

ORIGINAL ARTICLE

Comparison of Mean Decrease in Glycated Hemoglobin in Vitamin D Supplementation with Placebo in the Treatment of Type II Diabetes Mellitus

JAHAN SARDAR¹, HAJRA REHMAN², SEHER OBAID³, SUSAN KAKAKHEL⁴, MOHAMMAD ZAIB⁵, MUHAMMAD IBRAHIM KHALIL⁶, MUHAMMAD AMJAD CHISHTI⁷, SYED SAOUD ZAIDI⁸

¹Assistant professor Medicine, Kuwait Teaching Hospital, Peshawar

²House Officer, Kuwait Teaching Hospital, Peshawar

^{3,4}Assistant Professor, Northwest School of Medicine

⁵Assistant Professor (Medicine), Gajju Khan Medical College Swabi

⁶Biochemistry Mphil, Faculty Health Science, Hazara University Mansehra

⁷Department of Basic Clinical Science, Faculty of Eastern Medicine, Hamdard University Karachi, Pakistan

⁸Assistant professor, Pharmaceutics, Faculty of Pharmacy, Dow University of Health Sciences

Corresponding author: Mohammad Zaib, Email: doctorzaib1@yahoo.com

ABSTRACT

Introduction: Diabetes is common in Pakistan, with prevalence rates ranged from 7.6 -11%. Diabetics especially type 2 diabetes mellitus have a much higher odds of being vitamin d deficient.

Objective: To compare mean decrease in glycated hemoglobin in vitamin D supplementation with placebo in the treatment of type I diabetes mellitus

Methodology: This study design was randomized controlled trial carried out at the medicine department Lady Reading Hospital Peshawar for duration of six months after synopsis approval from July 2021 to December 2021. Sixty patients were included in our study. Patients in group A were subjected to routine diabetes therapy plus vitamin D supplementation in a dose of 600000 units per oral every two weeks for 3 months and patients in group B were subjected to only routine diabetes therapy. Data was entered and analyzed by statistical package for social sciences (SPSS) version 20.

Results: Base line HbA1C Level among Group A patients was analyzed as Mean was 9.27 and Std. Deviation was 1.58 whereas in group B subjects, the mean HbA1C Level was 9.28 and Std. Deviation was 1.59. Post HbA1C Level in Group A patients was analyzed as Mean was 7.29 and Std. Deviation was 1.40 whereas in group B subjects, the post mean HbA1C Level was 7.51 and Std. Deviation was 1.73

Conclusion: Our study concludes that supplementation of Vitamin D could improve Vitamin D level in blood but have no significant association with the reduction of HbA1c level in patients with Type II diabetes mellitus.

Keywords: Glycated hemoglobin; Vitamin D supplementation, Type II diabetes mellitus

INTRODUCTION

Globally, according to the World Health Organization (WHO), diabetes is the fifth largest cause of mortality among adults in many wealthy countries and in numerous emerging and newly industrialized nations, including Pakistan¹. One of the most prevalent endocrine illnesses seen in clinical practice is diabetes mellitus. Hyperglycemia is caused by a complete or partial absence of insulin, as well as insulin resistance^{2,3}. Type 2 non-insulin-dependent diabetes may affect anybody at any age, although it is more prevalent between the ages of 40 and 80 years, and it has a significant hereditary component⁴.

Diabetes is common in Pakistan, with prevalence rates ranged from 7.6 -11%⁵. As one of the most important soluble vitamins, vitamin d plays a critical role in bone health, but it also has a wide range of other skeletal health benefits⁶. Vitamin D insufficiency is the most frequent dietary deficit that has been documented in recent years in people of all ages all over the globe^{7,8}. Vitamin D deficiency is regarded as a public health issue since it has been linked to a number of chronic illnesses, including diabetes of both type 1 and type 2, hypertension, obesity, multiple sclerosis, cardiovascular disease and cancer, particularly colon and prostate cancer⁹.

Many cellular, preclinical and observational studies support a role of vitamin d in the pathogenesis of both

types of diabetes (type I& type 2), and possible role of vitamin replacement in prevention and or treatment of diabetes^{4,10}.

Diabetics especially type 2 diabetes mellitus have a much higher odds of being vitamin d deficient. Among African- American and Hispanics, the frequency of vitamin d deficiency in Type 2 diabetics is 67% and 59% respectively¹¹.

