



Original Article

Impact of 25(OH) Vitamin D and Insulin Resistance in Diabetic and Non-Diabetic Chronic Kidney Disease

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ABSTRACT

Background: Chronic kidney disease (CKD) is commonly associated with low 25-hydroxyvitamin D [25(OH)D] and insulin resistance, and diabetes can intensify both abnormalities.

Objectives: To compare 25(OH)D and insulin resistance between diabetic and non-diabetic CKD, and to examine the association of 25(OH)D with HOMA-IR and kidney function.

Methods: A comparative cross-sectional study was conducted on one hundred adults with CKD stages 3–5 were enrolled: diabetic CKD (D-CKD, n=50) and non-diabetic CKD (ND-CKD, n=50). Fasting glucose, fasting insulin, HbA1c, creatinine and serum 25(OH)D were measured. Estimated GFR (eGFR) was calculated and insulin resistance was assessed using HOMA-IR. Group comparisons, correlation analyses and multivariable linear regression were performed; $p < 0.05$ was considered significant.

Results: Mean age was 55.6 ± 11.2 years and 62% were males; 70% were in CKD stage 3–4. Mean 25(OH)D was 18.2 ± 7.6 ng/mL and was lower in D-CKD than ND-CKD (16.1 ± 7.1 vs 20.3 ± 7.6 ng/mL; $p=0.003$). Vitamin D deficiency (<20 ng/mL) was more frequent in D-CKD (76%) than ND-CKD (58%). HOMA-IR was higher in D-CKD than ND-CKD (4.1 ± 1.9 vs 2.3 ± 1.2 ; $p < 0.001$). 25(OH)D correlated inversely with HOMA-IR overall ($r = -0.46$; $p < 0.001$) and correlated positively with eGFR ($r = 0.29$; $p = 0.004$). After adjustment for age, sex, BMI, eGFR, CKD stage and diabetes status, 25(OH)D remained independently associated with lower HOMA-IR ($\beta = -0.08$ per 1 ng/mL; 95% CI -0.12 to -0.04 ; $p < 0.001$).

Conclusion: Vitamin D deficiency and insulin resistance were highly prevalent in CKD, with more marked abnormalities in diabetic CKD. The independent inverse association between 25(OH)D and insulin resistance supports routine metabolic and vitamin D evaluation in CKD care.

Keywords: chronic kidney disease; 25-hydroxyvitamin D; insulin resistance; HOMA-IR; diabetic CKD; eGFR.

INTRODUCTION

Chronic kidney disease (CKD) is a major non-communicable disease burden and is tightly linked to cardiovascular morbidity and premature mortality. Current CKD guidance recommends staging with estimated glomerular filtration rate (eGFR) to support risk stratification and treatment planning [1-3]. Diabetes mellitus remains a dominant driver of CKD progression and vascular complications, and diabetic kidney disease accounts for a substantial share of CKD care in tertiary hospitals. Beyond hyperglycaemia, CKD is accompanied by endocrine–metabolic derangements that worsen outcomes. Insulin resistance is increasingly recognised as an early abnormality in CKD and becomes more common as kidney function declines; skeletal muscle insulin signalling defects, inflammation and uremic toxins have been implicated [4-6]. In diabetic CKD, insulin resistance, adiposity and chronic inflammation often coexist and can amplify cardio-metabolic risk.

Vitamin D deficiency is also frequent in CKD. Limited sunlight exposure, dietary restrictions, obesity, urinary loss of vitamin D binding protein in proteinuric states, and reduced renal mass together contribute to low circulating 25-

hydroxyvitamin D [25(OH)D] levels [12]. Stage-wise evaluations demonstrate that deficiency rates increase with worsening CKD stage, with particularly high prevalence in stages 4–5 [10]. Clinically, serum 25(OH)D is the accepted marker for vitamin D status, and the Endocrine Society guideline defines deficiency as <20 ng/mL and sufficiency as ≥30 ng/mL [5]. In routine nephrology practice, vitamin D testing is often ordered for bone–mineral health, yet its extra-skeletal associations have become increasingly relevant.

