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Evaluating the Role of the Calcitriol and Renal Indices in the Patients with the Chronic Renal Failure and their Correlation with the Impairments Severity

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ABSTRACT

Chronic kidney disease (CKD) alters vitamin D metabolism, but circulating 1,25-dihydroxyvitamin D [1,25(OH)$_2$D] is not a measure of vitamin D stores. This exploratory cross-sectional study examined its primary association with estimated glomerular filtration rate (eGFR) and secondary associations with urine albumin-to-creatinine ratio (ACR) and GFR categories in 53 complete records of patients with investigator-diagnosed CKD in Baghdad, Iraq. Analyses used Spearman's rank correlation with bootstrap confidence intervals (CIs), Kruskal–Wallis tests, and regression of natural-log-transformed 1,25(OH)$_2$D with HC3 robust standard errors, adjusted for age, sex, and log$_{10}$ ACR. Mean age was 61.0 ±17.1 years; 28 participants (52.8%) were male. Median eGFR was 41.0 mL/min/1.73 m² and median ACR was 533.0 mg/g. The reported 1,25(OH)$_2$D median was 2,279.5 fmol/L (interquartile range, 1,609.6–3,377.8), but assay identity, units, and calibration must be resolved before biological interpretation. Correlations were weak and nonsignificant for eGFR (ρ = 0.096; 95% CI, −0.165 to 0.341; P = .495) and ACR (ρ = 0.102; P = .466). Differences across G2–G4 categories were also nonsignificant (P = .442). The adjusted eGFR ratio was 1.115 per 10 mL/min/1.73 m² (95% CI, 0.984–1.264; P = .086). These exploratory estimates are inconclusive: nonsignificance does not establish absence of association. Assay and eligibility limitations preclude clinical classification or treatment recommendations. Validated assays and adequately powered prospective studies are needed.

Keywords: Chronic Kidney Disease, Calcitriol, 1,25-Dihydroxyvitamin D, Albuminuria, Cross-Sectional Study, Iraq

INTRODUCTION

Chronic kidney disease (CKD) is defined as the presence of structural or functional abnormalities for 3 or more months and is classified on the basis of its etiology, glomerular filtration rate concentration and albuminuria ([KDIGO], 2024). According to the Global Burden of Disease 2017 study, 697.5 million individuals are thought to have chronic kidney disease, with a all-stage prevalence of 9.1% (Bikbov et al., 2020).

CKD related deaths in 2017 were estimated 1.2 million (Bikbov et al., 2020). Describing the significance of CKD research, we should note that they are not prevalence estimates derived from the selected hospital cohort. CKD leads to perturbations in vitamin D metabolism. Hepatic hydroxylation produces 25-hydroxyvitamin D [25(OH)D], the main nutritional vitamin D status marker, which is hydroxylated to produce biologically active [1,25(OH)$_2$D; calcitriol] (Bikle, 2014; Kim & Kim, 2014). Activity of the kidney enzyme CYP27B1 leads to the activation of vitamin D, while the substrate availability, kidney function, parathyroid hormone level, calcium, phosphate and FGF23 regulates the catabolism of CYP24A1 (see discussions in Bilke et al., 2014 and Bosworth & de Boer, 2013). Administration of recombinant FGF23 in animal experiments led to lowered circulating 1,25(OH) 2 D, reduced renal 1α-hydroxylase expression and an upregulation of 24-hydroxylase expression (Shimada et al., 2004). In the Chronic Renal Insufficiency Cohort (CRIC), we identified higher FGF23 at increasing eGFR strata relative to against PTH or phosphate abnormalities but ultimately this cross-sectional pattern does not demonstrate within-person time order (Isakova et al., 2011).

Clinical studies have correlated vitamin D metabolites with indices of renal function. In the 1,814-person SEEK study, lower eGFR, higher urine albumin-to-creatinine ratio (ACR), and diabetes were independently associated with lower 1,25OH2D (Levin et al., 2007). Higher baseline levels of eGFR were also associated with higher circulating 1,25(OH)$_2$ (OH)$_2$D levels in a cohort of prospective CKD referrals (Ravani et al., 2009). Findings involving 24,25-dihydroxyvitamin D and 25(OH)D vary across kidney-function strata and clinical groups (Bosworth et al., 2012; Chonchol & Scragg, 2007; Mehrotra et al., 2008). These biomarkers are not interchangeable, thus, the 25(OH)D deficiency thresholds should not be adopted for measuring 1,25(OH)$_2$D measurements.

