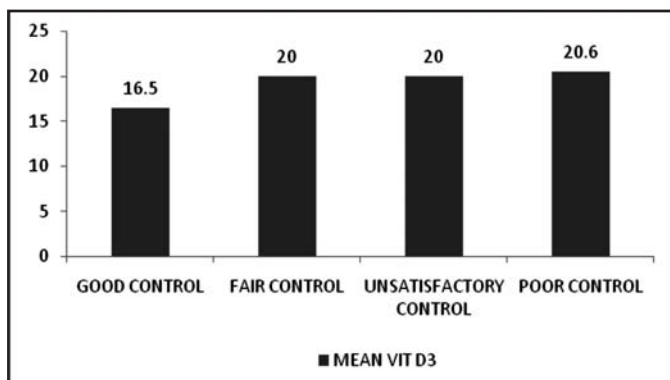


Fig. 1. Bar Diagram of Mean Vit D3 for HBA1C(%)

when compared for 16 'Unsatisfactory control' patients with 20.0 ± 0.91 issued a t-value = 2.45 ($P = 0.02$) and for the 3 'Poor control' patients with 20.6 ± 0.66 issued a Statistically Significant t-value = 2.89 ($P = 0.01$). This is presented in Fig 1. The ANOVA of Vit D3 for glycemic control groups was observed to be $F = 2.84$ ($P = 0.055$) statistically significant.

DISCUSSION

Type 2 diabetes mellitus is recognized as a worldwide public health problem due to the high medical and socioeconomic costs that result from complications associated with the disease⁹. In our study there existed a statistically insignificant correlation between HBA1C and Vit D3 for all 34 patients. But when we removed 8 patients under 'good control' we observed a negative correlation between HBA1C and Vit D3 with a magnitude of $r = -0.369$ ($P = 0.044$) but gender didn't show any significant association with all glycemic parameters along with Vitamin D3.

Since this is a time bound (8 months) study and the limited cost involved for Vit D3 investigation, we couldn't arrive at large number of patients without comorbid illness, but we could find a minimal negative correlation which is of Clinical Significance. The Chi-Square = 0.766 ($P = 0.858$) showed an insignificant association between sex and HBA1C.

The present study observed that type 2 diabetic individuals with vitamin D insufficiency showed poor glycemic control. According to various references¹⁰ vitamin D has a potential influence on glucose

homeostasis as suggested by the following factors.

Effect of vitamin D on insulin secretion : Pancreatic β cells express 1 alpha hydroxylase which is responsible for an active vitamin D3 synthesis¹¹ and also by increasing the insulin response to the glucose stimulation, but not affecting the basal insulin secretion¹². In some populations, type 1 diabetes is associated with certain polymorphisms within the VDR gene¹³ which is present in the human insulin gene promoter and also in the skeletal muscle and in adipose tissues¹⁴. The insulin secretion and sensitivity is influenced by Vitamin D mediated intracellular calcium secretion that enhances the binding of the calcium binding protein to the IRS - 1 (Insulin receptor substrate 1), stimulating tyrosine phosphorylation and PI3 kinase activation and thus promoting insulin secretion¹⁵.

Vitamin D deficiency may also impair the insulin secretion through its associated increase in the PTH levels which may impair the calcium signal which is needed for glucose-induced insulin secretion¹⁶. Of significance is the finding, that the vitamin D potentiation of glucose-induced insulin secretion is seen in normal individuals but not in patients with established type-2 DM¹⁷. Whether the insulin secretion is influenced by the direct action of Vitamin D or through its receptor or through changes in calcium, or PTH, is a matter of ongoing studies. It is also possible that the insulin secretion may be influenced by a combination of different mechanisms.

Effect of vitamin D on the insulin sensitivity : Type-2 DM, a state of chronic systemic inflammation has been found to increase the insulin resistance¹⁷. Type-2 DM was found to be associated with an increase in the levels of the tumour necrosis factor- α and β , the C reactive protein, the plasminogen activator inhibitor-1 (PAI-1), and interleukin-6 (IL-6)¹⁸. The increase in these inflammatory mediators may precede and even predict the development of type-2 DM. In support of this concept, is the finding that VDR has been found on almost all the cells of the immune system and that vitamin D can repress the type 1 cytokines, inhibit dendritic cell maturation, and upregulate the regulatory T cells. Vitamin D also

suppresses the antigen-presenting capacity of the macrophages, it modulates the development of the CD4 lymphocytes and it inhibits the production of IFN γ (interferon γ) and IL-2 (interleukin 2) ¹⁹, among other cytokines. These cytokines are known to activate the macrophages and the cytotoxic T cells, which in turn can lead to the destruction of the pancreatic islets. By the modulation of the immune and the inflammatory processes, vitamin D may also decrease insulin resistance and increase the insulin secretion in type-2 DM ²⁰, which are the two characteristic defects in this condition. From the above discussion, it is clear that vitamin D has a significant role to play in the molecular mechanisms of the synthesis, secretion and the peripheral sensitivity of insulin. Hence, hypovitaminosis D may be associated with insulin resistance and beta cell dysfunction. A variety of limitations of this study need however to be addressed. The small sample size did not allow a multivariate approach incorporating additional, potentially meaningful factors modifying the levels of serum 25(OH) D but it should be declared that from the evidence provided that improving vitamin D status will help establishing better glycemic control in people with DM type 2. Nevertheless, it seems that routine screening for vitamin D insufficiency may provide meaningful information and could be considered for diabetic care. Interventional studies are needed to evaluate whether vitamin D long-term supplementation could reduce morbidity in diabetic population with awareness of side effects.

