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Original Communication

Seasonal Variation in Vitamin D Levels and Association With Albuminuria in Patients With Diabetic Nephropathy: A Retrospective Cross-Sectional Study

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Abstract

Background: Diabetic nephropathy (DN) is a major cause of chronic kidney disease and remains a substantial contributor to morbidity worldwide. This study aimed to assess seasonal variation in serum 25-hydroxyvitamin D (25(OH)D) concentrations among patients attending the clinic and to examine associations between these concentrations and albuminuria, as well as other metabolic and biochemical parameters, in patients with DN. **Methods:** This retrospective cross-sectional study included 298 patients with DN admitted to a tertiary university hospital between 2017 and 2023. Patients were divided into four groups based on the season in which their blood samples were collected. Serum 25(OH)D levels, albuminuria, lipid profiles, and glycemic markers were measured. Differences in clinical parameters across seasons among clinic attendees and their associations with serum 25(OH)D levels were assessed using group comparisons, correlation analysis, and multiple linear regression. **Results:** The mean serum 25(OH)D concentration was 16.1 ± 8.2 ng/mL and varied significantly across seasons ($p < 0.001$). Vitamin D concentrations were lowest in winter and spring and highest in summer and autumn. Albuminuria levels differed significantly across the four seasonal groups ($p = 0.016$); however, none of the pairwise comparisons remained significant after Bonferroni correction. In multivariable regression analysis, albuminuria was independently and inversely associated with serum Vitamin D levels ($p < 0.001$). **Conclusions:** Serum 25(OH)D concentrations varied by the season of sample collection, and lower concentrations were cross-sectionally associated with higher urine albumin-to-creatinine ratio (UACR). Prospective longitudinal and interventional studies are needed to establish temporality and determine whether Vitamin D supplementation affects renal outcomes.

Keywords: diabetic nephropathy; Vitamin D; albuminuria; seasonal differences

1. Introduction

Diabetes mellitus is one of the most significant public health challenges worldwide due to its increasing prevalence and the wide range of systemic complications associated with the disease. Diabetic nephropathy (DN), a major microvascular complication of diabetes, is one of the leading causes of chronic kidney disease (CKD) and is strongly associated with increased cardiovascular morbidity and mortality [1]. According to a recent global epidemiological study published in 2025, approximately 107.6 million people worldwide were living with DN in 2021, corresponding to an age-standardized prevalence rate of 1259.6 per 100,000 population [2]. In patients with DN, albuminuria is the primary indicator of renal function decline and is considered an independent risk factor for disease progression [1].

Reducing albuminuria is an important therapeutic goal in clinical management, as reductions in albuminuria are associated with slower progression of kidney disease [3]. Although renin–angiotensin–aldosterone system (RAAS) blockers are recommended as standard therapy for patients with diabetes, hypertension, and albuminuria, target albuminuria levels are not always achieved, and substantial residual kidney risk persists [4]. This necessitates the investigation of additional mechanisms involved in the pathogenesis.

In recent years, interest has grown regarding the pleiotropic effects of Vitamin D beyond its classic role in calcium-bone metabolism. Experimental and clinical studies have suggested that Vitamin D inhibits RAAS at the receptor level and that 1,25-dihydroxyvitamin D exerts an antiproteinuric effect by suppressing renin gene transcription [5,6]. However, since Vitamin D synthesis is largely dependent on ultraviolet (UV) exposure, serum levels vary according to geographical and seasonal factors. Indeed, a large-scale analysis covering 46 countries reported significant seasonal fluctuations in Vitamin D levels depending on the duration of sunlight exposure [7].

Although seasonal variation in Vitamin D levels and the association between Vitamin D deficiency and renal dysfunction have been well documented, evidence regarding whether seasonal fluctuations in Vitamin D levels trans-

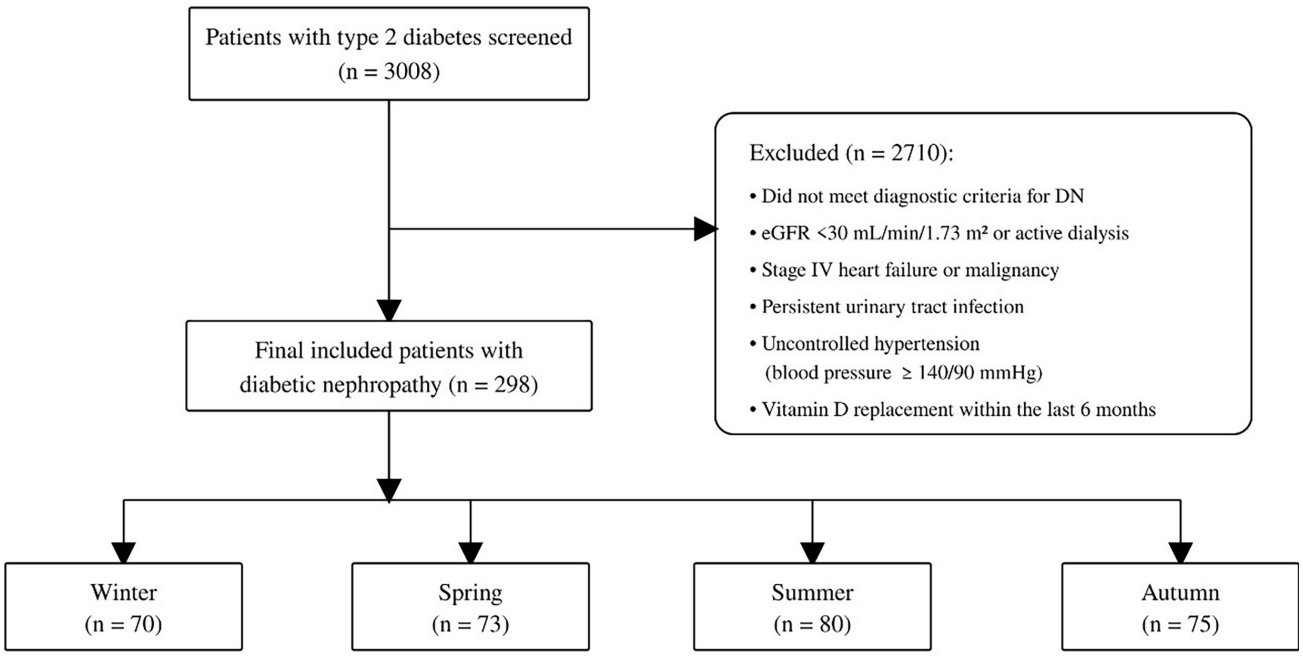

Fig. 1. Flowchart of patient selection and seasonal grouping. DN, diabetic nephropathy; eGFR, estimated glomerular filtration rate.

late into clinically meaningful changes in renal parameters, particularly albuminuria, in patients with DN remains limited. Therefore, this study aimed to compare Vitamin D levels between patients with DN attending the clinic in different seasons and to evaluate the associations of these between-group differences with metabolic and renal parameters, particularly albuminuria.

