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"Study of vitamin D status in chronic kidney disease patients and its correlation with the severity of chronic kidney disease in Gwalior region at tertiary care centre"

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Background: Vitamin D deficiency is highly prevalent in patients with chronic kidney disease (CKD) and contributes significantly to metabolic, skeletal, cardiovascular, and immunological complications. Impaired renal conversion of 25-hydroxyvitamin D to its active form, reduced sun exposure, dietary restrictions, and chronic inflammation predispose CKD patients to hypovitaminosis D, which worsens with disease progression.

Objectives: To assess serum vitamin D status in CKD patients and to evaluate its correlation with demographic factors, CKD severity, renal biochemical markers, and the effect of hemodialysis on vitamin D levels.

Methods: This prospective observational study was conducted at a tertiary care centre in Gwalior, India, from May 2023 to April 2025, including 180 CKD patients. Serum 25(OH)D levels were measured using chemiluminescent immunoassay (CLIA). Renal function was assessed using serum urea, creatinine, and estimated glomerular filtration rate (eGFR) calculated by the MDRD equation. CKD staging was done according to KDIGO guidelines. Statistical analysis was performed using IBM SPSS version 26.0.

Results: The mean age of patients was 44.64 ± 14.94 years, with male predominance (57.8%). Vitamin D deficiency was observed in 72.8% of patients, while only 7.8% had sufficient levels. More than half of patients (52.78%) were in Stage V CKD. A significant association was found between CKD stage and vitamin D deficiency ($p < 0.0001$). Vitamin D levels showed negative correlation with serum creatinine and urea and positive correlation with eGFR. In hemodialysis patients, deficiency remained highly prevalent despite a statistically significant post-dialysis rise in vitamin D levels.

Conclusion: Vitamin D deficiency is highly prevalent in CKD patients and worsens with disease severity and declining renal function. Routine screening and early supplementation should be integrated into standard CKD management to improve clinical outcomes.

Keywords: Chronic kidney disease, Vitamin D deficiency, eGFR, Hemodialysis, Renal dysfunction, Hypovitaminosis D.

Introduction: Vitamin D is an essential micro-nutrient that plays a crucial role in maintaining the health of bones, muscles, the nervous system, and the immune system[1]. Historically recognized primarily for its role in bone homeostasis, Vitamin D has recently been "rediscovered" as a multifunctional or "pleiotropic" vitamin. Beyond skeletal health, it has been implicated in the regulation of various physiological systems, including the cardiovascular,

endocrine, and immune systems[2]. Due to its broad biological activity and the increasing global prevalence of Vitamin D deficiency, there has been a surge in scientific interest and research focused on Vitamin D in recent years. CKD is the one of the non-communicable diseases that closely associated with Vitamin D deficiency. In addition to its classical roles in calcium and phosphate regulation, Vitamin D exhibits important antibacterial, anti-inflammatory, and immunomodulatory properties, which collectively contribute to its renoprotective effects[3]. CKD represents a major global health burden, affecting approximately 5–10% of the world's population[4]. According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is diagnosed based on an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² and/or the presence of structural or functional abnormalities of the kidneys persisting for more than three months [5,6]. CKD is classified into five stages based on eGFR values, with higher stages indicating progressively advanced renal dysfunction [6].

A clear understanding of CKD and its classification is essential for accurate diagnosis and appropriate management, as outlined by the National Kidney Foundation (NKF). The eGFR remains the best overall indicator of renal function in stable, non-hospitalized patients [7].

Kidney damage is defined by the presence of one or more of the following criteria:

- Pathological abnormalities in kidney tissue
- Persistent proteinuria
- Abnormal urine findings (e.g., hematuria)
- Structural abnormalities detected on imaging studies
- eGFR <60 mL/min/1.73 m² on at least two occasions, 90 days apart, not associated with reversible conditions such as dehydration or acute illness[8]

The commonly used method to estimate GFR is the four-variable Modification of Diet in Renal Disease (MDRD) equation, which calculates eGFR based on serum creatinine, age, gender, and ethnicity[9]. CKD is a strong predictor of premature cardiovascular morbidity and mortality. Disturbances in mineral metabolism are common as CKD progresses and are linked to complications such as bone loss, vascular calcification, cardiovascular disease, immune dysfunction, and increased mortality[10,11]. A critical metabolic consequence of CKD is the impaired renal synthesis of calcitriol (1,25-dihydroxyvitamin D), primarily due to decreased

renal mass and reduced activity of the enzyme 1α-hydroxylase. Emerging evidence suggests that hypovitaminosis D not only results from CKD but can also contribute to its progression. Patients with CKD often exhibit Vit. D deficiency due to their diminished ability to convert 25(OH)D to $1,25(OH)_2D$, the active hormonal form of Vit. D[11].

