

A Study to Assess the Relation between Serum Creatinine and Urine Microalbumin with Serum 25 Hydroxy Vitamin D in Type II Diabetes Mellitus

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Conflict of interest: Nil

Abstract:

Background: Diabetic Nephropathy is a common complication of Diabetes Mellitus that frequently progresses to ESRD and has a high mortality rate. When there is associated proteinuria, DN increases cardiovascular mortality by a factor of two to three. All of these structural and hemodynamic changes eventually lead to ESRD. Microalbuminuria is a precursor to Diabetic Nephropathy. Extracellular glucose acts directly on glomerular, tubular, interstitial, and vascular cells, resulting in the release of cytokines and growth factors such as angiotensin II, TGF- β , and monocyte chemo attractant protein (MCP)-1, all of which play an important role in the development of Diabetic Nephropathy.

Material & Methods: The current study on serum 25(OH) D in patients with Type 2 diabetes with and without nephropathy is a case-control study conducted at several hospitals in Indore. This work was carried out after receiving approval from the Institutional Ethical Committee.

The study group included a total of 200 known diabetics with a duration of more than 5 years, with the control group consisting of Type 2 DM patients (100 samples) without nephropathy and the case group consisting of patients with Diabetic Nephropathy (100 samples).

Design: Case control Design: A case-control study is a type of observational study that is commonly used to investigate factors linked to diseases or outcomes.

Conclusion: The study concluded that. Serum 25(OH) vitamin D levels are lower in patients with diabetic nephropathy (Vitamin D deficiency) and type 2 Diabetes Mellitus without nephropathy (Vitamin D insufficiency). The association between 25(OH)D and UACR is independent of age and gender. Vitamin D levels drop significantly when a diabetic patient progresses from Normoalbuminuria to Microalbuminuria. Significant vitamin D deficiency is associated with renal impairment in diabetic

Keywords: Serum Creatinine, Urine Microalbumin, Serum 25 Hydroxy Vitamin D, II Diabetes Mellitus.

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Introduction

A healthy life is a valuable gift that an individual can provide to others; if a person is well enough, he is the richest person in his own world. To most people, "healthy living" indicates that a person's physical and mental health are in harmony or that they work well together. Diabetes is the most common metabolic illness, affecting people in all parts of the world.

According to the World Health Organization's most recent 2016 data, 422 million persons worldwide are expected to have diabetes mellitus (WHO). Diabetes prevalence is steadily increasing; prior International Diabetes Federation estimates from 2013 estimated the population at 381 million diabetics. By 2030, the figure is expected to nearly double. Type 2 diabetes accounts for 85-90 percent of all cases. Sicree R, Shaw J, Zimmet P.(2018)

Diabetes Nephropathy (DN) is a long-term consequence of Diabetes Mellitus (DM). Microalbuminuria is the first clinical sign of diabetic nephropathy. End-Stage Renal Disease (ESRD), a terrible disease caused mostly by diabetic nephropathy, is the leading cause of diabetes morbidity and mortality.(D. de Zeeuw DR, Z. Zhang et al. 2006)

Renal failure accounts for 10–20% of diabetes-related deaths. Diabetic Nephropathy-related chronic kidney damage eventually leads to Renal Replacement Therapy.(G. Remuzzi AS, and P. Ruggenenti, 2002)

Kidney disease may progress as a result of Vitamin D deficiency vs insufficiency⁶. A vitamin D metabolite, namely ,25(OH)₂ vitamin D blocked by the RAS, has been demonstrated in vitro to

highlight its protective effect in DN. (Klaus G. 2008)

Epidemiology

According to the World Health Organization (WHO), approximately 250 million people worldwide have diabetes, with this figure expected to rise to 380 million by 2030.

Diabetes Nephropathy (DN) is a long-term complication of Diabetes Mellitus (DM). Microalbuminuria is the first clinical sign of diabetic nephropathy.

End-Stage Renal Disease (ESRD), a devastating disease caused primarily by diabetic nephropathy, is the leading cause of diabetes morbidity and mortality[2]. Renal failure accounts for 10–20% of diabetes-related deaths. Diabetic Nephropathy-related chronic kidney disease eventually leads to Renal Replacement Therapy.[3]

These modifications may be especially beneficial to people suffering from Diabetic Nephropathy.

When adequate vitamin D levels are maintained, there is an increase in insulin secretion by pancreatic cells, as well as a decrease in insulin resistance and arterial pressure. The potentially modifiable factor, arterial blood pressure for diabetic nephropathy, is said to decrease when insulin resistance decreases and insulin secretion increases, both of which are accomplished by adequate vitamin D levels¹⁰. The role of vitamin D levels in decreasing insulin resistance and thus the formation of overt hyperglycemia in our population needs to be investigated.

The purpose of this study is to compare serum 25-hydroxyvitamin D levels between Type 2 Diabetes Mellitus patients with and without nephropathy.

Material and Methods

The current study on serum 25(OH) D in patients with Type 2 diabetes with and without nephropathy is a case-control study conducted at several hospitals in Indore. This work was carried out after receiving approval from the Institutional Ethical Committee.

The study group included a total of 200 known diabetics with a duration of more than 5 years, with the control group consisting of Type 2 DM patients (100 samples) without nephropathy and the case group consisting of patients with Diabetic Nephropathy (100 samples).

