



## A PROSPECTIVE STUDY OF EFFECT OF VITAMIN D SUPPLEMENTATION ON GLYCEMIC CONTROL IN PATIENTS OF TYPE 2 DIABETES MELLITUS

### Medicine

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### ABSTRACT

The management of diabetes mellitus remains an enigma even though its symptoms were described more than 2000 years ago [9]. This is because the central therapeutic goal of diabetes management, euglycemia, is influenced by complex physiologic and pathologic processes, some of which are clearly understood, while others are less clear. Suboptimal glycemic control is a recognized risk factor for acute and chronic complications of diabetes including microvascular and macrovascular diseases. Various Oral Hypoglycemic Agents (OHA) have been widely used for the same. However, there is recent evidence in humans and animal models suggesting that vitamin D may play an important role in modifying the risk of diabetes [10]. This study aims at establishing the role of Vitamin D in Type 2 Diabetes Mellitus. Hope this study resolves the disputed role of Vitamin D and would be a useful tool in managing Type 2 Diabetes Mellitus in the future.

### KEYWORDS

Vitamin D, Hypoglycemia, 25-Hydroxy cholecalciferol

### INTRODUCTION

The World Health Organization defines Diabetes Mellitus as a metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipidemia, negative Nitrogen balance and sometimes Ketonemia [1]. There is an alarming increase in prevalence of Diabetes Mellitus (DM) worldwide, with 246 million diabetics residing world over as of 2010 [9]. The International Diabetes Federation (IDF) recognizes India as *Diabetes Capital of the World*, with 40.9 million diabetics as of 2006 [9]. All of this call for aggressive measures to reduce the diabetic burden that today has shaped up as a major public health concern economically, politically as well as socially. An appropriate drug therapy is needed to achieve optimal glycemic control in diabetic management. Attaining and maintaining a good glycemic control, by use of Oral Hypoglycemic Agents (OHA) and insulin preparations, is important to prevent the microvascular, macrovascular and acute metabolic complications [2]. Non-pharmacological measures like lifestyle modification and physical activity have an equally important role as does the drug therapy.

However, prevention and treatment of DM remains a major public health challenge. Several reports exist on worsening of glycemic control in Type 2 Diabetes patients with overt Vitamin D deficiency [4]. Evidence suggesting role of Vitamin D in glucose homeostasis and insulin secretions are: Vitamin D Receptors (VDRs) presence on beta cells and skeletal muscle, VDR Responsive element in Human Insulin gene promoter and expression of alpha 1 Hydroxylase enzyme [4].

The aim of this study is to find effect of Vitamin D supplementation on Glycemic control in patients of Type 2 DM. The objectives of the study include:

- 1) To assess and study the effect of Vitamin D supplementation on Fasting Blood Sugar levels in diagnosed patients of Type 2 Diabetes Mellitus
- 2) To assess and study the effect of Vitamin D supplementation on Post meal Blood sugar levels in diagnosed patients of Type 2 Diabetes Mellitus
- 3) To assess and study the effect of Vitamin D supplementation on Glycosylated Hemoglobin (HbA1c) levels in diagnosed patients of Type 2 Diabetes Mellitus
- 4) To assess any adverse drug reaction expected per se related to Vitamin D supplementation in terms of patients recording adverse effects

