

ORIGINAL ARTICLE

The Effect of Vitamin D Supplementation on Proteinuria in Type 2 Diabetes Mellitus Patients in DHQ Hospital Faisalabad

ATIKA AKRAM¹, ASAD MAHMOOD KHAN², OBAID ANWAR³, MUHAMMAD ARIF⁴, AMIN ANJUM⁵

¹Assistant Professor, Nursing/ Principal Mohi-Ud-Din Institute of Nursing and Allied Sciences Mirpur AJK

²Associate Professor Pharmacology Sahiwal Medical College Sahiwal

³Assistant Professor Pharmacology ABWA Medical College Faisalabad

⁴Assistant Professor Medicine Faisalabad Medical University Faisalabad

⁵Assistant Professor of Medicine Faisalabad Medical University

Correspondence to: Atika Akram, Email: atikaakram.68@gmail.com, Cell: 03202233202

ABSTRACT

Objectives: To evaluate the effect of Vitamin D supplementation on proteinuria in type 2 Diabetes Mellitus patients in attending DHQ Hospital Faisalabad.

Materials and Methods: The design of this study was Quasi-experimental study design and the duration of this study was from December 2021 to June 2022. This study was conducted in the Department of medicine, in DHQ Hospital Faisalabad. Total 30 patients who were suffering from type 2 diabetes mellitus disease were enrolled. Their Vitamin D levels, proteinuria, HbA1c and FBS level were evaluated. Oral Vitamin D 50,000 IU weekly was given to patients with Vit D deficiency for 8 weeks. At the end of 8 week vitamin D levels, FBS, HbA1c and proteinuria level were evaluated again. All the demographic details and study results were recorded on a predesigned data collection proforma.

Results: Out of total 30 patients, 11 were male and 19 were female with mean age of 34.73 ± 9.14 years. The most common age group was 41-50 years in which 36.7%, followed by age group of 31-40 years in which 33.3% and 30.0% patients were in age group of 41-50 years. The statistical difference between pre-intervention and post-intervention was calculated, and p-value was significant. In our study as Vit. D level increases while proteinuria decreases.

Practical Implication: In diabetic patients its deficiency lead to a number of serious conditions such as ischemic heart disease, CKD and Diabetic nephropathy. Vit D play its role in the inhibition of the renin-angiotensin system. It also have a protective role in the kidney by preventing of glomerulosclerosis and anti-proteinuric effect.

Conclusion: Vitamin D supplementation is helpful in decreasing proteinuria in Vit. D deficient T2DM patients.

Keywords: Vitamin D, Proteinuria, Type 2 Diabetes Mellitus, Albumin Level, Proteinuria, Threatening Disorder.

INTRODUCTION

Diabetes is a rapidly growing and life threatening disorder across the low-and-middle-income countries⁽¹⁾. Diabetes Mellitus is a worldwide disorder with prevalence rate of 7.1% in 2012. Recently in 2022, the Centers for Disease Control and Prevention (CDC) stated that there are 130 million adults suffering from diabetic mellitus in the United States. And in 2019, about 1.4 million adults with diabetes mellitus were diagnosed. It has been stated that the incidence of DM would be 69.9 million in Indian population and 11.6 million in Pakistani population by 2025^(2, 3). It is the main cause of many other complicated comorbidities. Nephropathy is one of these complicated disorder which is defined by the development of proteinuria.