Design case control study

Inclusion criteria

Glucose

➤ Fasting Plasma Glucose (FPG) \geq 126mg/dL(7.0mmol/L)(or)

➤ Hyperglycemia symptoms and Random Plasma glucose levels \geq 200mg/dL(11.1mmol/L)(or)

➤ 2hour Plasma glucose \geq 200mg/dL(11.1mmol/L)

B. Hemoglobin A1C (HbA1C) \geq 6.5%

Exclusion criteria:

- Liver failure patients,
- Vitamin D deficiency patients,
- Type 1 diabetes mellitus patients with and without nephropathy,
- Parathyroid disorders,
- Patients with diabetic nephropathy with other coexisting disease like obstructive uropathy, chronic glomerulonephritis
- Patients having malabsorption syndrome,
- Patients on drugs like barbiturates, phenytoin, Rifampicin, calcium, vitamin D
- Pregnant and lactating mothers.

Sample Collection

Blood was drawn after an overnight fast of 8-12 hours. Approximately 5ml of blood was drawn from the study subjects' ante-cubital veins and transferred into red-topped serum tubes, from which all study parameters were estimated.

Within 4 hours of blood collection, the blood samples were analysed. The following methodologies were used to analyse the biochemical parameters relevant to the study.

Urine Sample Collection

Urine samples were collected after giving proper instructions to the patient

- Early morning Mid-stream urine specimen was collected

Estimation Of Urine Albumin creatinine ratio (UACR)

Step1: Estimation of Albumin Concentration in Urine Sample

Latex Agglutination method / Immunoturbidimetry Kit from **Biosystems Reagents & Instruments**

Lot number: **COD31924(1 x 50mL)**

Reference interval

Urine Albumin = 3.9 to 24.4mg/day

Estimation of creatinine concentration in the urine sample

Method; Jaffe’s method

Reference interval

Urine creatinine: Adult Male = 14 to 26 mg/kg/day

Adult Female = 11 to 20 mg/kg/day

Urine Albumin Creatinine Ratios calculated by the following equation:

Urine Albumin (mg/L) UACR=

Urine Creatinine(g/L)

UACR=mg/g of Creatinine.

Normal UACR = <30 mg of albumin/gm of creatinine, Microalbuminuria=30-300 mg of albumin/gm of creatinine, Macroalbuminuria= >300 mg of al-

bumin/gm of creatinine.

Estimation of 25 hydroxyvitamin D by immunoassay

Methodology:

Quantitative competitive enzyme immunoassay Kit from LiLoDiagnostics

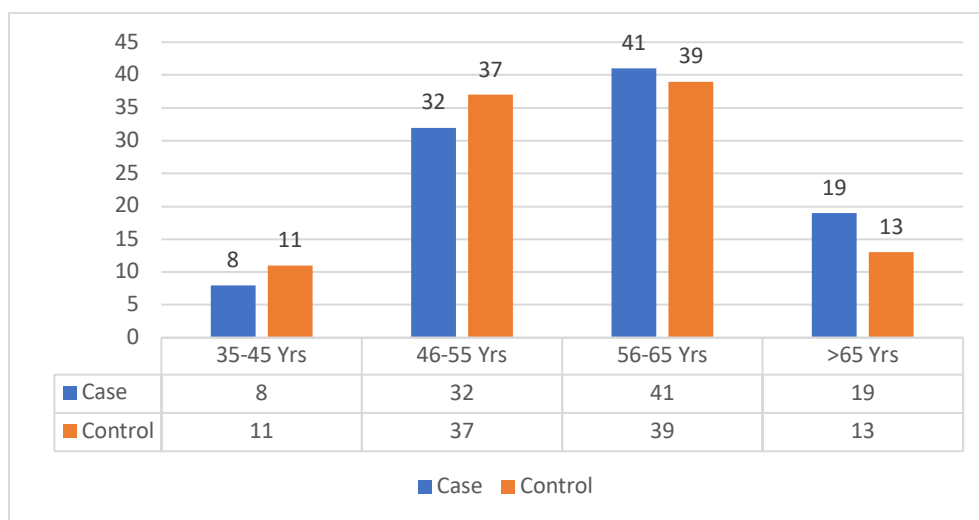
Results- The study and interpretation of data collected is discussed in this section from 200 diabetic patients (100 with nephropathy, 100 without nephropathy).

SECTION I: Demographic variables among participants.

Table 1: Participants by their age

Age	Variables	Case		Control	
		Case(f)	%	Control(f)	%
35-45 years		08	08	11	11
46-55 years		32	32	37	37
56-65 years		41	41	39	39
> 65 years		19	19	13	13
Total		100	100	100	100