2. Materials and Methods

2.1 Study Population

Electronic health records of patients attending the outpatient clinics of Süleyman Demirel University Research and Application Hospital between January 1, 2017, and December 31, 2023, were retrospectively reviewed. Among 3008 screened records, 298 adult patients (≥19 years) diagnosed with type 2 diabetes mellitus according to the American Diabetes Association (ADA) criteria [8] and who fulfilled the predefined diagnostic criteria for DN were included in the study. DN was defined as a spot urine albumin-to-creatinine ratio (UACR) of ≥30 mg/g confirmed on repeated measurements obtained at least three months apart or by the presence of diabetic retinopathy. To avoid duplicate observations, only data from each patient's first eligible visit after the diagnosis of DN were analyzed.

2.2 Exclusion Criteria

Conditions that could affect Vitamin D metabolism or renal parameters were determined as exclusion criteria. Accordingly, patients with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73m^2 (Stage 4–5 CKD), stage IV heart failure, receiving active dialysis treatment, having a known malignancy, persistent urinary tract infection, uncontrolled hypertension (blood pressure ≥140/90 mmHg), or those determined to have received Vitamin D replacement therapy within the last 6 months were excluded from the study. The patient selection process and seasonal grouping are presented in the flowchart (Fig. 1).

2.3 Data Collection and Seasonal Grouping

Demographic data (age, gender), duration of diabetes, and laboratory parameters, glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), serum creatinine, blood urea nitrogen (BUN), uric acid, calcium, phosphorus, albumin, total protein, lipid profile, thyroid-stimulating hormone (TSH), parathyroid hormone (PTH), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and 25-hydroxyvitamin D (25(OH)D) were recorded from the hospital information management system.

Routine biochemical parameters, including FPG, serum creatinine, BUN, uric acid, calcium, phosphorus, albumin, total protein, AST, ALT, and lipid profile, were analyzed using the Beckman Coulter AU5800 Clinical Chemistry Analyzer (Beckman Coulter Inc., Brea, CA, USA). HbA1c levels were measured using the Tosoh HLC-723G8 Automated Glycohemoglobin Analyzer (Tosoh Corporation, Tokyo, Japan). Serum 25(OH)D, TSH, and PTH levels were measured using the Siemens Atellica Immunoassay Analyzer (Siemens Healthineers, Erlangen, Germany).

Participants were categorized according to the season in which their blood samples were collected, based on the conventional Northern Hemisphere calendar: spring (March 21–June 20), summer (June 21–September 22), autumn (September 23–December 21), and winter (December 22–March 20). Each patient was included only once, based

on the first eligible visit after the diagnosis of DN. Therefore, the four seasonal groups comprised different patients and did not represent repeated measurements of the same individuals across seasons. Serum 25(OH)D concentrations were further categorized as deficiency (<12 ng/mL), insufficiency (≥12 to <20 ng/mL), and sufficiency (≥20 ng/mL).

2.4 Statistical Analysis

Statistical analyses were performed using the SPSS 22.0 (IBM Corp., Armonk, NY, USA) software package. The normality of all continuous variables was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests, together with histogram inspection, quantile–quantile (Q–Q) plots, and skewness and kurtosis values. Normality was evaluated separately within each study group (seasonal groups and Vitamin D groups) before selecting the appropriate statistical tests. Continuous variables with normal distribution were presented as mean ± standard deviation (SD), while those without normal distribution were presented as median and interquartile range (IQR: 25th–75th percentile).

Missing data occurred because some laboratory parameters were not measured or recorded during routine clinical evaluation. Data were available for 140 patients for PTH, 284 for LDL cholesterol, and 297 for calcium, phosphorus, FPG, uric acid, total cholesterol, HDL cholesterol, triglycerides, and TSH; complete data were available for the remaining variables. Missing data were not imputed. Available-case analysis was used for group comparisons, whereas complete-case analysis was used for multiple linear regression analysis. PTH was not included in the multivariable regression model because of the high proportion of missing data.

For comparisons between groups, the independent-samples *t*-test or Mann-Whitney U test was used for two groups. For the comparison of three or more groups (seasons and Vitamin D groups), one-way analysis of variance (ANOVA; post hoc: Tukey's honestly significant difference (HSD) test) was used for parametric data, and the Kruskal-Wallis test followed by pairwise Mann-Whitney U tests with Bonferroni correction was used for non-parametric data. Relationships between variables were analyzed using Pearson or Spearman correlation analyses. Multiple linear regression analysis was performed to identify the independent factors associated with serum Vitamin D levels. Variables found to be significant in the univariate analyses were entered into the multivariable model. Season was included in the model as three dummy variables (spring, summer, and autumn), with winter serving as the reference category. A *p*-value of <0.05 was considered statistically significant in all analyses.

3. Results

3.1 Demographic and Clinical Characteristics

A total of 298 patients with DN were included in the study. Of the patients, 51.7% (n = 154) were male, and the mean age was 59.8 ± 13.1 years. The mean HbA1c level of the total population was 9.0 ± 2.5%, and the mean serum Vitamin D level was determined to be 16.1 ± 8.2 ng/mL.

3.2 Comparison of Patients Attending in Different Seasons

In the seasonal analysis, a statistically significant difference was detected between serum Vitamin D levels ($p < 0.001$). The lowest Vitamin D levels were observed in winter (13.1 ng/mL) and spring (14.8 ng/mL), whereas the highest levels were detected in summer (18.9 ng/mL) and autumn (17.4 ng/mL). Mean levels in all seasonal groups were below the sufficiency threshold (<20 ng/mL).

Albuminuria levels differed significantly across the four seasonal groups ($p = 0.016$); however, none of the pairwise comparisons remained significant after Bonferroni correction. Correlation analysis demonstrated a moderate negative correlation between serum Vitamin D and albuminuria (Spearman's rho = –0.430, $p < 0.001$). Furthermore, significant differences between the seasonal patient groups were observed in diabetes duration, body mass index (BMI), calcium, HbA1c, FPG, and PTH levels (Table 1).

3.3 Clinical Presentation According to Vitamin D Levels

Vitamin D deficiency (<12 ng/mL) was detected in 31.2% (n = 93) of the patients, insufficiency (≥12 to <20 ng/mL) in 42.6% (n = 127), and sufficiency (≥20 ng/mL) in 26.2% (n = 78).

