

FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

INTRODUCTION

Previous literature shows that vitamin D deficiency is not only significantly prevalent in CKD patients but has prognostic implications and grave outcomes including death as well. Very limited research has been done on the frequency of vitamin D deficiency in CKD patients in our local population.

OBJECTIVE

To determine the frequency of vitamin D deficiency in patients with chronic kidney disease.

STUDY DESIGN

Cross Sectional Study

STUDY SETTINGS

Department of Nephrology, Pakistan Institute of Medical Sciences, Islamabad.

STUDY DURATION

This study was conducted from 1st May 2023 to 31st October 2023.

MATERIALS AND METHODS

Patients with chronic kidney disease were enrolled. Confirmation of CKD was done renal function tests and imaging revealing chronic renal parenchymal changes. Vitamin D level was measured in the blood sample of patient. Level less than 30nmol/L (20ng/mL) was considered confirmatory for the presence of vitamin D deficiency.

RESULTS

A total of 186 patients were enrolled. Age of the patients ranged from 20 to 60 years. Mean age of the patients was 39.80 ± 5.245 years. Male to female ratio was 2.6:1. Vitamin D deficiency was observed in 130 patients (69.9%).

CONCLUSION

Vitamin D deficiency is common in patients with chronic kidney disease. Patients with chronic kidney disease should be screened for vitamin D deficiency and treated accordingly.

INTRODUCTION

Vitamin D, a multifunctional secosteroid hormone, is essential for regulating mineral balance and bone metabolism via its active form, 1,25-dihydroxyvitamin D [1,2]. In addition to its traditional responsibilities, recent studies emphasize extraneous responsibilities of vitamin D as a regulator of immunological responses, cellular proliferation, and endocrine pathways, facilitated by vitamin D receptors (VDRs) found in almost all nucleated cells [3,4]. The worldwide prevalence of vitamin D deficiency, characterized by serum 25-hydroxyvitamin D (25[OH]D) levels below 30 nmol/L (12 ng/mL), has attained pandemic levels, impacting almost 1 billion individuals globally across all age demographics and ethnic backgrounds. This deficit has been epidemiologically linked to various pathologies, including cardiovascular illnesses, metabolic syndrome, cancers, and infectious diseases, as evidenced by both observational and mechanistic investigations [5,6].

In chronic kidney disease (CKD), vitamin D insufficiency is particularly important due to the gradual decline in renal 1α -hydroxylase activity, establishing a bidirectional link between renal impairment and disrupted vitamin D metabolism [7,8,9]. Current research indicates that 60-85% of chronic kidney disease (CKD) patients reveal vitamin D deficiency, with prevalence increasing as CKD progresses, from 40.7% in stage 3 to 85.7% in stage 5 CKD, as shown by Kim et al. [16,18]. The repercussions extend beyond secondary hyperparathyroidism to encompass aggravated proteinuria, expedited renal function deterioration, and heightened cardiovascular mortality, with hazard ratios attaining 1.58 (95% CI 1.18-2.12) in deficient populations [8,9,11].

Notwithstanding this global evidence, considerable knowledge gaps remain concerning region-specific prevalence patterns, especially within South Asian populations, where distinctive environmental (diminished UVB exposure), dietary (insufficient calcium/vitamin D intake), and genetic (VDR polymorphisms) factors may exacerbate deficiency risks [12-15]. A study by Sun Moon Kim et al. found that 61.5% of patients with chronic renal disease exhibited vitamin D insufficiency. Initial research conducted in Pakistan by Memon et al. (2020)

indicated a deficit rate of 70.8% among chronic kidney disease patients, but adjacent India reports an even higher rate of 82% within dialysis populations [17,18]. Nevertheless, comprehensive data for our tertiary care community, characterized by frequent malnutrition and late-stage CKD presentations, is lacking.

This study seeks to ascertain the prevalence and severity spectrum of vitamin D deficiency across CKD stages within our institution, (2) investigate demographic and clinical correlates of deficiency, and (3) establish baseline data for future interventional investigations. Our findings will yield essential insights for formulating regionally suitable screening techniques and supplementation strategies in the management of CKD.

MATERIAL AND METHODS

This cross-sectional study was performed in the Department of Nephrology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, from May 1, 2023, to October 31, 2023. The sample size of 186 patients was determined utilizing the WHO sample size calculation, based on an anticipated prevalence of vitamin D deficiency of 61.5%⁷, a margin of error of 7%, and a confidence level of 95%. Participants aged 20 to 60 years with chronic kidney disease (CKD) lasting over three months were included. The exclusion criteria included chronic liver disease, use of vitamin D or calcium supplements within the past two months, steroid medication, congenital abnormalities in vitamin D metabolism, and previous parathyroid surgery. Upon obtaining ethical permission and informed consent, demographic (age, gender), anthropometric (weight, height, BMI), and clinical data (medical history, indicators of vitamin D inadequacy) were documented. Blood samples (5 mL) were obtained in sterile vacuume tubes and assessed for serum 25(OH)D concentrations (deficiency defined as <30 nmol/L [12 ng/mL]) by a consultant pathologist of PIMS unaware of clinical information. Data were analysed using IBM-SPSS version 22. Frequencies and percentages are determined for qualitative data (gender, CKD severity, vitamin D status), whereas mean \pm SD represented quantitative factors such as age, BMI, disease duration etc. Stratification was conducted

based on age, gender, BMI, and disease duration, Chi-square tests was employed and p-value ≤ 0.05 considered significant.