A growing body of evidence connects vitamin D status with glucose metabolism. In a population-based analysis, lower 25(OH)D was associated with higher insulin resistance across strata of kidney function [6]. CKD-focused studies have also reported inverse relationships between 25(OH)D and insulin resistance in predialysis CKD, including non-diabetic CKD cohorts, and in dialysis settings [7]. These associations are biologically plausible because vitamin D influences insulin secretion, intracellular calcium handling, inflammatory pathways and adipokine profiles. Interventional evidence remains heterogeneous, but systematic reviews indicate that vitamin D supplementation can improve glycaemic indices and insulin sensitivity in selected populations, particularly among individuals with baseline deficiency. Data directly comparing diabetic and non-diabetic CKD patients using a uniform approach for 25(OH)D and HOMA-IR in Indian teaching hospitals remain limited. Clarifying whether diabetic CKD has a distinct vitamin D and insulin resistance profile, and whether 25(OH)D remains associated with insulin resistance after accounting for eGFR and body mass index (BMI), can inform practical screening strategies in CKD clinics.

Objectives: (1) To compare serum 25(OH)D levels and insulin resistance (HOMA-IR) between diabetic and non-diabetic adults with CKD stages 3–5; (2) to evaluate the correlation of 25(OH)D with HOMA-IR and eGFR; and (3) to assess the independent association between 25(OH)D and HOMA-IR after adjusting for demographic and clinical covariates.

MATERIALS AND METHODS

Study design and setting: A hospital-based comparative cross-sectional study was carried out at Government Siddhartha Medical College, Vijayawada, Andhra Pradesh, India, from 14th August 2025 to November 2025.

Participants and eligibility: Adults (≥18 years) with established CKD stages 3–5 attending outpatient clinics or admitted during the study period were screened consecutively. CKD staging was assigned using KDIGO eGFR categories [3], with eGFR estimated by the CKD-EPI creatinine equation [2]. Participants were grouped as diabetic CKD (D-CKD) or non-diabetic CKD (ND-CKD). Diabetes status was defined by documented diabetes treatment and/or American Diabetes Association diagnostic criteria [4]. Patients with acute kidney injury, pregnancy, active infection, malignancy, decompensated liver disease, and those receiving vitamin D supplementation or active vitamin D analogs within the preceding 3 months were excluded to reduce measurement bias.

Clinical and laboratory measurements: A structured proforma captured demographic data, comorbidities, CKD stage, and relevant medications. Height and weight were measured using standardized equipment and body mass index (BMI) was calculated (kg/m²). After an overnight fast (≥8 hours), venous blood was collected for fasting plasma glucose, fasting serum insulin, serum creatinine, and serum 25(OH)D. HbA1c was measured for glycemic characterization. Serum creatinine was measured by an enzymatic method traceable to isotope-dilution mass spectrometry. Serum 25(OH)D was measured using a chemiluminescence immunoassay. Vitamin D status was categorized using Endocrine Society thresholds [5]: severe deficiency (<10 ng/mL), deficiency (10–19.9 ng/mL), insufficiency (20–29.9 ng/mL), and sufficiency (≥30 ng/mL).

Assessment of insulin resistance: Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR) using the original formula [1]: $HOMA-IR = \text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glucose } (\text{mg/dL}) / 405$.

Sample size and outcomes: A pragmatic sample size of 100 (50 D-CKD and 50 ND-CKD) was planned to permit group comparisons and correlation analyses during the 4-month recruitment window. Primary outcomes were group differences in serum 25(OH)D and HOMA-IR. Secondary outcomes included correlations of 25(OH)D with HOMA-IR and eGFR, and multivariable predictors of HOMA-IR.

Ethical Considerations: Ethics Committee (IEC) approval was obtained from the Institutional Ethics Committee, Government Siddhartha Medical College, Vijayawada, Andhra Pradesh (IECSMCGGH/2025/AP/196 dates 02 August 2025), prior to initiation of the study, and written informed consent was obtained from all participants.

Statistical Analysis: Data were analyzed using standard statistical software. Continuous variables were summarized as mean ± SD or median (IQR) and compared using independent t-test or Mann–Whitney U test. Categorical variables were compared using chi-square test. Correlations were assessed using Pearson coefficients. Multivariable linear regression was performed with HOMA-IR as the dependent variable and 25(OH)D, diabetes status, BMI, age, sex, eGFR and CKD stage as covariates. A two-sided $p < 0.05$ was considered statistically significant.