According to the Endocrine Society guidelines, serum 25(OH)D levels are interpreted as follows: • Sufficiency: >30 ng/mL • Insufficiency: 20–30 ng/mL • Deficiency: <20 ng/mL • Severe deficiency: <10 ng/mL

The KDIGO 2017 guidelines recommend maintaining serum 25(OH)D levels above 30 ng/mL in

CKD patients, across all stages, to mitigate complications associated with CKD–Mineral and Bone

Disorder (CKD–MBD) and to improve clinical outcomes.[12,13]

Objectives

Primary Objective

- To study vitamin D status in chronic kidney disease patients.

Secondary Objectives

- To assess vitamin D levels in CKD patients in the predialysis stage.
- To evaluate vitamin D status in post-dialysis patients.
- To study changes in serum vitamin D levels with severity of CKD.
- To correlate hypo/hypervitaminosis D with CKD stage and disease severity.

Materials and Methods

Study Design: Prospective observational study

Study Centre: Department of Pathology, Gajra Raja Medical College, Gwalior (M.P.)

Study Duration: May 2023 to April 2025 (2 years)

Sample Size: 180 CKD patients

Study Population: Patients admitted in the Departments of Medicine and Nephrology, J.A. Group of Hospitals, Gwalior.

Sample size: A total of 180 CKD patients were included in the study using a standard sampling technique. From the study of Arulananthan (2016) the overall prevalence of vitamin D deficiency among the CRF patient 69% and 5% level of significance and 95% confidence absolute precision of 10% and sample size calculated by formula:

$$N = z^2\alpha_{/2} \times p \times q \ /d^2$$

$$N = 2 \times 69 \times 31/6.9^2 = 180$$

Inclusion Criteria

- All diagnosed CKD patients admitted during the study period in Jayarogya group of hospital, Department of Medicine and Department of Nephrology.

Exclusion Criteria

- Pediatrics patients (<15 years)
- Patients receiving vitamin D supplementation
- Patients on chemotherapy for malignancy

Laboratory Evaluation

- Serum vitamin D measured using Access 25(OH) Vitamin D Total Assay (CLIA method)
- Serum urea and creatinine measured using Beckman Coulter Analyzer
- eGFR calculated using MDRD equation
- CKD staging done according to KDIGO classification

Sample Collection and Processing: Venous blood samples (2–5 mL) were collected aseptically from the antecubital vein into serum separator tubes. In dialysis patients, samples were collected 30 minutes before and immediately after the dialysis session. Samples were allowed to clot at room temperature and centrifuged at 3000–3500 rpm for 10–15 minutes to obtain serum. All samples were processed within one hour of collection.

Laboratory Analysis: Serum 25-hydroxyvitamin D [25(OH)D], serum urea, and serum creatinine were measured using a Beckman Coulter automated analyzer. Vitamin D estimation was performed using the Access 25(OH) Vitamin D Total assay based on a competitive

chemiluminescent immunoassay (CLIA) principle. Serum creatinine was measured by the kinetic Jaffé method, and serum urea was estimated using the urease–GLDH enzymatic method.

Calibration and Quality Control: Calibration was performed using manufacturer-provided calibrators according to standard protocols. Internal quality control was maintained using low, medium, and high concentration controls, and all assays were performed only after quality control values were within acceptable ranges.

Renal Function Assessment: Estimated glomerular filtration rate (eGFR) was calculated using the MDRD equation, and CKD staging was done according to KDIGO classification.

Interpretation of Results: Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20–30 ng/mL), sufficient (30–100 ng/mL), and toxicity risk (>100 ng/mL).

Statistical Analysis: Data were analyzed using IBM SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation. Statistical significance was assessed using appropriate tests, and a p-value <0.05 was considered statistically significant.

Result: The study population had a mean age of 44.64 ± 14.94 years, indicating that chronic kidney disease predominantly affected individuals in the economically productive middle-age group. The most common age group was 31–40 years (25.6%), followed by 41–50 years (22.8%).
Gender distribution revealed a male predominance, with 57.8% males and 42.2% females,

