Original Articles

Effect of Vitamin D on Fasting Blood Sugar and HbA1c in Type 2 Diabetes Mellitus Patients

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ABSTRACT:

Objective: To evaluate the impact of vitamin D supplementation on fasting blood sugar & HbA1c in Type 2 diabetes mellitus patients.

Methodology: This was an analytical case control study and was carried out by the Pharmacology Department at the Basic Medical Sciences Institute (BMSI, JPMC) with the collaboration of Diabetic OPD, JPMC, Karachi for the duration of 6 months. In this study 80 patients were selected by non-probability purposive sampling method and open EPI 3.01 version was used to estimate the sample size.

Results: The study revealed that pre and post plasma vitamin D proportions in the intervention group were significant (P<0.001) as compared to the group labeled as control which did not show any difference at the end of study (P 0.16). However, there was an insignificant relationship between Vit D and HbA1c with no improvement observed in glycemic control (P 0.74) or HbA1c levels (P 0.20) in the intervention group.

Conclusion: According to the study's findings, vitamin D addition has improved plasma vitamin D3 levels and improved insulin sensitivity in patients with T2DM. The current analysis did not find a significant contribution to reducing HbA1c or enhancing glycemic control in individuals with T2DM.

KEYWORDS: Vitamin D, Type 2 Diabetes Mellitus, Fasting Blood Sugar

INTRODUCTION

This analysis was piloted in order to estimate the impact of vitamin D in type 2 diabetes mellitus patients which will help physicians in achieving improved compliance with a reduced amount of treatment and minimize the adverse effects of multiple drug interaction and also contributes in reducing financial load in T2DM patients. Diabetes is one of the most dangerous and prevalent chronic illnesses in the world, and can lead to crippling complications. It is not only an economic but also a societal problem for the patients, as well as a socio-economic burden for nation's budget due to its rising incidence and death rate.[9,19] Among the fitness concerns of current era, the figure of affected people has increased more than threefold over the past 20 years. Furthermore, percentage of American adults over the age of 18 (roughly 30 million citizens) also fall into this category and is predicted to ascend up to 300 million in 2025.[10,11] WHO estimated that type 2 diabetes mellitus claimed lives of almost 1.5 million people in 2019 and, was the leading cause of mortality.

Pakistan is among the most vulnerable nations suffering from diabetes, as the disease is more common in poor and middle-class nations. According to the International Diabetes Federation, around 33,000,000 adults in Pakistan (or 26.7% of

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the country's total grown-up population) had diabetes in 2021.[13,27] Furthermore, it is concerning that a significant number of people continue to live without a diagnosis, which may increase the incidence of the disease and the risk of complications from untreated diabetes.[19] Diabetes mellitus (DM) is a group of hormonal disorders which cause blood sugar levels to rise consistently. Among the two most frequent types of diabetes are Type 1 Diabetes Mellitus which is categorized by predominant absence of insulin as a result of an autoimmune attack on the islets of Langerhans whereas Type 2 Diabetes Mellitus is caused by decreased insulin sensitivity to the peripheral cells.[20] Based on the guidelines of American Diabetes Association, HbA1c is an investigative test for diabetes and an assessment of blood glucose levels in diabetic patients.[23]