Bonferroni-adjusted pairwise comparisons showed that albuminuria was significantly higher in the Vitamin D deficiency group (<12 ng/mL) than in both the insufficiency (≥12 to <20 ng/mL; adjusted $p < 0.001$) and sufficiency groups (≥20 ng/mL; adjusted $p < 0.001$), whereas no significant difference was observed between the insufficiency and sufficiency groups (adjusted $p = 1.000$). Additionally, in this group, the duration of diabetes was longer, and calcium, albumin, and eGFR levels were significantly lower (Table 2). In the gender-based evaluation, albuminuria levels were significantly higher in males compared to females ($p = 0.007$) (Fig. 2).

3.4 Correlation and Regression Analysis

Correlation analysis revealed a significant negative relationship between serum Vitamin D levels and albuminuria (rho = –0.430, $p < 0.001$), HbA1c (r = –0.142, $p = 0.014$), and PTH (rho = –0.206, $p = 0.014$) (Table 3, Fig. 3).

Multiple linear regression analysis was performed using complete data from 296 patients to identify independent factors associated with serum Vitamin D levels, and the model was statistically significant (F = 6.881, $p < 0.001$). The model explained 20.6% of the variance in Vitamin D

Table 1. Comparison of clinical and biochemical characteristics of patients by seasons.

Parameter	Winter		Spring		Summer		Autumn		*p*-value
	Number	Mean ± standard deviation - median (interquartile range)	Number	Mean ± standard deviation - median (interquartile range)	Number	Mean ± standard deviation - median (interquartile range)	Number	Mean ± standard deviation - median (interquartile range)	
Duration of diabetes (years)	70	9.0 (7.0–13.0)	73	9.0 (7.0–14.0)	80	8.0 (5.0–9.0)	75	7.0 (4.5–9.0)	<0.001[1]
Albuminuria (mg/g)	70	116.5 (57.0–382.0)	73	125.0 (66.0–267.0)	80	76.0 (39.5–215.0)	75	81.0 (36.0–283.0)	0.016[1]
BMI (kg/m^2)	70	33.0 (30.6–34.6)	73	33.5 (31.6–34.8)	80	31.6 (28.6–34.4)	75	31.5 (28.5–33.7)	0.008[1]
Systolic blood pressure (mmHg)	70	132.9 ± 10.9	73	131.0 ± 12.9	80	128.6 ± 12.9	75	129.8 ± 12.8	0.188[2]
Diastolic blood pressure (mmHg)	70	80.2 ± 11.0	73	78.9 ± 10.7	80	78.2 ± 9.9	75	78.9 ± 9.2	0.678[2]
ACEI/ARB use (%)									
Yes	30	42.9	32	43.8	37	46.3	41	54.7	0.464[3]
No	40	57.1	41	56.2	43	53.8	34	45.3	
Vitamin D (ng/mL)	70	13.1 ± 8.2	73	14.8 ± 6.8	80	18.9 ± 8.7	75	17.4 ± 7.8	<0.001[2]
Calcium (mg/dL)	70	9.2 ± 0.5	73	9.2 ± 0.6	79	9.4 ± 0.6	75	9.5 ± 0.5	0.004[2]
Phosphorus (mg/dL)	70	3.7 (3.0–4.0)	73	3.6 (3.2–4.0)	79	3.8 (3.0–4.0)	75	3.8 (3.2–4.0)	0.818[1]
Albumin (g/dL)	70	3.8 ± 0.4	73	3.8 ± 0.6	80	3.8 ± 0.5	75	3.9 ± 0.4	0.770[2]
Total protein (g/dL)	70	6.7 ± 0.7	73	6.9 ± 0.7	80	6.9 ± 0.6	75	6.8 ± 0.6	0.327[2]
HbA1c (%)	70	9.6 ± 2.7	73	9.3 ± 2.6	80	9.2 ± 2.5	75	8.0 ± 2.1	<0.001[2]
Fasting glucose (mg/dL)	70	213.5 (157.0–267.0)	73	208.0 (144.0–270.0)	79	169.0 (127.0–240.0)	75	167.0 (125.5–218.5)	0.012[1]
eGFR (mL/min/1.73 m^2)	70	73.3 ± 22.8	73	75.3 ± 21.8	80	76.5 ± 20.2	75	78.2 ± 17.8	0.542[2]
Creatinine (mg/dL)	70	0.94 (0.82–1.23)	73	0.94 (0.80–1.15)	80	1.00 (0.85–1.22)	75	0.96 (0.85–1.12)	0.765[1]
BUN (mg/dL)	70	16.0 (12.0–20.0)	73	16.0 (13.0–21.0)	80	17.0 (14.0–21.0)	75	17.0 (14.0–22.0)	0.458[1]
Uric acid (mg/dL)	70	5.8 (4.0–6.9)	73	5.3 (4.3–6.5)	80	5.3 (4.2–6.8)	74	5.4 (4.3–6.8)	0.896[1]
Total cholesterol (mg/dL)	70	206.0 (178.0–227.0)	73	203.0 (167.0–230.0)	80	184.5 (152.0–223.5)	74	203.5 (164.0–233.0)	0.273[1]
LDL cholesterol (mg/dL)	67	123.0 (99.5–139.0)	68	114.0 (82.0–144.0)	77	104.0 (83.0–129.0)	72	108.5 (95.0–150.0)	0.153[1]
HDL cholesterol (mg/dL)	70	45.0 (39.0–52.0)	73	45.0 (38.0–52.0)	80	46.0 (38.5–52.0)	74	43.5 (38.0–52.0)	0.952[1]
Triglyceride (mg/dL)	70	181.0 (124.0–246.0)	73	182.0 (117.0–245.0)	80	148.5 (100.5–245.5)	74	149.0 (106.0–230.0)	0.266[1]
TSH (mIU/L)	70	1.57 (1.00–2.30)	73	1.10 (0.77–1.60)	80	1.43 (1.10–2.30)	74	1.42 (0.86–2.30)	0.014[1]
Parathormone (pg/mL)	40	61.0 (38.0–87.5)	28	67.0 (39.5–87.5)	41	41.0 (32.0–57.0)	31	53.0 (36.0–69.5)	0.019[1]
AST (U/L)	70	21.0 (16.0–27.0)	73	20.0 (16.0–25.0)	80	20.0 (15.5–28.0)	75	20.0 (14.5–30.5)	0.970[1]
ALT (U/L)	70	14.5 (11.0–23.0)	73	21.0 (15.0–30.0)	80	20.0 (14.0–30.0)	75	21.0 (12.5–31.5)	0.004[1]

BMI, body mass index; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; HbA1c, glycated hemoglobin; BUN, blood urea nitrogen; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TSH, thyroid-stimulating hormone; AST, aspartate aminotransferase; ALT, alanine aminotransferase. [1], Kruskal-Wallis Test; [2], One-way analysis of variance; [3], Pearson Chi-square Test. For albuminuria, the Bonferroni-adjusted *p*-values were 1.000 for winter versus spring, 0.280 for winter versus summer, 0.248 for winter versus autumn, 0.065 for spring versus summer, 0.098 for spring versus autumn, and 1.000 for summer versus autumn; none of these pairwise comparisons were statistically significant.