Participants by their age

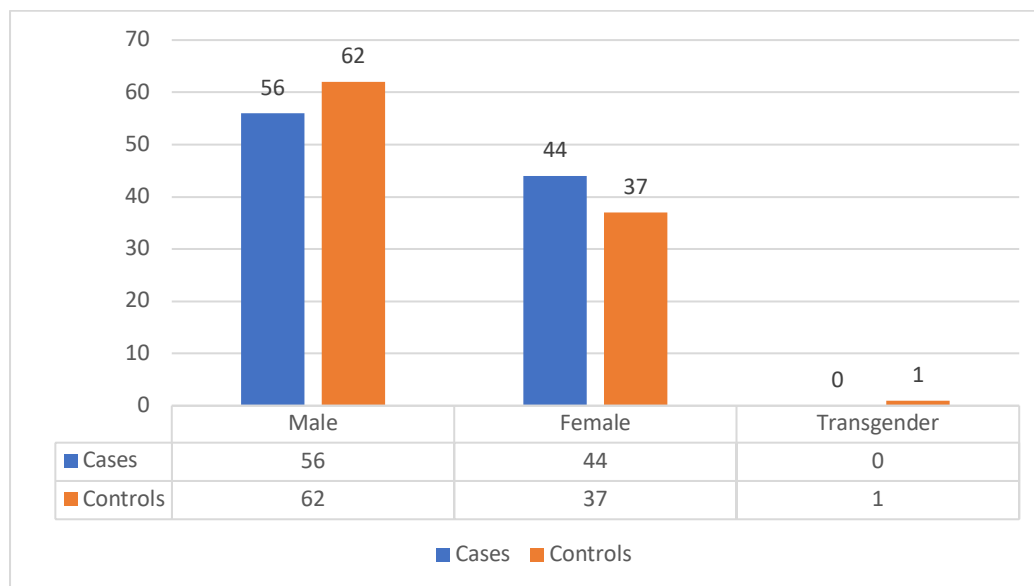


Interpretation

Table 1 and Figure-1 depicts that the age group of majority of the cases were 41% from 55 to 65 years and in controls 39% from 55 to 65 years, only 8% from 35 to 45 yrs. in cases and in controls it is 11%.

Table 2: Participants by Gender

Gender	Variables	Case		Control	
		Case(f)	%	Control(f)	%
	Male	56	56	62	62
	Female	44	44	37	37
	Transgender	00	00	01	01
	Total	100	100	100	100



Interpretation: Table 2 and Figure-2 depicts that the in cases and controls males constituted higher percentage than females. in control group, 1% of the samples were transgender.

Table 3: Participants by Educational status

Educational Status	Variables	Case(f)	%	Control(f)	%
		Primary	10	10	13
Secondary School	40	40	37	37	
UG Degree	30	30	22	22	
PG Degree	06	06	08	08	
Illiterate	04	04	10	10	
Total		100	100	100	100

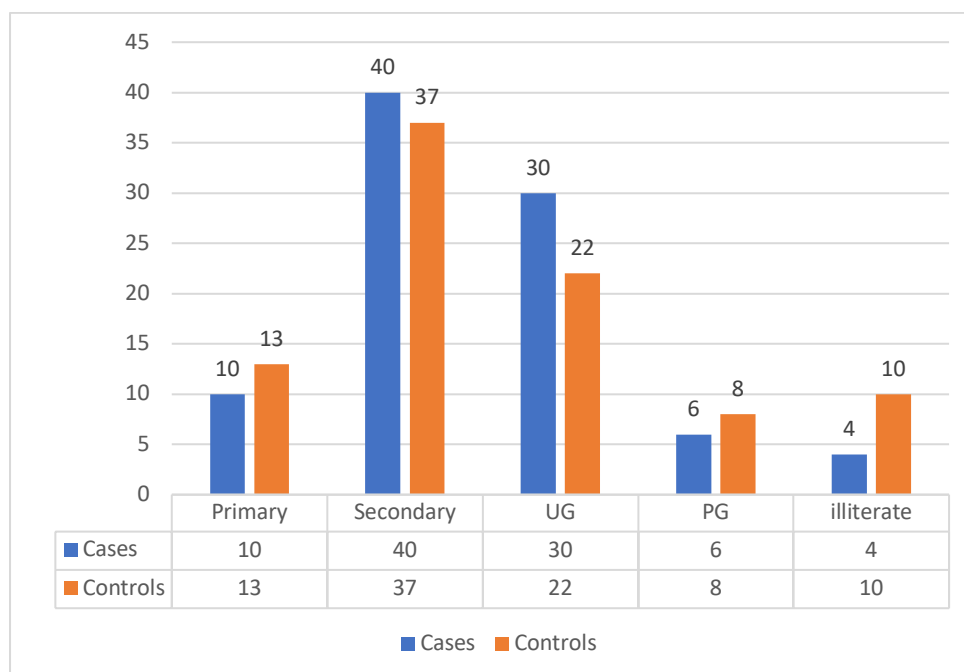


Figure 3: Participants by Educational status

Interpretation: Table -3 and Figure-3 depicts that, majority of the cases have secondary education 40% and in control group 37% with secondary education and only 4% were illiterate in cases and in controls were 10%.

Table 4: Participants by Employment status

Employment status	Variables				
		Case(f)	%	Control(f)	%
	Coolie	6	6	9	9
	Business	12	12	17	17
	Government employee	16	16	11	11
	Private employee	28	28	33	33
	Retired	38	38	30	30
	Total	100	100	100	100