KDIGO guidance situates vitamin D assessment within the CKD–mineral and bone disorder (CKD-MBD) framework and emphasises serial assessment of calcium, phosphate, PTH, and alkaline phosphatase, with 25(OH)D measurement considered where appropriate, rather than interpreting isolated calcitriol results (KDIGO CKD-MBD, 2017). Interpretation in a small hospital-based study must therefore account for assay comparability, clinical heterogeneity. The aim of this study was to evaluate the primary cross-sectional association between reported serum 1,25(OH)$_2$D and eGFR in

53 patients with CKD, with secondary analyses of ACR and differences across G2–G4 categories.

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted at the Teaching Hospital in Baghdad, Iraq. This study incorporated 53 patients that were identified by investigators to have CKD. Exclusion criteria of the study protocol were primary hyperparathyroidism, previous parathyroidectomy, pregnancy and lactation. Eligibility for the analytical dataset was determined as age, sex, eGFR, and renal biochemistry, ACR, and serum $1,25(OH)_2D$. All of the 53 records were included for the selected variables; no imputation has been carried out. No clinical criteria for CKD or evidence of chronicity for at least 3 months were noted in the documentation retained. Two participants had eGFR ≥60 mL/min/1.73 m² and ACR <30 mg/g but without other documented markers of kidney damage. These investigator-classified CKD records were retained in the main analysis and removed in a separate sensitivity analysis. One of the participants was a 14-year-old child. Since adult CKD-EPI equations are meant to be used in individuals aged ≥18 years NIDDKD (2025), an additional sensitivity analysis was limited to adults. These sensitivity analyses examine the impact of the records on the reported estimates; it does not determine eligibility for CKD of the paediatric eGFR.

Sample Collection

The reported collection protocol appointed 5 mL of venous blood in a gel tube. Blood was clotting at room temperature for 20 minutes, then centrifuged at 3,000 rpm for 20 minutes to separate serum. Serum was used to test the urea and creatinine levels; about 0.5 mL alkio-alb, aliquots destined for vitamin D measurement, were placed in an Eppendorf tube at -20 ºC..

Morning urine samples were collected from fasting participants and transferred to test tubes. Samples were centrifuged at 3,000 rpm for approximately 4–5 minutes, and the supernatant was retained for urinary albumin and creatinine measurements.

Biochemical Measurements and Variable Definitions

Serum urea, serum creatinine, and urinary creatinine were assayed using kits identified in the study documentation as BIOLABO/MALZY, France. Microalbumin Test cartridges from AGAPPE Diagnostic, India were used to assess urinary albumin. Competitive enzyme-linked immunosorbent assays from Bioassay Technology Laboratory (BT LAB), China described in the protocol for $1,25(OH)_2D$ and 25(OH)D.

Recorded eGFR values were used without recalculation. The study documentation specified CKD-EPI but did not identify the equation version or creatinine standardisation. The 2009 creatinine-based and 2021 race-free CKD-EPI equations have distinct specifications, so the equation used cannot be inferred from the recorded values (Inker et al., 2021; Levey et al., 2009). GFR categories were assigned from recorded eGFR as G2, 60–89; G3a, 45–59; G3b, 30–44; and G4, 15–29 mL/min/1.73 m². Albuminuria categories were assigned from recorded ACR as A1, <30; A2, 30–<300; and A3, ≥300 mg/g (KDIGO, 2024). No records were classified as G1 or G5. Combined GFR–albuminuria categories were derived from these numerical values rather than the inconsistent pre-existing category label. Recorded ACR was used in the main analyses; ACR recalculated from the urinary components was examined separately in sensitivity analysis using Equation (1).

$$\text{ACR (mg/g)} = [\text{urinary albumin (mg/dL)} / \text{urinary creatinine (mg/dL)}] \times 1{,}000 \quad (1)$$