There is a mean decrease in hba1c of 0.70+0.77 in type 2 diabetic with vitamin d replacement¹². In an another study there is a mean decrease of hba1c 0.2+0.5 in type 2 diabetic with without vitamin d supplement¹³. In another study, the hba1c decreased significantly after 12 weeks of consuming vitamin d fortified yogurt as compared to placebo group (p 0.001)¹⁴. No studies have been published so far in Pakistan regarding vitamin d deficiency in type 2 diabetics or the effects of its treatment on glycemic control though both type 2 diabetes and vitamin d deficiency are highly prevalent in this population⁸.

The present study is designed to compare the mean decrease in glyacted hemoglobin between patients of type ii diabetes mellitus subjected to vitamin d supplementation among similar group subjected to placebo. The rationale behind doing this study is that as mentioned above, vitamin d deficiency is not only common in Asian countries but also the role of vitamin d in diabetes control is controversial. The results of this study will provide us with local statistics for

decrease in glycated hemoglobin between two groups and if the mean decrease in vitamin d supplementation group is found to be significantly different from placebo group, we will suggest recommendations for routine vitamin d supplementation among patients with newly diagnosed type ii diabetes mellitus.

MATERIALS AND METHODS

This study design was randomized controlled trial carried out at the medicine department Lady Reading Hospital Peshawar. The duration of study was six months after synopsis approval from July 2021 to December 2021. Sixty patients were included in our study. For sampling non probability consecutive sampling technique was used. The inclusion criterion for our study was all the patients of both the sex and having age ≥ 35 , newly diagnosed with Type II DM and have no history of antidiabetic drugs while the criterion for exclusion was all the patients with chronic kidney disease, chronic liver disease acute myocardial, having allergy to metformin and gliclazide. Informed consent in written was signed from all the participants. History and detailed examination was done for all the subjects. Patients were randomly allocated in two groups. Patients in group A were subjected to routine diabetes therapy (Metformin 1 gm twice daily with gliclazide 60 mg) plus vitamin D supplementation in a dose of 600000 units per oral every two weeks for 3 months (12 weeks) and patients in group B were subjected to only Metformin 1 gm twice daily with gliclazide 60 mg. Vitamin D supplementation was provided to all patients free of cost from the hospital. The subjects were followed up to three months and then blood samples were taken to determine the HbA1C level. All the information like name, address, age, height, weight, BMI (kg/m²), gender, residence, smoking status, hypertension, socioeconomic status, occupation status, lifestyle, baseline HbA1C level, follow up HbA1C level after three months and mean decrease between the two groups was recorded in a pre-designed proforma. Data was entered and analyzed by statistical package for social sciences (SPSS) version 20. Mean + SDs was calculated for numerical variables like age, height, weight, BMI, baseline HbA1C level, follow up HbA1C level and mean decrease between the two groups. For categorical variables like gender, residence, smoking status, hypertension, socioeconomic status, occupation status, and lifestyle, frequencies and percentages were calculated.

RESULTS

Age wise distribution among 60 patients was analyzed as 16(26.7%) subjects in age group 35-40 Years, 14(23.3 %) in age range of 41-45 Years, 18(30.0%) in age range of 46-50 Years and 12(20.0%) subjects were observed in age range of 51-60 Years. (Figure 1) Male participants in our study were 38 (63.3%) and females were 22 (36.7%). (Figure 2) Base line HbA1C Level among Group A patients was analyzed as Mean was 9.27 and Std. Deviation was 1.58 whereas in group B subjects, the mean HbA1C Level was 9.28 and Std. Deviation was 1.59. (Figure 3) Post HbA1C Level in Group A patients was analyzed as Mean was 7.29 and Std. Deviation was 1.40 whereas in group B

subjects, the post mean HbA1C Level was 7.51 and Std. Deviation was 1.73. (Figure 4)

