Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/9452xv71

TO ASSESS THE IMPACT OF VITAMIN D SUPPLEMENTATION ON PROTEINURIA IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS, CONSIDERING THE AVERAGE ALTERATION IN THE URINARY ALBUMIN/CREATININE RATIO (UACR)

Kalsoom Ali Shah[1], Muhammad Junaid[2], Usman Saeed[3*], Talal Safdar[4], Bisma Fatima Aslam[5], Sauda Usmani[6]

[1]Jinnah Medical College, KPK, Pakistan
[2]Registrar, Department of Rheumatology, University Hospital Waterford, Ireland
[3*]Associate Professor, Department of Pharmacology, Fatima Memorial Hospital College of Medicine & Dentistry, Pakistan
[4]Assistant Professor of Medicine, Fauji Foundation Hospital Rawalpindi, Pakistan
[5]Assistant Professor, Department of Pharmacology & Therapeutics Azra Naheed Medical College, Lahore, Pakistan
[6]Associate Professor, Department of Physiology, Pak Red Crescent Medical and Dental College Lahore, Pakistan

***Corresponding author:** Usman Saeed
***Email:** dr.usman214@gmail.com

Abstract

Introduction: Vitamin D is normally low in T2DM patients and low levels make the damage of diabetic kidneys worse. Blood tests formerly known as UACR help to determine levels of proteins in urine to identify kidney damage at its early stages in patients with T2DM.

Objectives: The present study was designed to measure the efficacy of vitamin D supplementation in modifying proteinuria in T2DM patients through the evaluation of UACR after 6 months.

Materials and Methods: A group of investigators conducted a trial with 150 patients afflicted by both type-2 diabetes and high urinary albumin excretion by forming groups. The study divided the subjects into two equal groups and administered 1000 IU of vitamin D daily supplements to the first group while the second group was given a placebo for six months.

Results: The vitamin D intervention was also found to have achieved better outcome in the lowering of UACR than the placebo group and improved the serum levels of vitamin D.

Conclusion: Vitamin D helps reduce protein loss from the kidneys of type 2 diabetes patients to stop the progression of kidney damage.

Keywords: Vitamin D, Type 2 Diabetes Mellitus, proteinuria, urinary albumin-to-creatinine ratio, diabetic nephropathy, supplementation.

INTRODUCTION

The importance of Vitamin D deficiency in the worsening of multiple complications of diabetes has been identified, including diabetic nephropathy. This ascending stage of chronic kidney disease (CKD) affects thousands of patients with Type 2 Diabetes Mellitus (T2DM) and is characterized by

increased proteinuria as a sign of kidney deterioration. There is interest in the relation between vitamin D status and proteinuria since the vitamin may influence immune modulation, inflammation, and fibrosis, all critical to kidney disease progression (1). Microalbuminuria, especially using UACR, is one of the first indications of DN and the primary marker of renal disease in T2DM patients (2). Some investigations indicate that supplementation with vitamin D could prevent and counteract the negative impact of hyperglycemia on renal function through its well-established anti-inflammatory and antioxidant activities, which play a role in the development of kidney disease in people with diabetes (3).

Recent studies suggest that adaptation of vitamin D levels should be an essential factor in advancing renal function, particularly in T2DM patients. Vitamin D impacts the kidneys, particularly by modulating the renin-angiotensin-aldosterone system, which significantly affects blood pressure and fluid retention. Abnormalities in this system are observed in the Kimmelstiel-Wilson lesion and are responsible for further deterioration of the disease and progression to chronic renal failure stage 4. Furthermore, vitamin D has successfully lowered albuminuria in patients with T2DM – a factor indicating that it can supplement the treatment of proteinuria (5). This specific aspect of vitamin D has also been investigated alongside other therapies, such as antioxidants and omega-3 fatty acids, which decrease kidney inflammation and have a positive impact on kidney function (6). The effects of vitamin D in lipid metabolism have also been studied, showing that vitamin D may help manage kidney lipid deposition implicated in nephropathy. This is well illustrated in advanced diabetic renal disease, where dyslipidemia is common and tends to worsen the course of renal disease (7). However, current research also proved that vitamin D increases the process of autophagy in kidney cells, which is beneficial in removing damaged compositions within kidney cells for protection from kidney damage (8).