Table 2. Comparison of clinical and biochemical characteristics by Vitamin D levels.

Parameter	Vitamin D Levels						*p*-value
	<12 ng/mL		≥12 to <20 ng/mL		≥20 ng/mL		
	Number	Mean ± standard deviation - median (interquartile range)	Number	Mean ± standard deviation - median (interquartile range)	Number	Mean ± standard deviation - median (interquartile range)	
Duration of diabetes (years)	93	9.0 (7.0–13.0)	127	8.0 (5.0–10.5)	78	7.5 (5.0–10.0)	0.003[1]
Albuminuria (mg/g)	93	318.0 (124.0–616.0)	127	74.0 (42.0–152.5)	78	68.0 (40.0–118.0)	<0.001[1]
BMI (kg/m^2)	93	31.9 ± 3.6	127	31.6 ± 4.0	78	32.1 ± 3.5	0.635[2]
Systolic blood pressure (mmHg)	93	128.7 ± 12.3	127	132.5 ± 13.3	78	129.5 ± 10.9	0.056[2]
Diastolic blood pressure (mmHg)	93	78.5 ± 8.9	127	79.8 ± 11.2	78	78.2 ± 9.9	0.466[2]
ACEI/ARB use (%)							
Yes	39	41.9	65	51.2	36	46.2	0.392[3]
No	54	58.1	62	48.8	42	53.8	
Calcium (mg/dL)	93	9.1 ± 0.6	126	9.5 ± 0.5	78	9.4 ± 0.5	<0.001[2]
Phosphorus (mg/dL)	93	3.7 (3.2–4.0)	126	3.8 (3.2–4.0)	78	3.5 (3.0–4.0)	0.059[1]
Albumin (g/dL)	93	3.6 ± 0.6	127	4.0 ± 0.4	78	3.9 ± 0.4	<0.001[2]
Total protein (g/dL)	93	6.7 ± 0.7	127	7.0 ± 0.6	78	6.9 ± 0.6	0.003[2]
HbA1c (%)	93	9.5 ± 2.7	127	8.9 ± 2.5	78	8.5 ± 2.3	0.051[2]
Fasting glucose (mg/dL)	93	208.0 (150.0–260.0)	126	178.5 (138.0–248.0)	78	168.0 (126.0–250.0)	0.148[1]
eGFR (mL/min/1.73m^2)	93	69.7 ± 23.2	127	79.5 ± 17.5	78	77.3 ± 20.8	0.002[2]
Creatinine (mg/dL)	93	1.03 (0.87–1.40)	127	0.94 (0.80–1.10)	78	0.94 (0.81–1.17)	0.002[1]
BUN (mg/dL)	93	19.0 (15.0–23.0)	127	16.0 (13.0–19.5)	78	15.5 (12.0–21.0)	0.001[1]
Uric acid (mg/dL)	93	5.7 (4.3–7.5)	127	5.3 (4.2–6.5)	77	5.3 (4.5–6.6)	0.160[1]
Total cholesterol (mg/dL)	92	196.0 (164.5–227.0)	127	195.0 (170.5–233.0)	78	203.0 (157.0–224.0)	0.773[1]
LDL cholesterol (mg/dL)	90	106.0 (83.0–135.0)	122	115.5 (92.0–144.0)	72	113.0 (80.0–143.0)	0.448[1]
HDL cholesterol (mg/dL)	92	45.0 (36.5–52.0)	127	44.0 (38.0–52.0)	78	46.0 (40.0–53.0)	0.217[1]
Triglyceride (mg/dL)	92	200.5 (130.5–251.0)	127	153.0 (105.5–242.0)	78	151.5 (100.0–225.0)	0.051[1]
TSH (mIU/L)	92	1.30 (0.83–2.00)	127	1.40 (1.00–2.00)	78	1.55 (0.80–2.30)	0.539[1]
Parathormone (pg/mL)	59	58.7 (37.5–88.5)	52	49.5 (30.0–70.5)	29	46.0 (32.0–62.0)	0.112[1]
AST (U/L)	93	19.0 (14.0–27.0)	127	20.0 (15.5–27.5)	78	21.0 (17.0–27.0)	0.394[1]
ALT (U/L)	93	17.0 (12.0–29.0)	127	21.0 (14.0–29.5)	78	20.5 (14.0–30.0)	0.250[1]

ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; [1], Kruskal–Wallis Test; [2], One-way analysis of variance; [3], Pearson Chi-square Test. For albuminuria, the Bonferroni-adjusted *p*-values were <0.001 for <12 versus ≥12 to <20 ng/mL, <0.001 for <12 versus ≥20 ng/mL, and 1.000 for ≥12 to <20 versus ≥20 ng/mL.

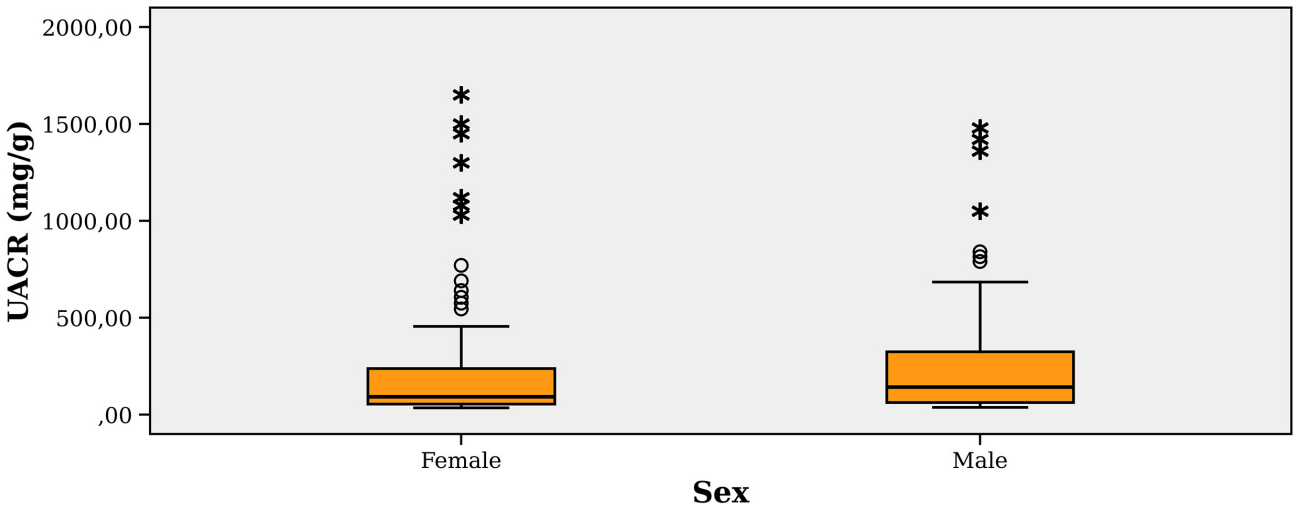

Fig. 2. Comparison of urinary albumin-to-creatinine ratio (UACR) levels between female and male patients. Circles (○) represent outliers, and asterisks (*) represent extreme outliers.