However, after different experimental studies, it is well established that there are direct connections among low vitamin D and variables like obesity, and especially type 2 diabetes mellitus which may also raise the risks of pandemic diseases like COVID-19 severity.[22] Currently, vitamin D has gained massive significance for its contribution in a variety of additional natal functions. In recent years, its other functions within the human body have become a focus of attention.[24] The serum glucose level is associated with various biological processes happening inside the human body but its altered volume can be associated with several harmful results. Carbohydrate and lipid metabolism are interrelated, and an imbalance in the body's levels of free fatty acids is a contributing factor to type 2 diabetes mellitus (T2DM), insulin resistance, and various complications including chronic inflammation, pancreatic β-cell impairment and myocardial infarction. In people with satisfactory health, metabolism of fat is tightly regulated. Since extra fatty acids will collect inside the body and interfere with the fatty tissue signal process which is the source of varied medical conditions particularly type 2 diabetes mellitus.[17] Recent data reveals that over 50% of Pakistan's population (53.5 percent) is affected by vitamin D3 deficiency. Hypovitaminosis D is principally influenced by cultural norms and environmental factors, though different sectors have minimum impression on its serum value. Because of this, in Pakistan grown-ups, infants and pregnant women are mainly vulnerable sector due to their limited motion within their residence settings in accordance with their cultural standards.[12] Experts suggest that approximately 25 minutes of sunlight exposure to the face and upper body, without sunscreen, around 9 a.m.at most geographic altitudes, at least 3 times a week, may provide the necessary amount of vitamin D and increase its levels in the blood. Moreover, the biological production of vitamin D varies throughout the day and is also influenced by different seasons and geographic locations on Earth.[14,15]

The key point of this study is to observe the results of vitamin D administration in type 2 diabetic patients. The positive outcome will benefit the patients in achieving improved compliance with less treatment and dropping financial load in T2DM patients as well as minimizing drug interactions with several drug therapies. Unluckily, sufficient research work wasn't carried out on Pakistani population with T2DM. They take multiple medicines to sustain their normal glycemic level but there are additional endocrine components which participate in managing raised blood glucose. Similarly, depression is quite common among individuals with diabetes due to dietary restrictions, complications and unmanageable glycemia. While they may be prescribed various antidepressants, tolerance can develop over time, leading to adverse effects. In various experiments it has been noticed that individuals with hyper-glycemia and mental illness also lack vitamin D.

METHODOLOGY

It was an experimental case control analysis that was carried out in the department of pharmacology in Collaboration with diabetic OPD JPMC, Karachi. Non-probability purposive collection

choice was preferred for this study. Study Period was 6 months after approval of synopsis. Ethical approval was obtained from Institutional Review Board (IRB) of BMSI JPMC Karachi (vide letter No. F.2-81/2020-GENL/3932/JPMC).

In this study, we included both genders with type 2 diabetes mellitus aged 18-60 years[18] whose duration of type 2 diabetes mellitus is not more than 10 years and were on insulin and oral hypoglycemic drugs and gave consent to take part in this analysis. In the exclusion criteria, children, elderly individuals over sixty years old, pregnant or lactating women, patients with type 1 diabetes mellitus (T1DM), individuals with unsatisfactory clinical conditions and those who have taken vitamin D or calcium supplements in the last six months were exempted from the study. The sample size was assessed using Open Epi software version 3.01 and 80 participants were chosen and mean difference was determined as well. With a 95% confidence interval and a power of 80%, for sample size calculation the prevalence of disease, was at least 31 in each intervention and control group. As a result, we engaged 40 people for single group.[8]

On the basis of vitamin D administration, participants were divided into two groups. The control one received no vitamin D supplementation, while the intervention group got 600,000 IU/month of vitamin D supplementation via intramuscular (I/M) method, administered sequentially for 3 months.[21,28] Each box of 5 ampoules containing 1 ml, 600,000 IU of vitamin D3 manufactured by Shanxi Shuguang Pharmaceutical Co., Ltd, China, with batch number 81126. SPSS Version 21.0 (Chicago, SPSS Inc.) was used to analyze the data. IBM SPSS version 22.0 was utilized in statistical examination. To investigate the relationship between vitamin D and plasma glucose levels Chi Square test was applied. Incidence and percentages were recorded for the descriptive qualities. For the analytical significance of the link between vitamin D and type 2 diabetes Chi square test was used.

