ORIGINAL ARTICLE

Association of Vitamin D Deficiency with Microalbuminuria in Type II Diabetics

MUDDASSIR AHMED[1], FAZL-E-MATEEN[2], AHMED AYYAZ[3], *MARIA MUDDASSIR[4], AHMAD BASIRAT[5], SAJAD AHMED[6]*
[1]*Sheikh Zayed Hospital Lahore,*
[2]*Assistant Professor Nephrology Department Mayo Hospital Lahore,*
[3]*Sheikh Zayed Hospital Lahore ,*
[4]*M Islam Medical College Gujranwala,*
[5]*Tallaght University Hospital Ireland,*
[6]*Assistant Professor Nephrology Department Mayo Hospital Lahore*
Correspondence to Dr. Muddassir Ahmed, Email: muddassir4u@hotmail.com , cell 0300-6403607

ABSTRACT

Aim: To find out whether or not an association exists between Microalbuminuria and deficiency of Vitamin D in our diabetic population.
Methods: This cross sectional analytical study was carried out in out-patient department of Nephrology and Diabetes Centre, Sheikh Zayed Hospital, Lahore after approval from Ethical Committee and IRB, over a period of one year. The study included 312 patients, 156 patients had microalbuminuria and 156 patients were normoalbuminuric. Their 25(OH) vitamin D levels were measured by a single specified laboratory. Effect modifiers like age and gender were controlled through stratification. The comparison in Vitamin D levels amongst both groups was done using independent sample t-test.
Results: Out of 156 patients who had no microalbuminuria (ACR<30 mg/g of creatinine), 51 patients had vitamin D deficiency (32.6%). However in patients with microalbuminuria (ACR 30-300mg/g of creatinine), 115 out of 156 patients (73.7%) had vitamin D deficiency.
Conclusion: This study states that an association exists between Vitamin D deficiency and microalbuminuria in type 2 diabetes. It is also reported that incidence of Vitamin D deficiency is more as compared to normo-albuminuric patients.
Keywords: Microalbuminuria, Vitamin D deficiency, Urinary creatinine levels, Type 2 Diabetes.

INTRODUCTION

Diabetes mellitus can be classified as a disorder with improper hyperglycemia and deranged metabolism due to both decrease in the secretion of insulin or an aggregate of resistance to insulin and decreased secretion to compensate. It is a main cause of mortality and morbidity worldwide. The huge majority of diabetics are categorized into one of two main types: type 1, in which there is complete insulin deficiency and type 2 diabetes, which is marked by the combination of insulin resistance with an insufficient redeeming increase in the secretion of insulin. Apart from the two main types it can also develop during pregnancy and secondary to pancreatic disorders, endocrinopathies and drugs[1].

The initial clinical sign of the kidney injury in diabetics is generally microalbuminuria[2], which occurs in 2-5% of patients in a year with prevalence around 25%. Vitamin D is involved in many metabolic pathways including maintenance of bone health. Deficiency of Vitamin D is very prevalent in Pakistan and much so in CKD population[3].

There are two theories regarding relationship between deficiency of Vitamin D & albuminuria. It has been proved that presence of Vitamin D (25-OH D3) deficiency has led to development and progression of albuminuria[4]. Vitamin D can act as a potent inhibitor of both the renin-angiotensin system and nuclear factor–kB pathways. On the other hand it has also been hypothesized that overt proteinuria can cause urinary excretion of VDBP, which is a carrier of vitamin D. This urinary loss of VDBP might have an effect on vitamin D levels[5].

We aim to ascertain whether an association exists between microalbuminuria and deficiency of Vitamin D among our diabetic patients. If such an association is established, it could potentially warrant the early screening of levels of vitamin D in patients having type 2 diabetes resulting in earlier prevention of complications related to diabetes.

METHODS

This cross sectional study was carried out in the out-patient department of Nephrology and Diabetes Centre, Sheikh Zayed Hospital Lahore over a period of one year. A total of 156 patients in each group were estimated by using 90% confidence level, 80% power of test with expected odds ratio 2.41 of deficiency of Vitamin D in albuminuria as compared to normoalbuminuric with expected prevalence of Vitamin D deficiency in normoalbuminuric patients of about 8%. It was calculated by using PS – Power and sample size calculation software. Non-probability purposive consecutive sampling was done. Patients having type 2 diabetes mellitus were studied.

Both male and female patients having type 2 diabetes mellitus for 5 yrs or more duration were included. Patients who were excluded were those who had taken vitamin D supplements in the last 2 months, those with albumin-creatinine ratio of more than 300mg/g of creatinine, known case of rickets and patients with BUN greater than 25 mg/dl and creatinine levels greater than 1.2 mg/dl.