levels (Adjusted R^2 = 0.206). To account for differences associated with the season of clinic attendance, season was incorporated into the multivariable regression model using dummy variables, with winter as the reference category. After adjustment for diabetes duration, calcium, phosphorus, albumin, HbA1c, FPG, creatinine, BUN, triglycerides, and season, albuminuria remained independently and inversely associated with serum Vitamin D levels (β = –0.330, $p < 0.001$). In addition, summer (β = 0.285, $p < 0.001$) and autumn (β = 0.181, $p = 0.009$) were independently associated with higher serum Vitamin D levels compared with winter, whereas spring was not significantly associated with Vitamin D levels ($p = 0.124$). None of the other variables included in the model showed an independent association with Vitamin D levels (Tables 4,5).

Table 3. Correlation between Vitamin D and other numeric parameters.

Variables	Vitamin D (ng/mL)		
	n	r–rho	*p*-value
Age (years)	298	0.046	0.432[1]
Duration of diabetes (years)	298	–0.165	0.004[1]
Albuminuria (mg/g)	298	–0.430	<0.001[2]
BMI (kg/m^2)	298	0.006	0.914[1]
Systolic blood pressure (mmHg)	298	0.006	0.913[1]
Diastolic blood pressure (mmHg)	298	–0.021	0.721[1]
Calcium (mg/dL)	297	0.134	0.021[1]
Phosphorus (mg/dL)	297	–0.127	0.028[2]
Albumin (g/dL)	298	0.196	0.001[1]
Total protein (g/dL)	298	0.096	0.099[1]
HbA1c (%)	298	–0.142	0.014[1]
Fasting glucose (mg/dL)	297	–0.140	0.016[2]
eGFR (mL/min/1.73m^2)	298	0.112	0.052[1]
Creatinine (mg/dL)	298	–0.164	0.005[2]
BUN (mg/dL)	298	–0.189	0.001[2]
Uric acid (mg/dL)	297	–0.044	0.450[1]
Total cholesterol (mg/dL)	297	0.009	0.880[2]
LDL (mg/dL)	284	0.019	0.746[2]
HDL (mg/dL)	297	0.067	0.251[2]
Triglyceride (mg/dL)	297	–0.128	0.027[2]
TSH (mIU/L)	297	0.097	0.095[2]
Parathormone (pg/mL)	140	–0.206	0.014[2]
AST (U/L)	298	0.068	0.241[2]
ALT (U/L)	298	0.101	0.080[2]

[1], Pearson Correlation Test; [2], Spearman's Correlation Test.

4. Discussion

DN continues to be the most common cause of end-stage renal disease worldwide and shows a strong association with increased cardiovascular mortality. In this study, differences in Vitamin D levels according to the season of sample collection and their association with albuminuria, an important marker of renal involvement, were examined in patients with DN. Furthermore, multivariable regression analysis demonstrated that the season of sample collection remained independently associated with serum Vitamin D levels even after adjustment for renal and metabolic parameters. Although Vitamin D levels in patients with diabetes have previously been investigated, studies evaluating differences in Vitamin D levels according to the season of sample collection and their associations with renal and metabolic parameters specifically in patients with DN remain limited.

Vitamin D synthesis begins primarily with the exposure of the skin to ultraviolet B (UV-B) radiation at a wavelength of 290–315 nm [9]. However, this process is directly affected by age, physical activity, skin pigmentation, and most importantly, seasonal factors [10]. In our study, Vitamin D levels were found to be below the suffi-

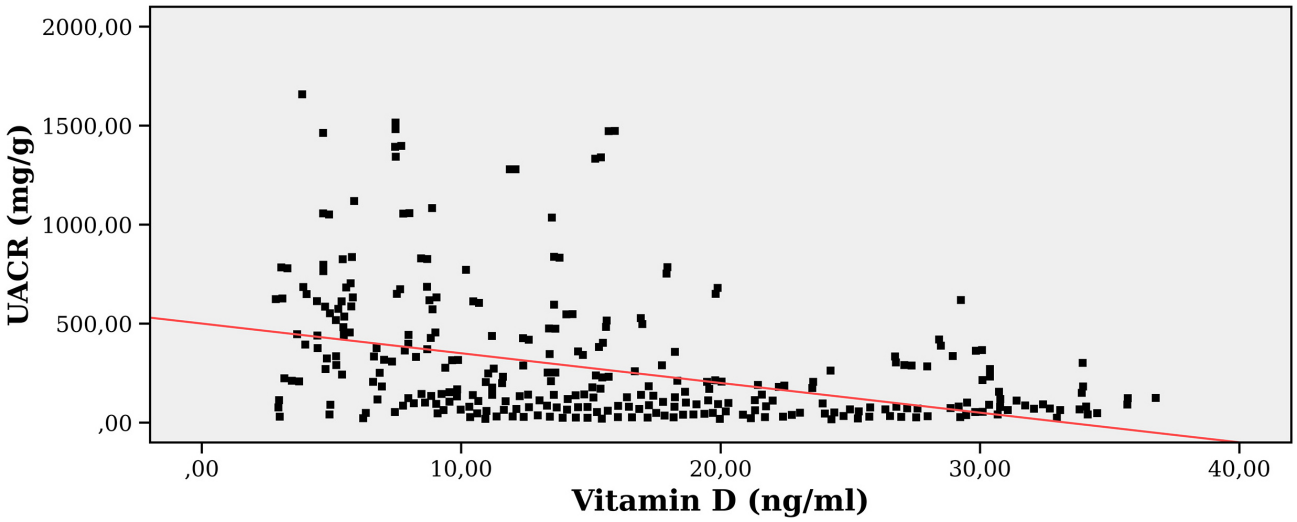

Fig. 3. Relationship between serum 25-hydroxyvitamin D (25(OH)D) concentrations and urinary albumin-to-creatinine ratio (UACR) in patients.

