

A Study on Association of Vitamin D3 With Diabetic Nephropathy

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Abstract:-

➤ *Background:*

Vitamin D has important actions on glucose metabolism. These include improved insulin exocytosis, direct stimulation of insulin receptor, improved uptake of glucose by peripheral tissues, improving insulin resistance. It has got various pleiotropic effects like suppression of cell mediated immunity, regulation of cell proliferation, stimulation of neurotropic factors such as nerve growth factor, Glial cell line-derived neurotrophic factor, neurotrophin, suppression of RAAS, reduction of albuminuria, immunomodulatory effects, and anti-inflammatory effects. Thus, vitamin D is implicated in many ways in the pathogenesis of retinopathy, neuropathy and nephropathy.

➤ *Aim of the Study :*

The purpose of the study is to assess the levels of 25- hydroxyl vitamin D in patients with type 2 diabetes mellitus and its association with diabetic nephropathy.

➤ *Materials and Methods :*

In this cross sectional study, the association between circulating 25-hydroxy vitamin D level and the presence of diabetic nephropathy in type 2 diabetes mellitus who attended medicine outpatient clinic and inpatients of medical wards.

Our study included 206 patients which includes two groups, one group with 25(OH) D <30ng/ml of 72 patients and another group with 134 patients who had 25(OH)D>30ng/ml. Venous blood was drawn from the patients after an overnight fasting and serum creatinine was calculated using Jaffe method, Glycated haemoglobin - HbA1c was measured by an automated High performance liquid chromatography analyser. Serum 25(OH)D concentrations were measured using chemiluminescent immunoassay. Estimated Glomerular

Filtration Rate e-GFR was estimated with the Four variable Modification of Diet in Renal Disease (MDRD) study equation.

➤ *Observation and Results :*

In our study total of 206 patients, 104 patients were female and 102 were males. With gender comparison, there occurs a statistically significant 'p value' in female patients with Vit D<30ng/ml a mean of 61.2% compared with males with a mean of 38.8%. Here 71 patients with vitamin D deficiency which constitutes about 53% found to have diabetic nephropathy and in vitamin D sufficient patients, 30 patients which constitutes about 41.7% found to have diabetic which is statistically insignificant.

➤ *Conclusion :*

Vitamin D is found to have both direct action through vitamin D receptor activation and indirect action through regulation of calcium homeostasis and its effects on various pathogenesis and type2 diabetes which includes dysfunction of pancreatic beta cells, insulin action impairment and systematic information. Vitamin D is considered to be an important factor in modifying the risk of type2 diabetes mellitus and In type 2 Diabetes mellitus about 65% people found to have vitamin D deficiency according to our study.

I. INTRODUCTION

Diabetes Mellitus is a fast growing epidemic accounting for about 90% globally. Its incidence rate is increasing year by year in both developed and developing countries. India has an alarming epidemic of diabetes and is a major public health problem, according to Indian Council of Medical Research sponsored INDIAB study, published in 2011. It is now estimated to have 387 million people are diabetic across the world and the number is projected to extend to 592 million by the year 2035. This diabetes

epidemic is right now progressing across rural and hilly areas which were previously thought as untouched. Although the prevalence of both the types of diabetes mellitus is increasing worldwide, the prevalence of type 2 diabetes mellitus is rapidly rising than other types those are attributed to more of obesity and sedentary lifestyle, high calorie density-fast food as countries become more and more industrialized¹. Worldwide estimates project that more number of individuals with diabetes mellitus will be in the age group of 45–64 years in 2030.

In India, there is an estimated 45 million people with diabetes mellitus in 2007, has risen to 62 million in 2009 and it is predicted to rise about 100 million people by 2025 by which time every 5th diabetic person in the world would be an Indian, as per to the Diabetes Atlas published by the International Diabetes Federation (IDF). There is an estimate that around 200 diabetic patients were underdiagnosed and are at higher risk for development of complications such as Renal failure, Atherosclerosis, stroke, myocardial infarction, diabetic foot amputations.

There is an estimate that 5 million deaths are contributed by diabetes and its complications in 2015². On studying the complications of diabetes, 63% of patients with diabetic nephropathy have type II DM and The risk of developing diabetic nephropathy is not constant over the duration of diabetes.