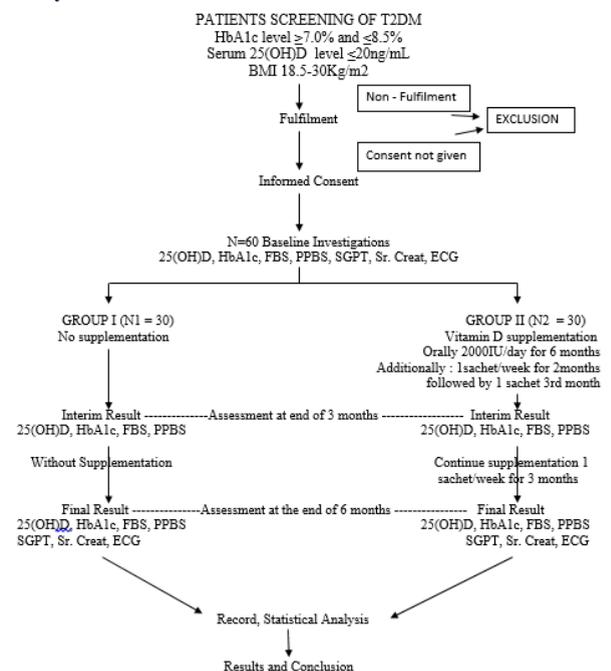
### MATERIALS AND METHODS

The present study is an open-label, randomized, single-centered, comparative, prospective and parallel, two-arm interventional study of 11 months duration. Study was carried out from 10/02/2018 to 04/01/2019. The study is designed according to norms and principles of ICH GCP (International Conference on Harmonization Good Clinical Practice) guidelines. The Study was conducted at MGM Medical College, Aurangabad after obtaining approval of study

protocol from Institutional Ethics Review Committee (IERC). The selection of the patients was strictly as per designed in inclusion and exclusion criteria. Informed written consent was obtained from all patients at the time of enrollment.

Total 60 patients suffering from T2DM were enrolled in the study. They were randomly allotted into 2 groups of 30 each by using Random number table. Group 1 or the Control Group were patients not receiving any Vitamin D supplement during the study period. They continued regularly with their OHA for diabetic control. Group 2 or the Treatment group were patients supplemented with Vitamin D as per Schedule. The Vitamin D supplement was a single sachet: dose equivalent to 1gm containing 60,000IU of Cholecalciferol. To be supplemented once a week for 2 months followed by once a month for 4 months. Additionally, 2000IU of Cholecalciferol Capsule to be supplemented once daily [11]. The study was conducted as per the flowchart shown aside.

### Study Flowchart



At each visit patient was assessed for glycemic control and history pertaining to any adverse effect. Patient was advised to follow healthy diet, do regular exercise and not take any other anti-diabetic drug or

vitamin supplement. All statistical analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows, Version 7.0. Bar graph, pie charts and other methods of graphical representations are used to portray the results of the experiments and Fischer's t test and student's t test (Paired and Unpaired) were used to measure the differences among the groups.

**3.0 RESULTS**

Total 60 patients were analyzed in the entire study.

Of the total 60 diabetic patients selected, 33 were male and 27 were female patients. Group C consisted of 16 male patients (53.33%) and 14 female patients (46.66%) while Group T had 17 male patients (56.66%) and 13 female patients (43.33%).

	Group C		Group T	
	Male	Female	Male	Female
Age				
30 - 40 years	3	2	5	6
40 - 50 years	7	7	9	6
50 - 60 years	6	5	3	1
	16	14	17	13

**Table 2**

FBS (mg%)	Baseline Mean ± SD	After 3 months Mean ± SD	After 6 months Mean ± SD
Group C	162.90 ± 31.33	138.70 ± 34.05	127.2 ± 36.60
Group T	157.90 ± 37.27	124.07 ± 39.64	94.93 ± 15.35

**On evaluating the Fasting Blood sugar (FBS)** at baseline, 3 months and 6 months in Group C and Group T, the following results were obtained.

In Group C, Mean FBS is reduced from 162.9 ± 31.33 to 138.7 ± 34.05 after 3 months and further to 127.2 ± 36.60 after 6 months of study reflecting total reduction of 21.6%. In Group T, a sharper fall was seen in Mean FBS which reduced from 157.90 ± 37.27 to 124.07 ± 39.64 after 3 months and more pronounced in next 3 months to 94.93 ± 15.35 reflecting total reduction of 39.89%.