Table 4. Summary of the multiple linear regression model for factors associated with serum Vitamin D levels.

R	R^2	Adjusted R^2	F (ANOVA)	*p*	Durbin-Watson
0.491	0.241	0.206	6.881	<0.001	1.635

R, multiple correlation coefficient; R^2, coefficient of determination; adjusted R^2, adjusted coefficient of determination; F, F-statistic; ANOVA, analysis of variance.

ciency threshold (<20 ng/mL) in the vast majority of patients (73.8%). This finding is consistent with the results of Ngai et al. [11] and Dean et al. [12], who reported that deficiency is common in the CKD population due to reduced renal 1α-hydroxylase activity. From a seasonal perspective, González-Parra et al. [13] in hemodialysis patients and Klingberg et al. [14] in healthy individuals reported that Vitamin D levels dropped dramatically in winter months. Similarly, mean Vitamin D levels were higher among patients attending during summer than among those attending during winter (18.9 vs. 13.1 ng/mL), while remaining below the sufficiency threshold in all four groups ($p < 0.001$).

The most critical finding of our study is the strong negative correlation detected between Vitamin D levels and albuminuria (rho = –0.430, $p < 0.001$). In the multiple regression analysis, albuminuria was independently and inversely associated with serum Vitamin D levels ($p < 0.001$). In addition, after adjustment for renal and metabolic variables, summer and autumn remained independently associated with higher serum Vitamin D levels compared with winter, whereas spring was not significantly associated with serum Vitamin D levels. This relationship can be explained through the RAAS, which plays a critical role in the pathogenesis of DN. Vitamin D exerts its biological effects through the Vitamin D Receptor (VDR), and VDR activation negatively regulates RAAS by suppressing renin gene transcription [15]. Excessive activation of RAAS leads to efferent arteriolar vasoconstriction, increased intraglomerular pressure, and consequently, proteinuria [16]. Proteinuria is currently accepted not only as a consequence of kidney damage but also as an independent risk factor accelerating progression [17]. Despite dietary and medical treatments, target albuminuria levels cannot be reached in many patients [18]. Literature indicates that reduced eGFR and increased albuminuria are associated with Vitamin D deficiency [19] and that the use of Vitamin D analogs slows albuminuria and glomerular filtration rate loss [20]. Recent evidence has also demonstrated an association between Vitamin D deficiency and adverse renal outcomes in diabetic kidney disease; however, whether Vitamin D supplementation improves renal outcomes remains uncertain [21].

This mechanistic relationship is supported by experimental and clinical studies. Wang et al. [22] showed that the deletion of VDR in diabetic mice resulted in severe albuminuria and glomerulosclerosis, while Mizobuchi et al. [19] demonstrated that paricalcitol treatment reduced albuminuria. Clinically, Zomorodian et al. [23] also reported that albuminuria was more severe in patients with Vitamin D <20 ng/mL. Although albuminuria differed significantly overall across the seasonal groups, none of the pairwise comparisons remained significant after Bonferroni correction.

Another noteworthy finding in our study is the gender difference. Although no significant difference was detected between women and men in terms of Vitamin D levels, albuminuria levels were found to be significantly higher in male patients compared to females ($p = 0.007$). In the literature, Gould et al. [24] and Yudkin et al. [25] stated that male gender could be a risk factor for microvascular complications, while Zacharias et al. [26] noted that this could stem from hormonal factors and lifestyle differences. Addition-

Table 5. Multiple linear regression analysis for factors associated with serum Vitamin D levels.

Model	B	Standard error	β	*t*	*p*	Tolerance	VIF
Constant	24.306	8.600	-	2.826	0.005	-	-
Duration of diabetes	–0.026	0.105	–0.014	–0.247	0.805	0.812	1.232
Albuminuria	–0.009	0.002	–0.330	–5.585	<0.001	0.772	1.295
Calcium	–1.005	1.058	–0.069	–0.951	0.343	0.505	1.979
Phosphorus	–0.593	0.688	–0.047	–0.862	0.389	0.909	1.100
Albumin	1.906	1.173	0.116	1.626	0.105	0.529	1.891
HbA1c (%)	–0.307	0.228	–0.095	–1.350	0.178	0.540	1.851
Fasting glucose	–0.002	0.006	–0.021	–0.309	0.757	0.585	1.710
Creatinine	–1.189	1.802	–0.048	–0.660	0.510	0.502	1.990
BUN	–0.004	0.075	–0.004	–0.052	0.959	0.535	1.869
Triglyceride	0.000	0.003	0.008	0.138	0.890	0.892	1.121
Spring	1.900	1.233	0.100	1.541	0.124	0.637	1.571
Summer	5.271	1.237	0.285	4.260	<0.001	0.600	1.666
Autumn	3.410	1.300	0.181	2.623	0.009	0.567	1.762

B, unstandardized regression coefficient; β, standardized regression coefficient; VIF, variance inflation factor. Dependent variable: Serum Vitamin D level.

Season was entered into the model as dummy variables, with winter serving as the reference category. The regression analysis included 296 complete cases. Missing data were handled using complete-case analysis, and no imputation was performed.

ally, the protective effect of estrogen on podocytes may be a factor slowing nephropathy progression in women. This finding emphasizes that gender should also be taken into consideration in the risk stratification of DN.

The positive correlation we detected between Vitamin D deficiency and serum albumin levels (r = 0.196, p = 0.001) is consistent with the literature. Yonemura et al. [27] reported that Vitamin D deficiency is associated with hypoalbuminemia. The anti-inflammatory properties of Vitamin D are well known; in its absence, increased systemic inflammation can suppress the synthesis of albumin, which is a negative acute-phase reactant. However, the cross-sectional design of the present study does not allow conclusions regarding whether Vitamin D supplementation could improve mineral metabolism or nutritional status.

When mineral metabolism was examined, a positive relationship was found between Vitamin D and calcium, and a negative relationship with PTH, consistent with the literature [28,29]. However, the negative correlation observed between phosphorus levels and Vitamin D (rho = –0.127) differs from some literature data. It is thought that this situation may originate from treatment-related factors such as dietary restrictions or the use of phosphate binders in our diabetic patient population.

Regarding glycemic control, it was determined that HbA1c and FPG levels were higher in winter and spring months and showed a negative correlation with Vitamin D. HbA1c tends to rise in winter, showing seasonal fluctuations [30,31]. This situation has been associated with increased caloric intake, decreased physical activity, and biological rhythm changes [32,33]. However, it is also suggested that the decline in Vitamin D levels may impair glycemic control [34,35]. FPG levels are also known to exhibit seasonal variation [36,37]. Wang et al. [38] showed that low Vitamin D is associated with insulin resistance. Our findings indicate that lower Vitamin D levels were associated with poorer glycemic parameters; however, the cross-sectional design does not permit conclusions regarding the direction or causality of this relationship. Previous meta-analyses have reported improvements in HbA1c, FPG, and insulin resistance following Vitamin D supplementation in patients with type 2 diabetes mellitus [39]; however, these findings cannot establish that the associations observed in the present study reflect a treatment effect.