The deficiency of Vitamin D is also most common disorder with global prevalence of 30-87% and in T2DM its prevalence is 70-90%⁽⁴⁾. In Chinese population Vit D deficiency is also common with prevalence rate of 34.3% specially in children^(5, 6). In diabetic patients its deficiency lead to a number of serious condition such as ischemic heart disease, CKD and Diabetic nephropathy. Vit D play its role in the inhibition of the renin-angiotensin system. It also have a protective role in the renal by preventing of glomerulosclerosis and anti-proteinuric effect. In proteinuria patients the glomerular filtration rate reduced to 10-12 mL annually. So life style changes can improve the proteinuria patients to some extent. The pervasiveness of type-II DM in Pakistan is 12%. It is a communal disorder with significant mortality and morbidity⁽⁵⁻⁶⁾. The common adverse effects of DM are due to complications in vascular system, both at the microvascular level (neuropathy, retinopathy, nephropathy) and at the macrovascular level (peripheral neuropathy, coronary artery disease, cerebrovascular disease). Hypertension is a communal comorbid disease that affects most patients, and its incidence varies with the diabetes mellitus type of the patient including ethnicity, obesity and age⁽⁷⁻⁸⁾. Various researches have revealed the effectiveness of monitoring cardiovascular risk factors in people with diabetes in delaying or preventing CVD in diabetic patients. The maximum advantages are achieved when numerous causing aspects are taken into account all over the world. Analyzing facts of the UK

Diabetic Outlook analysis, Stratton et al and Molyneaus et al institute that better control of glycemia in type-II diabetic patients reduces the complications and its incidence⁽¹⁰⁾. The decline in HbA1c is probable to decrease the complications risk, with the minimum risk of complications if HbA1c remains within the normal range⁽¹¹⁾. Maintaining good control of blood sugar in diabetic patients is significant to delay or prevent problems. In Pakistan, there are few studies assessing glycemic status in subjects with hypertension and normotension among type-II diabetics⁽¹²⁾. In this study we want to evaluate or measure the effect of Vitamin D supplementation on proteinuria in patients suffering from type 2 Diabetes Mellitus.

Objective: To evaluate the effect of Vitamin D supplementation on proteinuria in type 2 Diabetes Mellitus patients in attending DHQ Hospital Faisalabad.

MATERIALS AND METHODS

Study Design and Setting: This Quasi-experimental study, was done at the department of medicine in DHQ Hospital Faisalabad.

Duration of the Study: Duration of the study was 6 months (Dec 2021 – June 2022).

Sample Size: Sample size of 30 was calculated by using WHO sample size calculator taking.

Level of significance = 5%

Urine ACR at baseline = 2.54 ± 0.28

Urine ACR after 2 months = 2.29 ± 0.29 (7)

Power of test=99%

Inclusion Criteria:

- Vitamin D deficiency (Vitamin D <20 ng/ml) or insufficiency (Vitamin D between 21-30ng/ml)
- Patient on stable doses of Angiotensin-converting enzyme Inhibitors or Angiotensin receptor blockers for at least 3 months.
- HbA1C $\leq 9\%$
- Urine ACR > than 30 mg/g.
- Glomerular filtration ratio greater than 50 mL/min or serum creatinine < 2 mg/dL
- Age between 18 and 50 years.

- Both gender.
- Patients who will be willing to give consent.

Exclusion Criteria:

- Patients with uncontrolled diabetes HbA1C greater than 9%.
- $\text{Ca} \times \text{Phosphorus} > 55 \text{ mg/dL}^2$,
- Ca supplement consumption during the last 8 weeks and Pt who had used Vitamin D in prior 4 weeks.
- $\text{Ca} > 10 \text{ mg/dL}$ and Vitamin D $> 30 \text{ ng/ml}$.
- Active systemic or urinary infection
- History of steroids use.

METHODS

Totally 30 patients with Vit D deficiency and also suffering from type 2 Diabetes Mellitus were enrolled in this study. Consecutive non probability sampling technique was used by the researcher to recruit the affected individuals. After obtaining ethical approval from hospitals ethical committee, an informed consent was obtained from the patients. A predesign questioner was used to collect data. Vitamin D levels Proteinuria, HbA1c and FBS level was evaluated. Oral VITAMIN D 50,000 IU weekly dose was given to Patients with Vit D deficiency for 8 weeks. At the end of 8 week the Vitamin D levels, FBS, HbA1c and Albumin level was evaluated again.