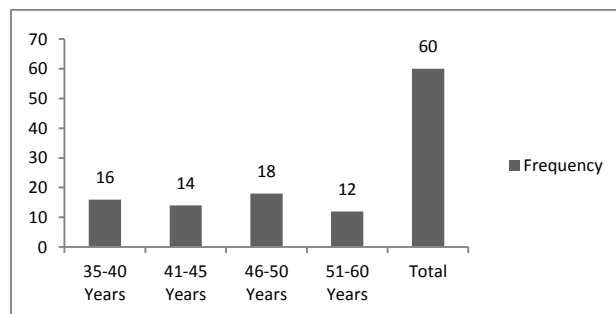


Figure 1: Age wise distribution of subjects

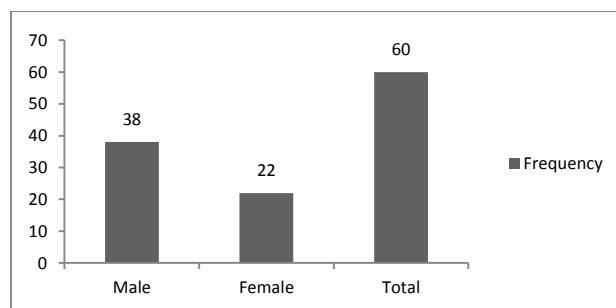


Figure 2: Gender wise distribution of subjects

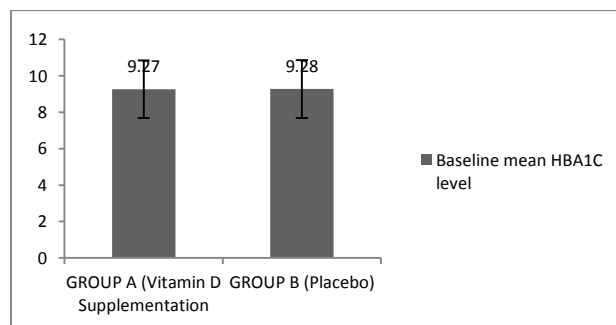


Figure 3: Group wise distribution of base line HbA1C level

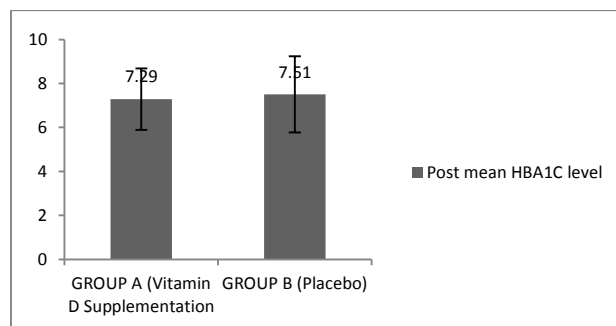


Figure 4: Group wise distribution of Post HbA1C level

DISCUSSION

Regardless of the fact that vitamin D may have a role in the prevention of diabetes and heart disease, as well as its risk factors, the data is inconsistent, and there are few randomized controlled studies in this area. When compared to other investigations, the findings of this study were very

contradictory. One explanation for the study's contradictory findings is that HbA1c was much higher in the combination group than in the metformin alone group, which explains why the mean HbA1c in the metformin group alone was likewise low at the end follow-up. In our study, Base line HbA1C Level among Group A patients was analyzed as Mean was 9.27 and Std. Deviation was 1.58 whereas in group B subjects, the mean HbA1C Level was 9.28 and Std. Deviation was 1.59. Post HbA1C Level in Group A patients was analyzed as Mean was 7.29 and Std. Deviation was 1.40 whereas in group B subjects, the post mean HbA1C Level was 7.51 and Std. Deviation was 1.73 in our study.

With increased Vitamin D intake as part of a medication regimen, substantial improvements in HbA1c may be achieved in Type II diabetes mellitus over time. In a cohort of overweight and obese individuals with Type I diabetes mellitus, researchers found the first evidence of a link between increased supplementation of Vitamin D as part of a pre-existing medication regime followed over time and predictors of Type II diabetes mellitus¹⁵.

Vitamin D deficiency has been shown to have a significant impact on glucose metabolism in studies. Low Vitamin D levels have been linked to insulin resistance and/or Type 2 diabetes mellitus in the most of epidemiological research. Nonetheless, the results of randomized controlled studies are unclear¹⁶.

After three months of Vitamin D treatment, Type II diabetes mellitus patients had a substantial rise in 25(OH)D ($p = 0.015$), according to Nwosu et al. This research found a clinically meaningful drop in HbA1c in Type II diabetes individuals, from 8.5 (2.9%) at baseline to 7.7 (2.5%) at the end¹⁷.