Vitamin D has been traditionally known as anti-ricketic factor or sunshine vitamin. Vitamin D is unique because it is synthesized by the body and it functions as a hormone. Besides its pivotal role in calcium homeostasis and bone mineral metabolism, evidences link Vitamin D with chronic diseases like Diabetes, Hypertension, Myopathic disorder, infections, autoimmune disorder and cancer. The natural substance cholecalciferol is originally called vitamin D3. Vitamin D2 is the artificially produced ergocalciferol. The natural source of cholecalciferol is by the action of short wavelength ultraviolet light from the sun on 7- dehydrocholesterol in the skin. Cholecalciferol also occurs in a small minority of our foods. Vitamin D deficiency is Epidemic in India despite of plenty of sunshine. All Indian studies uniformly point to low 25(OH)D levels in the populations studies despite abundant sunshine. It is a multifunctional fat soluble vitamin requiring for humans' growth and development and its non-classical functions has more attention for close association between vitamin D deficiency and complications of DM. the prevalence of vitamin D deficiency is high in type 2 DM and its complications³. This study is undertaken to evaluate the effect of vitamin D deficiency in the development of microvascular complications like diabetic nephropathy⁴ in type 2 DM.

Vitamin D, traditionally known for its role in regulating bone and calcium metabolism, has recently been implicated in a multitude of systems including the cardiovascular, immune, and reproductive systems^{5,6}. The

ubiquitous expression of vitamin D receptors in the human body is closely related to these findings, suggesting that vitamin D plays an important role in the regulation of the expression of multiple genes beyond those involved in calcium metabolism⁷.

Several large epidemiologic studies on the impact of vitamin D on metabolic and cardiovascular diseases demonstrated that lower vitamin D levels were associated with the incidence of type 2 diabetes mellitus (T2DM)^{8,9}. Vitamin D deficiency reportedly reduced intracellular calcium levels and decreased insulin secretion in pancreatic beta cells¹⁰. Vitamin D deficiency also decreases the insulin receptor expression, leading to peripheral insulin resistance¹¹. Furthermore, vitamin D deficiency has an atherosclerotic action, promoting myocardial hypertrophy and renin activation¹².

Vitamin D deficiency is prevalent in South Korea. The 2006 to 2008 Korea National Health and Nutrition Examination Survey (KNHANES), which included adults aged 19 years or older, reported vitamin D deficiency in 47.3% of men and 64.5% of women¹³. Another international study reported that Korean postmenopausal osteoporotic women had the lowest 25-hydroxyvitamin D (25OHD) levels among 18 countries¹⁴. These findings suggest that vitamin D deficiency may be even more prevalent in T2DM patients in Korea and related to poor glycemic control and/or various complications of T2DM.

However, studies on the association between vitamin D deficiency and micro- and macrovascular complications in T2DM showed conflicting results and are currently inconclusive. Several studies reported that vitamin D deficiency increased the risk of diabetic polyneuropathy¹⁵, nephropathy, and retinopathy¹⁶. However, other studies found no association between vitamin D deficiency and diabetic polyneuropathy¹⁷ or retinopathy¹⁸. While vitamin D deficiency was reportedly associated with a lower low-density lipoprotein cholesterol (LDL-C) level and a higher triglyceride level and diastolic blood pressure than those in T2DM patients with sufficient vitamin D level¹⁹, other studies reported no relationship²⁰.

➤ *Aim of the Study:*

To assess the levels of 25- hydroxyl vitamin D in patients with type 2 diabetes mellitus and its association with diabetic nephropathy.

➤ *Materials & Methods:*

This study was conducted in Katuri Medical College, Guntur for duration of 6 months from June 2022 to Dec 2022. A proper ethical approval was obtained from the Institutional Ethical Committee .The study was conducted after getting informed consent from all the Subjects involved in this study.

- Study Design: Cross Sectional Study
- Period: 6 months
- June 2022 to Dec 2022

- Conflict of Interest: Nil
- Study population: Study population will consist of patients and general population in the hospitals diagnosed with Diabetes above 30 years of age.

➤ *Inclusion Criteria:*

- Cases: Diabetics in this study will be defined by the American Diabetes Association as either
- Fasting plasma glucose (FBS) of >125 mg/dl, or
- Postprandial blood sugars at 2Hr (PPBS) > 200 mg/dl.