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A specifically devised proforma was used to gather all the related information. The proforma include analytical information like age, name and sex. Their early morning voided urine samples were gathered and kept at -20°C till analysis. Urine samples were analyzed for microalbuminuria by using a commercially available ELISA kit. Urinary creatinine levels were measured by using a commercially available kit. Their spot urine albumin to creatinine ratio was calculated (cut off value of ACR<30mg/g of creatinine for normoalbuminuric). These tests were performed in RIA Lab at NHRC Sheikh Zayed Medical Complex. Two groups were made depending upon the presence or absence of microalbuminuria, 156 patients in each group. Their 25–hydroxyvitamin D levels were measured by a single specified laboratory. Effect modifiers like age and gender were controlled through stratification.

Data was collected and compiled in the computer and analyzed using SPSS 22. The quantitative variables included age, vitamin D levels, albumin/creatinine ratio and duration of diabetes. The measured variables were expressed in mean and standard deviation. Vitamin D levels were compared between 2 groups by using independent sample t-test. The qualitative variables included gender, presence or absence of microalbuminuria and Vitamin D deficiency. They were presented by calculating frequencies and percentages. Use of Binary logistic regression was done to see the effect of albuminuria on deficiency of Vitamin D by controlling duration of diabetes, gender and age as confounders.

RESULTS

The study included 312 patients who were separated into 2 groups, each comprising of 156 patients depending on the presence and absence of microalbuminuria. From 312 patients, males were 157(50.3%) and females were 155(49.7%). 29 years was the minimum age and 70 years was the maximum age. 53.09±11.4 was the mean age. Three age groups were made of the patients. 13 patients were between 25 to 35 years, 141 patients were present in age group of 36 to 50 years and 158 patients included in age group of 51 to 70 years. All the patients were checked for their vitamin D levels, minimum level was 12 and the maximum was 26. Mean was 19.7±2.3. Independent T test was applied on both groups and P value was found to be less than 0.1 (P=0.028). Hence proven that a positive association exists between levels of vitamin D & microalbuminuria.

Table 1: Cross tabulation of presence and absence of deficiency of vitamin D and microalbuminuria

Vitamin D groups	Group		Total
	ACR<30mg/g of Creatinine	ACR 30-300mg/g of Creatinine	
Deficient	51	115	166
Not deficient	105	41	146
Total	156	156	312

Table 2 shows that males have slightly higher incidence of microalbuminuria. Out of a total of 157 male patients, 50.3% patients were having vitamin D deficiency (79/157). Out of 155 female patients, 56.13% patients were having vit D deficiency (87/155). Showing thereby that more %age of females are Vitamin D deficient as compared to males.

Fig. 1: Percentage of patients according to different age groups

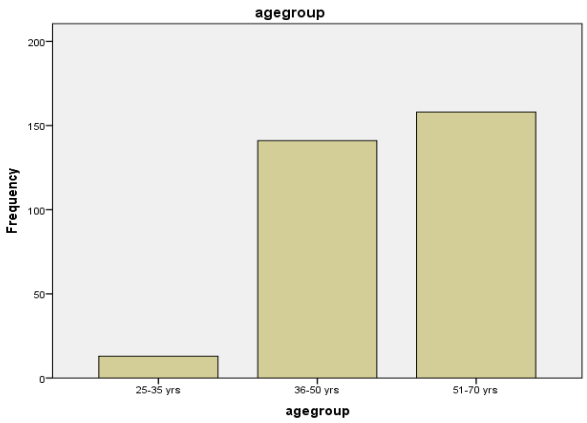

Table 2: %age and absence of microalbuminuria in both genders

Group	Gender		Total
	Male	Female	
ACR<30mg/g of Creatinine	73	83	156
ACR 30-300mg/g of Creatinine	84	72	156
Total	157	155	312

Fig. 2: Presence and absence of microalbuminuria in both genders

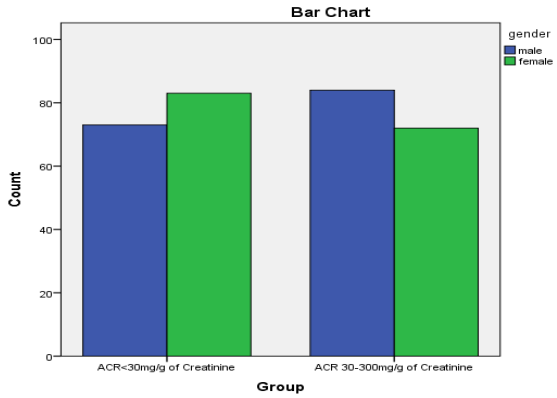

Table 3: Status of vitamin D in the two genders.