Statistical Analysis

Analyses used all 53 records complete for the selected variables, without imputation. Spearman's rank correlations with reported serum $1,25(OH)_2D$ were estimated with percentile 95% CIs from 10,000. The primary eGFR correlation was not adjusted for multiple testing; Benjamini–Hochberg q values were calculated for six secondary correlations. Reported $1,25(OH)_2D$ and ACR were compared across G2–G4 categories using Kruskal–Wallis tests. Multivariable ordinary least-squares regression modelled natural-log-transformed reported $1,25(OH)_2D$ as a function of eGFR, age, sex, and $\log_{10}$ ACR, as specified in Equation (2). HC3 heteroscedasticity-consistent robust standard errors and t-based 95% CIs were used. Exponentiated coefficients were presented as geometric-mean ratios, with eGFR and age expressed per 10-unit increment. Sensitivity analyses separately excluded the paediatric record, the two G2A1 records, and the highest vitamin D measurement, and examined recalculated ACR. All tests were two-sided, and all analyses were exploratory.

$$\ln(Y_i) = \beta_0 + \beta_1(eGFR_i/10) + \beta_2(age_i/10) + \beta_3 male_i + \beta_4 \log_{10}(ACR_i) + \varepsilon_i \quad (2)$$

Here, Y_i is the reported serum $1,25(OH)_2D$ value in the supplied fmol/L unit, $eGFR_i$ is expressed in mL/min/1.73 m², age_i in years, ACR_i in mg/g, and $male_i$ is coded 1 for male and 0 for female. β_0 is the intercept, β_1–β_4 are regression coefficients, and ε_i is the residual. Ratios are $\exp(\beta_1)$ per 10-unit higher eGFR, $\exp(\beta_2)$ per 10 years, $\exp(\beta_3)$ for male versus female, and $\exp(\beta_4)$ per 10-fold higher ACR.

Ethics Approval

Ethical approval was obtained from Ibn Sina University of Medical and Pharmaceutical Sciences. Study procedures were reported to comply with institutional and national ethical requirements and the Declaration of Helsinki and its subsequent revisions.

RESULTS AND DISCUSSION

Patient Characteristics and Data Quality

All 53 linked records were complete for the selected variables. Mean age was 61.0 ±17.1 years, with a median of 62.0 years and a range of 14–90 years. There were 28 male participants (52.8%) and 25 female participants (47.2%). GFR categories comprised 8 patients (15.1%) in G2 and 15 patients (28.3%) in each of G3a, G3b, and G4. Most participants had A3 albuminuria (35; 66.0%), compared with 15 (28.3%) in A2 and 3 (5.7%) in A1 (Table 1).

Table 1: Overall Characteristics of the 53 Patient Records

Variable	Median (IQR) or n (%)	Range
Age (years)	62.0 (53.0–70.0)	14.0–90.0
eGFR (mL/min/1.73 m²)	41.0 (27.0–54.0)	15.0–87.0
Serum urea (mg/dL)	73.2 (55.2–102.0)	24.0–198.7
Serum creatinine (mg/dL)	1.62 (1.30–1.99)	0.92–4.80
Urinary creatinine (mg/dL)	35.52 (23.98–86.87)	8.37–497.51
Urinary albumin (mg/dL)	22.50 (10.60–82.00)	0.50–283.00
ACR (mg/g)	533.0 (235.0–2,570.0)	10.6–15,338.0
1,25(OH)₂D (fmol/L)*	2,279.5 (1,609.6–3,377.8)	779.9–29,039.3
Male sex	28 (52.8%)	—
Female sex	25 (47.2%)	—

Two G2A1 participants had no additional documented markers of kidney damage. One pre-existing combined category label was G2A3, whereas the recorded eGFR of 81 mL/min/1.73 m² and ACR of 252.57 mg/g corresponded to G2A2; classification by the numerical values was used. Another participant had a recorded ACR of 1,174.0 mg/g and a recalculated ACR of 1,835.0 mg/g.