➤ *Exclusion Criteria:*

- Type 1 Diabetes mellitus
- Gestational Diabetes mellitus
- Chronic Kidney Disease
- Hypertension
- Coronary artery disease
- Hypoparathyroidism
- Severe infection
- Severly impaired hepatic function
- Multiple myeloma
- Malignancy
- HIV – AIDS

Diagnosis of Type 2 diabetes mellitus was made by clinical records and blood investigations including fasting and postprandial blood glucose values. For the diagnosis of diabetes mellitus, WHO criteria were employed.

II. METHODOLOGY

After obtaining informed written consent, basic demographic details, detailed clinical history and physical examination will be done. Blood samples were taken for the determination of serum 25 hydroxy vitamin D level, HbA1C, serum creatinine and urinary albumin excretion rate was also done, and eGFR was also calculated. Presence of nephropathy is defined as abnormal albuminuria which is urine albumin excretion rate >30mg/day and /or eGFR <60ml/min/1.73 m2.

➤ *Data Collection & Analysis:*

The data of each patient will be collected on a proforma specially designed for this study and which includes demographic details, past medical history, diabetic profile. The information collected regarding all the selected subjects were recorded in a Master Chart. The collected data was analyzed to identify the vitamin D deficiency and its association in the development of nephropathy in Type 2 Diabetes Mellitus patients. The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value .05 is considered as significant level.

III. OBSERVATION AND RESULTS

➤ *Comparison Between Age with Groups:*

Table 1 Comparison between Age with Groups

		Groups			Total	□ 2 – value	P- value
		> 30 ng/ml	< 30 ng/ml				
Age range	30 – 39 yrs	Count	17	18	35	5.370	0.147 #
		%	23.6%	13.4%	17.0%		
	40 – 49 yrs	Count	20	35	55		
		%	27.8%	26.1%	26.7%		
	50 – 59 yrs	Count	26	51	77		
		%	36.1%	38.1%	37.4%		
	>= 60 yrs	Count	9	30	39		
		%	12.5%	22.4%	18.9%		
Total		Count	72	134	206		
		%	100.0%	100.0%	100.0%		

No Significant at P < 0.05 level

Age of the patients were categorized and in the range of 30-39 yrs, 40-49 yrs , 50-59 yrs & >= 60 yrs, Vit D level was compared and grouped as one group with vit D level > 30 ng/ml & other <30 ng/ml and there is no significant difference.

