Evaluating the Role of Vitamin D3 in Modulating Insulin Resistance and Glycemic Control Among Type 2 Diabetic Nephropathy Patients

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Abstract- Type 2 diabetes mellitus (T2DM) is a major global health concern, often complicated by diabetic nephropathy (DN), a leading cause of end-stage renal disease. Vitamin D3 has been implicated in various metabolic and inflammatory processes, potentially influencing insulin sensitivity and renal outcomes. However, the exact relationship between vitamin D3 levels, glycemic control, and insulin resistance in T2DM patients with different stages of DN remains unclear. This study aims to evaluate serum vitamin D3 levels in T2DM patients with varying degrees of albuminuria and to assess their correlation with markers of insulin resistance and glycemic control, compared with healthy controls. A case-control study was conducted involving 180 T2DM patients—divided into normoalbuminuria (n=60), microalbuminuria (n=60), and macroalbuminuria (n=60) groups—and 60 healthy controls. Glycemic Profile (Fasting blood glucose [FBS], HbA1c, fasting insulin), lipid profile (total cholesterol, triglycerides, LDL, HDL, VLDL), renal function markers (urea, creatinine, albumin-to-creatinine ratio [ACR], glomerular filtration rate [GFR]), calcium, and vitamin D3 levels were measured. Insulin resistance was assessed using the HOMA-IR index. Serum vitamin D3 levels were significantly lower in all T2DM subgroups than in controls (P<0.001), with the lowest levels observed in the macroalbuminuria group. A significant positive correlation was observed between vitamin D3 and FBS only in the microalbuminuria group (r= +0.437, P=0.016). No significant associations were found between vitamin D3 and HOMA-IR or other glycemic parameters across the groups. Markers of renal dysfunction, including serum creatinine, urea, and ACR, were significantly elevated with increasing severity of albuminuria. Vitamin D deficiency is prevalent in T2DM patients with nephropathy, especially those with advanced renal impairment. While no strong associations were found between vitamin D3 and insulin resistance, a positive correlation with FBS in early-stage nephropathy suggests a potential role for vitamin D in glycemic regulation during the progression of DN. Further longitudinal studies are warranted to explore the therapeutic implications of vitamin D supplementation in T2DM patients at risk of nephropathy.

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, peripheral and hepatic insulin resistance, and progressive beta-cell dysfunction (1). It is a major public health challenge, with over 500 million people affected worldwide—more than 90% of whom have T2DM—driven by rising obesity, sedentary lifestyles, and aging populations (2).

Among the microvascular complications associated with T2DM, diabetic nephropathy (DN) is one of the

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most severe and life-threatening conditions. DN is a major cause of end-stage renal disease (ESRD), contributing significantly to increased morbidity, mortality, and healthcare costs. The progression of DN typically follows a predictable course: glomerular hyperfiltration and hypertrophy, then microalbuminuria, which may progress to overt proteinuria (macroalbuminuria), and ultimately to a decline in glomerular filtration rate (GFR) and chronic kidney disease (CKD). Patients with DN also face a heightened risk of cardiovascular complications, further exacerbating their overall prognosis (3,4).

Insulin resistance plays a central role not only in the pathogenesis of T2DM but also in the development and progression of its complications, including nephropathy. Insulin signaling defects contribute to impaired glucose uptake, enhanced hepatic gluconeogenesis, and dyslipidemia, all of which promote oxidative stress, inflammation, and endothelial dysfunction—key mechanisms underlying diabetic kidney injury. Moreover, poor glycemic control exacerbates these pathways, leading to the formation of advanced glycation end products (AGEs), activation of protein kinase C (PKC), and increased production of reactive oxygen species (ROS), all of which accelerate renal damage (5,6).

Given these pathways, there is growing interest in modifiable factors that may mitigate insulin resistance and slow DN progression. Vitamin D3 (cholecalciferol), a fat-soluble secosteroid best known for its role in calcium homeostasis and bone metabolism, has attracted considerable attention. Beyond its classical functions, vitamin D3 exerts pleiotropic effects on multiple physiological systems, including the immune, cardiovascular, and metabolic systems. Evidence suggests that vitamin D3 has anti-inflammatory, anti-fibrotic, and immunomodulatory properties, which may confer protective effects against both insulin resistance and renal dysfunction (7).