RESULTS

A total of 100 adults with CKD stages 3–5 were included, comprising 50 patients with diabetic CKD (D-CKD) and 50 with non-diabetic CKD (ND-CKD). The overall mean age was 55.6 ± 11.2 years and 62% (n=62) were males. Seventy percent of participants were in CKD stage 3–4.

Baseline profile and kidney function: The D-CKD group was older than the ND-CKD group (57.9 ± 10.4 vs 53.3 ± 11.7 years; $p=0.041$) and had higher BMI (25.6 ± 3.7 vs 24.0 ± 3.3 kg/m²; $p=0.028$). Sex distribution, CKD stage distribution, eGFR and serum creatinine were comparable between groups (Table 1).

Table 1. Baseline profile and kidney function (n = 100)

Variable	Total (n=100)	D-CKD (n=50)	ND-CKD (n=50)	p-value
Age (years), mean \pm SD	55.6 ± 11.2	57.9 ± 10.4	53.3 ± 11.7	0.041
Male sex, n (%)	62 (62.0)	34 (68.0)	28 (56.0)	0.214
BMI (kg/m ²), mean \pm SD	24.8 ± 3.6	25.6 ± 3.7	24.0 ± 3.3	0.028
CKD stage 3, n (%)	38 (38.0)	16 (32.0)	22 (44.0)	0.215
CKD stage 4, n (%)	32 (32.0)	18 (36.0)	14 (28.0)	0.390
CKD stage 5, n (%)	30 (30.0)	16 (32.0)	14 (28.0)	0.657
eGFR (mL/min/1.73m ²), mean \pm SD	27.4 ± 11.6	25.8 ± 11.3	29.0 ± 11.7	0.169
Serum creatinine (mg/dL), median (IQR)	2.8 (2.1–4.1)	3.0 (2.2–4.3)	2.6 (2.0–3.9)	0.223

Vitamin D status: Mean serum 25(OH)D for the cohort was 18.2 ± 7.6 ng/mL. Vitamin D levels were significantly lower in D-CKD than ND-CKD (16.1 ± 7.1 vs 20.3 ± 7.6 ng/mL; $p=0.003$). Vitamin D deficiency (<20 ng/mL) was more frequent in D-CKD (76%) compared with ND-CKD (58%), and severe deficiency (<10 ng/mL) was also numerically higher in D-CKD (24% vs 12%) (Table 2).

Table 2. 25(OH) Vitamin D distribution (n = 100)

Vitamin D category	Total (n=100)	D-CKD (n=50)	ND-CKD (n=50)	p-value
Severe deficiency (<10 ng/mL), n (%)	18 (18.0)	12 (24.0)	6 (12.0)	0.112
Deficiency (10–19.9 ng/mL), n (%)	46 (46.0)	26 (52.0)	20 (40.0)	0.230
Insufficiency (20–29.9 ng/mL), n (%)	28 (28.0)	10 (20.0)	18 (36.0)	0.074
Sufficiency (\geq 30 ng/mL), n (%)	8 (8.0)	2 (4.0)	6 (12.0)	0.145
Mean 25(OH)D (ng/mL), mean \pm SD	18.2 ± 7.6	16.1 ± 7.1	20.3 ± 7.6	0.003

Insulin resistance and glycemic indices: Insulin resistance was higher in D-CKD than ND-CKD, with significantly elevated mean HOMA-IR (4.1 ± 1.9 vs 2.3 ± 1.2 ; $p<0.001$). Fasting glucose, fasting insulin and HbA1c were also higher in the diabetic CKD group (Table 3).

Table 3. Insulin resistance markers (n = 100)

Parameter	Total (n=100)	D-CKD (n=50)	ND-CKD (n=50)	p-value
Fasting glucose (mg/dL), mean \pm SD	118.6 ± 42.1	152.4 ± 38.6	84.8 ± 12.4	<0.001
Fasting insulin (μ IU/mL), mean \pm SD	15.1 ± 7.8	19.2 ± 7.6	11.0 ± 5.2	<0.001
HOMA-IR, mean \pm SD	3.2 ± 1.8	4.1 ± 1.9	2.3 ± 1.2	<0.001
HbA1c (%), mean \pm SD	6.7 ± 1.4	7.8 ± 1.2	5.6 ± 0.5	<0.001

