IMPACT OF VITAMIN D_3, ON HBA1C IN INDIVIDUALS WITH PRE-DIABETES

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ABSTRACT

Objective: To determine the effect of vitamin D_3 supplementation on HbA1c in individuals with pre- diabetes
Study Design: Quasi experimental study.
Place and Duration of Study: Study was executed in department of Pharmacology and Therapeutics, Army Medical College, Rawalpindi in collaboration with Chemical Pathology department, Army Medical College and Armed Forces Institute of Pathology (AFIP), Rawalpindi Pakistan, from Jan to Dec 2019.
Methodology: One hundred and forty individuals with pre-diabetes and co-existing hypovitaminosis D_3 were selected, with serum 25(OH) D (<50 nmol/L) and elevated glycosylated hemoglobin (HbA1c) (5.7-6.4%). Individuals were randomly assigned to receive 2000000 IU of vitamin D_3 (Vit D_3; n=70) or placebo (n=70) one stat at the beginning of study and one after one month. The primary outcome was amelioration of HbA1c. Results of HbA1c and vitamin D_3 were compared after completion of study with the initial values.
Results: A considerable inverse association was found between vitamin D_3 and HbA1c in individuals with pre-diabetes. Median with inter-quartile range of baseline serum 25(OH) D_3 was 43 and 41 nmol/L in the Vitamin D_3 and placebo group, respectively. Post treatment serum 25(OH) D_3 was significantly increased to 54nmol/L (p<0.0001) in the Vitamin D_3 group. HbA1c level was decreased in the vitamin D_3 group.
Conclusion: This study evaluated the correlation between vitamin D_3 in individuals with pre-diabetes. A statistically significant improvement in Glycosylated hemoglobin (HbA1c) was observed in the patients selected in the pre-diabetic range.

Keywords: Glycemic, Hypovitaminosis, Insulin sensitivity, Parameters, Pre-diabetes, Supplementation, treatment, Vitamin D deficiency, 25-hydroxyvitamin D.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder caused by gradual impairment of beta cell function, paired with insulin resistance (IR). It has affected one hundred and seventy one million people in the year two thousand, and the number is expected to increase to three hundred and sixty six million by year two thousand and thirty. Increased morbidity and mortality is associated with T2DM[1].

The role of vitamin D_3 in glucose regulation is well established and several studies have shown that vitamin D_3 deficiency has an inverse relationship with pre-diabetes and T2DM[2]. Many observational studies have concluded that increase plasma 25(OH) D concentration is related with reduced risk of diabetes[3]. Animal studies have also projected a role for vitamin D_3 in both the occurrence and treatment of T2DM[4]. Supplementation of vitamin D_3 can have a possible therapeutic role in preventing the intensity and progression of T2DM. There is sufficient data indicating that vitamin D_3 deficiency is a global health problem and effects patients irrespective of latitude of residence, age, gender and race[5]. A deficiency in vitamin D_3 can result from inadequate exposure to sunlight, impaired synthesis in skin, not having enough of vitamin D_3 in your diet or reduced intestinal absorption. Pakistan, which is situated near the equator with sufficient sunlight, has a high occurrence of vitamin D_3 deficiency. "Pre-diabetes" is a condition in which glucose levels are not high enough for diagnosis of diabetes but are too high to be measured as normal[6]. People who have pre-diabetes have greater chance to develop T2DM[7]. HbA1c ≥6.5%

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is diagnosed as diabetic; while, HbA1c between 5.7% and 6.4% as pre-diabetic[5].

Pakistani people have a high prevalence of T2DM and vitamin D_3 deficiency[8]. It has been suggested that vitamin D_3 plays a part in the development of T2DM. Pancreatic β cells express a lot of vitamin D-binding protein and vitamin D receptors (VDR). There are several studies which have proved the binding of the circulating active form, 1, 25(OH) $2D_3$ to the VDR expressed in pancreatic β cells[9].

Although, the pharmacotherapy of T2DM is well studied and explored, but is very costly and may result in untoward adverse effects. If preventive measures are employed while the patient is in the pre-diabetic stage, it will be helpful in delaying the onset of full blown diabetes mellitus[10]. Keeping this in our mind, we planned a study whose purpose was to observe the outcome of vitamin D_3 supplementation on HbA1c in individuals who are pre-diabetics. If vitamin D_3 is found to have ameliorating effect, it may become a useful tool in preventing the onset of full blown T2DM.