Diabetic nephropathy is mainly diagnosed and evaluated by measuring albuminuria because this protein is an indicator of damaged kidneys. The UACR is a sensitive and accurate marker for early nephropathy in patients with T2DM, and results on screening may be substantial (9). The use of UACR count can also measure proteinuria, an aspect associated with kidney damage in diabetic patients and the progress to kidney failure in T2DM patients (10). Research has recommended that vitamin D supplementation cut albuminuria by 36 % and brought down the UACR, giving a probable key to postponing the progression to severe kidney ailment (11). The effect of Vitamin D on kidney function may be attributed to the fact that it helps to modulate inflammations, which tend to be higher among diabetic nephropathy patients (12). Although vitamin D supplementation seems to have a kidney-protecting effect in patients with T2DM, the dosing and duration of supplementation are still unclear. There is evidence that higher doses of Vitamin D are needed to see better results in Halbuminuria and the general function of the kidneys (13). Nevertheless, the over-supplementation with vitamins, especially Vitamin D, poses clinical problems such as hypercalcemia, requiring constant monitoring of serum levels (14). In addition, the interaction between vitamin D and the kidney may be modulated by other factors like dietary intake, ultraviolet light exposure, and the presence of other co-morbid illnesses, which may sometimes place the research in a contentious position (15).

Objective: The aim of the present research is to evaluate the effects of vitamin D supplementation on proteinuria among people with Type 2 Diabetes Mellitus by comparing differences in UACR.

MATERIALS AND METHODS

Study Design: Cross Sectional.

Study setting: The research will be carried out at the Jinnah Medical College, KPK, Pakistan. The hospital treats people from many different backgrounds, which makes it perfect for studying how vitamin D supplements affect those with type 2 diabetes.

Duration of the study: The duration of the study was from January 2024 to December 2024.

Inclusion Criteria:

The study is looking for adults who fit these criteria. A minimum of two years' diagnosis of type 2 diabetes mellitus and a UACR between 30 and 300 mg/g. No current vitamin D supplements or kidney function treatments will be a factor in selection. This study is limited to participants who have no ongoing vitamin D treatment or kidney-related medical interventions. Each participant must demonstrate stable diabetic care along with steady adherence to complete study demands.

Exclusion Criteria

The study excludes pregnant women and nursing mothers, as well as patients who have severe kidney problems or vitamin D overuse. The research team does not accept participants with stage 3-5 kidney disease or excessive vitamin D intake; it only studies men and non-pregnant women. Study participants with serious medical conditions, including heart failure, need to avoid taking part due to data integrity concerns. The study will exclude anyone taking medications that might affect kidney or vitamin D functions, such as corticosteroids and immunosuppressant drugs.

Methods

Two groups participated in the study. While the control group was given a daily placebo, the intervention group consumed 1000 IU of vitamin D. The participants were divided into these groups at random. The computer software will be used in the intended allocation to minimize any partiality in the group selection process. Gender, age, BMI, medical history, vitamin D levels, renal function tests, and uric acid creatinine ratio will all be measured at baseline to begin this study. The population will have their UACR assessed at baseline and at the three-month and six-month follow-up by using spot urine samples. Blood measures of vitamin D, calcium, and phosphate will also be taken to check for any side effects of supplementation. Self-report, pill count and monthly follow-up phone calls will be used to assess the degree of compliance with supplementation. At the end of the study, statistical analyses will be used to compare the differences in UACR between the two groups before and after the intervention, controlling for age and diabetes duration.

RESULTS

The study required 150 participants where we selected 75 people to take real vitamin D supplements while another 75 individuals received placebo pills. The mean age of participants was 58.3 ± 6.5 years, with a male-to-female ratio of 1.2:1. To start the study we created balanced teams with matched diabetes histories and health measurements. Table 1 shows the basic information about study participants when the research began.