Limitations

Our study has some limitations. The single-center and retrospective design prevent the definitive establishment of a causal relationship. Importantly, the four seasonal groups comprised different patients, and the same individuals were not followed with repeated measurements across different seasons. Therefore, the observed findings represent differences between patients attending the clinic in different seasons rather than within-patient seasonal changes. The cross-sectional design also precludes assessment of temporal changes and limits causal interpretation. Additionally, factors such as patients' dietary habits and duration of sun exposure could not be standardized at the individual level. Furthermore, because this was a retrospective study based on routinely collected medical records, several potential confounders affecting Vitamin D metabolism, including disorders such as hyperparathyroidism, malabsorption syndromes, granulomatous diseases, pregnancy/lactation, and

medications influencing Vitamin D metabolism, could not be systematically assessed. Some laboratory parameters, particularly PTH, had missing data because they were not routinely measured in all patients. Therefore, PTH was excluded from the multivariable regression model, and the regression analysis was based on complete cases. In addition, detailed information regarding antidiabetic medications and comorbidities was not consistently available for all patients; therefore, only angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB) use was evaluated. Consequently, residual confounding cannot be completely excluded. However, the large sample size and the dataset covering four seasons increase the power of the study.

5. Conclusions

This study demonstrated that serum 25(OH)D concentrations differed among patients with DN according to the season of sample collection, with higher concentrations observed in summer and autumn than in winter. Lower serum 25(OH)D concentrations were cross-sectionally associated with higher albuminuria. However, because of the retrospective cross-sectional design, the temporal and causal nature of these associations cannot be determined. Prospective longitudinal and interventional studies are required to establish temporality and determine whether Vitamin D supplementation affects albuminuria or other renal outcomes in patients with DN.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author.

Author Contributions

Concept – MY, AA; Design – MY, AA; Supervision – AA; Resources – AA, HK; Materials – MY, HK; Data Collection and/or Processing – MY, HK; Analysis and/or Interpretation – MY, AA; Literature Search – MY, HK; Writing Manuscript – MY; Critical Review – AA, HK. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the Süleyman Demirel University Clinical Research Ethics Committee (Date: 29.12.2023, Decision No: 301). The study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for written informed consent was waived by the Clinical Research Ethics Committee due to the retrospective nature of the study and the use of anonymized data.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR54395.

References

[1] Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. Diabetes Care. 2005; 28: 164–176. https://doi.org/10.2337/diacare.28.1.164

[2] Zhang L, Jiang L, Xu R, Zhang X, Zhang B, Yue R. Epidemiological research on diabetic nephropathy at global, regional, and national levels from 1990 to 2021: an analysis derived from the global burden of disease 2021 study. Frontiers in Endocrinology. 2025; 16: 1647064. https://doi.org/10.3389/fendo.2025.1647064

[3] Heerspink HJ, Kröpelin TF, Hoekman J, de Zeeuw D, Reducing Albuminuria as Surrogate Endpoint (REASSURE) Consortium. Drug-Induced Reduction in Albuminuria Is Associated with Subsequent Renoprotection: A Meta-Analysis. Journal of the American Society of Nephrology. 2015; 26: 2055–2064. https://doi.org/10.1681/ASN.2014070688

[4] Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney International. 2022; 102: S1–S127. https://doi.org/10.1016/j.kint.2022.06.008

[5] Yuan W, Pan W, Kong J, Zheng W, Szeto FL, Wong KE, et al. 1,25-dihydroxyvitamin D3 suppresses renin gene transcription by blocking the activity of the cyclic AMP response element in the renin gene promoter. The Journal of Biological Chemistry. 2007; 282: 29821–29830. https://doi.org/10.1074/jbc.M705495200

[6] Isakova T, Gutiérrez OM, Patel NM, Andress DL, Wolf M, Levin A. Vitamin D deficiency, inflammation, and albuminuria in chronic kidney disease: complex interactions. Journal of Renal Nutrition: the Official Journal of the Council on Renal Nutrition of the National Kidney Foundation. 2011; 21: 295–302. https://doi.org/10.1053/j.jrn.2010.07.002

[7] Khanna T, Shraim R, Zarkovic M, van Weele M, van Geffen J, Zgaga L. Comprehensive Analysis of Seasonal and Geographical Variation in UVB Radiation Relevant for Vitamin D Production in Europe. Nutrients. 2022; 14: 5189. https://doi.org/10.3390/nu14235189

[8] American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024; 47: S20–S42. https://doi.org/10.2337/dc24-S002

[9] Holick MF. Vitamin D deficiency. The New England Journal of Medicine. 2007; 357: 266–281. https://doi.org/10.1056/NEJMra070553

[10] Costanzo PR, Elías NO, Kleiman Rubinsztein J, Garcia Basavilbaso NX, Piacentini R, Salerni HH. Ultraviolet radiation im-

pact on seasonal variations of serum 25-hydroxy-vitamin D in healthy young adults in Buenos Aires. Medicina. 2011; 71: 336–342. (In Spanish)

[11] Ngai M, Lin V, Wong HC, Vathsala A, How P. Vitamin D status and its association with mineral and bone disorder in a multi-ethnic chronic kidney disease population. Clinical Nephrology. 2014; 82: 231–239. https://doi.org/10.5414/CN108182

[12] Dean YE, Elawady SS, Shi W, Salem AA, Chotwatanapong A, Ashraf H, et al. Progression of diabetic nephropathy and vitamin D serum levels: A pooled analysis of 7722 patients. Endocrinology, Diabetes & Metabolism. 2023; 6: e453. https://doi.org/10.1002/edm2.453

[13] González-Parra E, Avila PJ, Mahillo-Fernández I, Lentisco C, Gracia C, Egido J, et al. High prevalence of winter 25-hydroxyvitamin D deficiency despite supplementation according to guidelines for hemodialysis patients. Clinical and Experimental Nephrology. 2012; 16: 945–951. https://doi.org/10.1007/s10157-012-0642-2

[14] Klingberg E, Oleröd G, Konar J, Petzold M, Hammarsten O. Seasonal variations in serum 25-hydroxy vitamin D levels in a Swedish cohort. Endocrine. 2015; 49: 800–808. https://doi.org/10.1007/s12020-015-0548-3