Epidemiological studies have reported an inverse association between serum levels of 25-hydroxyvitamin D3 [25(OH)D], the primary circulating form of vitamin D, and markers of insulin resistance such as the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Additionally, lower vitamin D levels have been linked to increased risk and severity of diabetic complications, particularly nephropathy. Vitamin D receptors (VDRs) are expressed in various tissues relevant to glucose metabolism and kidney function, including pancreatic beta cells, skeletal muscle, adipose tissue, and renal tubular epithelium, suggesting a direct biological plausibility for its involvement in these processes (8,9).

Despite accumulating evidence, the role of vitamin D3 in glycemic control and insulin sensitivity among patients with established DN remains unclear. Furthermore, findings from existing studies are often inconsistent, likely due to differences in population characteristics, nephropathy staging, and methods of vitamin D assessment.

Therefore, this study was designed to investigate the relationship between serum vitamin D3 levels and key markers of insulin resistance and glycemic control in patients with type 2 diabetes and varying degrees of albuminuria, compared to healthy controls. By examining these associations across different stages of diabetic nephropathy, we aim to provide novel insights into the potential utility of vitamin D3 as a biomarker or therapeutic target in the early detection and management of renal complications in T2DM patients.

Materials and Methods

Study design and participants

This case-control study was conducted between February and May 2023 at the National Diabetes Center affiliated with Al-Mustansiriya University in Baghdad, Iraq. The study protocol was approved by the Research Ethics Committee of the School of Public Health, Tehran University of Medical Sciences (Approval ID: IR.TUMS.SPH.REC.1402.046). Written informed consent was obtained from all participants prior to enrollment. A total of 240 subjects were enrolled and divided into two groups:

Control group: 60 healthy individuals without a history of chronic diseases, cancer, or regular medication use.

Case group: 180 patients diagnosed with type 2 diabetes mellitus (T2DM) and diabetic nephropathy, further classified based on urinary albumin excretion levels into:

Normoalbuminuria (n=60, urinary albumin< 30 mg/day)

Microalbuminuria (n=60, urinary albumin 30–300 mg/day)

Macroalbuminuria (n=60, urinary albumin> 300 mg/day)

Inclusion criteria included T2DM for more than 5 years and HbA1c> 6.5%. Exclusion criteria were chronic kidney disease, neoplastic disorders, severe liver disease, active infections, hematological diseases,

pregnancy, stroke, insulin use, urinary tract infection, or fever.

Sample collection

10 mL of venous blood was collected from each participant after a 10-12-hour overnight fast. Urine samples were collected in sterile containers and stored at 4° C until analysis.

Biochemical assays

All biochemical parameters were analyzed using standardized methods and commercial diagnostic kits:

Fasting blood glucose (FBS), lipid profile, urea, serum creatinine, and calcium were analyzed using an AutoAnalyzer (Human, Germany).

Insulin levels were quantified via electrochemiluminescence immunoassay using the cobas e 411 analyzer (Roche, Germany) (LOT No. 1066065001).

HbA1c was determined using the AFIAS-6 device (Boditech, South Korea).

Vitamin D3 levels were also confirmed using enzyme-linked fluorescent assay (ELFA) with Mini VIDAS (BioMérieux, France) (LOT No. 1009608510).

Statistical analysis

Data were analyzed using SPSS software version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as mean±standard deviation (SD), while categorical variables were presented as frequencies and percentages.

Normality of data distribution was assessed using the Shapiro-Wilk test. While some variables, such as fasting insulin and HOMA-IR, showed skewed distributions in certain groups, the large and equal sample sizes (n=60 per group) justify the use of parametric tests (one-way ANOVA) based on the Central Limit Theorem. As a sensitivity analysis, non-parametric Kruskal-Wallis tests were also performed for key metabolic variables, yielding results consistent with the parametric analyses.