Table 1: Baseline Characteristics of Participants

Characteristic	Vitamin D Group (n=75)	Placebo Group (n=75)	p-value
Age (years)	58.1 ± 6.3	58.5 ± 6.8	0.762
Male/Female ratio	1.3:1	1.1:1	0.426
Duration of diabetes (years)	5.2 ± 3.0	5.3 ± 3.2	0.798
HbA1c (%)	7.8 ± 1.2	7.7 ± 1.1	0.653
UACR (mg/g)	56.3 ± 22.4	55.8 ± 23.1	0.911

Patients taking vitamin D supplements experienced a notable 18.5 mg/g UACR decrease, but the placebo group showed just 3.4 mg/g improvement during the same period of time. The vitamin D group showed additional UACR reductions from 18.5±7.3 mg/g at three months to 32.7±10.5 mg/g at six months, while the placebo group maintained its initial UACR levels ($p<0.001$). Table 2 shows how UACR values changed during the research period.

Table 2: Changes in UACR from Baseline to 6 Months

Time Point	Vitamin D Group (n=75)	Placebo Group (n=75)	p-value
Baseline	56.3 ± 22.4	55.8 ± 23.1	0.911
3 months	37.8 ± 15.1	52.4 ± 21.6	<0.001
6 months	23.6 ± 12.0	55.2 ± 22.9	<0.001

The vitamin D treatment led to an 18.5 mg/g reduction in UACR levels compared to 3.4 mg/g in patients in the placebo group during the 3-month study period. At the 6-month assessment, the vitamin D group reached a mean decrease in UACR of 32.7±10.5 mg/g, but the placebo group maintained similar UACR levels without significant changes ($p<0.001$). Table 2 shows how UACR values changed during the research period.

Table 3: Serum Vitamin D Levels at Baseline and 6 Months

Time Point	Vitamin D Group (n=75)	Placebo Group (n=75)	p-value
Baseline	18.4 ± 8.2	17.9 ± 7.5	0.723
6 months	34.5 ± 15.3	18.7 ± 7.2	<0.001

Regular checks revealed participants in the vitamin D group took their supplements at least 94% of the time based on pill counts and participant feedback. The participants showed no adverse medical effects during testing, which led to sustained participation without any withdrawals. Research demonstrates that taking vitamin D supplements helps lower proteinuria levels and shows safe effects when used as a long-term treatment for individuals with Type 2 Diabetes Mellitus.

DISCUSSION

Research shows that vitamin D treatment reduces protein leaking into urine samples from T2DM patients based on UACR readings. Previous studies show low vitamin D levels can trigger diabetic nephropathy and the new study back up these findings.(1) Research supports that vitamin D supplements can protect diabetic kidneys against inflammation and fibrosis which leads to kidney damage. Research shows vitamin D can help both reduce inflammation and promote kidney cell repair which suggests its use as an extra treatment for diabetic kidney disease. Vitamin D impacts kidney function in multiple ways. Vitamin D directly affects the renin-angiotensin-aldosterone system, which controls blood pressure and fluid regulation in the body. Those who have diabetes and kidney problems typically develop RAAS system issues that create harmful pressure buildup within the kidneys and damage their structures. The vitamin D receptors in kidney tissues connect with vitamin D to inhibit RAAS enzymes, which decreases high blood pressure and protein leakage from the glomerular filter. Participants who took vitamin D supplements showed noticeable kidney health benefits by reducing UACR levels over a 6-month testing period.

The vitamin D group's better UACR results demonstrate how this vitamin fights oxidative stress and inflammation that make diabetic nephropathy progress faster. Kidney damage occurs when high blood sugar levels trigger both reactive oxygen species and inflammatory molecules to build up. Research proves that vitamin D protects against inflammation through its ability to control molecules that trigger inflammation, such as IL-6 and TNF-α (4). Vitamin D helps activate enzymes that fight free radicals in kidney cells to protect against damage from oxidative stress. UACR decreased in participants treated with vitamin D through these protective processes that showed kidney health benefits for type 2 diabetes patients. Research shows that vitamin D supports podocyte health, which prevents diabetic nephropathy by fighting inflammation and harmful molecules. Podocytes function as specialized filtering cells in glomeruli to keep the filtration barrier strong. High blood sugar and inflammation damage podocytes, which allow albumin to leak into urine through proteinuria. New studies reveal that vitamin D supplements improve podocytes' autophagy function by removing

defective proteins and cell parts. The protective action restores the filtration barrier and reduces future kidney damage. Vitamin D helped protect kidney filtration capacity through its beneficial effects on podocyte function during our study.