REFERENCES

1. Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, Marks JS. Prevalence of Obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA*. 2003;(289):76–79.
2. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, et al. High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. *Diabetologia*. 2001;44(9):1094–101.
3. Mathieu C., Gysemans C., Vitamin D and diabetes; Laboratory of Experimental Medicine and Endocrinology (LEGENDO). *Diabetol*. 2006; 22(3): 187-193
4. Bikle DD, Siiteri PK, Ryzen E, Haddad JG. Serum protein binding of 1, 25- dihydroxyvitamin D: a re-evaluation by the direct measurement of the free metabolite levels. *J Clin Endocrinol Metab*. 1985;(61):969-975.
5. Thacher TD, Clarke BL. Vitamin D insufficiency. *Mayo Clin Proc* 2011; (86):50-60
6. Parker J, Hashmi O, Dutton D, Mavrodaris A, Stranges S, Kandala NB et al. The levels of vitamin D and the cardiometabolic disorders: a systematic review and meta-analysis. *Maturitas* 2010; (65):225-236
7. Kleinbaum DG, Kupper LL, Morganstern H, Epidemiological research: principles and quantitative methods. Van nostrand Reinhold, New York:1982
8. Kirkwood BR, Essentials of Medical Statistics, Kwell Scientific Publications Lt., London
9. Hennekens CH, Burings JE, Epidemiology in Medicine, LittleBrown and Company, Boston/Toronto
10. Beatriz A. Díaz-Apodaca,1 Shah Ebrahim,2 Valerie McCormack,3 Federico G. De Cosío,4 and Rosalba Ruiz-Holguín5 "Prevalence of type 2 diabetes and impaired fasting glucose: cross-sectional study of multiethnic adult population at the United States-Mexico border", *Rev Panam Salud Publica* 28(3), 2010.
11. Pittas A.J., Lau J., Hu F.B., Dawson-Hughes B. The role of Vitamin D and calcium in type 2 diabetes mellitus. A systemic review and meta-analysis. *Journal of Clinical Endocrinology and Metabolism*. 2007;92(6):2017-2029.
12. Johnson J.A., Grande J.P., Roche P.C., Kumar R. Immuno histochemical localization of the 1,25 (OH) 2 D3 receptor and calbindin D 28K in human and rat pancreas. *American Journal of Physiology*. 1994; 267 (3), E356-E360
13. Bland R, Markovic., Hills C.E, et al. Expression of 25-hydroxy vitamin D3-1 alpha hydroxylase in the pancreatic islets. *Journal of Steroid Biochemistry and Molecular Biology*. 2004 ;89-90:121-125

14. Boursillon P.M., Billaudel B., Faure-Dussert A., J. Endocrinol. 1999;(160):87-90.
15. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. Diabetologia. 2006; 49 (1): 217-218
16. Simpson R.U., Thomas G.A., Arnold A.J., "Identification of the 1,25 – di hydroxy vitamin D3 receptors and their activities in the muscle. The Journal of Biological Chemistry. 1985; 260(15): 8882-8891.
17. Fujita T., Palmieri G.M, J. Bone Miner. Metab. 2000;(18): 109–125
18. Kadowaki S., Norman A.W, J. Clin. Invest. 1984;(73): 759–766
19. Bastard J.P, Maachi M., Lagathu C., Kim M.J., Caron M., Vidal H, Capeau J., Feve B., Eur. Cytokine Netw. 2006;(17): 4–12.
20. Kolb H., Mandrup-Poulsen T., Diabetologia .2005;(48): 1038-1050
21. Vendrell J., Gutierrez C., Pastor R., Richart C., Metabolism. 1995; (44):691–694
22. Ferná'ndez-Real J.M, Vendrell J., Ricart W., Broch M., Gutie'rrez C., Casamitjana R, Oriola J., Richart C., Diabetes Care.2000;(23): 831–837.
23. Vozarova B.et al. Hum. Genet. 2003; (112):409–413.
24. Hoffstedt J., Andersson I.L, Persson L, Isaksson B, Arner P. Diabetologia. 2002;(45):584–587.
25. Wolford J.K., Gruber J.D., Ossowski V.M., Vozarova B., Antonio P. Tataranni, Bogardus C., Hanson R.L. Mol. Genet. Metab. 2003;(78):136–144.

1. **P. J. Parameaswari**
Asst. Prof. Biostatistics
Department of Community Medicine
Sree Balaji Medical College,
Bharath University,
No.7, CLC Works Road,
Chromepet, Chennai- 600044, India
Email : dr.parameaswari@rocketmail.com

2. **Carnagarin Revathy**
Post Graduate
Department of Biochemistry
Sree Balaji Medical College,
Bharath University,
No.7, CLC Works Road,
Chromepet, Chennai-600044, India
Email : revathycarnagarin@yahoo.com

3. **Balasubramanian Shanthi**
Associate Professor
Department of Biochemistry
Sree Balaji Medical College,
Bharath University,
No.7, CLC Works Road,
Chromepet, Chennai-600044, India
Email : shanthibio@gmail.com