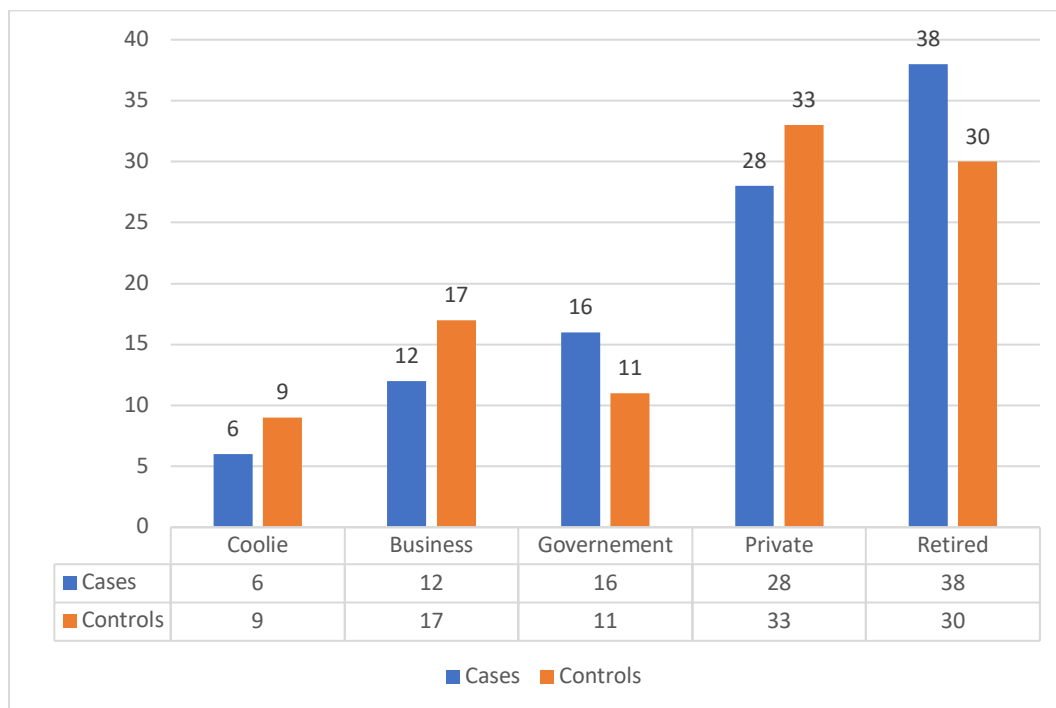


Figure-4 Participants by Employment status

Interpretation Table -4 and Figure-4 depicts that, majority of the cases were retired employees 38% and in control group 30% were retired employees and only 6% were coolies in cases and in controls were 9%.

Table-5 Participants by Monthly Income

Employment status	Variables				
		Case(f)	%	Control(f)	%
	>10000	12	12	14	14
	10001-20000	42	42	37	37
	20001-30000	24	24	29	29
	>30000	22	22	20	20
	Total	100	100	100	100

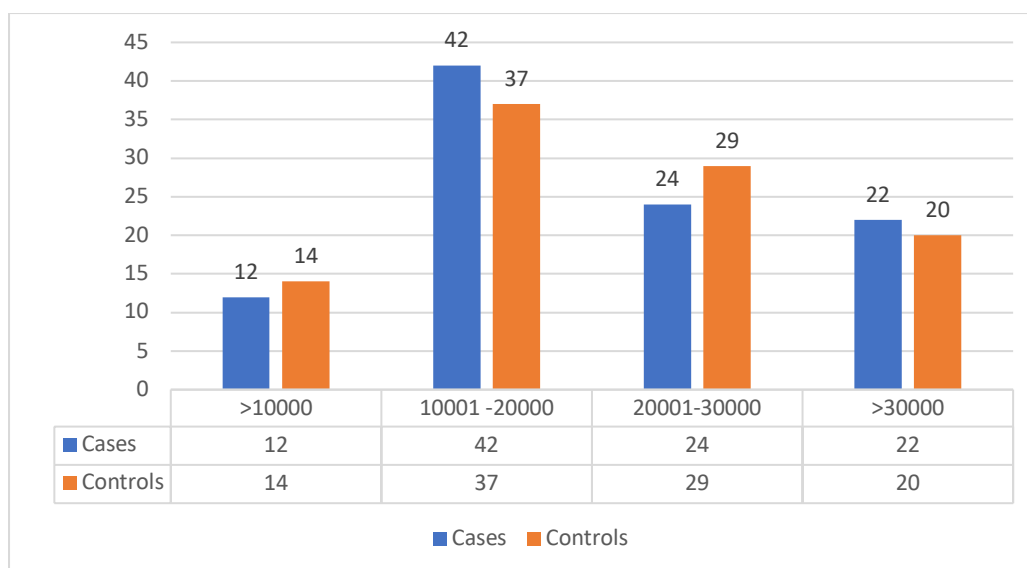


Figure 5: Participants by Monthly Income

Interpretation: Table -5 and Figure-5 depicts that, majority of the cases(42%) were earning between 10001 to 20000 and in control group 37% were earning between 10001 to 20000 and only 12% were earning less than 10000 in cases and in controls were 14%.

Section II: clinical variables of the participants.

Table 6: Clinical Variables Of The Participants

	Clinical Variables	Controls	Cases	P Value
1	Alcoholism	10(10%)	10(10%)	0.84-NS
2	Smoking	18(18%)	20(20%)	0.69-NS
3	BMI	28.11±1.73	28.91± 2.34	0.01- S
4	Hypertension	37(37%)	44(44.%)	0.64-NS
5	Fasting Glucose	128.44 ± 26.13	190.20±68.11	0.001-S
6	UACR	3.24± .73	123.76± 89.03	0.001-S
7	Calcium	9.88±.42	9.87±.44	0.67-NS
8	Phosphorus	4.01 ± .35	4.02±.38	0.58-NS
9	Creatinine	.61 ± .07	.69±.09	0.001-S
10	e GFR	123 ± 8.12	110.33 ± 5.04	0.001-S

Table 6 reveals that UACR, eGFR, fasting glucose, serum creatinine, serum calcium, and serum phosphorus are just a few of the many variables that can be compared between cases and controls in order to determine the mean, standard deviation, and p values.

UACR, eGFR, fasting glucose, and serum creatinine (p value<0.001) were all significantly different between cases and controls.

. There was a significant (p value 0.05) disparity in BMI between the cases and controls. Smoking, drinking, and alcohol consumption were not significantly different between cases and controls in terms of hypertension, serum calcium, and serum phosphorus.

Section III: assess the serum 25-hydroxy vitamin d levels in cases and controls.