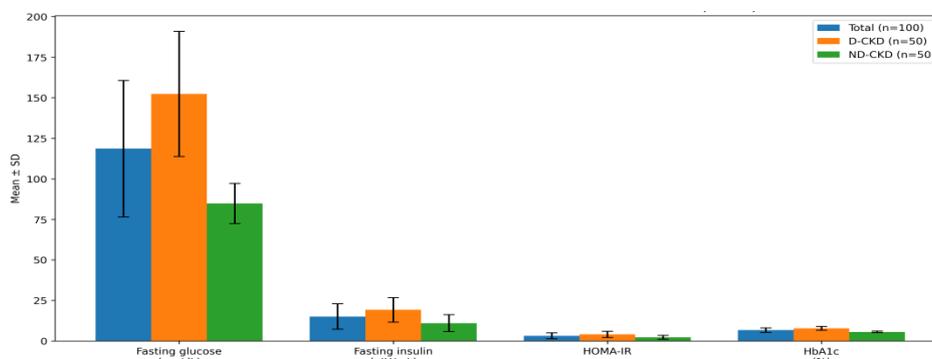
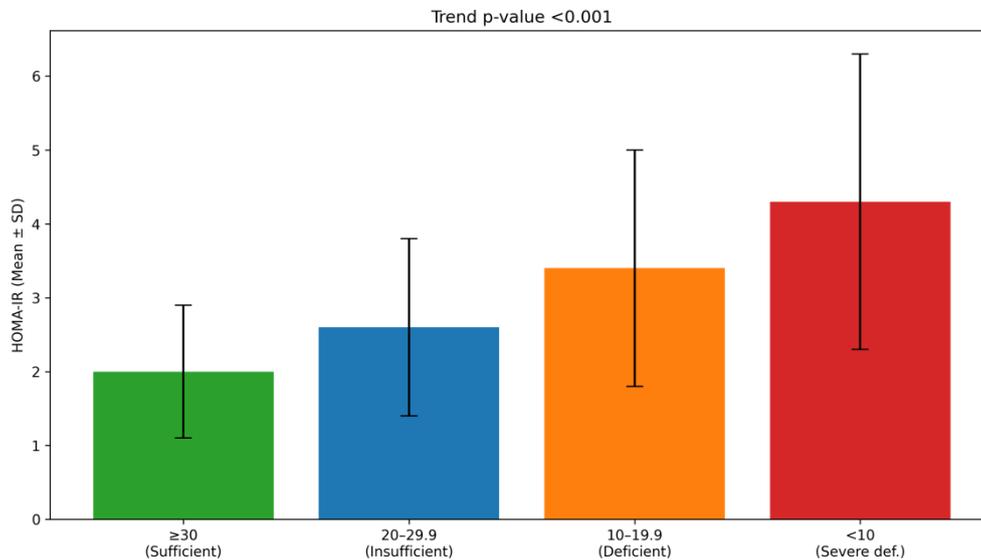


Figure 1: Insulin resistance markers in CKD: Total vs Diabetic vs Non Diabetic

Association between vitamin D and insulin resistance: In the overall cohort, 25(OH)D showed a significant inverse correlation with HOMA-IR ($r=-0.46$; $p<0.001$). Similar inverse associations were observed within both subgroups: D-CKD ($r=-0.41$; $p=0.003$) and ND-CKD ($r=-0.32$; $p=0.021$). Serum 25(OH)D correlated positively with eGFR ($r=0.29$; $p=0.004$). When stratified by vitamin D category, mean HOMA-IR increased stepwise with worsening vitamin D deficiency (p for trend <0.001) (Table 4).

Table 4. HOMA-IR by vitamin D category (n = 100)

Vitamin D category	n	HOMA-IR (mean ± SD)	p-value (trend)
≥30 ng/mL (sufficient)	8	2.0 ± 0.9	
20–29.9 ng/mL (insufficient)	28	2.6 ± 1.2	
10–19.9 ng/mL (deficient)	46	3.4 ± 1.6	
<10 ng/mL (severe deficient)	18	4.3 ± 2.0	<0.001

**Figure 2: HOMA-IR by 25(OH) Vitamin D category**

Multivariable analysis: In linear regression adjusting for age, sex, BMI, eGFR, CKD stage and diabetes status, 25(OH)D remained independently associated with lower HOMA-IR ($\beta=-0.08$ per 1 ng/mL increase; 95% CI -0.12 to -0.04 ; $p<0.001$). Diabetes status ($\beta=+1.20$; $p<0.001$) and BMI ($\beta=+0.10$ per kg/m^2 ; $p=0.012$) were independent predictors of higher HOMA-IR.

