Original Research Article

Vitamin D in different stages of type 2 Diabetic nephropathy –A cross sectional study.

ABSTRACT:

Background: Diabetic nephropathy is a microvascular complication of diabetes mellitus and the prevalence of which increasing in every year. Monitoring of Vitamin D status in diabetic nephropathy patients is important, as the deficiency of vitamin D appears as a risk factor for the development of diabetic nephropathy. The aim of this study is to analyze vitamin D status in different stages of type 2 diabetic nephropathy. **Methods:** A 1.5-year cross-sectional research of 12- diabetic patients, 60 with nephropathy and 60 without nephropathy patients enrolled to MES Medical College. Patients with heart, liver, or thyroid disease, as well as those on dialysis, were excluded from the study. The VITROS 5600 integrated system measured fasting blood sugar, HbA1c, creatinine and vitamin D. According to HbA1c and estimated glomerular filtration rate (eGFR) values, the study population is separated into two groups. The statistical package for the social sciences (SPSS) software was used to conduct the analysis. The level of significance was calculated at 95%. **Results:** The level of vitamin D in diabetic individuals with nephropathy is much lower than in diabetic patients without nephropathy. In diabetic nephropathy patients, serum creatinine, urea, and HbA1c exhibited a highly significant negative correlation with vitamin D status, but eGFR showed a highly significant positive correlation. **Conclusion:** Vitamin D status has been found to be poor in all patients, with a greater drop in diabetic nephropathy patients. In diabetic nephropathy patients, serum creatinine, urea, and HbA1c exhibited a highly significant negative association with vitamin D status, but eGFR showed a highly significant positive link.

Keywords: Diabetic Nephropathy, Vitamin D, Serum Creatinine, Estimated Glomerular Filtration Rate.

1. INTRODUCTION:

Diabetes mellitus is a disease having more importance as the incidence and prevalence is increasing globally. Untreated diabetes mellitus results in micro and macro vascular complications, among these Diabetic Nephropathy incidence is more. It is a very serious problem as if not treated will lead to end stage renal disease and death. Vitamin D have many functions and this complexity of interaction is related to the long-term changes in renal function (1).

Most vertebrates can manufacture sufficient levels of vitamin D if their skin is exposed to enough sunlight (UVB rays). The sufficient amount of vitamin D can be obtained either from their diet or via adequate skin exposure to sunlight (2).

Vitamin D insufficiency is caused mostly by a lack of sun exposure and a decrease in consumption. Many studies from all over the world have found decreasing levels of vitamin D (3,4). Despite the abundance of sunlight in India, vitamin D deficiency affects 50 to 90 percent of the population, and this shortage affects people of all ages and genders (5).

The action of vitamin D is receptor mediated, which are expressed in almost all cell types in the kidney (6,7). Vitamin D deficiency/insufficiency is associated with insulin resistance, reduced beta cell function leading to an increase in blood glucose (8).

The protective role of vitamin D in diabetic nephropathy is suggested in recent years (7,9). The improvement in renal function of diabetic nephropathy patients with Vitamin D

administration was shown in a recent study (10). In spite of these positive findings, contrasting reports are also available on the association of vitamin D with diabetic nephropathy (11–14). Researches are going on to confirm the renal protective effects of vitamin D and to evaluate a therapeutic dose.

Contrasting results are still available and it is important to measure vitamin D level in different stages of diabetic nephropathy. The objective of this study is to measure vitamin D level in different stages of diabetic nephropathy in type 2 diabetic patients of Kerala.