Table 7: Compare the serum 25-hydroxy vitamin D levels among cases and controls. n-200

	Variables	Controls		Cases		Student's t test
		Mean	SD	Mean	SD	
1	Serum 25-Hydroxy Vitamin D	16.277	2.18	6.611	1.35	0.001-S t-6.98 df-199

The mean and standard deviation of the 25 Hydroxy vitamin D levels among DN patients and controls were presented in Table 7

The mean 25 Hydroxy vitamin D concentration in cases was 6.61± 1.35 ng/ml, while in controls it was 16.277±2.18ng/ml. The computed value of 6.98 indicates that the calculated t-value is greater

than the table value(2.83) at a significance level of 5%. Therefore, The difference in 25 Hydroxy vitamin D values between cases and controls were highly significant ($p < 0.001$).

Section- IV assess the correlation between serum 25-hydroxyvitamin d levels and selected clinical variables among case and controls.

Table 8: Assess the relationship between UACR and e GFR.

	Cases	Controls
correlation	0.022	0.25
pvalue	0.830	0.142
N	100	100

Table 8 depicts that Pearson correlation coefficient was used to calculate the relationship between UACR and eGFR. A Pearson coefficient correlation was performed on variables such as UACR and eGFR to determine the linear relationship in both groups. In both cases and controls, there was a weaker positive correlation between UACR and eGFR.

Table 9: Assess the relationship between e GFR and vitamin D.

	Cases	Controls
correlation	-0.13	0.12
pvalue	0.37	0.611
N	100	100

Table 9 depicts Pearson correlation coefficient was used to calculate the relationship between e GFR and vitamin D. A Pearson coefficient correlation was performed on variables such as e GFR and vitamin D to determine the linear relationship in

both groups. It was observed that, the concentration of eGFR increases, the concentration of vitamin D decreases In both cases and controls, hence there was a weaker negative correlation between e GFR and vitamin D.

Table 10: Assess the relationship between UACR and vitamin D.

	Cases	Controls
correlation	-0.113	0.061
pvalue	0.39	0.602
N	100	100

Table 10 depicts Pearson correlation coefficient was used to calculate the relationship between UACR and vitamin D. A Pearson coefficient correlation was performed on variables such as UACR and vitamin D to determine the linear relationship in both groups. In both cases and

controls, It was observed that in cases, the concentration of UACR increases, the concentration of vitamin D decreases, hence there was a weaker negative correlation between UACR and vitamin D

Table 11: Assess the relationship between vitamin D and serum creatinine.

	Cases	Controls
correlation	-0.021	-0.027
pvalue	0.722	0.798
N	100	100

Table 11 depicts Pearson correlation coefficient was used to calculate the relationship between vitamin D and serum creatinine. A Pearson coefficient correlation was performed on variables such as vitamin D and serum creatinine to determine the linear relationship in both groups. In

both cases and controls, It is observed that in cases, as the concentration of serum creatinine increased, the concentration of vitamin D was decreased, hence there was a weaker negative correlation between vitamin D and serum creatinine

Table 12: Assess the relationship between vitamin D and fasting glucose.

	Cases	Controls
correlation	-0.021	-0.027
pvalue	0.722	0.798
N	100	100

Table 12 depicts Pearson correlation coefficient was used to calculate the relationship between vitamin D and fasting glucose. A Pearson coefficient correlation was performed on variables such as vitamin D and fasting glucose to determine the linear relationship in both groups. In both cases

and controls. It was observed that in cases, as the concentration of fasting glucose increased, the concentration of vitamin D decreased, hence there was a weaker negative correlation between vitamin D and fasting glucose.

Table 13: Assess the relationship between vitamin D and fasting glucose.

	Cases	Controls
Correlation	-0.019	-0.027
P-value	0.722	0.798
N	100	100

Table 13 depicts Pearson correlation coefficient was used to calculate the relationship between vitamin D and fasting glucose. A Pearson coefficient correlation was performed on variables such as vitamin D and fasting glucose to determine the linear relationship in both groups. In both cases

and controls. It was observed that in cases, as the concentration of fasting glucose increased, the concentration of vitamin D decreased, hence there was a weaker negative correlation between vitamin D and fasting glucose.

Table 14: Assess the relationship between serum 25 hydroxy vitamin D and calcium.

	Cases	Controls
Correlation	-0.191	-0.249
P-value	0.126	0.129
N	100	100

Table 14 depicts Pearson correlation coefficient was used to calculate the relationship between serum 25 hydroxy vitamin D and calcium. A Pearson coefficient correlation was performed on variables such as serum 25 hydroxy vitamin D and calcium to determine the linear relationship in both

groups. It was observed that as the concentration of serum calcium increases, the concentration of serum vitamin D decreases, hence there was a weaker negative correlation between serum 25 hydroxy vitamin D and calcium.

Table 15: Assess the relationship between serum 25 hydroxy vitamin D and phosphorus.

	Cases	Controls
Correlation	0.039	-0.054
P-value	0.682	0.571
N	100	100

Table 15 depicts Pearson correlation coefficient was used to calculate the relationship between serum 25 hydroxy vitamin D and phosphorus. A Pearson coefficient correlation was performed on variables such as serum 25 hydroxy vitamin D and phosphorus to determine the linear relationship in both groups. It was observed that as the concentration of serum calcium increases, the concentration of serum vitamin D decreases, hence

there was a weaker positive correlation between serum 25 hydroxy vitamin D and phosphorus in cases and also there was a weaker negative correlation between serum 25 hydroxy vitamin D and phosphorus in controls.

Section V-compare the serum 25-hydroxy vitamin d levels with selected clinical variables among cases and controls.