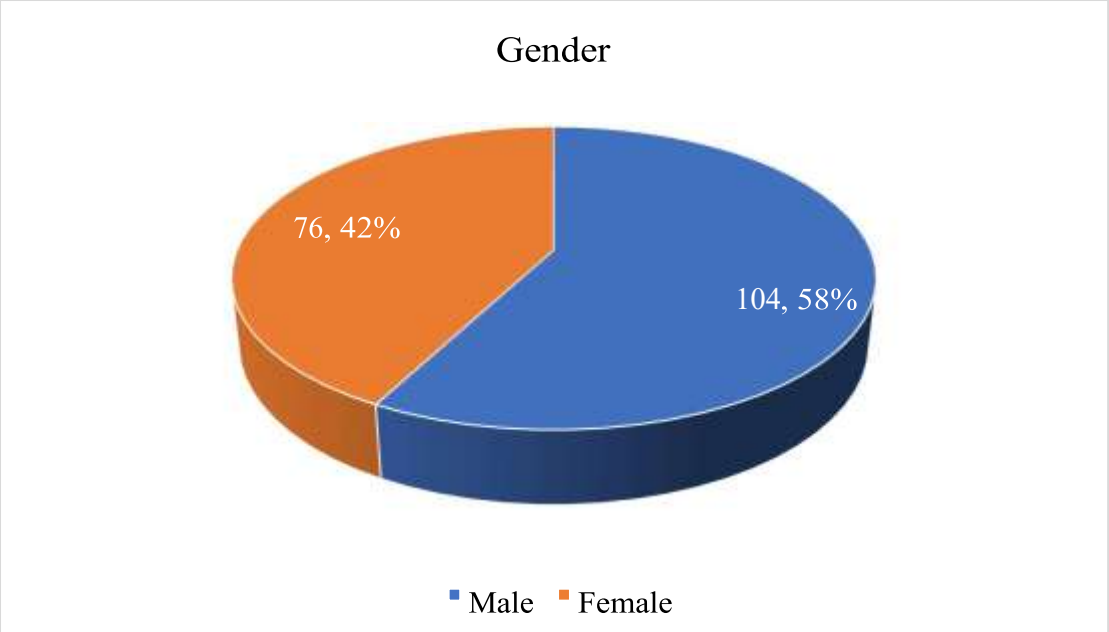

Fig. 1: showing distribution of study population according to Gender

Table 1: Summary of Demographic, Biochemical Parameters, Vitamin D Status, and Renal Function in CKD Patients (180)

Parameter	Findings
Age Distribution	Most common: 31–40 years (25.56%)
Gender Distribution	Male: 104 (57.78%)Female: 76 (42.23%)
Serum Urea (mg/dL)	Mean ± SD: 153.40 ± 79.53 (Min: 34.70, Max: 390.00)
Serum Creatinine (mg/dL)	Mean ± SD: 5.17 ± 3.12 (Min: 0.80, Max: 12.70)
eGFR (mL/min/1.73 m²)	Mean ± SD: 19.47 ± 15.91 (Min: 3.20, Max: 86.68)

Vitamin D Status	Deficient: 131 (72.8%) Insufficient: 34 (18.9%) Sufficient: 14 (7.8%) Upper safety limit: 1 (0.6%)
CKD Stages (KDIGO)	Stage II: 7 (3.89%) Stage III: 32 (17.78%) Stage IV: 46 (25.56%) Stage V: 95 (52.78%)
Vitamin D vs Age	Not significant ($\chi^2 = 16.746$, $p = 0.541$)
Vitamin D vs Gender	Not significant ($\chi^2 = 1.303$, $p = 0.728$)
Vitamin D vs CKD Stage	Significant association ($\chi^2 = 55.370$, $p < 0.0001$)
Gender vs CKD Stage	Not significant ($p = 0.705$)
Age vs CKD Stage	Not significant ($p = 0.227$)
Correlation Analysis	Vitamin D vs Creatinine: $r = -0.278$ ($p<0.001$) Vitamin D vs Urea: $r = -0.204$ ($p=0.006$) Vitamin D vs eGFR: $r = +0.451$ ($p<0.001$)
Hemodialysis Subgroup (n = 50)	Vitamin D Deficient: 74% Insufficient: 22% Sufficient: 4%
Vitamin D (Dialysis Patients)	Before dialysis: 16.74 ± 13.66 ng/mL After dialysis: 17.02 ± 12.34 ng/mL

Effect of Dialysis on Vitamin D	Significant improvement after dialysis (Wilcoxon test, $p < 0.0001$)

The present study demonstrates a high burden of vitamin D deficiency in CKD patients, with nearly three-fourths (72.8%) of the study population showing deficient vitamin D levels. Only 7.8% of patients had sufficient vitamin D levels, highlighting widespread hypovitaminosis D in CKD.

Renal function parameters showed severe impairment, with markedly elevated serum urea and creatinine levels and a low mean eGFR (19.47 ± 15.91 mL/min/1.73 m²), indicating advanced renal dysfunction in the study population. More than half of the patients (52.78%) belonged to Stage V CKD, reflecting late-stage disease predominance.

A statistically significant association between CKD stage and vitamin D deficiency ($p < 0.0001$) was observed, demonstrating that vitamin D deficiency worsens with increasing severity of CKD. Stage V CKD patients showed the highest proportion of vitamin D deficiency (62.6%), confirming a disease-severity relationship.