Comparisons between groups were performed using one-way ANOVA followed by post-hoc Tukey's test for normally distributed data. Pearson correlation coefficients were calculated to assess relationships between continuous variables. A $P<0.05$ was considered statistically significant.

Results

A total of 120 participants were enrolled in this case-control study, including 60 healthy controls and 180 patients with type 2 diabetes mellitus (T2DM) and nephropathy, categorized by albuminuria status as normoalbuminuria (n=60), microalbuminuria (n=60), or macroalbuminuria (n=60). There was no significant difference in gender distribution ($P=0.760$), age ($P=0.070$), BMI ($P=0.693$), or diabetes duration ($P=0.293$) across the groups (Table 1).

Table 1. Demographic and clinical characteristics of study groups

Variables	Macroalbuminuria (n=60)	Microalbuminuria (n=60)	Normoalbuminuria (n=60)	Control Group (n=60)	*P*
Age (years), Mean±SD	52.27±7.49	59.27±7.41	52.67±12.10	56.90±9.6	0.07
BMI (kg/m²), Mean±SD	29.58±4.67	29.73±4.05	28.49±5.13	28.85±4.66	0.69
Gender, n (%)					0.76
Male	18 (28.6%)	16 (25.4%)	15 (23.8%)	14 (22.2%)	
Female	12 (21.1%)	14 (24.6%)	15 (26.3%)	16 (28.1%)	
Duration of DM (years)	11.20±4.43	11.97±5.42	10.10 ± 3.80	–	0.29

DM=Diabetes Mellitus; BMI=Body Mass Index

Biochemical parameters

Significant differences were observed among all groups in lipid profile parameters, including total cholesterol ($P<0.001$), triglycerides ($P<0.001$), HDL ($P<0.001$), VLDL ($P<0.001$), and LDL ($P<0.001$). Patients with macroalbuminuria had the highest levels of total cholesterol (198.57±33.55 mg/dL), triglycerides (186.03±108.02 mg/dL), and LDL (120.83±31.96 mg/dL), indicating a more severe dyslipidemic profile compared to other groups (Table 2).

Fasting blood glucose (FBS) and HbA1c levels were significantly elevated in all diabetic subgroups compared to controls ($P<0.001$). The macroalbuminuria group showed the highest mean FBS (261.5±70.6 mg/dL) and HbA1c (10.0±1.0%) values, reflecting poorer glycemic control in this subgroup.

No significant differences were found in fasting insulin levels ($P=0.320$) or HOMA-IR ($P=0.740$) between the groups, although a trend toward higher insulin resistance was observed in the macroalbuminuria

group.

Serum urea and creatinine levels differed significantly among the groups (P<0.001 for both). The macroalbuminuria group had the highest serum creatinine (2.1±0.67 mg/dL) and urea (43.53±20.02 mg/dL) levels, consistent with advanced renal impairment.

Albumin-to-creatinine ratio (ACR) was markedly elevated in the macroalbuminuria group (81.66±23.04 mg/d) compared to microalbuminuria (25.44±9.06 mg/d), normoalbuminuria (3.20±0.13 mg/d), and controls (3.09±0.21 mg/d; P<0.001). Glomerular filtration rate (GFR) was significantly lower in the macroalbuminuria group (29.53±0.72 mL/min/1.73m²) compared to microalbuminuria (48.09±0.93 mL/min/1.73m²), normoalbuminuria (65.86±2.29 mL/min/1.73m²), and controls (71.49±1.33 mL/min/1.73m²; P<0.001).

Serum calcium levels varied significantly among the groups (P<0.001), with the highest levels observed in the macroalbuminuria group (10.17±0.52 mg/dL). In contrast, vitamin D3 levels were significantly lower in all T2DM subgroups compared to controls (P<0.001), with the lowest levels in the macroalbuminuria group (14.26±7.73 ng/mL) compared to microalbuminuria (15.13±6.89 ng/mL), normoalbuminuria (15.10±4.72 ng/mL), and controls (46.40±15.58 ng/mL).