From November 2020 to March 2021, 80 patients with type 2 diabetes mellitus were enrolled from the diabetic Clinic and completed four appointments. The initial records were acquired from contributors based on their medical history. Vital signs, serum vitamin D levels, fasting blood sugar, and HbA1c levels were routinely measured during the first consultation and evaluation. All basic investigations in both groups were completed after fully explaining the method to the study participants on the very first visit in November 2020 (designated as day 0). Intervention group was summoned in December 2020 for vitamin D delivery (designated as visit 1). In between, all expected lab results for all blood variables were obtained and documented. The first visit for vitamin D delivery occurred in December, during which 600,000 IU of Vit D3 were administered intramuscularly to the deltoid muscle of the members of the intervention group. In a similar way the second and third visits occurred in January and February 2021, with patients receiving a similar amount of vitamin D3 intramuscularly. The fourth and final visit occurred in March 2021, and participants from both the intervention and control groups were summoned, and preliminary investigations were repeated once more. The blood samples were processed in JPMC laboratory that adheres to regular procedures regarding assays. FPG was determined using glucose hexokinase catalytic analysis (Olympus Glucose OSR 6121), glycosylated hemoglobin was quantified using the Roche 2nd series HbA1c immunochemical assay. Using the Roche Modular Analytics E170 Vit D (25-OH) test, vitamin D samples were assessed using standard laboratory techniques.

The reference level of Vit D:[25]

>30 ng/mL (75 nmol/L) -------- Normal levels
20–30 ng/ml (50–75 nmol/L) -------- Vit D insufficiency.
< 20 ng/ mL (50 nmol/L) ---------- Vit D absence

The cut-off reference values of HbA1c:[26]

< 5.7% -------- Normal
5.7%–6.4% -------- Pre diabetes
> /= 6.5% --------- Diabetes Mellitus

RESULT

This study included 80 type 2 diabetes mellitus individuals, 28 of whom were men and 52 of whom were women as demonstrated in Table 1.

Screening for added co morbidities revealed that 33 participants had a prior diagnosis of hypertension 20 had diabetes for less than 5 years, and 20 had T2DM for longer than 5 years. In the Intervention batch, 31 people took hypoglycemic medications, 4 used insulin, and 5 used both. Whereas 32 had a previous record of hypertension, while 20 cases had type 2 diabetes mellitus (T2DM) for less than 5 years, and a similar number of controls had T2DM for more than 5 years.

Table I: Demographic characteristics of participants in both groups (n=80)

Variable		n	%
Age (years)	40- <50	42	52.5
	50 – 60	38	47.5
Gender	Male	28	35.0
	Female	52	65.0

As demonstrated in Table 2, 26 people took hypoglycemic medications and 11 people used insulin, whereas three people used both in the control group.

Table 2: Frequency of co morbidities with medicine in both group

Variable		Intervention (n=40) n(%)	Control (n=40) n(%)
Hypertension	Yes	33 (82.5%)	32 (80.0%)
	No	7 (17.5%)	8 (20.0%)
Duration of diabetes	<5years	20 (50.0%)	20 (50.0%)
	>5 years	20 (50.0%)	20 (50.0%)
Hypoglycemic intake	Oral drugs	31 (77.5%)	26 (65.0%)
	Insulin	4 (10.0%)	11 (27.5%)
	Both	5 (12.5%)	3 (7.5%)

A statistical analysis of measurements taken before and after therapy for vitamin D, fasting blood sugar, and HbA1c revealed a significant change in vitamin D levels (P 0.001) between pre and post therapy values.

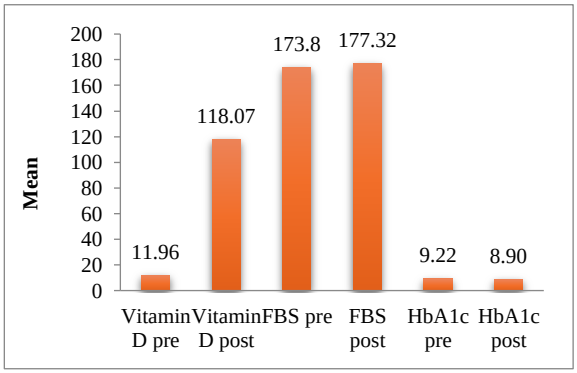
Meanwhile, an insignificant difference was observed between Pre- and Post-therapy fasting blood sugar levels (FBS) (P 0.74). Similarly, no meaningful change was found in HbA1c levels before and after therapy (P 0.20) in intervention group, as shown in table 3.