Vitamin D Measurements across GFR Categories

The reported serum 1, 25(OH)₂D (lowest number, 779.9 fmol/L to mean, 29,039.3 fmol/L) (median, 2,279.5; IQR, 1,609.6–3,377.8); The unit, supplied, remains unverified. Highest Medians in G2, substantial overlap across categories and no monotonic trend across the other groups. The Kruskal-Wallis statistic was H = 2.687 with 3 degrees of freedom (P = 0.442). ACR varied across the same categories (H = 16.800; P < 0.001). These are shown in Table 2 and Figure 1. The Per Figure 1 that uses a logarithmic vertical axis incorporates the highest value overall, 29,039.3 fmol/L, into G3b.

Table 2: Renal Indices and Vitamin D across GFR Categories

Category	n	eGFR	1,25(OH)₂D*	ACR
G2	8	71.0 (65.8–75.8)	3,566.6 (2,305.7–4,913.4)	48.4 (36.1–131.9)
G3a	15	50.0 (47.5–54.5)	2,043.8 (1,269.5–3,088.9)	303.4 (168.1–510.6)
G3b	15	36.0 (32.0–40.5)	2,246.6 (1,379.9–3,833.3)	879.5 (280.5–1,999.5)
G4	15	22.0 (18.5–24.5)	2,279.5 (1,737.0–2,500.0)	1,488.0 (721.5–5,399.0)

*The 1, 25(OH)₂D unit remains unverified. For 1, 25(OH)₂D: H = 2.687, P = 0.442; for ACR: H = 16.800, P < 0.001; exploratory Kruskal–Wallis tests with 3 degrees of freedom.

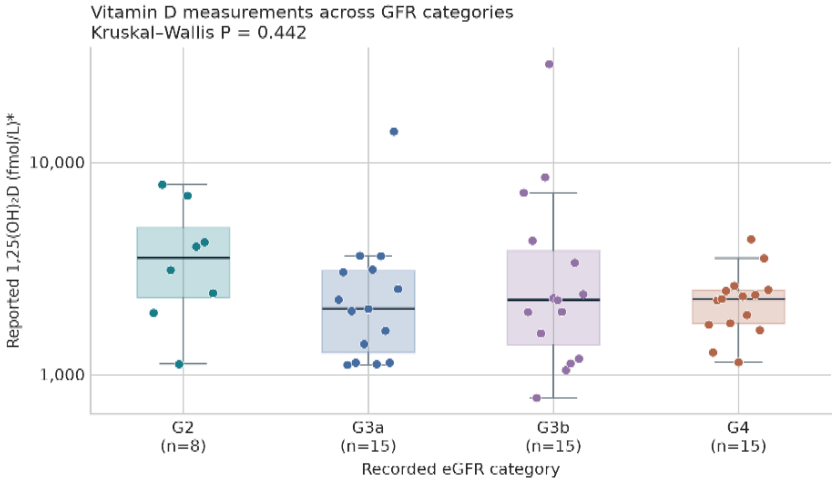


Figure 1: Serum 1,25(OH)₂D by GFR category. Y-axis is on a log scale. Boxes show the median and interquartile range (IQR); whiskers go to the most extreme observation that's no more than 1.5 times the IQR of the quartiles. Each data point is a patient observation; the largest value in G3b is 29,039.3 fmol/L

Bivariate Associations

The correlation between reported serum 1, 25(OH)₂D and eGFR was weak and nonsignificant (ρ = 0.096; 95% CI, −0.165 to 0.341; P = 0.495). The ACR correlation was also weak and nonsignificant (ρ = 0.102; 95% CI, −0.187 to 0.379; P = 0.466). These estimates are inconclusive and do not establish equivalence or absence of association. Table 3 summarises the correlation estimates, and Figure 2 displays the individual values. Age had a negative unadjusted correlation (ρ = −0.340; P = 0.013), but this did not meet the false-discovery-rate threshold after adjustment for the six secondary comparisons (q = 0.077).