Study findings demonstrate that vitamin D helps regulate the metabolism of fats in patients who develop type 2 diabetes and diabetic kidney disease. Type 2 diabetes patients often develop dyslipidemia with high triglyceride levels and low HDL, which makes their kidney damage worse. Research shows that vitamin D can enhance cholesterol levels in the body while decreasing triglyceride levels. Vitamin D's impact on lipid levels may help protect kidney function by limiting lipid buildup in the kidneys and reducing tissue damage. Study data showed participants who received vitamin D supplements had a notable rise in their serum vitamin D levels throughout the six-month study. Both groups showed low baseline vitamin D levels, which points to widespread vitamin D deficiency in T2DM patients. Research shows that vitamin D deficiency affects many diabetic patients, according to earlier studies(8).The ability of vitamin D supplementation to significantly raise serum vitamin D levels in this study indicates that supplementation can effectively address vitamin D deficiency in individuals with T2DM, potentially improving their overall health and reducing the risk of complications such as diabetic nephropathy.

The findings from this study support that vitamin D treatment reduces proteinuria, but we need to recognize several study limitations. This study spanned six months in total. The effects of vitamin D on kidney functioning and kidney failure prevention require additional testing across more extended observation periods. The study showed UACR improvement but did not evaluate detailed kidney examinations or GFR levels. Studies going forward should monitor these kidney indicators and vitamin D effects to gain a complete picture of diabetic nephropathy treatment. The researchers failed to account for dietary calcium intake as a potential factor affecting vitamin D metabolism and kidney function. Research reveals that vitamin D supplements have potential benefits in reducing the proteinuria rate among patients with type 2 diabetes. Researchers need to find the best vitamin D therapy protocols for T2DM patients to ensure their kidney protection over time. Research teams must conduct extensive studies in multiple locations to confirm these results and study vitamin D's impact on diverse population types. Vitamin D supplements provide kidney protection to individuals with Type 2 Diabetes. Studies indicate vitamin D supplements enhance existing diabetic nephropathy therapies by lowering protein levels in urine tests. Taking vitamin D supplements supports kidney preservation in type 2 diabetes patients through proper regulation of inflammation and tissue stress, plus protection of kidney cells and fat control.

CONCLUSION

The study findings demonstrate that vitamin D treatment leads to reduced protein loss in people with Type 2 Diabetes Mellitus (T2DM) based on UACR measurements. Vitamin D shows promise in protecting kidney health and slowing down diabetic nephropathy by reducing the UACR value. Vitamin D's benefits come in several different ways - by controlling inflammation and oxidative stress, healing damaged podocytes, and changing how the body handles lipids. Higher vitamin D levels in T2DM patients after supplementation show that this treatment is successful in correcting their widespread vitamin D deficiency. The research shows promise, but we require additional studies spanning multiple centres to assess vitamin D's lasting impact on kidney health in T2DM patients.

References

1. El Askary, A., Gharib, A.F., Almehmadi, M., Bakhuraysah, M.M., Al Hajjiahmed, A.A., Al-Hejji, L.I., Alharthi, M.S. and Shafie, A., 2021. The role of vitamin D deficiency and elevated inflammatory biomarkers as risk factors for the progression of diabetic nephropathy in patients with type 2 diabetes mellitus. Open Chemistry, 19(1), pp.1174-1183.
2. Mahemuti, N., Zou, J., Liu, C., Xiao, Z., Liang, F. and Yang, X., 2023. Urinary albumin-to-creatinine ratio in normal range, Cardiovascular Health, and all-cause mortality. JAMA Network Open, 6(12), pp.e2348333-e2348333.