Correlation analysis revealed that vitamin D levels negatively correlated with serum creatinine and serum urea, and showed a moderate positive correlation with eGFR, indicating that declining renal function is associated with worsening vitamin D status.
No significant association was found between vitamin D status and age or gender, nor between age/gender and CKD stage, suggesting that biochemical and disease severity factors play a more dominant role than demographic variables.

In hemodialysis patients, vitamin D deficiency remained highly prevalent (74%). However, a statistically significant improvement in vitamin D levels after dialysis ($p < 0.0001$) was observed, indicating a modest biochemical improvement post-dialysis, though deficiency largely persisted.

Discussion: The study population had a relatively younger mean age (44.64 ± 14.94 years), with the majority of patients being below 50 years, indicating an early onset of CKD in this region. This finding aligns with recent Indian studies by Kumar M et al. (2020)[14] and Ravindra K et al. (2021)[15], who reported increasing CKD prevalence among younger adults, contrasting with earlier registry data that showed older age predominance. A male predominance (57.8%) was observed, consistent with the Indian CKD Registry (2012) and studies by Agarwal SK et al.

(2017)[16], suggesting biological, hormonal, and healthcare-access-related gender disparities in CKD burden.

Biochemically, patients demonstrated markedly elevated serum urea and creatinine levels with a low mean eGFR (19.47 ± 15.91 mL/min/1.73 m²), indicating advanced renal dysfunction. Similar findings have been reported by Kumar V et al. (2019)[17] and Chowta MN et al. (2020)[18], who also documented that most hospital-based CKD cohorts present in Stage IV–V disease. In the present study, more than half of patients (52.78%) were in Stage V CKD, highlighting delayed diagnosis and referral patterns common in low- and middle-income settings.

A key finding of this study was the very high prevalence of vitamin D deficiency (72.8%), with only 7.8% of patients having sufficient levels. These results are consistent with national and international studies, including Molina MC et al. (2017)[19], Gonzalez EA et al. (2004)[20], and Saxena A et al. (2018)[21], all of which reported vitamin D deficiency rates ranging from 68% to over 80% in CKD populations. This widespread deficiency is attributable to reduced renal conversion of vitamin D, urinary loss of vitamin D–binding protein, dietary restrictions, limited sun exposure, and chronic inflammation in CKD patients, as described by Holick MF et al.(2007)[1].

Importantly, the study demonstrated a statistically significant association between CKD stage and vitamin D deficiency ($p < 0.0001$), with the highest deficiency observed in Stage V CKD, confirming a progressive decline in vitamin D levels with worsening renal function. Similar stagedependent declines in vitamin D have been reported by Gonzalez EA et al. (2004)[20], Molina MC et al. (2017)[19], and Saxena A et al. (2018)[21]. Correlation analysis further supported this relationship, showing negative correlations of vitamin D with serum creatinine and urea, and a positive correlation with eGFR, findings consistent with previous observations by Nigwekar SV et al. (2014)[22] and Holick MF et al. (2007)[1].

In the hemodialysis subgroup, although a statistically significant rise in vitamin D levels postdialysis was observed, the mean levels remained in the deficient range, indicating that dialysis alone does not correct vitamin D deficiency. This is consistent with studies by Del Valle et al. (2011)[23] and Nigwekar SV et al. (2014)[22], which demonstrated that 25(OH)D is largely dialysisinsensitive, and that meaningful correction requires active supplementation. The KDIGO guidelines (2017) also recommend routine monitoring and treatment of vitamin D deficiency in all CKD patients, including those on dialysis.

Conclusion: The present study demonstrates a high prevalence of vitamin D deficiency among CKD patients, which worsens with advancing disease severity and declining renal function. Vitamin D levels showed significant associations with CKD stage and renal biochemical markers, while minimal improvement was observed with hemodialysis alone. These findings highlight that vitamin D deficiency is an integral and under-recognized component of CKD pathology.

Routine screening and early, stage-wise vitamin D supplementation should be incorporated into standard CKD management protocols. Integrating vitamin D monitoring as a core component of nephrology care, in accordance with KDIGO recommendations, may help improve metabolic balance, reduce complications, and enhance overall patient outcomes.

Recommendation: Routine screening and early correction of vitamin D deficiency should be made a standard component of chronic kidney disease (CKD) management across all stages. Vitamin D supplementation should be initiated from early CKD, especially before progression to advanced stages, and structured replacement therapy must be provided to dialysis patients, as hemodialysis alone does not restore adequate vitamin D levels. Integrating vitamin D monitoring into routine nephrology care may help reduce complications and improve long-term outcomes in CKD patients.

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Ethical Consideration: The study protocol was approved by the Institutional Scientific and Ethics Committees of G. R. Medical College, Gwalior. Ethical certificate- D.No:/234/IEC-GRMC/2023 dated 01/10/2023

Conflicts of Interest: The authors no conflicts of interest.

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