Table 3: Spearman's Rank Correlations with Serum 1, 25(OH)₂D (N = 53)

Variable	ρ	95% CI	P	q
eGFR (mL/min/1.73 m²)	0.096	−0.165 to 0.341	0.495	Not adjusted
Age (years)	−0.340	−0.574 to −0.064	0.013	0.077
Serum urea (mg/dL)	−0.149	−0.416 to 0.134	0.286	0.699
Serum creatinine (mg/dL)	−0.002	−0.269 to 0.265	0.987	0.987
Urinary creatinine (mg/dL)	0.003	−0.271 to 0.278	0.981	0.987
Urinary albumin (mg/dL)	0.119	−0.183 to 0.402	0.395	0.699
ACR (mg/g)	0.102	−0.187 to 0.379	0.466	0.699

CIs are percentile intervals from 10,000 paired bootstrap resamples. P values are from two-sided asymptotic Spearman tests. Benjamini–Hochberg q values are reported for six secondary correlations; the primary eGFR correlation was not adjusted.

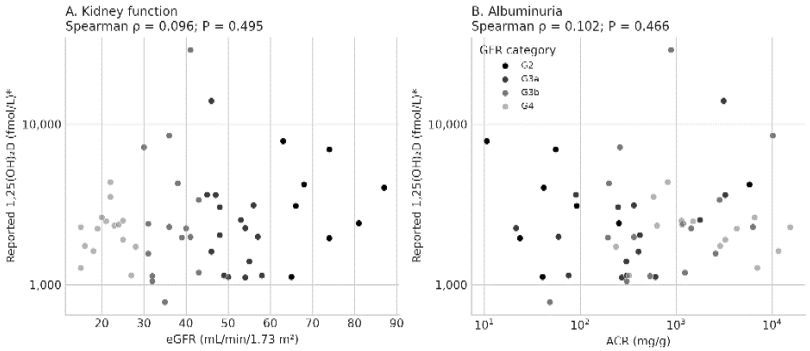


Figure 2: Sera 1,25(OH)₂D levels associated with eGFR (Fig. a) and ACR (Fig. b). Each point represents a patient record. GFR groupings are color-coded by shades of grey, from darkest to lightest: G2, G3a, G3b, and G4 (the legend uses the same scheme). The 1,25(OH)₂D axes and the ACR axis are logarithmic. The asterisk the unconfirmed supplied unit fmol/L. The displayed P values are from unadjusted Spearman tests; the ACR correlation has Benjamini–Hochberg q value 0.699

Multivariable Regression

After adjustment for age, sex, and $\log_{10}$ ACR, each 10 mL/min/1.73 m² higher eGFR was associated with a geometric-mean ratio of 1.115 for serum 1, 25(OH)₂D (95% CI, 0.984–1.264; P = 0.086). Although the point estimate was positive, its confidence interval included unity. The geometric-mean ratio for ACR per 10-fold increase was 1.154 (95% CI, 0.784–1.698; P = 0.461). The confidence intervals for age and sex also included unity. Model R^2 was 0.146, and adjusted R^2 was 0.075. Table 4 and Figure 3 present the adjusted estimates.

Table 4: Adjusted Linear Regression of Natural-Log-Transformed Serum 1, 25(OH) ₂D

Predictor	β	HC3 SE	Geometric-mean ratio (95% CI)	P
eGFR, per 10 mL/min/1.73 m²	0.109	0.062	1.115 (0.984 to 1.264)	0.086
Age, per 10 years	−0.116	0.081	0.890 (0.756 to 1.049)	0.160
Male versus female	−0.177	0.194	0.838 (0.568 to 1.237)	0.366
ACR, per 10-fold increase	0.143	0.192	1.154 (0.784 to 1.698)	0.461

n = 53; R^2 = 0.146; adjusted R^2 = 0.075. β denotes the natural-log-scale regression coefficient. HC3 SE.

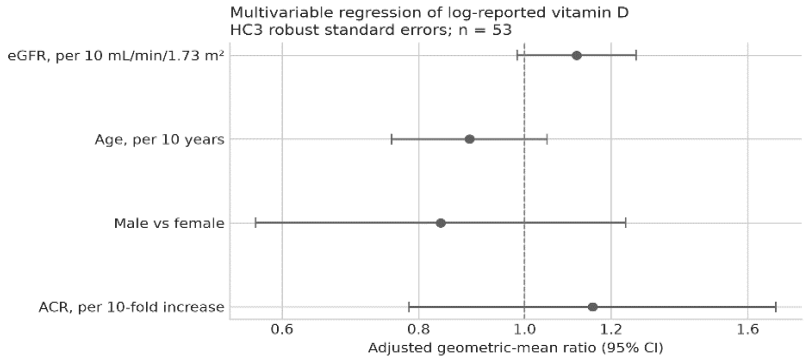


Figure 3: Exponentiated coefficients and 95% confidence intervals (CIs) from the regression of natural-log-transformed reported serum 1,25(OH)₂D, adjusted for the other displayed covariates. Points and intervals are presented in grayscale. HC3 robust standard errors and t-based intervals were used