Correlation analysis

Pearson correlation analysis revealed no significant associations between vitamin D3 levels and most clinical or biochemical parameters in the macroalbuminuria and normoalbuminuria groups (Table 3). However, in the microalbuminuria group, a significant positive correlation was observed between vitamin D3 and fasting blood glucose (r=0.437, P=0.016), suggesting a potential relationship between glycemic control and vitamin D status in early-stage nephropathy.

Table 2. Biochemical parameters in study groups

Parameters	Macroalbuminuria (n=60)	Microalbuminuria (n=60)	Normoalbuminuria (n=60)	Control group (n=60)	*P*
Glycemic Profile					
FBS (mg/dL), Mean ± SD	261.5 ± 70.6	176.6 ± 51.1	155.7 ± 55.5	94.7 ± 9.0	<0.001
HbA1c (%), Mean ± SD	10.0 ± 1.0	7.8 ± 0.8	6.9 ± 0.4	4.8 ± 1.0	<0.001
Fasting insulin (µU/mL)	8.1 ± 15.0	9.8 ± 12.6	8.4 ± 7.0	12.7 ± 5.5	0.320
HOMA-IR	5.0 ± 8.8	4.1 ± 4.9	3.5 ± 4.1	3.7 ± 3.9	0.740
Lipid Profile					
Cholesterol (mg/dL)	198.57 ± 33.55	179.70 ± 44.35	180.20 ± 35.32	146.20 ± 26.65	<0.001
Triglycerides (mg/dL)	186.03 ± 108.02	191.83 ± 100.45	170.10 ± 88.03	97.67 ± 25.50	<0.001
LDL (mg/dL)	120.83 ± 31.96	101.00 ± 33.74	105.31 ± 28.95	83.83 ± 28.09	<0.001
HDL (mg/dL)	40.53 ± 8.16	40.33 ± 8.72	40.87 ± 10.88	21.83 ± 3.19	<0.001
VLDL (mg/dL)	37.21 ± 21.60	38.37 ± 20.09	34.02 ± 17.61	19.53 ± 5.10	<0.001
Renal Function Markers					
Blood Urea (mg/dL)	43.53 ± 20.02	32.42 ± 14.60	23.20 ± 5.15	24.77 ± 3.95	<0.001
Serum Creatinine (mg/dL)	2.1 ± 0.67	1.33 ± 0.21	0.95 ± 0.22	0.87 ± 1.17	<0.001
Albumin/Creatinine Ratio	81.66 ± 23.04	25.44 ± 9.06	3.20 ± 0.13	3.09 ± 0.21	<0.001
GFR (mL/min/1.73m²)	29.53 ± 0.72	48.09 ± 0.93	65.86 ± 2.29	71.49 ± 1.33	<0.001
Bone and Calcium Metabolism					
Calcium (mg/dL)	10.17 ± 0.52	8.97 ± 1.19	7.23 ± 1.53	9.43 ± 0.75	<0.001
Vitamin D3 (ng/mL)	14.26 ± 7.73	15.13 ± 6.89	15.10 ± 4.72	46.40 ± 15.58	<0.001

FBS = Fasting Blood Sugar; HbA1c = Glycated Hemoglobin; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; LDL = Low-Density Lipoprotein; HDL = High-Density Lipoprotein; VLDL = Very-Low-Density Lipoprotein; GFR = Glomerular Filtration Rate

Table 3. Pearson correlation coefficients between serum vitamin D3 levels and biochemical parameters in different albuminuria groups