2. MATERIALS AND METHODS:

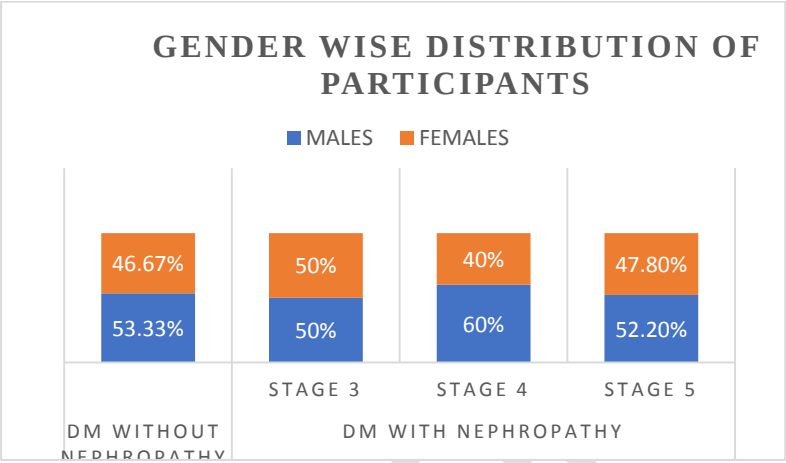
The cross-sectional study including 120 Type 2 Diabetic patients, out of which 60 with nephropathy and 60 without nephropathy was conducted after obtaining approval from the Institutional Ethics Committee in MES Medical College, Kerala. Patients with a history of cardiac, liver, thyroid dysfunction, those under dialysis were excluded from the study. Diabetic nephropathy patients sub grouped according to different stages of nephropathy, determined by eGFR value (15). eGFR is calculated using MDRD equation. Serum creatinine, serum urea, fasting blood sugar, HbA1c were measured by VITROS 5600 integrated system and vitamin D estimated using VITROS ECi/ECi Immunodiagnostic Systems using Intellicheck R Technology. Pearson correlation coefficient and unpaired t test used for statistical analysis at a level of significance of 5%.

3. RESULTS AND DISCUSSION:

Type 2 Diabetic patients of age group 40-60 years, with and without nephropathy were enrolled in this study. This study was to investigate the vitamin D status in Type 2 Diabetic patients with (n=60, 48.33 % females and 51.67 % males) and without nephropathy (n=60, 46.67 % females and 53.33 % males). Based on eGFR value Diabetic nephropathy patients are distributed in stage 3, 4 and 5. Among this stage 3 comprised 38 % (50% females

& 50% males) of the patients, 22 % (40 % females and 60% males) in stage 4 and 40% in stage 5 (47.8 % females & 52.2 % males) (Figure 1).

Figure 1: Distribution of study subjects according to gender



The parameters analysed were expressed as Mean± SD. We could find a highly significant difference in the vitamin D status between Diabetic patients with and without nephropathy. It has been observed that vitamin D status is low for all the patients and further decrease in diabetic nephropathy patients (Table-1). Vitamin D level is significantly lowered in diabetic patients with nephropathy than in patients without nephropathy.

Table 1: Comparison of parameters among diabetic patients with and without nephropathy:

Parameters	DM	DN	t Value	p Value
AGE	53.4 ± 5.9	55.9 ± 5.7	2.44	0.02*
SBP	130.8 ±14.7	139.2 ± 17.8	2.79	0.01*
DBP	82.3 ± 7.6	83.8 ± 8.4	1.02	0.31
FBS	170.1 ± 58.3	164.7 ± 50.1	0.54	0.58

Urea	24.5 ± 8.04	74 ± 48.1	7.86	<0.001*
Creatinine	0.75 ± 0.13	4.08 ± 3.48	7.39	<0.001*
HbA1c	7.44 ±1.88	8.9 ± 2.08	4.17	<0.001*
eGFR	99.3 ± 24.3	25.3 ±17.5	19.12	<0.001*
Vitamin D	30.9 ± 4.02	17.1 ± 4.4	17.95	<0.001*

*Indicates significant difference; significance is measured at the level of $p<0.05$

Recent observations have demonstrated that kidney disease seems to be associated with a high incidence of vitamin D insufficiency or deficiency (16). Studies by Gonzalez et al. (17) demonstrated that 25-hydroxyvitamin D values are 30 ng/ml, believed be the lower limit of normal, in the majority of patients with CKD. Al-Badr et al reported that vitamin D has the potential to have a favourable impact in diabetic nephropathy (18). Banerjee D et al also suggested a link between of vitamin D deficiency with cardiovascular events in patients with CKD (19). But in contrast Kayzer C A et al concluded Plasma 1,25(OH)2D is not associated with risk of developing increased albuminuria or reduced eGFR (20).