METHODOLOGY

A quasi experimental study was conducted in department of Pharmacology, Army Medical College, Rawalpindi in collaboration with Chemical Pathology Department Army Medical College and Armed Forces Institute of Pathology (AFIP), Rawalpindi Pakistan, from January to December 2019. Study protocol approval was sought from Ethics Review Committee of Army Medical College, Rawalpindi and Center for Research in Experimental and Applied Medicine (CREAM), Army Medical College (AMC), Rawalpindi prior to the study. Sample size was 70 as calculated by G*Power version 3 by keeping the level of significance at 5% and power of test as 80%.

For the study, a sample of 140 individuals with pre-diabetes and coexisting hypovitaminosis D_3 between the ages of 21 to 60 years of age, were selected through non probability consecutive sampling. Their serum 25(OH)D was <(50 nmol/L)[11] and had elevated glycosylated hemoglobin (HbA1c) in the pre-diabetic range HbA1c (5.7-6.4%)[7]. Patients suffering from full blown T2DM, vitamin D_3 in sufficient range, diagnosed kidney or liver diseases, any mental illness or patients taking anti-epileptic drugs were excluded from the study. Moreover, patients with hemoglobinopathies and pregnant or lactating females were also not included. Patients were duly intimated about the nature and purpose of the study by the researcher. Written informed consent was obtained from them. The demographic details of the patients were recorded by using individual questionnaires. Their fasting blood samples were collected after an overnight fasting of greater than twelve hours, and measured in the Department of Chemical Pathology Department Army Medical College, Rawalpindi.

Individuals selected were randomly assigned by lottery method to receive orally placebo group 1 (n=70) or group 2 vitamin D3 (n=70) 200,000 IU one stat and at the beginning of study and one after one month.

Data was analyzed on IBM Statistical Package for Social Sciences version 22. Shapiro-Wilk test was applied for normality of data. Kruskal-Wallis-H test (a nonparametric test) was used for quantitative variables; HbA1c and vitamin D_3 status. A *p*-value ≤0.05 was considered as significant. Quantitative variables were presented as median and interquartile range [IQR]. Qualitative variables like age, gender, and family history of diabetes were measured as frequency and percentages.

RESULTS

Two groups were comparable to each other with respect to age, gender, and family history of diabetes (fig-1 & 2).

Present study showed that there was statistically significant and inverse relationship between the serum level of vitamin D_3 and HbA1c in pre-diabetic subjects as compared to placebo at the end of the study. In group 1, there was no significant change in the level of HbA1c, when compared to baseline (table). However, HbA1c decreased significantly in patients treated with D_3

than in the placebo group (mean: 5.8 interquartile range: 5.9-5.7) significant (p=0.01). HbA1c was analyzed on ADVIA 1800 Siemens by turbidimetric inhibitory immunoassay (TINIA).

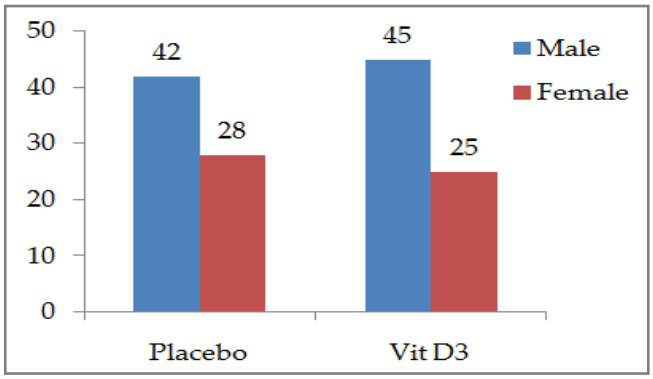

Figure-1: Gender wise distribution between the two study groups.

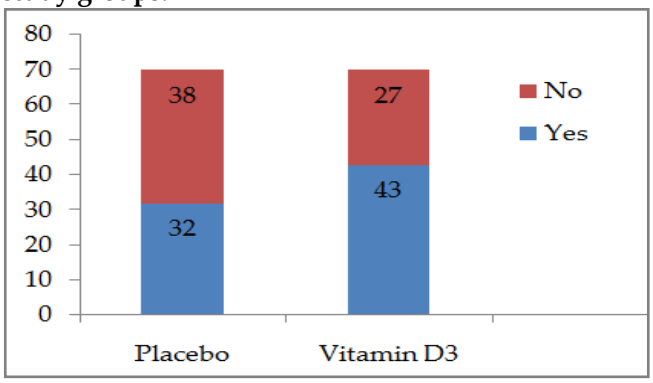

Figure-2: Family history of diabetes in the two study groups.