Statistical Analysis: By using the SPSS version 23.0, all the collected data were analyzed. Frequency & percentage was used to present qualitative (categorical) variables i.e. gender. Mean and standard deviation will be calculated for quantitative variables like age, HbA1C levels, levels of vitamin D levels, FBS and Albumin level before and after the intervention. The paired Student's t-test was used to compare data before and after intervention. P value < 0.05 was significant.

RESULTS

Out of total 30 patients, 11 were male and 19 were female with mean age of 34.73 ± 9.14 years (Table 1, Fig 1-0). The most common age group was 41-50 years in which 36.7%, followed by age group of 31-40 years in which 33.3% and 30.0% patients were in age group of 41-50 years (Table 2, Fig 2-0).

Table 1: Distribution of patients according to gender (n=179)

Variable	Frequency	Percentage
Gender:		
Male	11	36.7
Female	19	63.3
	Mean	SD
Age (Years)	34.73	9.14

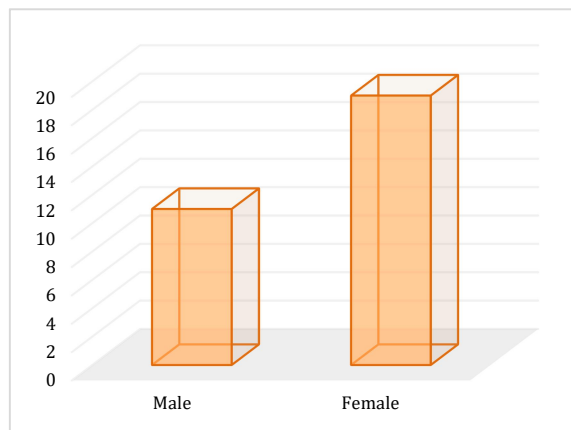


Figure 1: Graphical Representation of gender

Table 2: Distribution of patients according to age group (n=30)

Age Group (Years)	Frequency	Percentage
18-30	9	30.0

31-40	10	33.3
41-50	11	36.7
Total	50	100.0

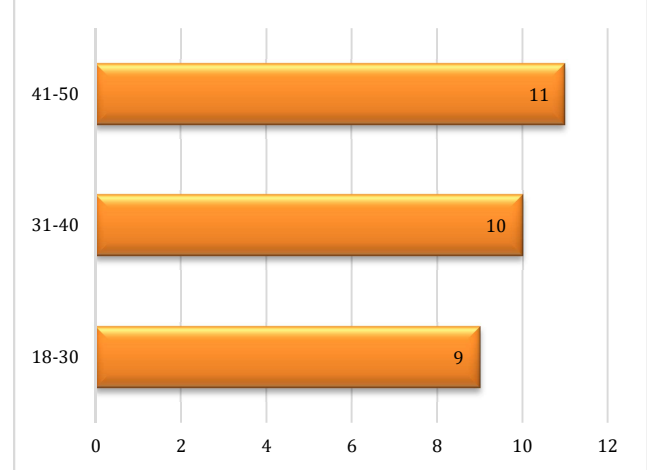


Figure 2: Graphical Representation of distribution of patients according to age group (n=30)

In order to determine the statistical difference between Pre-intervention and post-intervention, p-value was calculated through Paired Sample T-Test.

Table 3: Pre-intervention and post-intervention comparison (n=30)

Variables	Pre intervention	Post intervention	Difference	P-Value
Vit D (nmol/L)	26.02 \pm 3.63	29.91 \pm 3.12	3.89 \pm 0.51	0.00
Proteinuria (mg/day)	978.63 \pm 10.8	954.40 \pm 9.2	24.23 \pm 1.6	0.00
HbA1c	7.3 \pm 0.87	8.1 \pm 0.79	0.8 \pm 0.87	0.00
FBS (mg/dL)	145.5 \pm 11.0	157.20 \pm 10.2	11.7 \pm 0.8	0.00

DISCUSSION

Diabetic Mellitus has become a global epidemic. This study was conducted on patients attending DHQ Hospital Faisalabad in order to evaluate or measure the effect of Vitamin D supplementation on proteinuria in type 2 Diabetes Mellitus patients. The prevalence of T2DM in high amount globally and in Pakistan, and the effect of the status of vitamin D under different conditions make it very important to determine or evaluate the relationship between vitamin D and T2DM.