Table 16: Compare Fasting Glucose and the serum 25-hydroxy vitamin D levels in cases. n-100

Group		Mean	SD	Paired t-test
Cases	Serum 25 Hydroxy vitamin D	5.39	1.12	df-99
Cases	Fasting Glucose	190.20	68.11	t=11.09 S P<0.001

p<0.001, S- Significant

Table 16 depicts the compare the mean between Fasting Glucose and vitamin D in diabetic nephropathy, The computed value of 11.09

indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, and there was an inverse relationship

between Fasting Glucose and vitamin D in case groups in Type 2 Diabetes Mellitus.

Discussion

This Article discusses the findings of a data analysis to Assess the Relation Between Serum Creatinine and Urine Microalbumin with Serum 25 Hydroxy Vitamin D in Non-Insulin Dependent Diabetes Mellitus With Nephropathy Patients. The discussion is based on the study's objectives and the hypothesis stated in the study.

Objectives

1. To determine serum 25-hydroxy vitamin D levels in patients with Type 2 Diabetes Mellitus with and without Diabetic Nephropathy.
2. To assess how serum 25-hydroxyvitamin D levels correlated with urine microalbumin and serum creatinine levels in diabetic nephropathy patients.
3. To compare the role of vitamin D sufficiency versus deficiency in the progression of diabetic nephropathy.

Diabetic Nephropathy is a common complication of Diabetes Mellitus that frequently progresses to ESRD and has a high mortality rate. When there is associated proteinuria, DN increases cardiovascular mortality by a factor of two to three.

The glomerular and tubular basement membranes thicken in the early stages of DN, followed by hyperfiltration, albuminuria, glomerulosclerosis, and tubular-interstitial fibrosis. All of these structural and hemodynamic changes eventually lead to ESRD. Microalbuminuria is a precursor to Diabetic Nephropathy.

Extracellular glucose acts directly on glomerular, tubular, interstitial, and vascular cells, resulting in the release of cytokines and growth factors such as angiotensin II, TGF- β , and monocyte chemo attractant protein (MCP)-1, all of which play an important role in the development of Diabetic Nephropathy.

RAS has been shown to be important in the progression of renal injury in DN.

Clinical studies have shown that treatment with ACE inhibitors or Angiotensin II type 1 receptor blockers can slow the progression of glomerulosclerosis, tubulointerstitial fibrosis, and proteinuria.

The hormonal form of vitamin D, 1,25(OH) $_2$ D, has numerous physiological functions. Adequate levels of 1,25(OH) $_2$ D are required for bone metabolism 140, and there is evidence that it has anti-proliferative effects in cellular differentiation, immune modulation, and RAS inhibition.

Renin biosynthesis is inhibited by 1,25(OH) $_2$ D. Null- mutant mice lacking the vitamin D receptor (VDR) gene develop hyperreninemia in studies. Renin elevation causes increased blood pressure and cardiac hypertrophy¹³⁹. In this study, we found that 1,25(OH) $_2$ D acts as a negative regulator of the RAS.

The goal of this article was to identify the scientific evidence on the role of 25(OH) D in patients with DN and Type 2 DM without nephropathy.

We recruited 200 subjects for this study and divided them into two groups. Cases (100) are DN patients, while controls (100) are type 2 DM patients without nephropathy.

Patients with liver failure, vitamin D deficiency, type 1 diabetes mellitus, malabsorption syndrome, other co-existing renal disease such as chronic glomerulonephritis, obstructive uropathy, pregnant and lactating mothers, and patients on drugs such as barbiturates, phenytoin, and rifampicin were excluded.

Demographic Variables

Results revealed that regarding age group of majority of the cases were 41% from 55 to 65 years and in controls 39% from 55 to 65 years, only 8% from 35 to 45 yrs. in cases and in controls it is 11%. Cases and controls males constituted higher percentage than females. In control group, 1% of the samples were transgender majority of the cases have secondary education 40% and in control group 37% with secondary education and only 4% were illiterate in cases and in controls were 10%. Regarding education majority of the cases were retired employees 38% and in control group 30% were retired employees and only 6% were coolies in cases and in controls were 9%. In the case of income majority of the cases (42%) were earning between 10001 to 20000 and in control group 37% were earning between 10001 to 20000 and only 12% were earning less than 10000 in cases and in controls were 14%.

Clinical Variables

Study reveals that UACR, eGFR, fasting glucose, serum creatinine, serum calcium, and serum phosphorus are just a few of the many variables that can be compared between cases and controls in order to determine the mean, standard deviation, and p values.

UACR, eGFR, fasting glucose, and serum creatinine (p value <0.001) were all significantly different between cases and controls. There was a significant (p value 0.05) disparity in BMI between the cases and controls. Smoking, drinking, and alcohol consumption were not significantly different between cases and controls in terms of

hypertension, serum calcium, and serum phosphorus.

The above result was supported by Hajeong Lee., et.al(2012) Serum phosphorus levels above the normal range have been linked to cardiovascular (CV) morbidity. Low-grade albuminuria (LGA) has been linked to an increase in CV events in several studies. The current study sought to look into the relationship between serum phosphorus levels and LGA in the general population. We examined the people who had been subjected to health inspections. We looked at the relationship between serum phosphorus and LGA in 8953 people (mean age 47.4 years) with eGFRs of 60 mL/min/1.73m² and urinary albumin-to-creatinine ratios (UACRs) of 30 mg/g. Participants who had a colonoscopy were not eligible. The uppermost quartile group of serum phosphorus concentrations had a significantly higher mean UACR than the other quartile groups. Serum phosphorus remained an independent predictor of increased UACR in the multivariate regression analysis (B = 0.610, P 0.001). Subgroup analyses revealed that this association held true regardless of age, gender, presence of hypertension or diabetes, body mass index, or eGFR. Higher serum phosphorus was independently related to LGA in individuals without evidence of renal dysfunction in our population-based study. More research is needed to determine the precise mechanism of the association between serum phosphorus and LGA.