Variable	Macroalbuminuria group		Microalbuminuria group		Normoalbuminuria group	
	r	*P*	r	*P*	r	*P*
Age	-0.257	0.171	0.071	0.708	-0.206	0.275
BMI	0.267	0.154	0.102	0.590	-0.115	0.545
Duration of Diabetes	-0.238	0.205	-0.055	0.774	-0.093	0.626
Cholesterol	-0.092	0.630	0.029	0.880	0.014	0.943
Triglycerides	-0.169	0.373	0.173	0.362	0.029	0.878
HDL	-0.007	0.971	0.254	0.175	0.250	0.182
VLDL	-0.169	0.373	0.173	0.362	0.029	0.878
LDL	0.020	0.918	-0.131	0.492	-0.095	0.616
FBS	-0.013	0.945	+0.437	0.016*	-0.106	0.578
HbA1c	-0.289	0.121	0.192	0.311	-0.289	0.121
Fasting Insulin	0.041	0.828	0.087	0.646	-0.107	0.575
HOMA-IR	0.032	0.866	0.241	0.200	-0.102	0.590
Blood Urea	0.221	0.240	-0.125	0.509	0.129	0.496
Serum Creatinine	0.091	0.632	0.006	0.974	0.186	0.326
ACR	0.118	0.533	-0.018	0.334	0.265	0.157
GFR	-0.241	0.200	0.018	0.927	0.135	0.477
Calcium	-0.316	0.089	-0.244	0.194	-0.179	0.345

A significant positive correlation between vitamin D3 and FBS was observed only in the microalbuminuria group (r = +0.437, *P*=0.016).
In the macroalbuminuria group, a near-significant trend was found between vitamin D3 and calcium (r = -0.316, *P*=0.089)

Discussion

This study demonstrates a significant association between serum vitamin D3 levels and the severity of DN in patients with T2DM. Serum vitamin D3 concentrations were markedly lower in all T2DM subgroups compared with healthy controls, with the lowest levels observed in patients with macroalbuminuria, consistent with the growing body of evidence linking vitamin D deficiency to advanced renal dysfunction in diabetes.

Despite the well-documented role of vitamin D in insulin signaling and glucose metabolism (10,11), we found no significant correlation between vitamin D3 levels and HOMA-IR or fasting insulin across any of the study groups. This absence of association aligns with some clinical studies that failed to demonstrate a clear link between vitamin D status and insulin resistance, particularly in populations with established diabetes or chronic kidney disease. The inconsistency with other reports may be attributed to differences in study design, population characteristics, or baseline vitamin D status.

Moreover, vitamin D exhibits anti-inflammatory properties by suppressing nuclear factor-kappa B (NF-κB) signaling and reducing the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), all of which are elevated in T2DM and contribute to insulin resistance and endothelial dysfunction (12,13). These anti-inflammatory effects may also extend to the kidneys, where vitamin D inhibits the renin-angiotensin system (RAS), reduces podocyte injury, and attenuates glomerulosclerosis, thereby potentially slowing the progression of DN (14,15).

Despite these plausible biological mechanisms, our results showed no significant correlation between vitamin D3 levels and HOMA-IR or other markers of insulin resistance across all groups. This lack of association is consistent with some prior reports, although it contradicts others that have found inverse relationships between 25-hydroxyvitamin D levels and insulin resistance indices. The discrepancy could be attributed to several factors, including the stage of nephropathy, variations in ethnicity, age, body mass index, duration of diabetes, and differences in the methods used to measure vitamin D (16,17).

Interestingly, we observed a significant positive

correlation between vitamin D3 and FBS specifically in the microalbuminuria group. This unexpected finding suggests a potential paradoxical relationship during early-stage nephropathy. One possible explanation is that vitamin D may exert differential effects at different stages of disease. In early DN, elevated fasting blood glucose may stimulate compensatory vitamin D activity to preserve insulin sensitivity and reduce inflammation, but this effect may diminish or be masked as renal function declines.

Another notable observation was the progressive elevation of renal dysfunction markers—such as serum creatinine, urea, ACR, and reduced GFR—with increasing severity of albuminuria. These findings are consistent with the established pathophysiology of DN and highlight the importance of monitoring these parameters in clinical practice.

Serum calcium levels were significantly higher in the macroalbuminuria group, possibly reflecting disturbances in mineral metabolism associated with CKD. Given that vitamin D plays a central role in calcium homeostasis, future studies should consider evaluating parathyroid hormone (PTH) levels to better understand the interplay between vitamin D, calcium, and phosphorus in DN.