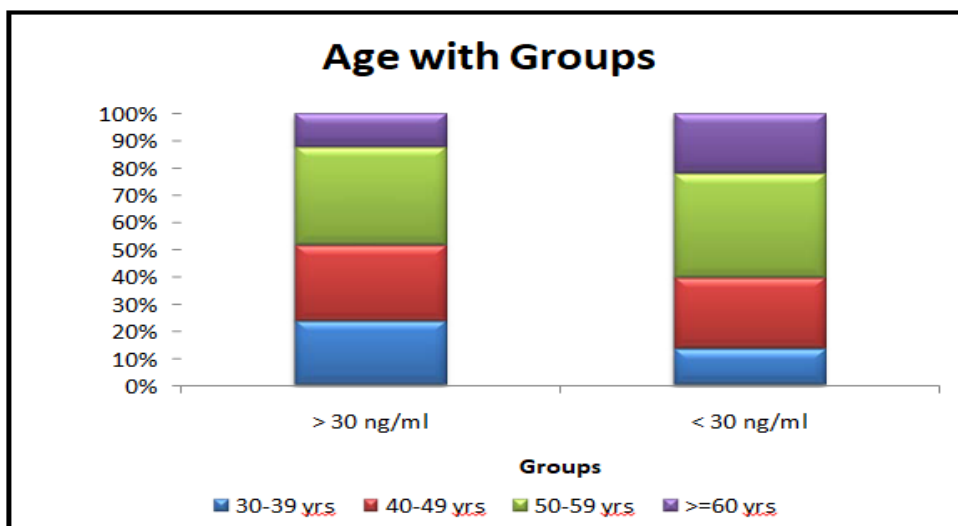


Fig 1 Comparison between Age with Groups

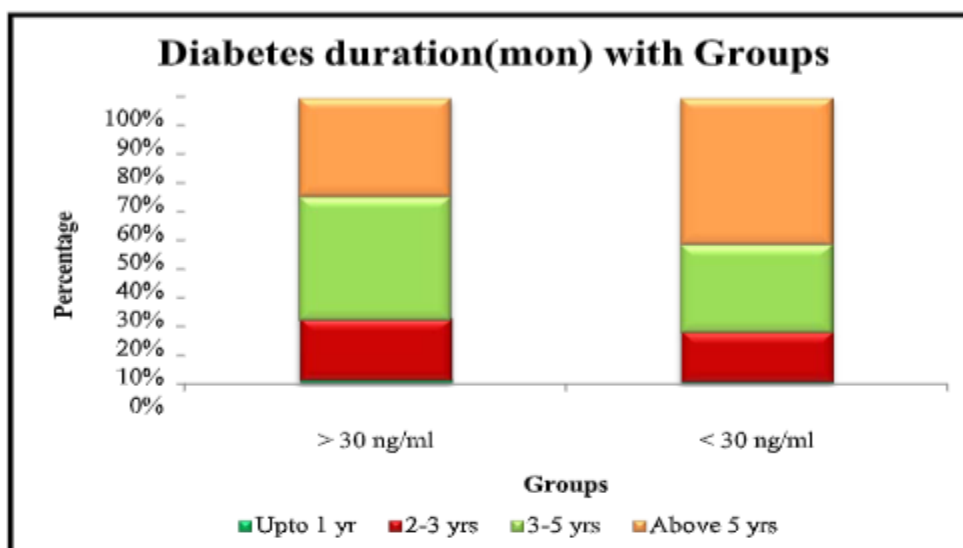


Fig 2 Comparison between Diabetes Duration with Groups

On comparing the groups with duration of diabetes categorised as upto 1 yr., 2-3 yrs, 3-5 yrs & above 5 yrs there found no significant differences.

Table 2 Comparison between Diabetes duration with Groups

		Groups			Total	□ 2 - value	P- value
		> 30 ng/ml	< 30 ng/ml				
Diabetes Duration	Up 1 yr	Count	1	1	2	5.508	0.1 38 #
		%	1.4%	.7%	1.0%		
	2 – 3 yrs	Count	15	23	38		
		%	20.8%	17.2%	18.4%		
	3 – 5 yrs	Count	31	41	72		
		%	43.1%	30.6%	35.0%		
	Above 5 yrs	Count	25	69	94		
		%	34.7%	51.5%	45.6%		
Total		Count	72	134	206		
		%	100.0%	100.0%	100.0%		

No Significant at P < 0.05 level

Table 3 Comparison between Urine Albumin with Groups

			Groups		Total	□ 2 - value	P- value
			> 30 ng/ml	< 30 ng/ml			
Urine Albumin	A	Count	42	63	105	2.401	0.121 #
		%	58.3%	47.0%	51.0%		
P	Count	30	71	101			
	%	41.7%	53.0%	49.0%			
Total		Count	72	134	206		
		%	100.0%	100.0%	100.0%		

No Significant at P < 0.05 level

In Patients with 25(OH)D <30ng/ml, albuminuria is found in 71 patients which comprises about 55% of study population whereas in group with 25(OH)D>30 ng/ml 30 patients had albuminuria which comprises about 41.7% with a ‘p’ value of 0.121 which is not statistically significant and so there is no association between vitamin D deficiency and albuminuria in this study.