Sensitivity Analyses

The highest serum 1, 25(OH)$_2$D corresponded to the record with the largest Cook's distance (0.308); five records exceeded the conventional screening threshold of 4/n. Excluding this measurement yielded an adjusted eGFR ratio of 1.110 (95% CI, 0.981–1.256; P = 0.097). Restriction to adults, exclusion of the two G2A1 records, and use of recalculated ACR yielded similar estimates. All confidence intervals for the eGFR estimates in the sensitivity analyses included unity (Table 5).

Table 5: Sensitivity Analyses of the Egfr–Vitamin D

Analysis	n	ρ	P, ρ	Adjusted ratio (95% CI)	P, model
Main analysis	53	0.096	0.495	1.115 (0.984 to 1.264)	0.086
Adults only	52	0.085	0.549	1.122 (0.989 to 1.273)	0.072
Exclude two G2A1 records	51	0.073	0.610	1.117 (0.986 to 1.265)	0.080
Exclude highest vitamin D value	52	0.098	0.491	1.110 (0.981 to 1.256)	0.097
Recalculated ACR	53	0.096	0.495	1.116 (0.985 to 1.264)	0.083

Adjusted ratios are expressed per 10 mL/min/1.73 m² higher eGFR, with adjustment for age, sex, and $\log_{10}$ ACR. Exclusions were applied separately. The recalculated ACR analysis included all participants and used Equation (1).

Discussion

In this exploratory analysis of 53 investigator-diagnosed CKD records, reported serum 1,25(OH)$_2$D showed weak, nonsignificant correlations with eGFR (ρ = 0.096; P = 0.495) and ACR (ρ = 0.102; P = 0.466) with overlapping values across G2–G4 categories. The adjusted eGFR ratio was 1.115 (95% CI, 0.984–1.264; P = 0.086). These estimates are not contradictory but are no stronger than pure noise. Assay harmonization, units and calibration needed to interpret biologically relevant concentration, or are comparable to other studies in magnitude.

As part of the observational SEEK study 1,814 participants were identified to have lower eGFR, higher ACR, and diabetes as independent predictors of lower concentrations of calcitriol (Levin et al., 2007). A parametric current prospective cohort of 168 CKD referrals, baseline 1,25(OH)$_2$D correlated positively with eGFR (r = 0.46; P < 0.001), and these adjusted dialysis and mortality analyses were focused primarily on 25(OH)D (Ravani et al., 2009). In contrast the present study did not identify a comparable clear unadjusted association. However, differences in sample size, recruitment, clinical characteristics, correlation methods, and assay-specific reporting limit comparison. And the definition of low calcitriol used in the SEEK study as it relates to its assay was not validated for the concentrations reported in this analysis.

Studies of other vitamin D metabolites provide complementary, not interchangeable, evidence. In a 278 participant CKD cohort, lower eGFR was linked to lower 24,25-dihydroxyvitamin D, a marker of vitamin D catabolism (Bosworth et al., 2012). Altered activation, transport of its substrates, and catabolism may coexist in CKD (Bosworth & de Boer, 2013), but the single vitamin D variable in the dataset used in the current project does not allow us to tease apart these pathways.

Observational studies examined 25(OH)D in relation to kidney function and clinical characteristics (Chonchol & Scragg, 2007; Mehrotra et al., 2008). Their findings concern nutritional vitamin D status rather than circulating calcitriol. Accordingly, their concentration thresholds and deficiency classifications were not applied to the present 1,25(OH)$_2$D measurements.

A study of 61 children receiving dialysis, with 40 controls, reported a bimodal association between 1,25(OH)$_2$D and vascular measures; all dialysis patients were prescribed alfacalcidol (Shroff et al., 2008). This treated paediatric population differs from the present predominantly adult sample. The current analyses do not establish a nonlinear or bimodal relationship.