[15] Zhang Z, Sun L, Wang Y, Ning G, Minto AW, Kong J, et al. Renoprotective role of the vitamin D receptor in diabetic nephropathy. Kidney International. 2008; 73: 163–171. https://doi.org/10.1038/sj.ki.5002572

[16] Phillips AO, Steadman R. Diabetic nephropathy: the central role of renal proximal tubular cells in tubulointerstitial injury. Histology and Histopathology. 2002; 17: 247–252. https://doi.org/10.14670/HH-17.247

[17] Remuzzi G, Bertani T. Is glomerulosclerosis a consequence of altered glomerular permeability to macromolecules? Kidney International. 1990; 38: 384–394. https://doi.org/10.1038/ki.1990.217

[18] Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney International. 2007; 71: 31–38. https://doi.org/10.1038/sj.ki.5002009

[19] Mizobuchi M, Morrissey J, Finch JL, Martin DR, Liapis H, Akizawa T, et al. Combination therapy with an angiotensin-converting enzyme inhibitor and a vitamin D analog suppresses the progression of renal insufficiency in uremic rats. Journal of the American Society of Nephrology: JASN. 2007; 18: 1796–1806. https://doi.org/10.1681/ASN.2006091028

[20] Li YC, Qiao G, Uskokovic M, Xiang W, Zheng W, Kong J. Vitamin D: a negative endocrine regulator of the renin-angiotensin system and blood pressure. The Journal of Steroid Biochemistry and Molecular Biology. 2004; 89-90: 387–392. https://doi.org/10.1016/j.jsbmb.2004.03.004

[21] Chackochan A, Rashid M, Reghunath SR, Poojari PG, Thunga G, Nagri SK, et al. Role of vitamin D in the development and progression of diabetic kidney disease: an overview of meta-analyses. Therapeutic Advances in Endocrinology and Metabolism. 2025; 16: 20420188251319476. https://doi.org/10.1177/20420188251319476

[22] Wang Y, Deb DK, Zhang Z, Sun T, Liu W, Yoon D, et al. Vitamin D receptor signaling in podocytes protects against diabetic nephropathy. Journal of the American Society of Nephrology. 2012; 23: 1977–1986. https://doi.org/10.1681/ASN.2012040383

[23] Zomorodian SA, Shafiee M, Karimi Z, Masjedi F, Roshanshad A. Assessment of the relationship between 25-hydroxyvitamin D and albuminuria in type 2 diabetes mellitus. BMC Endocrine Disorders. 2022; 22: 171. https://doi.org/10.1186/s12902-022-01088-2

[24] Gould MM, Mohamed-Ali V, Goubet SA, Yudkin JS, Haines AP. Microalbuminuria: associations with height and sex in non-diabetic subjects. BMJ (Clinical Research Ed.). 1993; 306: 240–242. https://doi.org/10.1136/bmj.306.6872.240

[25] Yudkin JS, Forrest RD, Jackson CA. Microalbuminuria as predictor of vascular disease in non-diabetic subjects. Islington Diabetes Survey. Lancet (London, England). 1988; 2: 530–533. https://doi.org/10.1016/s0140-6736(88)92657-8

[26] Zacharias JM, Young TK, Riediger ND, Roulette J, Bruce SG. Prevalence, risk factors and awareness of albuminuria on a Canadian First Nation: a community-based screening study. BMC Public Health. 2012; 12: 290. https://doi.org/10.1186/1471-2458-12-290

[27] Yonemura K, Fujimoto T, Fujigaki Y, Hishida A. Vitamin D deficiency is implicated in reduced serum albumin concentrations in patients with end-stage renal disease. American Journal of Kidney Diseases: the Official Journal of the National Kidney Foundation. 2000; 36: 337–344. https://doi.org/10.1053/ajkd.2000.8984

[28] Jean G, Terrat JC, Vanel T, Hurot JM, Lorriaux C, Mayor B, et al. Daily oral 25-hydroxycholecalciferol supplementation for vitamin D deficiency in haemodialysis patients: effects on mineral metabolism and bone markers. Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2008; 23: 3670–3676. https://doi.org/10.1093/ndt/gfn339

[29] Piirainen R, Englund E, Henriksson AE. The impact of seasonal variation of 25-hydroxyvitamin D and parathyroid hormone on calcium levels. Clinical Biochemistry. 2016; 49: 850–853. https://doi.org/10.1016/j.clinbiochem.2016.06.009

[30] Ferrie CD, Sharpe TC, Price DA, Surtees RA. Seasonal variation of glycosylated haemoglobin. Archives of Disease in Childhood. 1987; 62: 959–960. https://doi.org/10.1136/adc.62.9.959

[31] Higgins T, Saw S, Sikaris K, Wiley CL, Cembrowski GC, Lyon AW, et al. Seasonal variation in hemoglobin A1c: is it the same in both hemispheres? Journal of Diabetes Science and Technology. 2009; 3: 668–671. https://doi.org/10.1177/193229680900300408

[32] Hawkins RC. Circannual variation in glycohemoglobin in Singapore. Clinica Chimica Acta; International Journal of Clinical Chemistry. 2010; 411: 18–21. https://doi.org/10.1016/j.cca.2009.09.031

[33] Hamilton SL, Clemes SA, Griffiths PL. UK adults exhibit higher step counts in summer compared to winter months. Annals of Human Biology. 2008; 35: 154–169. https://doi.org/10.1080/03014460801908058

[34] Honeyman MC, Elkassaby S, Harrison LC. Seasonal changes in preprandial glucose, A1C, and blood pressure in diabetic patients: response to Liang. Diabetes Care. 2007; 30: e118; author reply e119. https://doi.org/10.2337/dc07-1405

[35] McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. Nutrition Journal. 2008; 7: 4. https://doi.org/10.1186/1475-2891-7-4

[36] Liang WW. Seasonal changes in preprandial glucose, A1C, and blood pressure in diabetic patients. Diabetes Care. 2007; 30: 2501–2502. https://doi.org/10.2337/dc07-0597

[37] Suarez L, Barrett-Connor E. Seasonal variation in fasting plasma glucose levels in man. Diabetologia. 1982; 22: 250–253. https://doi.org/10.1007/BF00281300

[38] Wang C, Li H, Huo L, Wang Q, Zhang T, He X, et al. Serum 25-Hydroxyvitamin D Levels in Type 2 Diabetes Patients in North China: Seasonality and the Association between Vitamin D Status and Glycosylated Hemoglobin Levels. Interna-

tional Journal of Clinical Practice. 2023; 2023: 4151224. https://doi.org/10.1155/2023/4151224

[39] Chen W, Liu L, Hu F. Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: An updated systematic review and meta-analysis of randomized controlled trials. Diabetes, Obesity & Metabolism. 2024; 26: 5713–5726. https://doi.org/10.1111/dom.15941