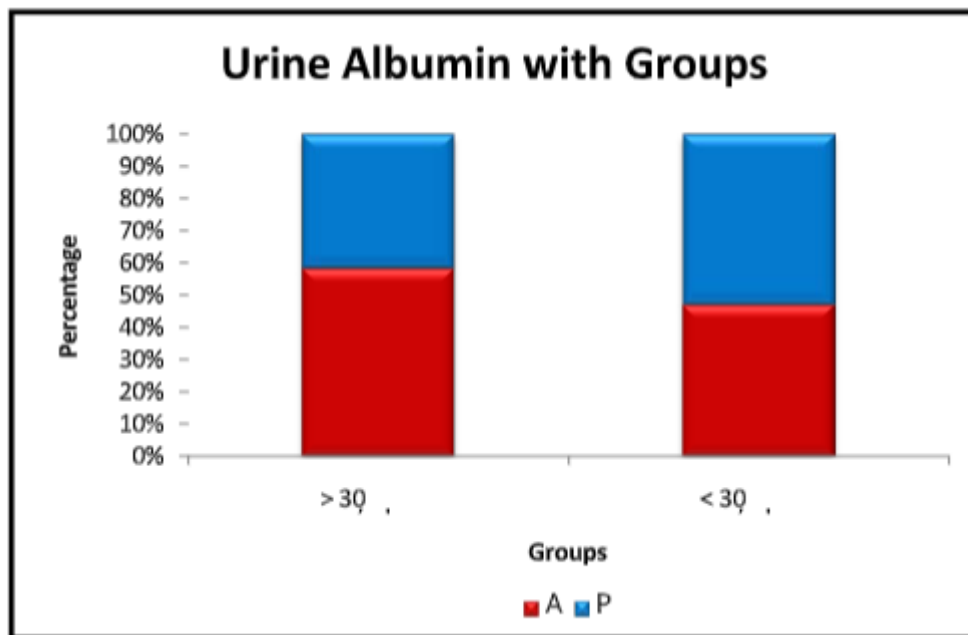


Fig 3 Urine Albumin with groups

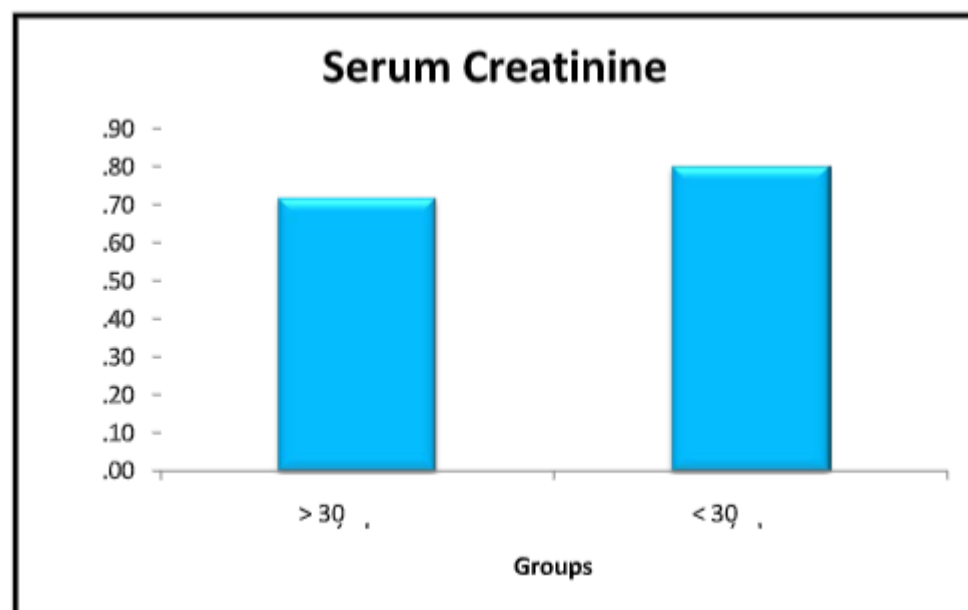


Fig 4 Comparison of Serum Creatinine

Table 4 Comparison of Serum Creatinine by Independent Sample T-test

Groups		N	Mean	S.D	t- value	P- value
SC	> 30 ng/ml	72	.72	0.09	3.909	0.0005 **
	< 30 ng/ml	134	.80	0.22		
** Highly Significant at P < 0.01 level						

In groups with vitamin D deficiency the mean value of serum creatinine found to be 0.8 mg/dl and in patients with sufficient vitamin D mean serum creatinine was 0.72mg/dl and the ‘p’ value is 0.0005 which is statistically significant and hence there occurs a significant association between serum creatinine and vitamin D deficiency.