Table 3: Comparison of the mean values of vitamin D, FBS & HbA1c before and after therapy between the two groups

Variable		Mean±SD	P value
Intervention group	Pre-therapy Vitamin D level	11.96±7.07	<0.001
	Post-therapy Vitamin D level	118.07±39.66	
	Pre-therapy Fasting blood sugar (FBS)	173.80±69.20	0.74
	Post-therapy Fasting blood sugar FBS	177.32±73.51	
	Pre-therapy HbA1c	9.22±2.14	0.20
	Post-therapy HbA1c	8.90±1.97	
Control group	Pre-therapy Vitamin D level	12.71±8.89	0.16
	Post-therapy Vitamin D level	12.72±8.89	
	Pre-therapy Fasting blood sugar (FBS)	167.92±78.71	<0.001
	Post-therapy Fasting blood sugar FBS	180.45±80.73	
	Pre-therapy HbA1c	9.28±1.64	<0.001
	Post-therapy HbA1c	9.66±1.87	

P value ≤ 0.05 taking significant

Fig 1 Schematic representation of the correlation between pre- and post-intervention mean levels of vit D, FBS and HbA1c in the treated group.



No noteworthy change was seen between the means of pre- and post-therapy vitamin D levels in the untreated group. (P 0.16), however the P value of pre-and post-therapy FBS and HbA1c showed a significant difference (P <0.001) in control group.

Fig2: Statistical representation of the comparison between pre- and post- intervention mean levels of vitamin D, FBS, HbA1c in the untreated group.