3. Zhuang, N.N. and You, H.J., 2024. Role of vitamin D3 in lipid metabolism and chronic pain in advanced diabetic kidney disease and its rehabilitation. Healthcare and Rehabilitation, 1(1), p.100005.
4. Sun, Y., Jin, D., Zhang, Z., Zhang, Y., Zhang, Y., Kang, X., Jiang, L., Tong, X. and Lian, F., 2023. Effects of antioxidants on diabetic kidney diseases: mechanistic interpretations and clinical assessment. Chinese Medicine, 18(1), p.3.
5. Gameil, M.A., Marzouk, R.E., El-Sebaie, A.H. and Ahmed Eldeeb, A.A., 2023. Influence of time factor and albuminuria on characteristics of patients with type 2 diabetes Mellitus before, during and 1 year after COVID-19 recovery. Diabetology & Metabolic Syndrome, 15(1), p.126.
6. Dean, Y.E., Elawady, S.S., Shi, W., Salem, A.A., Chotwatanapong, A., Ashraf, H., Reddi, T., Dundi, P.O.R., Habash, W.Y., Habash, M.Y. and Ahmed, S., 2023. Progression of diabetic nephropathy and vitamin D serum levels: A pooled analysis of 7722 patients. Endocrinology, Diabetes & Metabolism, 6(6), p.e453.
7. Zhang, X., Zhang, L., Wen, Y., Zhang, M., Liu, S. and Xiao, H., 2023. Vitamin D ameliorates podocyte injury by enhancing autophagy activity in diabetic kidney disease. Kidney and Blood Pressure Research, 48(1), pp.314-325.
8. Elbarbary, N.S., Ismail, E.A.R. and Mohamed, S.A., 2023. Omega-3 fatty acids supplementation improves early-stage diabetic nephropathy and subclinical atherosclerosis in pediatric patients with type 1 diabetes: A randomized controlled trial. Clinical Nutrition, 42(12), pp.2372-2380.
9. Kamel, A.A., Elnaggar, M.G., Hamad, D.A., Zakhary, M.M. and Bakkar, S.M., 2022. The Role of Vitamin D, DKK1, Hepcidin and Oxidative Stress Biomarkers in Type 2 Diabetes Mellitus Patients With and Without Diabetic Nephropathy. The Egyptian Journal of Hospital Medicine, 89(2), pp.7137-7146.
10. He, X., Sun, J., Liu, C., Yu, X., Li, H., Zhang, W., Li, Y., Geng, Y. and Wang, Z., 2022. Compositional alterations of gut microbiota in patients with diabetic kidney disease and type 2 diabetes mellitus. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, pp.755-765.
11. ElSayed, N.A., Aleppo, G., Aroda, V.R., Bannuru, R.R., Brown, F.M., Bruemmer, D., Collins, B.S., Hilliard, M.E., Isaacs, D., Johnson, E.L. and Kahan, S., 2023. 11. Chronic kidney disease and risk management: standards of care in diabetes—2023. Diabetes Care, 46(Supplement_1), pp.S191-S202.
12. Zanchi, A., Jehle, A.W., Lamine, F., Vogt, B., Czerlau, C., Bilz, S., Seeger, H. and de Seigneux, S., 2023. Diabetic kidney disease in type 2 diabetes: a consensus statement from the Swiss Societies of Diabetes and Nephrology. Swiss medical weekly, 153(40004), p.40004.
13. shamim Khan, A., Zubair, M., Khan, S., Sultan, K. and Khan, M.K., 2022. The role of vitamin D deficiency and supplementation in onset and progression of diabetic nephropathy: A systematic review. Romanian Journal of Diabetes Nutrition and Metabolic Diseases, 29(1), pp.135-154.
14. He, A., Shi, C., Wu, X., Sheng, Y., Zhu, X., Yang, J. and Zhou, Y., 2024. Clusters of Body Fat and Nutritional Parameters are Strongly Associated with Diabetic Kidney Disease in Adults with Type 2 Diabetes. Diabetes Therapy, 15(1), pp.201-214.
15. Goldman, J.D., Busch, R. and Miller, E., 2024. Best Practice Perspectives on Improving Early Detection and Management of Chronic Kidney Disease Associated With Type 2 Diabetes in Primary Care. Clinical Diabetes, p.cd230074.