The AMPK pathway is a key regulator of energy homeostasis, enhancing insulin sensitivity and exerting renoprotective effects by reducing oxidative stress and fibrosis (18,19). Emerging evidence suggests that vitamin D may activate AMPK in various tissues, potentially linking vitamin D status to improvements in metabolism and renal function (20). However, in our study, low vitamin D levels were not associated with improved insulin sensitivity, possibly due to impaired AMPK responsiveness in advanced DN or concurrent metabolic dysregulation.

Similarly, Sodium-glucose co-transporter 2 (SGLT2) inhibitors have shown renoprotective and metabolic benefits in T2DM, potentially through AMPK activation and improved mitochondrial function. Some studies suggest these agents may also influence vitamin D metabolism by improving renal function (21). However, our study did not include patients on SGLT2 inhibitors, limiting the generalizability of our findings to real-world populations. Future research should explore potential synergistic effects between vitamin D supplementation and newer antidiabetic therapies.

Several epidemiological and interventional studies support our findings. A meta-analysis by Li *et al*., (22) reported that vitamin D supplementation significantly improved glycemic control and insulin sensitivity in T2DM patients, particularly those with baseline vitamin D deficiency. Rohold *et al.*, (23) found an inverse association between 25(OH)D levels and the risk of developing T2DM and related complications. Zhou *et al*., (24) demonstrated that low vitamin D levels were independently associated with an increased risk of incident CKD and progression to ESRD.

However, the evidence is not entirely consistent, as Forouhi *et al*., (25) reported no beneficial effect of vitamin D supplementation on glycemic control in a prospective study, suggesting that the effects of vitamin D may be context-dependent or require specific baseline deficiencies.

Cao *et al*., (26) also failed to show significant improvements in renal outcomes with vitamin D analogs in patients with CKD, suggesting that the therapeutic window may be limited or that different formulations may be required.

Our findings are limited by the cross-sectional design, which precludes causal inference. We did not measure PTH or $1,25(OH)_2$ D, limiting our understanding of the functional vitamin D endocrine system. Additionally, factors such as sun exposure, dietary intake, BMI, and inflammation—known to influence vitamin D status—were not assessed. The study population was also geographically restricted, which may affect generalizability.

In conclusion, our study highlights the high burden of vitamin D deficiency in T2DM patients with nephropathy, particularly in advanced stages. While no direct association with insulin resistance was found, the unexpected correlation with FBS in early-stage DN suggests a potentially dynamic role for vitamin D during disease progression. These findings support the need for longitudinal and interventional studies to determine whether vitamin D supplementation could modulate early metabolic changes in patients at risk of DN, rather than serving as a marker of disease severity.

References

1. Ahmad E, Lim S, Lamptey R, Webb DR, Davies MJ. Type 2 diabetes. Lancet 2022;400:1803-20.
2. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci 2020;21:6275.
3. Selby NM, Taal MW. An updated overview of diabetic nephropathy: diagnosis, prognosis, treatment goals and latest guidelines. Diabetes Obes Metab 2020;22:3-15.
4. Avogaro A, Fadini GP. Microvascular complications in diabetes: a growing concern for cardiologists. Int J