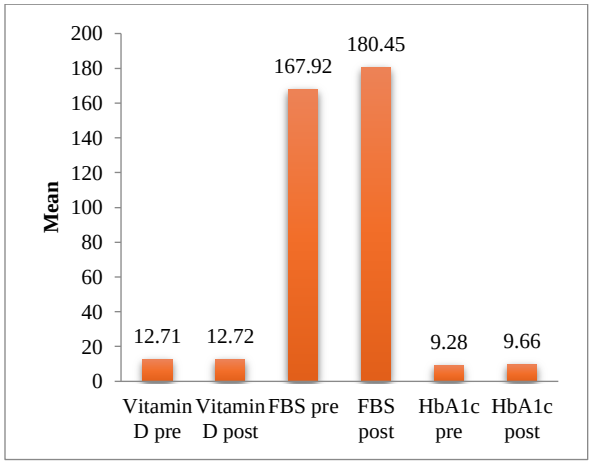


Fig 3: prior & later levels of vitamin D in both groups

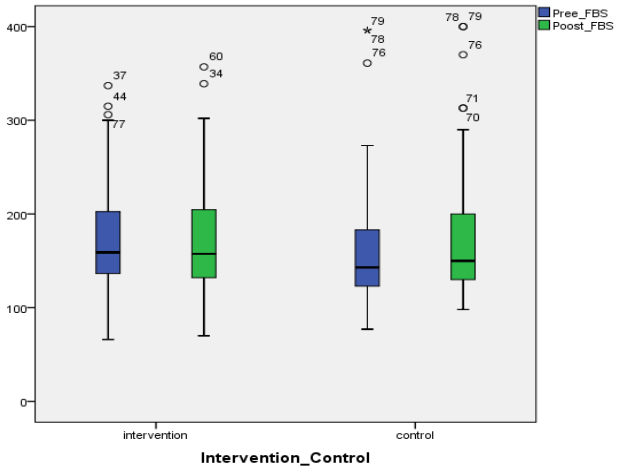


Fig 4: Before & after intervention, FBS levels in both groups

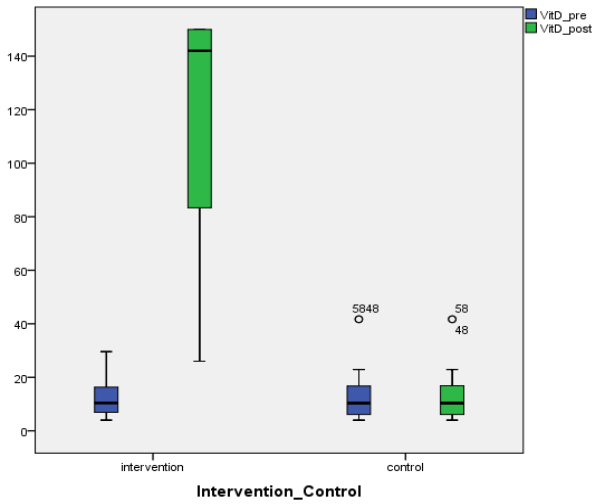
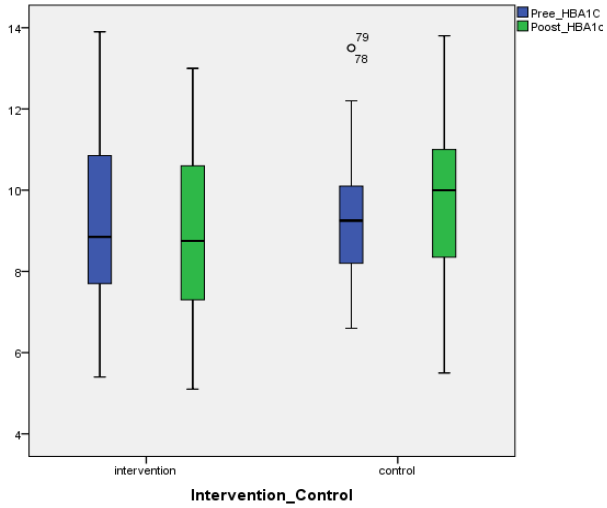


Fig 5: Pre and post intervention Fasting glycosylated hemoglobin values in both groups



DISCUSSION

The current analysis showed the enormous importance of vitamin D in increasing serum cholecalciferol levels and improving diabetic symptoms in experimental group. However, the observed changes were not statistically significant. Contrary to this, the control group which was not given vitamin D showed improved glycemic index. So according to our study vitamin D plays no significant role in decreasing FBS and HbA1c.

Our study is consistent with a meta-analysis which showed that vitamin D administration significantly reduces key inflammatory factors, and guards kidney function which may delay diabetic nephropathy but glycemic levels remain identical in both the groups.[6]

Contrary to this, Kazemi et al. conducted a study analyzing the efficacy of different vitamins and minerals including vitamin D, in diabetes. They concluded that vitamin D was more effective among others in lowering FBS and HbA1c.[3] Similarly, Zhang et al. performed study on prediabetic individuals and shared that blood sugar levels were reduced to normoglycemia.[7]

In the current era vitamin D is gaining incredible importance because of its positive effects on numerous medical conditions. Its beneficial effects are also seen in improving mental health. In a

systemic review that included six studies analyzed different doses of vitamin D against a placebo group for 12 weeks and found a positive effect on depression, anxiety and mental health.[2]

Hypovitaminosis D can lead to severe complications in diabetes, Tang et al found out that patients with diabetic foot had lower vitamin D levels in contrast to the individuals without diabetic foot. Moreover, people whose blood sugar levels are high tend to have lower levels of vitamin D.[5]

Another study highlighted sex differences in vitamin D3 levels, finding lower vitamin D3 levels in diabetic females compared to males.[1] A recent systemic review was done in 2021 and 29 case control studies were included to see the effect of vitamin D3 on Gestational Diabetes Mellitus and there came out a noteworthy relationship among lack of vitamin D3 & threat of developing Gestational Diabetes Mellitus.[4]

CONCLUSION

This research concluded that vitamin D supplementation enhanced serum cholecalciferol levels[16] and decreased insulin resistance in T2DM patients. In terms of its impact on improving blood glucose levels & minimizing HbA1c in individuals with Type II diabetes, it was not observed and was deemed unimportant.

Conflict of Interest: None
None to declare. None

Abbreviations:

T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
Vit D	Vitamin D
HbA1c	Glycosylated Hemoglobin
FBS	Fasting Blood Sugar

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