Assess The Serum 25-Hydroxy Vitamin D Levels In Cases And Controls.

Result revealed that the mean 25 Hydroxy vitamin D concentration in cases was 6.61 ± 1.35 ng/ml, while in controls it was 16.277 ± 2.18 ng/ml. The computed value of 6.98 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, The difference in 25 Hydroxy vitamin D values between cases and controls were highly significant ($p < 0.001$).

This study suggested that vitamin D levels may play a significant role in DN, and adequate levels of vitamin D must be maintained to slow the progression of Diabetic Nephropathy.

The above result was supported by Toossi, et. al.(2015) To investigate the serum levels of 25-hydroxy vitamin D3 [25(OH)D] in acne vulgaris patients and their relationship to clinical features. This cross-sectional study took months to complete. This study included 39 acne vulgaris patients and 40 healthy controls. Subjects were included if they had not used alcohol, vitamin D supplements, oral steroids, PUVA and/or NBUVB in the previous three months. The levels of 25(OH)D in the blood were determined. Baseline demographics, family history, and comorbidities such as PCO were all documented. SPSS 16.0.0

was used for statistical analysis. The median level of 25(OH)D in patients was 8.4 ng/mL (range: 1.4–99) and 10.4 ng/mL (range: 3.1–56.7) in controls, with no statistically significant difference. PCOS was a significant predictor of acne vulgaris occurrence (OR=6.25; 95 percent CI: 1.52–25.66; $p=0.01$). There were no significant associations between disease severity and serum 25(OH)D levels ($r_s=0.12$, $p=0.45$), age ($r_s=0.28$, $p=0.09$), BMI ($r_s=0.12$, $p=0.46$), age at disease onset ($r_s=0.08$, $p=0.63$), or disease duration ($r_s=0.10$, $p=0.54$). Based on previous research, it is highly likely that vitamin D will be a significant factor in acne patients, and more studies with a larger sample size may be beneficial in obtaining positive results.

Assess the correlation between serum 25-hydroxyvitamin d levels and selected clinical variables among case and controls.

Results shows that a Pearson coefficient correlation was performed on variables such as UACR and eGFR to determine the linear relationship in both groups. In both cases and controls, there was a weaker positive correlation between UACR and eGFR.

A Pearson coefficient correlation was performed on variables such as e GFR and vitamin D to determine the linear relationship in both groups. It was observed that, the concentration of eGFR increases, the concentration of vitamin D decreases In both cases and controls, hence there was a weaker negative correlation between e GFR and vitamin D

A Pearson coefficient correlation was performed on variables such as UACR and vitamin D to determine the linear relationship in both groups. In both cases and controls, It was observed that in cases, the concentration of UACR increases, the concentration of vitamin D decreases, hence there was a weaker negative correlation between UACR and vitamin D

A Pearson coefficient correlation was performed on variables such as vitamin D and serum creatinine to determine the linear relationship in both groups. In both cases and controls, It is observed that in cases, as the concentration of serum creatinine increased, the concentration of vitamin D was decreased, hence there was a weaker negative correlation between vitamin D and serum creatinine.

A Pearson coefficient correlation was performed on variables such as vitamin D and fasting glucose to determine the linear relationship in both groups. In both cases and controls. It was observed that in cases, as the concentration of fasting glucose increased, the concentration of vitamin D decreased, hence there was a weaker negative correlation between vitamin D and fasting glucose.

A Pearson coefficient correlation was performed on variables such as vitamin D and fasting glucose to determine the linear relationship in both groups. In both cases and controls. It was observed that in cases, as the concentration of fasting glucose increased, the concentration of vitamin D decreased, hence there was a weaker negative correlation between vitamin D and fasting glucose

A Pearson coefficient correlation was performed on variables such as serum 25 hydroxy vitamin D and calcium to determine the linear relationship in both groups. It was observed that as the concentration of serum calcium increases, the concentration of serum vitamin D decreases, hence there was a weaker negative correlation between serum 25 hydroxy vitamin D and calcium

A Pearson coefficient correlation was performed on variables such as serum 25 hydroxy vitamin D and phosphorus to determine the linear relationship in both groups. It was observed that as the concentration of serum calcium increases, the concentration of serum vitamin D decreases, hence there was a weaker positive correlation between serum 25 hydroxy vitamin D and phosphorus in cases and also there was a weaker negative correlation between serum 25 hydroxy vitamin D and phosphorus in controls .

Studies demonstrating a benefit in vitamin D supplementation to prevent the progression of renal disease suggested that this may be a strategy to consider in future studies.

