

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Vitamin D Deficiency And Its Independent Role In Renal Damage In Diabetes Mellitus.

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### ABSTRACT

The deficiency of Vitamin D is common among Indian population with a higher prevalence in diabetic patients. Recent researches point the crucial fact that Vitamin D deficiency could double the risk of albuminuria during five years follow up in Diabetes Mellitus. It is speculated that Vitamin D deficiency increases the risk of Diabetic nephropathy. Nephropathy is the common cause for morbidity and also death in Diabetes Mellitus. Hence early intervention of Vitamin D deficiency will have marked improvement in the quality of life for Diabetic patients. The aim of this study is to assess the degree of Vitamin D deficiency and concomitant albuminuria in diabetic patients. In a case series, 70 diabetic patients were selected and assessed for Vitamin D status and degree of albuminuria. The group of diabetic patients with Vitamin D deficiency ( $19.9 \pm 14$  ng/mL) has albuminuria ( $274 \pm 93$  mg/g) whereas the group of diabetic patients with normal Vitamin D ( $44.6 \pm 12$  ng/mL) has albuminuria ( $112 \pm 84$  mg/g). The study provides strong evidence to the hypothesis that deficiency of Vitamin D independently causes renal damage as proved by intense albuminuria. Hence therapy with Vitamin D is essential especially in Diabetes Mellitus to retard the progression of Diabetic Nephropathy and its related morbidity and mortality.

**Keywords:** Vitamin D, Renal Damage, Diabetic Nephropathy, Albuminuria

<https://doi.org/10.33887/rjpbcs/2021.12.3.15>

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## INTRODUCTION

Vitamin D helps in the intestinal absorption of calcium thus critical for strong bones and teeth. It has been known for centuries that Vitamin D deficiency causes Rickets/ Osteomalacia characterized by softening of bones and skeletal deformities. But recent researches throw light on myriad of health problems associated with Vitamin D deficiency. Decreased level of Vitamin D in serum has been associated with cognitive impairment, cardiovascular death and cancer<sup>(1,2)</sup>. Current researches point that Vitamin D deficiency in diabetes mellitus is associated with increased risk of renal damage as predicted by increased albumin in urine<sup>(3)</sup>.

Sunlight is the prime source of Vitamin D. Recent reports speculate that increased risk of skin cancer has reduced the duration of sun exposure thus increased the risk of Vitamin D deficiency in men and women alike<sup>(4)</sup>. Hence, Vitamin D deficiency has become common among the general population. The Vitamin D deficiency is a serious concern in diabetic population for it worsens the renal function even at the earlier stage. Vitamin D (Vit D) deficiency is a common disorder in diabetic Mellitus and may increase the risk for ischemic heart disease and Diabetic renal disease<sup>(5)</sup>.

It has been postulated that the metabolites from Vitamin D inhibit renin-angiotensin system. Hence reno-protective effect of Vitamin D is through preventing glomerulo-sclerosis and retarding proteinuria. Evenmore, prescription of Vitamin D has shown to decrease insulin resistance and also the blood pressure thus effective for the patient in multiple ways<sup>(6,7)</sup>.

Albuminuria is the forerunner for the diagnosis of kidney damage. It is critical in the current health scenario to clearly establish the one to one relationship between low levels of Vitamin D and development of kidney disease in Diabetes Mellitus. Hence, the purpose of this study is to evaluate the existence of association between the Vitamin D deficiency and albuminuria in diabetic patients.

## MATERIALS AND METHODS

After obtaining written consent, a detailed history was obtained from 70 known diabetics attending Master Health Check-Up of Tamil Nadu Government Multi Super Specialty Hospital, Chennai. Blood and urine samples were collected from every patient. Serum separated from centrifuged blood is used to assay fasting and post prandial blood glucose, Urea, Creatinine, Vitamin D and electrolytes. Plasma has been utilized to assay HbA1C for every patient. Urine samples are collected to quantify the albumin in urine.

The study population includes only the diabetic patients. Based on the Vitamin D status diabetic population is further divided into two groups:

- DM patients with normal Vitamin D
- DM patients with Vitamin D deficiency and insufficiency.

The serum level of Vitamin D greater than or equal to 30ng/mL is normal for the study population. Vitamin D of 20 to 30ng/mL is insufficient and those less than 20ng/mL is deficient for Vitamin D.

The degree of albuminuria is assessed in each group by collecting spot urine and calculating the albumin-creatinine ratio (ACR). Normal ACR is <30mg/g and ACR of 30-300mg/g is moderate albuminuria. ACR >300mg/g is severe albuminuria. The relationship between Vitamin D deficiency and renal damage is then calculated statistically.