In CRIC/Hispanic CRIC, FGF23 was inversely associated with eGFR and, in a subset, with calcitriol (Isakova et al., 2011). FGF23 abnormalities occurred at higher eGFR strata than PTH or phosphate abnormalities. This cross-sectional comparison describes differences across participants rather than serial progression within individuals and cannot establish temporal precedence in the present cohort.

Experimental evidence provides pathway context rather than a human causal explanation. Recombinant FGF23 reduced circulating 1,25(OH)$_2$D, downregulated renal CYP27B1 mRNA, and upregulated CYP24A1 mRNA in animals (Shimada et al., 2004). These findings are consistent with reviews of PTH stimulation and FGF23-mediated inhibition of renal calcitriol production (Bikle, 2014; Kim & Kim, 2014). Without linked FGF23, PTH, calcium, phosphate, or 25(OH)D measurements, the present study cannot attribute its findings to a specific regulatory mechanism.

The present observational ACR correlation must be distinguished from randomised evidence on vitamin D receptor activation. VITAL randomised 281 patients with type 2 diabetes and albuminuria to paricalcitol or placebo for 24 weeks. The combined paricalcitol groups had a between-group ACR difference of −15% (95% CI, −28% to 1%; P = 0.071) (de Zeeuw et al., 2010). This intervention estimate neither tests the endogenous calcitriol–ACR correlation nor establishes treatment implications for the present measurements.

PRIMO and OPERA similarly evaluated paricalcitol interventions rather than endogenous vitamin D correlations. In PRIMO, 227 patients were followed for 48 weeks; OPERA included 60 patients with CKD and left ventricular hypertrophy followed for 52 weeks. Both trials reduced PTH but did not demonstrate significant improvement in their primary left ventricular mass outcomes (Thadhani et al., 2012; Wang et al., 2014). These findings cannot be used to infer causality from the present cross-sectional associations.

Systematic reviews further distinguish biochemical responses from clinical outcomes. Nutritional vitamin D supplementation increased 25(OH)D and reduced PTH, while calcitriol findings were heterogeneous (Kandula et al., 2011). Active vitamin D increased hypercalcaemia risk in placebo-controlled trials involving non-dialysis CKD with secondary hyperparathyroidism (Cozzolino et al., 2021). These treatment effects do not define the clinical meaning of an isolated endogenous calcitriol measurement.

This review of 128 randomised studies including 11,270 adults with CKD found that vitamin D therapy probably had little or no impact on all-cause mortality (risk ratio 1.04; 95% CI, 0.84–1.24), while effects on fracture, cardiovascular and kidney outcomes were uncertain (Yeung et al., 2023).

Consistent with contemporary CKD-MBD assessment (KDIGO CKD-MBD, 2017), the present exploratory findings fail to support vitamin D deficiency classification or recommendations for supplementation or calcitriol treatment.

Strengths, Limitations, and Implications

The analysis used all 53 records complete for the selected variables, with bootstrap intervals, HC3 robust regression inference, and separate sensitivity analyses. These approaches describe uncertainty and the influence of selected records but do not establish assay validity or clinical eligibility. The principal limitations are the small, single-centre, cross-sectional sample; the 14-year-old participant; and two G2A1 records without additional documented kidney damage. Recruitment details, dialysis and medication exposure, the exact CKD-EPI equation. The findings therefore remain exploratory, and nonsignificant estimates should not be interpreted as established null relationships.

CONCLUSION

In this exploratory cross-sectional analysis of 53 investigator-diagnosed CKD records, reported serum 1,25(OH)$_2$D had weak, nonsignificant correlations with eGFR and ACR, with no significant differences across G2–G4 categories. The adjusted eGFR ratio of 1.115 (95% CI, 0.984–1.264; P = 0.086) remained inconclusive and did not establish absence of association. Unresolved assay identity, units, and calibration, together with incomplete CKD chronicity documentation and the paediatric and G2A1 eligibility issues, limit biological and clinical interpretation. These findings do not support vitamin D deficiency classification or treatment recommendations. Adequately powered prospective studies using validated assays and clearly documented CKD eligibility are needed.

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