Cardiol 2019;291:29-35.
5. Bhatti JS, Sehrawat A, Mishra J, Sidhu IS, Navik U, Khullar N, et al. Oxidative stress in the pathophysiology of type 2 diabetes and related complications: current therapeutic strategies and future perspectives. Free Radic Biol Med 2022;184:114-34.
6. Lee SH, Park SY, Choi CS. Insulin resistance: from mechanisms to therapeutic strategies. Diabetes Metab J 2022;46:15-37.
7. Contreras-Bolívar V, García-Fontana B, García-Fontana C, Muñoz-Torres M. Mechanisms involved in the relationship between vitamin D and insulin resistance: impact on clinical practice. Nutrients 2021;13:3491.
8. Yang Y, Zhang X, Bao M, Liu L, Xian Y, Wu J, et al. Effect of serum 25-hydroxyvitamin D3 on insulin resistance and β-cell function in newly diagnosed type 2 diabetes patients. J Diabetes Investig 2016;7:226-32
9. Del Gobbo LC, Song Y, Dannenbaum DA, Dewailly E, Egeland GM. Serum 25-hydroxyvitamin D is not associated with insulin resistance or beta cell function in Canadian Cree. J Nutr 2011;141:290-5.
10. Mitri J, Muraru M, Pittas A. Vitamin D and type 2 diabetes: a systematic review. Eur J Clin Nutr 2011;65:1005-15.
11. Bikle D. Vitamin D: production, metabolism, and mechanisms of action. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000.
12. Fenercioglu AK. The anti-inflammatory roles of vitamin D for improving human health. Curr Issues Mol Biol 2024;46:13514-25.
13. Dashti N, Einollahi N, Nabatchian F. Leptin and interleukin-6 in end-stage renal disease. Pak J Med Sci 2008;24:694-7.
14. Majidi Z, Hosseinkhani S, Amiri-Dashatan N, Emamgholipour S, Tutunchi S, Hashemi J, et al. Effect of rosiglitazone on circulating malondialdehyde (MDA) level in diabetes based on a systematic review and meta-analysis of eight clinical trials. J Investig Med 2021;69:697-703.
15. Soltani A, Aghakhani A, Dehghanbanadaki H, Majidi Z, Rezaei-Tavirani M, Shafiee G, et al. Association between liver fibrosis and osteoporosis in adults aged 50 and older: insights from the Bushehr Elderly Health Program. J Diabetes Metab Disord 2025;24:65.
16. Chiu KC, Chu A, Go VLW, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. Am J Clin Nutr 2004;79:820-5.
17. Gagnon C, Lu ZX, Magliano DJ, Dunstan DW, Shaw JE, Zimmet PZ, et al. Low serum 25-hydroxyvitamin D is associated with increased risk of metabolic syndrome at five years. J Clin Endocrinol Metab 2012;97:1953-61.
18. Safaie N, Idari G, Ghasemi D, Hajiabbasi M, Alivirdiloo V, Masoumi S, et al. AMPK activation: a potential strategy to mitigate TKI-induced cardiovascular toxicity. Arch Physiol Biochem 2024;1-13.
19. Wang Q, Sun J, Liu M, Zhou Y, Zhang L, Li Y. The new role of AMP-activated protein kinase in regulating fat metabolism and energy expenditure in adipose tissue. Biomolecules 2021;11:1757.
20. Chang E, Kim Y. Vitamin D ameliorates fat accumulation with AMPK/SIRT1 activity in C2C12 skeletal muscle cells. Nutrients 2019;11:2806.
21. Llorens-Cebrià C, Molina-Van den Bosch M, Vergara A, Jacobs-Cachá C, Soler MJ. Antioxidant roles of SGLT2 inhibitors in the kidney. Biomolecules 2022;12:143.
22. Li X, Liu Y, Zheng Y, Wang P, Zhang Y. The effect of vitamin D supplementation on glycemic control in type 2 diabetes patients: a systematic review and meta-analysis. Nutrients 2018;10:375.
23. Rohold CK, Jørgensen HL, Vojdeman FJ, Madsen CM, Olsen A, Heegaard AM, et al. Levels of plasma 25-hydroxy vitamin D and risk of developing type 2 diabetes in a large Danish primary health care population. Acta Diabetol 2025;62:397-404.
24. Zhou T, Shen L, Li Z, Jia J, Xing H, Wang N, et al. Severe 25-hydroxyvitamin D deficiency may predict poor renal outcomes in biopsy-proven diabetic nephropathy. Front Endocrinol 2022;13:871571.
25. Forouhi NG, Luan JA, Cooper A, Boucher BJ, Wareham NJ. Baseline serum 25-hydroxyvitamin D predicts future glycemic status and insulin resistance: the Ely Prospective Study 1990–2000. Diabetes 2008;57:2619-25.
26. Cao M, He C, Gong M, Wu S, He J. The effects of vitamin D on all-cause mortality in different diseases: an evidence-map and umbrella review of 116 randomized controlled trials. Front Nutr 2023;10:1132528.