The study results supported by Alkhatatbeh, M. J., & Abdul-Razzak, K. K. (2018). The purpose of this study was to look into the relationship between serum 25-hydroxyvitamin D concentration and glycemic control measures like haemoglobin A1c (HbA1c) and fasting blood glucose (FBG) in adult patients with diabetes mellitus (DM) from Jordan's north. Another goal was to compare serum levels of 25-hydroxyvitamin D between patients with well-controlled diabetes and patients with uncontrolled diabetes. This was a cross-sectional study with 261 diabetic participants. The concentration of 25-hydroxyvitamin D was determined by electrochemiluminescence immunoassay, HbA1c by turbidimetric inhibition immunoassay, and FBG by the hexokinase method. Other clinical variables' data were obtained from medical records or through self-reporting. Participants with good glycemic control had significantly higher levels of 25-hydroxyvitamin D than those with uncontrolled diabetes ($P=0.03$). Participants with adequate vitamin D status (>30 ng/ml in serum) had significantly lower HbA1c levels than participants with deficient vitamin D status (20 ng/ml) ($P=0.02$). Significant inverse correlations were found between 25-hydroxyvitamin D levels and HbA1c and FBG levels ($r=0.23$ and 0.17 ,

respectively, both $P0.01$). There were also significant correlations between the duration of diabetes and the levels of HbA1c and FBG (both $r=0.21$, $P0.01$). HbA1c levels were also found to be inversely related to participants' age ($r=0.19$, $P0.01$). Further multiple linear regression analysis revealed an inverse significant relationship between HbA1c and 25-hydroxyvitamin D levels ($F=12.95$, $R^2=0.48$, $P0.01$) but no such relationship between FBG and 25-hydroxyvitamin D levels. These findings may prompt additional research to determine whether vitamin D supplementation improves glycemic control and how vitamin D affects glucose homeostasis in patients with diabetes.

Compare the serum 25-hydroxy vitamin d levels with selected clinical variables among cases and controls.

Compare the mean between Fasting Glucose and vitamin D in diabetic nephropathy, The computed value of 11.09 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between Fasting Glucose and vitamin D in case groups in Type 2 Diabetes Mellitus.

Compare the mean between Fasting Glucose and vitamin D in diabetic nephropathy. The computed value of 7.53 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%.Thereforeand there was an inverse relationship between Fasting Glucose and vitamin D in control groups in Type 2 Diabetes Mellitus.

Compare the mean between BMI and vitamin D in diabetic nephropathy. The computed value of 4.27 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%.Thereforeand there was an inverse relationship between BMI and vitamin D in case groups in Type 2 Diabetes Mellitus.

Compare the mean between BMI and vitamin D in diabetic nephropathy. The computed value of 3.88 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between BMI and vitamin D in control groups in Type 2 Diabetes Mellitus.

Compare the mean between UACR and vitamin D in diabetic nephropathy. The computed value of 8.03 indicates that the calculated t-value is greater than the table value (2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between UACR and vitamin D in case groups in Type 2 Diabetes Mellitus.

Compare the mean between and vitamin D in diabetic nephropathy. The computed value of 5.09 indicates that the calculated t-value is greater than

the table value (2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between UACR and vitamin D in control groups in Type 2 Diabetes Mellitus.

Compare the mean between UACR and vitamin D in diabetic nephropathy. The computed value of 8.03 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between UACR and vitamin D in case groups in Type 2 Diabetes Mellitus.

Compare the mean between UACR and vitamin D in diabetic nephropathy. The computed value of 5.09 indicates that the calculated t-value is greater than the table value(2.83) at a significance level of 5%. Therefore, and there was an inverse relationship between UACR and vitamin D in control groups in Type 2 Diabetes Mellitus.

Compare the mean between Phosphorus and vitamin D in diabetic nephropathy. The computed value of 1.20 indicates that the calculated t-value is less than the table value(2.83) at a significance level of 5%. Therefore, and there was no relationship between Phosphorus and vitamin D in case groups in Type 2 Diabetes Mellitus.

Compare the mean between Phosphorus and vitamin D in diabetic nephropathy. The computed value of 1.32 indicates that the calculated t-value is less than the table value(2.83) at a significance level of 5%. Therefore, and there was no relationship between Phosphorus and vitamin D in control groups in Type 2 Diabetes Mellitus.

The above results were supported by Al-Timimi, D. J., & Ali, A. F. (2013). Serum 25(OH) D levels were measured in 337 Kurd patients with type 2 diabetes and 146 patients without type 2 diabetes. Its relationship with the glycemic control marker (HbA1c), as well as anthropometric parameters (age, gender, and BMI), diabetes duration, and serum blood glucose, was investigated. The mean SD values for serum 25hydroxy (OH) D levels in diabetic patients were 25.6 12.6 ng/ml and 34.1 14.7 ng/ml in controls (p0.01). Diabetic patients had a significantly higher prevalence of vitamin D deficiency than controls (53.7 percent vs. 29.4 percent, p0.001). This finding held true even after serum 25 (OH) D levels were adjusted to reflect severe vitamin D deficiency (4.4 percent vs. 0.68 percent). Patients with poor glycemic control had a 90 percent higher prevalence of low vitamin D status than those with adequate vitamin D levels (76 percent). When compared to diabetics with good and fair glycemic control, diabetics with poor glycemic control had lower 25(OH)D levels (p0.01) and a higher prevalence of low vitamin D status (89 percent vs. 4% and 7%, respectively). Patients with diabetes for more than 5 years had a higher prevalence of low vitamin D status than the

vitamin D sufficient group (51 percent vs. 40 percent). In diabetic patients, there was a statistically significant negative correlation between serum 25 (OH) D levels and HbA1c percent ($r=0.238$, $p0.01$). Two-thirds of diabetics with type 2 have low vitamin D levels, particularly those with poor glycemic control and those with longer diabetes durations. This could be attributed to the additive effect of glycemic control on vitamin D status.

Conclusion

The study concluded that• Serum 25(OH) vitamin D levels are lower in patients with diabetic nephropathy (Vitamin D deficiency) and type 2 Diabetes Mellitus without nephropathy (Vitamin D insufficiency). The association between 25(OH)D and UACR is independent of age and gender. Vitamin D levels drop significantly when a diabetic patient progresses from Normoalbuminuria to Microalbuminuria. Significant vitamin D deficiency is associated with renal impairment in diabetic

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