Serum creatinine, urea, HbA1c showed a highly significant negative correlation and eGFR showed a highly significant positive correlation with vitamin D status in diabetic nephropathy patients. SBP, DBP and FBS showed no significant correlation with vitamin D (Table-2).

Table 2: Correlation between Vitamin D and other parameters in Diabetic Nephropathy.

Parameters	Correlation with Vit D	
	r	p
AGE	0.26	0.04*
SBP	-0.05	0.67
DBP	-0.02	0.86

FBS	-0.15	0.25
Urea	-0.59	<0.001*
Creatinine	-0.67	<0.001*
HbA1c	-0.54	<0.001*
eGFR	0.86	<0.001*

*Indicates significant correlation; significance is measured at the level of $p<0.05$

Kim S G et al also reported that a positive association between vitamin D deficiency and decreased eGFR. They also reported a simultaneous decrease in vitamin D level with decrease in eGFR (21). In patients with early stages of CKD, Ravani et al.(22) proposed that serum 25(OH)D is an independent inverse predictor of renal disease progression and death. Previous study on the relationship between vitamin D and eGFR however, has shown mixed results. In Korean adults, Park et al.(23) found that 25(OH)D was positively associated with eGFR . In the Framingham Heart Study, O'Seaghdha et al.(24) found no link between 25(OH)D and eGFR. Kim S G etal reported that the prevalence of decreased eGFR levels were increased as an increase of age, but the prevalence of vitamin D deficiency was decreased (21). A weak positive correlation between vitamin D and eGFR was identified by Wang Y et al (25), implying that plasma vitamin D concentrations were lower in advanced-stage patients and those with a lower eGFR.

There is a significant difference in vitamin D status in these 3 groups (Table 3). There was a decrease in vitamin D as the nephropathy progressed from stage 3 to 5. We observed a positive correlation between eGFR and vitamin D status. This correlation was more significant in stage 3 of diabetic nephropathy.

Table 3: Correlation Between Vitamin D & eGFR at different stages of DN

DN	Mean ± SD	r Value	p Value

Stage 3	21.3 ± 2.8	0.52	0.01
Stage 4	17.5 ± 2.7	0.17	0.54
Stage 5	12.9 ± 1.5	0.31	0.15

Peng et al. (26) studied 448 individuals, including 144 with type 2 DM with CKD and 304 with CKD but no DM, and found that 93.1 percent of DN patients and 78.9% of patients without DN had low vitamin D status. In a retrospective observational study done by Xiao et al. (27) reported that the four DN groups had significantly lower serum 25(OH)D levels than the control group. Ray et al. (28) published a study that investigated the profile of CKD-related mineral bone abnormalities in 72 newly diagnosed DN patients with CKD stages 4 and 5. In 65.72 percent of them, the vitamin D level was less than 20 ng/mL. Serum 25(OH)D was 19.15 (IQR 13.6-23.4) ng/mL in the CKD stage 4 group, but it was 10.95 (IQR 9.3, 16.4) ng/mL in the CKD stage 5 group ($p = 0.006$).

4. **CONCLUSION**:

Vitamin D levels are low in all patients, with diabetic nephropathy patients having even lower levels. In diabetic nephropathy patients, serum creatinine, urea, and HbA1c all showed a highly significant negative association with vitamin D status, but eGFR showed a highly significant positive correlation. Renal protective effect of vitamin D is very important and can be used as a therapeutic target.

DECLARATIONS

Ethical approval: The study was approved by the Institutional Ethics Committee

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