This study shows that Vit D supplementation have positive effects on proteinuria patients. It has been stated that there is Vit D deficiency in patients suffering from type 2 DM (8). Vit D deficiency is also associated with diabetic retinopathy (9-11).

The enrolled patients of this study were mostly between the ages of 18 and 50 years. It was stated that severe Vit D deficiency can occur in young women with higher risk with age in a woman's lifecycle. In our study patients, female (63.3%) were dominant over male (36.7%). Same results were also stated in other studies. A study conducted by Khalid S Aljabri at Saudi population stated that the prevalence of Vit D deficiency in females suffering from T2DM is high (12). The perceived variation between the poor control of blood sugar levels and age and can be described by the change in peoples demographic features and age differences in the studies. Hypertension is the utmost common comorbidities in DM2 patients (17). In our study, 65.9% of the subjects had high blood pressure. Khattab et al, Benoit et al., Adham et al also institute that the maximum of the diabetic people in the study had hypertension 18-20. The research showed that the peoples having diabetes for long period of time significantly associated with high blood sugar level. The atherosclerosis was mostly seen among diabetic patients have high blood pressure with least control on blood sugar levels (2). In

addition, adverse effects of some antihypertensive drugs on glucose metabolism have been documented. All these aspects collectively subsidise to poor control of glycemia among diabetic patients with hypertension (12). Studies have shown that hypertension is independent control factor in diabetic patients with poor glycemic control. The potential role of vitamin D deficiency in cardiovascular morbidity and mortality has been summarized earlier. Hypovitaminosis D is associated with asymptomatic cardiovascular disease (CVD) in type 2 diabetic patients with nephropathy. Moreover, vitamin D deficiency was also found to be prevalent in hemodialysis patients and is associated with higher all-cause early mortality. The evidence supporting the role of vitamin D supplementation in such conditions is lacking. One study with Alphacalcidol showed survival advantage in chronic HD patients. However, a recent meta-analysis concludes that the clinical evidence on effect of vitamin D supplementation on cardiovascular mortality is insufficient.

The Vitamin D act as anti proteinuric affect and can be used for the treatment of proteinuria. The major contribution of this research study is the finding of an association between vitamin D and proteinuria in T2DM patients. In studies conducted by De Zeeuw et al.(13) and Huang et al. (14) stated that doses of cholecalciferol have antiproteinuric effects on Chinese diabetic patients. Our study find out clear difference between pre intervention and post intervention regarding increase in Vit D level. But fail to find association between using of Vit D and serum HbA1c. Other studies have find different results regarding the improvement and decrease of HbA1c level (15-18) (15-19).

CONCLUSION

It is concluded that by using Vit D supplementation in type 2 diabetic patients can improve the serum Vit D level and also helpful in decreasing proteinuria. However there is no improvement of glycemic control indices.