DISCUSSION

This comparative study of 100 adults with CKD stages 3–5 showed two consistent patterns: widespread vitamin D deficiency and substantial insulin resistance. Both abnormalities were more pronounced in diabetic CKD. Mean 25(OH)D in the cohort was in the deficient range, and the diabetic group had significantly lower 25(OH)D than the non-diabetic group, alongside markedly higher HOMA-IR and glycemic indices. The findings highlight that CKD and diabetes interact to magnify metabolic risk.

The inverse relationship between 25(OH)D and insulin resistance in our cohort aligns with prior population and CKD-specific evidence. Chonchol and Scragg, using NHANES data, reported that lower 25(OH)D was associated with higher HOMA-derived insulin resistance across strata of kidney function [6]. In CKD cohorts, similar inverse associations have been documented. A non-diabetic CKD study from Romania reported higher insulin resistance among patients with more severe 25(OH)D deficiency [7]. In another CKD cohort, insulin resistance correlated with both 25(OH)D and renal function, reinforcing a coupled metabolic–renal gradient [8]. Our subgroup correlations in both diabetic and non-diabetic CKD support the robustness of the relationship.

We also observed a modest positive correlation between 25(OH)D and eGFR, consistent with stage-related depletion described in CKD populations [10]. Reviews emphasize CKD-specific mechanisms that lower vitamin D stores, including reduced sun exposure, dietary constraints, urinary loss of vitamin D binding protein and impaired renal mass-dependent metabolism [12]. The diabetic group in our study had higher BMI, which can reduce circulating 25(OH)D through volumetric dilution and sequestration in adipose tissue and can independently worsen insulin resistance. BMI remained an independent predictor of HOMA-IR in our adjusted model, yet the association between 25(OH)D and HOMA-IR persisted after accounting for BMI and kidney function.

Biological plausibility exists for these findings. Vitamin D receptors are expressed in pancreatic β -cells, skeletal muscle and adipose tissue, and vitamin D has been linked to insulin secretion, intracellular calcium handling and inflammatory signalling. CKD itself promotes insulin resistance through inflammation, oxidative stress and post-receptor defects in skeletal muscle signalling pathways [13]. In this context, vitamin D deficiency can accompany insulin resistance and potentially contribute to it. The stepwise rise in HOMA-IR with worsening vitamin D category in our results is consistent with a dose–response pattern.

Clinically, these findings support routine assessment of vitamin D status and insulin resistance markers in CKD, especially when diabetes is present. While cross-sectional data do not establish causality, meta-analytic evidence in metabolic populations suggests that improving vitamin D status can improve insulin sensitivity and glycemic indices in deficient individuals [14]. High deficiency prevalence in CKD [10-12] and consistent observational associations justify prospective studies to test whether targeted repletion strategies translate into clinically meaningful metabolic and renal benefits.

Limitations

This study was single-centre with a short recruitment window, limiting external generalizability. The cross-sectional design prevents causal inference between 25(OH)D and insulin resistance. Albuminuria, dietary intake, sunlight exposure, parathyroid hormone, calcium and phosphate were not measured, so residual confounding remains. We relied on a single 25(OH)D measurement, and seasonal variation was not captured. The sample size limited subgroup analyses by CKD stage.

CONCLUSION

In adults with CKD stages 3–5, vitamin D deficiency and insulin resistance were common, and both were more pronounced in diabetic CKD than in non-diabetic CKD. Diabetic participants had lower mean 25(OH)D and higher fasting glucose, insulin, HbA1c and HOMA-IR. Across the cohort, 25(OH)D correlated inversely with HOMA-IR and positively with eGFR. In multivariable analysis, higher 25(OH)D remained independently associated with lower insulin resistance after adjustment for age, sex, BMI, CKD stage, eGFR and diabetes status. These findings support routine vitamin D assessment and integrated metabolic risk evaluation in CKD, and they justify prospective trials of correction strategies in practice.

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