**Table 3**

Comparison FBS	t-value	p-value	Significant / Not Significant
Group C at 6 months	6.859	<0.0001	Significant
Group T at 6 months	11.72	<0.0001	Significant

**Table 4**

PPBS (mg%)	Baseline Mean ± SD	After 3 months Mean ± SD	After 6 months Mean ± SD
Group C	213.40 ± 36.82	187.40 ± 31.72	176.17 ± 34.39
Group T	209.70 ± 41.30	175.93 ± 27.85	149.03 ± 16.86

**On evaluating the Post prandial Blood Sugar (PPBS)** at baseline, 3 months and 6 months in Group C and Group T, the following results were obtained.

In Group C, Mean PPBS is reduced from 213.40 ± 36.82 to 187.40 ± 31.72 after 3 months and further to 176.17 ± 34.39 after 6 months of study reflecting total reduction of 17.37%. In Group T, a sharper fall was seen in Mean PPBS which reduced from 209.70 ± 41.30 to 175.93 ± 27.85 after 3 months and more pronounced in next 3 months 149.03 ± 16.86 reflecting total reduction of 28.7%.

**Table 5**

Comparison PPBS	t-value	p-value	Significant / Not Significant
Group C at 6 months	6.487	<0.0001	Significant
Group T at 6 months	11.08	<0.0001	Significant

**Table 6**

HbA1c (mg%)	Baseline Mean ± SD	After 3 months Mean ± SD	After 6 months Mean ± SD
Group C	7.80 ± 0.47	7.42 ± 0.51	7.22 ± 0.59
Group T	7.76 ± 0.511	7.22 ± 0.513	6.70 ± 0.39

**On evaluating the Glycosylated Hemoglobin level (HbA1c)** at baseline, 3 months and 6 months in Group C and Group T, the following results were obtained.

In Group C, there was a minimal reduction in Mean HbA1c as it decreased from 7.80 ± 0.47 to 7.42 ± 0.51 after 3 months and further to 7.22 ± 0.59 after 6 months of study reflecting total reduction of 7.43%.

In contrast during the same period in Group T, the Mean HbA1c showed a decrease from 7.76 ± 0.511 to 7.22 ± 0.513 after 3 months and more pronounced in next 3 months 6.70 ± 0.39 reflecting total reduction of 13.66%.

**Table 7**

Comparison HbA1c	t-value	p-value	Significant / Not Significant
Group C at 6 months	7.403	<0.0001	Significant
Group T at 6 months	17.18	<0.0001	Significant

**Table 8**

Vitamin D	Baseline Mean ± SD	After 3 months Mean ± SD	After 6 months Mean ± SD
Group C	13.40 ± 3.26	13.03 ± 3.11	13.07 ± 2.26
Group T	13.17 ± 3.98	23.10 ± 4.18	34.53 ± 4.08

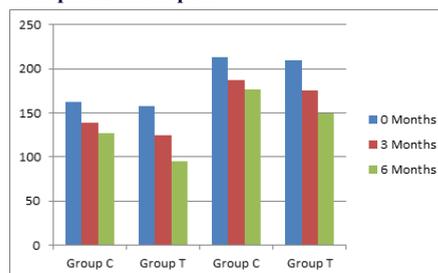
**On evaluating the Serum Vitamin D levels** at baseline, 3 months and 6 months in Group C and Group T, the following results were obtained.

In Group C it was observed that at all the three levels of study, the Mean Vitamin D levels remained almost constant from 13.40 ± 3.26 to 13.03 ± 3.11 after 3 months and to 13.07 ± 2.26 after 6 months. In group T, Mean Vitamin D increased rapidly from 13.17 ± 3.98 at the start of the study to 23.10 ± 4.18 after 3 months and further to 34.53 ± 4.08 after 6 months.