REFERENCES

- Hogerzeil HV, Recourt S. The importance of insulin donations for children in 43 low-and middle-income countries. *Journal of Public Health Policy*. 2019;40(2):253-63.
- Memon WU, Jadoon Z, Qidwai U, Naz S, Dawar S, Hasan T. Prevalence of diabetic retinopathy in patients of age group 30 years and above attending multicentre diabetic clinics in Karachi. *Pakistan Journal of Ophthalmology*. 2012;28(2).
- Mathur P, Leburu S, Kulothungan V. Prevalence, awareness, treatment and control of diabetes in India from the countrywide National NCD Monitoring Survey (NNMS). *Frontiers in public health*. 2022;205.
- Mori H, Okada Y, Tanaka Y. Incidence of vitamin D deficiency and its relevance to bone metabolism in Japanese postmenopausal women with type 2 diabetes mellitus. *Internal Medicine*. 2015;54(13):1599-604.
- Chen J, Yun C, He Y, Piao J, Yang L, Yang X. Vitamin D status among the elderly Chinese population: a cross-sectional analysis of the 2010–2013 Pakistan national nutrition and health survey (CNNHS). *Nutrition journal*. 2017;16(1):1-8.
- Yang C, Mao M, Ping L, Yu D. Prevalence of vitamin D deficiency and insufficiency among 460,537 children in 825 hospitals from 18 provinces in mainland Pakistan. *Medicine*. 2020;99(44).
- Kim MJ, Frankel AH, Donaldson M, Darch SJ, Pusey CD, Hill PD, et al. Oral cholecalciferol decreases albuminuria and urinary TGF- β 1 in patients with type 2 diabetic nephropathy on established renin-angiotensin-aldosterone system inhibition. *Kidney international*. 2011;80(8):851-60.
- Karau PB, Kirna B, Amayo E, Joshi M, Ngare S, Muriira G. The prevalence of vitamin D deficiency among patients with type 2 diabetes seen at a referral hospital in Kenya. *The Pan African Medical Journal*. 2019;34.
- Kaur H, Donaghue KC, Chan AK, Benitez-Aguirre P, Hing S, Lloyd M, et al. Vitamin D deficiency is associated with retinopathy in children and adolescents with type 1 diabetes. *Diabetes care*. 2011;34(6):1400-2.
- Alcubierre N, Valls J, Rubinat E, Cao G, Esquerda A, Traveset A, et al. Vitamin D deficiency is associated with the presence and severity of diabetic retinopathy in type 2 diabetes mellitus. *Journal of diabetes research*. 2015;2015.
- Nadri G, Saxena S, Mahdi AA, Kaur A, Ahmad M, Garg P, et al. Serum vitamin D is a biomolecular biomarker for proliferative diabetic retinopathy. *International Journal of Retina and Vitreous*. 2019;5(1):1-5.
- Aljabri KS. Vitamin D deficiency in female Saudis with Type 2 diabetes mellitus. *Age (years)*. 53:16.5.
- De Zeeuw D, Agarwal R, Amdahl M, Audhya P, Coyne D, Garimella T, et al. Selective vitamin D receptor activation with paricalcitol for reduction of albuminuria in patients with type 2 diabetes (VITAL study): a randomised controlled trial. *The Lancet*. 2010;376(9752):1543-51.
- Huang Y, Yu H, Lu J, Guo K, Zhang L, Bao Y, et al. Oral supplementation with cholecalciferol 800 IU ameliorates albuminuria in Chinese type 2 diabetic patients with nephropathy. *PLoS One*. 2012;7(11):e50510.
- Zhang Z, Sun L, Wang Y, Ning G, Minto AW, Kong J, Quigg RJ, Li YC. Renoprotective role of the vitamin D receptor in diabetic nephropathy *Kidney Int*. 2008;73:163-71.
- Ahmadi N, Mortazavi M, Iraj B, Askari G. Whether vitamin D3 is effective in reducing proteinuria in type 2 diabetic patients? *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*. 2013;18(5):374.
- Bonakdaran S, Hami M, Hatefi A. The effects of calcitriol on albuminuria in patients with type-2 diabetes mellitus. *Saudi Journal of Kidney Diseases and Transplantation*. 2012;23(6):1215.
- Momeni A, Mirhosseini M, Kabiri M, Kheiri S. Effect of vitamin D on proteinuria in type 2 diabetic patients. *Journal of nephropathology*. 2017;6(1):10.
- Saeed, A., Jahanzeb, Z., Batool, U., Kauser, S., Muhammad, M., & Mahmood, N. (2022). Relationship Of Glycemic Control With Level Of Blood Pressure Amongst Type 2 Diabetic Patients. *Pakistan Journal Of Medical & Health Sciences*, 16(07), 982-982.