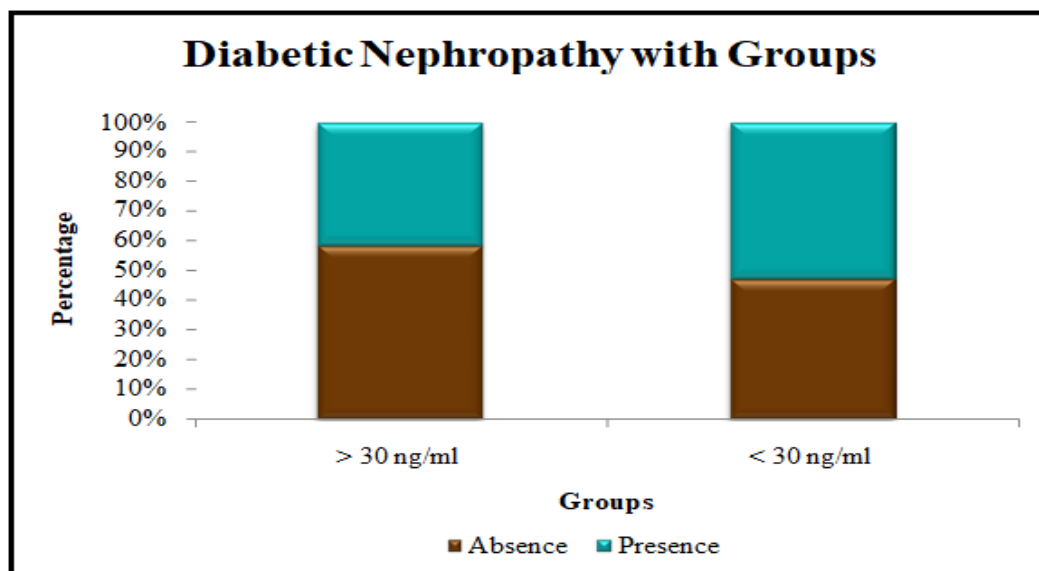


Fig 5 Comparison between Diabetic Nephropathy

Table 5 Comparison between Diabetic Nephropathy with Groups

			Groups		Total	χ ² – value	P- value
			> 30 ng/ml	< 30 ng/ml			
Diabetic Nephropathy	N	Count	42	63	105	2.401	0.121 #
		%	58.3%	47.0%			
	Y	Count	30	71	101		
		%	41.7%	53.0%			
Total	Count	72	134	206			
	%	100.0%	100.0%	100.0%			
# No Significant at P < 0.05 level							

Here 71 patients with vitamin D deficiency which constitutes about 53% found to have diabetic nephropathy and in vitamin D sufficient patients, 30 patients which constitutes about 41.7% found to have diabetic nephropathy with a ‘p’ value of 0.121 which is statistically insignificant.

IV. DISCUSSION

Our study included 206 patients which includes two groups, one group with 25(OH) D <30ng/ml of 72 patients and another group with 134 patients who had 25(OH)D>30ng/ml.

In groups with vitamin D deficiency the mean value of serum creatinine found to be 0.8 mg/dl and in patients with sufficient vitamin D mean serum creatinine was 0.72mg/dl and the ‘p’ value is 0.0005 which is statistically significant and hence there occurs a significant association between

serum creatinine and vitamin D deficiency. In our study , mean value of eGFR in vitamin D deficiency patients found to be 77.6 ml/min/1.73m² whereas the mean eGFR in vitamin D sufficient patients found to be 77.63ml/min/1.73m² with a ‘p’ value of 0.335 which is not statistically significant. In patients with vitamin D deficiency, mean value of 24 hours urinary protein was found to be 0.34g/day whereas in groups with sufficient vitamin D mean value found to be 0.28g/day with ‘p’ value of 0.188 and which is not statistically significant. Here 71 patients with vitamin D deficiency which constitutes about 53% found to have diabetic nephropathy and in vitamin D

sufficient patients, 30 patients which constitutes about 41.7% found to have diabetic nephropathy with a 'p' value of 0.121 which is statistically insignificant. Here 71 patients with vitamin D deficiency which constitutes about 53% found to have diabetic nephropathy and in vitamin D sufficient patients, 30 patients which constitutes about 41.7% found to have diabetic nephropathy with a 'p' value of 0.121 which is statistically insignificant and hence this study revealed that there is no significant association between vitamin D deficiency and Diabetic nephropathy.

Hypovitaminosis and albuminuria association could not be established with a Significant value in this study.

V. CONCLUSION

Vitamin D is found to have both direct action through vitamin D receptor activation and indirect action through regulation of calcium homeostasis and its effects on various pathogenesis and type2 diabetes which includes dysfunction of pancreatic beta cells, insulin action impairment and systematic information.

- Vitamin D is considered to be an important factor in modifying the risk of type2 diabetes mellitus and its microvascular complications.
- In type 2 Diabetes mellitus about 65% people found to have vitamin D deficiency according to our study.

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