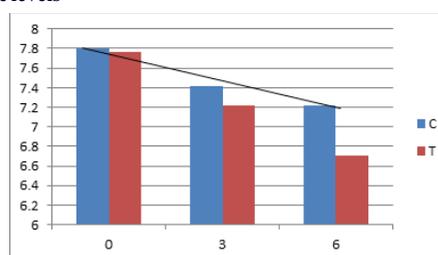
**Table 9**

Comparison Vitamin D	t-value	p-value	Significant / Not Significant
Group C at 6 months	1.109	<0.0001	Significant
Group T at 6 months	26.19	<0.0001	Significant

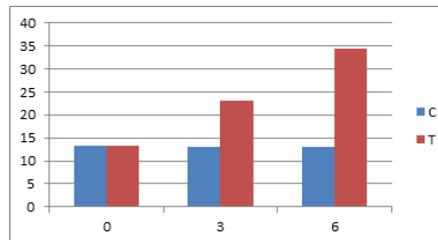
**Graph 1 - The graphical representation below shows the comparison of study parameters (FBS and PPBS) values at all levels in Group C and Group T.**



**Graph 2 - The graph below shows HbA1c values in both groups at all three levels**



**Graph 3 - The graph below shows Vitamin D values in both groups at all three levels**



The calculated values of t were compared with the tabulated values and it was inferred that the differences in the values of FBS, PPBS and HbA1c obtained in control and treated groups were statically non-significant up to 3 months. However, at the end of 6 months these values significantly decreased. The decrease was more pronounced in treatment group as compared to control group. It was also observed

that the Vitamin D levels significantly increased in treated group from 3rd month itself and by end of 6 months was nearly 2.6 times the baseline levels. These levels remained almost constant in Control Group all throughout the study.

## DISCUSSION

Several studies have previously demonstrated the relationship between Vitamin D and Type 2 Diabetes Mellitus. Dandona et al recognized this situation 25 years ago when he commented that '*whether Vitamin D deficiency contributes to pathogenesis of diabetes or vice versa is an area ripe for investigation.*' [7] This comment unfortunately holds true even today. Currently, there is insufficient evidence of beneficial effect to recommend vitamin D supplementation as a means of improving glycemia or insulin resistance in patients with diabetes, normal fasting glucose or impaired glucose tolerance.

Study conducted by Al-Daghri NM et al 2012 is an 18-month prospective interventional study on T2DM Saudi patients with Vitamin D supplement (2000IU/day) oral as an adjuvant therapy. 25(OH)D levels remained below normal 18 months after treatment onset. Yet, this 'suboptimal' supplementation significantly improved glycemic control with favorable change in blood sugar levels that were more pronounced in T2DM females [16].

Jacobs et al 2008 in a randomized, double-blind, placebo-controlled, parallel group trial in T2DM with low serum 25(OH)D levels showed oral vitamin D reduced FBS levels in patients with T2DM and Vitamin D insufficiency [17]. Torun et al showed that Vitamin D exerts its insulinotropic effect by the VDR, causing an increased Calcium influx through beta cell membrane and many other potential mechanisms of Vitamin D on T2DM have been demonstrated [18].

## RESULTS AND CONCLUSION

From the present study, it can be concluded that Vitamin D deficiency was seen concomitantly in Type 2 DM Patients. In Treatment Group, Vitamin D supplement was responsible for improved levels of FBS, PPBS, HbA1c and serum Vitamin D levels among the individuals and within the time intervals. The near normal values of study parameters resulted in good control of blood sugar levels following 6 months of Vitamin D supplementation.

In summation it can be said that when Vitamin D levels were adequate, the glycemic control was better with blood sugar levels in control. The limitations of the study include: pilot study with small sample size, double blinded study could not be conducted and determining the right dose of Vitamin D was difficult. Another important question that still remains unanswered is, "Is low Serum Vitamin D level a factor that predisposes, or is it somehow a by-product of illness?" Hence, the relationship between Vitamin D status and glucose tolerance in Type 2 DM requires further study to establish a definite result.

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