## RESULTS AND DISCUSSION

70 Diabetic patients have participated in the study. It was found that among the 70 patients, 39 are Vitamin D deficient and 31 patients have normal Vitamin D. Mean age of Vitamin D deficient and normal Vitamin D

groups were 52.9±8 and 52.4±8.2 years respectively ( $P=0.7980$ ). There were no significant difference between two groups of diabetic patients based on serum glucose(Fasting and Post-prandial), HbA<sub>1c</sub>, Urea, Creatinine and serum Electrolyte levels ( $P>0.05$ ). The mean serum Vitamin D level among the deficient population is 19.9±14 ng/mL. In the Vitamin D deficient population the mean ACR is 274±93 mg/g. The mean serum Vitamin D for diabetic population with normal Vitamin D is 44.6±12 ng/mL. This population has the mean ACR of 112± 84mg/g. The comparison of variables between the Vitamin D deficient and Normal Vitamin D diabetic population is given in table 1.

**Table 1: Comparison of variables between diabetic population (Vit D deficient and Normal Vit D)**

S.No	VARIABLE	DIABETIC POPULATION WITH DEFICIENT VIT D (19.9±14 ng/mL)	DIABETIC POPULATION WITH NORMAL VIT D (44.6±12 ng/mL)	P VALUE
1	Age (years)	52.9±8	52.4±8.2	0.7980
2	FBS (mg/dL)	136± 52.3	141.1± 53.6	0.6898
3	PPBS(mg/dL)	223±46.2	245±37.7	0.055
4	HbA <sub>1c</sub> (%)	8.13±1.0	8.01±0.9	0.60
5	Urea (mg/dL)	42.8±27	41.4±29	0.8354
6	Creatinine(mg/dL)	3.0±2.2	2.9±2.02	0.84
7	Albumin Creatinine ratio(mg/g)	274±93	112± 84	< 0.0001 (Significant)

The study showed significant difference between changes of albumin creatinine ratio between the two groups of diabetic patients ( $P=0.028$ ). Thus we concluded that Vitamin D deficiency is associated with worsening of renal damage in diabetic patients thus accelerating Diabetic Nephropathy.

Kim et al. has followed 63 diabetic patients with nephropathy and associated Vit D deficiency for the period of seven months. The study has proved that return of Vitamin D to normal levels could decrease the degree of albuminuria. The study also proposed that dietary Vit D supplementation even in patients with DN may have a beneficial effect in delaying the progression of disease<sup>(8)</sup>

Bonakdaran et al. followed 119 patients of diabetes Mellitus. In the clinical trial, 31 cases has Vit D deficiency. Therapy with Vitamin D for 8 weeks has significantly reduced the extent of Proteinuria<sup>(9)</sup>.

Huang et al. proved in the study, deficiency of serum Vitamin D levels has been associated with microalbuminuria(30 to 300 mg/g of creatinine) and therapeutic oral intake of Vitamin D has significantly decreased the degree of albuminuria in early stages. They concluded that conventional doses of cholecalciferol may have anti-proteinuric effects on Chinese diabetic population<sup>(10)</sup>.

Madar et al. showed 16-week oral therapeutic administration of Vit D<sub>3</sub> to healthy individuals with low Vit D status has no improvement for HbA<sub>1c</sub><sup>(11)</sup>. In the same line, Ahmadi et al reported no significant difference based on HbA<sub>1c</sub> in study groups by Vitamin D therapy<sup>(12)</sup>.

Zehnder *et al.* studied the relationship between the levels of inflammatory markers in blood of chronic kidney disease (CKD) patients with the level of Vitamin D. They found out that there is a relationship between the CKD and the level of Vitamin D. The higher levels of 25(OH) D subsequently reduces inflammation<sup>(13)</sup>.

The metabolites of vitamin D influence the renal endothelial function and inversely related to the degree of arterial calcification in CKD patients. Nevertheless, decrease in 25(OH) D in CKD patients results in poor prognosis and eventually progression to End Stage Renal Disease<sup>(14)</sup>. There are evidences supporting the fact, vitamin D decreases the renal fibrosis progression<sup>(15)</sup>.

In this study we found direct association between Vitamin D deficiency and risk of renal damage in Diabetes Mellitus.

### CONCLUSION

Oral or Intramuscular therapeutic administration of Vitamin D in type 2 diabetic patients with Vit D deficiency or insufficiency leads to normalization of serum Vit D level. This end results is reduction of renal protein excretion thus delays the progression of renal damage. Hence, we concluded that correction of Vit D deficiency may be an effective and much needed treatment to retard Diabetic Nephropathy.

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