Table: Comparison of HbA1c between the two groups by Kruskal-Wallis test.

HbA1c		Group 1 Placebo	Group 2 Vit. D_3	p-value
Pretreatment	Median	6.1	6.2	0.91*
	IQR	6.5-5.8	6.4-6.0	
12 Wks Post Treatment	Median	6.3	5.8	0.01**
	IQR	6.7-5.9	5.9-5.7	

*Not significant p-value >0.05, **Significant p-value <0.05.

DISCUSSION

T2DM is on the rise globally and has been declared as a world-wide pandemic[11]. It has extensive consequences on human health as well as on health care system costs[12]. The attainment of normal blood glucose levels is critical for diabetes control[13]. Although, the pharmacotherapy of T2DM is highly efficacious but it is associated with poor compliance, untoward side effects, and high costs. Hence, identification and implication of alternative therapeutic measures at the public health level are desired to decrease diabetes related burdens and costs[14]. A large pool of evidence has suggested that suboptimal vitamin D_3 levels are related with impaired glucose tolerance and diabetes mellitus. In the past few years, various researches have indicated higher vitamin D_3 intake is associated with a lower risk of T2DM[6]. The prevalence of T2DM in Pakistan is 26%, whereas of pre-diabetes is about 14%[1]. Diabetes has developed at an alarming rate and urgently requires strategies for early diagnosis as well as cost-effective prevention approaches in our country[1]. Therefore, individuals who are prediabetics with vitamin D_3 deficiency are at an increased risk of T2DM[15]. Bearing in mind the increasing incidence of T2DM and deficiency of vitamin D_3, it is imperative to study this relevance. In our 12 weeks study, vitamin D_3 supplementation to pre-diabetics individuals who had D_3 hypovitaminosis exhibited an excellent response.

HbA1c was performed as it is very specific for diagnosis of diabetes. The advantages of HbA1c over fasting blood sugar (FPG) are that it is better predictor of cardiovascular accidents (CVA), and microvascular complications with less daily variations. It also shows long-term glucose concentration[16]. It showed a notable response in this study. HbA1c level decreased significantly after vitamin D_3 supplementation. This finding is supported by the studies conducted by a large number of researchers. Khokhar and his colleagues concluded that after vitamin D_3 therapy, level of HbA1c decreased in individuals with type 2 diabetes[17]. Parental vitamin D_3 supplementation also resulted in decrease in HbA1c levels in another study[18]. Furthermore, Upreti and his research fellows in 2018, showed a decrease in HbA1c levels by supplementing vitamin D_3 to diabetic patients[19]. Our finding is consistent with the results of the study done by Almetwazi and his fellows in 2017. They concluded that there was a significant difference

in HbA1c between the diabetic patients having no vitamin D_3 deficiency and diabetic patients with a vitamin D_3 deficiency[20]. In agreement with our research, a cross-sectional study conducted on the pre-diabetic patients reported a significant inverse relationship between serum level of vitamin D_3 and HbA1c[21]. In addition, a meta-analysis was carried out by Angellotti and Pittas. They came up with similar findings that short-term supplementation with vitamin D_3 improved beta cell function and reduced the rise in HbA1c. Likewise research work of Prakash and his fellows acclaimed that there was a significant effect of vitamin D_3 therapy on glycemic control in diabetic patients. They evaluated that there was a decrease in HbA1c without any change in treatment of diabetes[22,23].

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CONCLUSION

This study evaluated the correlation between vitamin D_3 and individuals who were pre-diabetics. As the patients selected were having pre-diabetes, there was a statistically significant improvement in Glycosylated hemoglobin (HbA1c). The beneficial role of vitamin D_3 in pre-diabetic individuals looks very promising. Supplementation of vitamin D_3 may be safe, simple, and cost-effective strategy. Our research has important public health implications, essentially due to the beneficial effect of vitamin D_3 on glycemic parameters in pre-diabetic individuals.

Disclosure

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CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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