Gender	Status of Vitamin D		Total
	Deficient	Deficient	
Male	79	78	157
Female	87	68	155
Total	166	146	312

DISCUSSION

Type 2 Diabetes mellitus is a rapidly growing medical problem in developing countries that commonly complicates into diabetic nephropathy and is a well known cause of ESRD all over the world. Initial presentation of diabetic nephropathy is albuminuria. The renin-angiotensin system has a major role in development of diabetic nephropathy. ACE inhibitors and ARBs had proven role in preventing diabetic nephropathy by decreasing albuminuria. There have been ongoing studies to find alternative medication for controlling microalbuminuria. It is reported in many studies that vitamin D analogs are able to

suppress renin expression, inhibition of mesangial expansion and improvement of renal function[6].

In our study 157 patients were males and 155 patients were females, thereby sharing an almost equal number from both the genders. It is consistent with the previous studies where males were 54% and females 46%.

In this study, 29 years was the minimum and 70 years was the maximum age with 53.09 years being the mean age. Patients were separated in 3 age groups where 4.2% were between the ages of 25-35 years. 45.1% were between the age of 36-50 years and 50.6% patients were above 50 years. In the survey, total patients were 321 out of which 24.8% patients were in first group i.e., 25-35 years, 38% patients were in second group i.e., 36-55 years and 37% patients were above 55 years. It shows that patients were equally distributed in all age groups. However, in our study most of the patients belong to middle to elder age group. It shows that Type 2 diabetes mellitus is more prevalent in middle and older ages.

In our study, cut off value of vitamin D deficiency was 20ng/ml and when we compared two groups of patients i.e. with and without microalbuminuria, the deficiency of Vitamin D was more prevalent in the group with microalbuminuria i.e., 73.7% (115/156). On the other hand, those patients who had no microalbuminuria also had decreased incidence of vitamin D deficiency 32.6% (51/156). This finding is consistent with other studies like NHANES 2001-2006. Patients with microalbuminuria had higher incidence of vitamin D deficiency (12%) as compared to patients with no microalbuminuria (7.87%).

In a study done by Isakova T it was shown that patients with microalbuminuria were more likely to have decreased 25(OH) D3 levels and high IL6 levels[8]. This relation of deficiency of Vitamin D & microalbuminuria has been strengthened by many studies which measured the results of Vitamin D replacement on urine albumin excretion. Xu L carried out a meta-analysis of the randomized control trials and showed that vitamin D therapy decreased proteinuria and did not have any adverse effects on the renal profile in patients not undergoing haemodialysis[8]. However; few researchers like Ahmadi N have showed no convincing effects of Vitamin D on proteinuria[9].

In national health and nutrition examine study (NHANES III study), there is relation between albuminuria and vitamin D deficiency. Zehnder et al and Ibrahim I studied the relationship between inflammatory markers in CKD and existence of vitamin D deficiency. There was a relationship between development of chronic renal failure and decreasing vitamin D levels.[10] There are different proposed mechanisms of decreasing microalbuminuria and progression of chronic renal failure by Vitamin D replacement. According to the researchers, vitamin D deficiency is independently related to higher plasma renin and angiotensin II concentration. In addition to this there is evidence that vitamin D causes a decrease in the progression of renal fibrosis. It can be due to decrease in renal expression of renin as well as curbing the tumor necrosis alpha effect[10].

Design of our study is slightly different from the studies done previously to find relationship between vitamin D and microalbuminuria. We separated the patients into 2 groups in our study according to the presence and absence of microalbuminuria and then measured vitamin D level in two groups. However in previous studies done by Fernández-Juárez G and Isakova T, patients were divided according to presence and absence of vitamin D deficiency and then albuminuria was measured with or without vitamin D replacement[4,7].

Keeping in view the results of our study we can say that a relationship exists between vitamin D levels and degree of proteinuria. In order to prevent diabetic nephropathy in type 2 diabetics we should diagnose and treat the deficiency of vitamin D earlier in the course of disease, which is not an expensive modality. Thus, by treating vitamin D deficiency we can not only decrease proteinuria but can also maintain patient's bone health.

CONCLUSION

It is concluded that an association exists between vitamin D deficiency and microalbuminuria in type 2 diabetes. In patients with microalbuminuria, incidence of vitamin D deficiency is more as compared to normo-albuminuric patients. More studies are also needed to show the effect of vitamin D replacement on degree of albuminuria to strengthen this association.

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