Another study was carried out to determine the effect of daily vitamin D3 supplementation for 16 weeks on the level of HbA1C. This study reported that the level of 25(OH) D increased substantially in this period but the level of HbA1c was not improved¹⁸.

The main difference between this trial and the current one is that this one only included healthy people and replaced oral vitamin D twice a day in two doses, while the current study only gave vitamin D twice a week. Another study reported comparable results to our findings and reported that there was no significant effect of the vitamin D supplementation on the level of HbA1c¹⁹. The main limitation in current research study was small sample size. Other studies based on large sample size should be carried out to get better outcomes.

CONCLUSION

Our study concludes that supplementation of Vitamin D could improve Vitamin D level in blood but have no significant association with the reduction of HbA1c level in patients with Type II diabetes mellitus.

REFERENCES

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32(7):1335-43.
2. Kroder G, Bossenmaier B, Kellerer M, Capp E, Stoyanov B, Mühlhöfer A, et al. Tumor necrosis factor- α -and hyperglycemia-induced insulin resistance. Evidence for

different mechanisms and different effects on insulin signaling. *The Journal of clinical investigation*. 1996;97(6):1471-7.

3. Leontieva O, Demidenko Z, Blagosklonny M. Rapamycin reverses insulin resistance (IR) in high-glucose medium without causing IR in normoglycemic medium. *Cell Death Dis*. 2014;5(5):e1214-e.
4. David G, Gardner D, Dolores R. Greenspan's basic & clinical endocrinology. New York: McGraw Hill Medical. 2011.
5. Khan MY, Riaz R, Malik SA, Ali M, Afzal MS. Association of CTLA-4 polymorphisms and autoimmune type-1 diabetes mellitus susceptibility in Pakistani population. *Turkish Journal of Biochemistry*. 2018;43(2):173-5.
6. Cooke DW, Plotnick L. Type 1 diabetes mellitus in pediatrics. *Pediatr Rev*. 2008;29(11):374-85.
7. Lu H-K, Zhang Z, Ke Y-H, He J-W, Fu W-Z, Zhang C-Q, et al. High prevalence of vitamin D insufficiency in China: relationship with the levels of parathyroid hormone and markers of bone turnover. *PLoS One*. 2012;7(11):e47264.
8. Gennari C. Calcium and vitamin D nutrition and bone disease of the elderly. *Public Health Nutr*. 2001;4(2b):547-59.
9. Zhang R, Naughton DP. Vitamin D in health and disease: current perspectives. *Nutr J*. 2010;9:65-.doi:10.1186/1475-2891-9-65.
10. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *The Lancet*. 2010;375(9716):735-42.
11. Organization WH. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. 2006.
12. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. *N Engl J Med*. 2010;362(9):800-11.
13. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2007;298(22):2654-64.
14. Cavanagh PR, Ulbrecht JS. 28 Footwear for People with Diabetes. *The foot in diabetes*. 2006:336.
15. 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;24(3):335-41.
16. Gröbler M, Gaksch M, Kienreich K, Verheyen N, Schmid J, ó Hartaigh B, et al. Effects of vitamin D supplementation on glycated haemoglobin and fasting glucose levels in hypertensive patients: a randomized controlled trial. *Diabetes, Obesity and Metabolism*. 2016;18(10):1006-12.
17. Nwosu BU, Maranda L. The effects of vitamin D supplementation on hepatic dysfunction, vitamin D status, and glycemic control in children and adolescents with vitamin D deficiency and either type 1 or type 2 diabetes mellitus. *PLoS One*. 2014;9(6):e99646.
18. Madar AA, Knutsen KV, Stene LC, Brekke M, Meyer HE, Lagerlöv P. Effect of vitamin D3 supplementation on glycated hemoglobin (HbA1c), fructosamine, serum lipids, and body mass index: a randomized, double-blinded, placebo-controlled trial among healthy immigrants living in Norway. *BMJ Open Diabetes Research and Care*. 2014;2(1):e000026.
19. Krul-Poel YH, Westra S, ten Boekel E, ter Wee MM, van Schoor NM, van Wijland H, et al. Effect of vitamin D supplementation on glycemic control in patients with type 2 diabetes (SUNNY trial): a randomized placebo-controlled trial. *Diabetes Care*. 2015;38(8):1420-6.