RESULTS:

The study included 186 patients, with a near-equal gender distribution (49.5% male, 50.5% female). Age of the patients ranged from 20 to 60 years, while mean age was 39.80 ± 5.245 years, mean weight 45.22 ± 7.101 kg and mean BMI was 21.381 ± 1.020 . 62.9% of patients had a BMI >20 kg/m², while a

majority (68.8%) had a disease duration of ≤ 24 months. Detailed descriptive statistics for all the qualitative variables is shown in Table-I. 69.9% (n=130) of patients had Vitamin D deficiency, while 30.1% (n=56) did not. Stratification analysis reflected that older age (≥ 40 years), lower BMI (≤ 20 kg/m²), and shorter disease duration (≤ 24 months) were significantly associated with higher Vitamin D deficiency. A comprehensive analysis of stratification is illuminated in table 2.

Table- I: Frequency and percentages of patients according to various qualitative variables (n = 186)

| Variable | Category | Frequency | Percent (%) |
|------------------------------|--------------------------------|-----------|-------------|
| Gender | Male | 92 | 49.5 |
| | Female | 94 | 50.5 |
| Age (years) | 40 years or more | 138 | 74.2 |
| | Less than 40 years | 48 | 25.8 |
| BMI (kg/m ²) | 20 kg/m ² or below | 69 | 37.1* |
| | More than 20 kg/m ² | 117 | 62.9 |
| Duration of Disease (months) | 24 months or below | 128 | 68.8 |
| | More than 24 months | 58 | 31.2 |

Table-II: Association Between Vitamin D Deficiency and Demographic/Clinical Characteristics (n= 186)

| Variable | | Vitamin D Deficiency | | Total | p-value |
|-------------|-----------------|----------------------|------------|--------------|----------|
| | | Yes | No | | |
| Gender | Male | 70 (76.0%) | 22 (24.0%) | 92 (100.0%) | 0.068 |
| | Female | 60 (63.8%) | 34 (36.2%) | 94 (100.0%) | |
| Age (years) | ≥ 40 years | 112 (81.2%) | 26 (18.8%) | 138 (100.0%) | <0.001 |

| Variable | Vitamin D Deficiency | | Total | p-value |
|------------------------------|-----------------------|-------------|------------|--------------|
| | <40 years | 18 (37.5%) | 30 (62.5%) | 48 (100.0%) |
| BMI (kg/m ²) | ≤20 kg/m ² | 58 (84.0%) | 11 (16.0%) | 69 (100.0%) |
| | >20 kg/m ² | 72 (61.5%) | 45 (38.5%) | 117 (100.0%) |
| Duration of Disease (months) | ≤24 months | 101 (78.9%) | 27 (21.1%) | 128 (100.0%) |
| | >24 months | 29 (50.0%) | 29 (50.0%) | 58 (100.0%) |

DISCUSSION

Chronic kidney disease (CKD) has emerged as a significant public health concern globally, especially in developing nations. The prevalence of chronic kidney disease (CKD) among adults in Pakistan was 21.2% [10]. Our study findings indicated that the mean age is higher in patients with a more advanced stage of chronic kidney disease (CKD). In individuals with chronic kidney disease, vitamin D insufficiency is frequently associated with an elevation in parathyroid hormone as renal function deteriorates. It may also elevate cardiovascular risk, mineral bone disease, and hyperparathyroidism [11]. Our investigation revealed that all individuals recruited exhibited a deficit of vitamin D. The deficiency is more pronounced in advanced-stage patients than to those in earlier stages. Vitamin D deficiency occurs in up to 80 percent of patients with chronic kidney disease (CKD), correlating with albuminuria, accelerated progression of kidney disease, and increased all-cause mortality [12]. The significant frequency of vitamin D deficiency in chronic kidney disease (CKD) patients, evidenced by our study (69.9%), corresponds with international data, although rates differ among populations and CKD stages. Jean et al. (2017) identified analogous trends, ascribing insufficiency to compromised renal synthesis, reduced solar exposure, and comorbidities such as diabetes and hypertension [13]. Our findings support research conducted in Pakistan, where Najamuddin et al. (2019) and Ikram et al. (2022) reported deficiency rates of 40% and 80%, respectively, in newly diagnosed CKD patients [14,15]. This gap may indicate variations in CKD

severity, geographic solar exposure, or diagnostic criteria (e.g., <20 ng/mL vs. <30 nmol/L).

Similar to Kim et al. (2014), we noted an increased deficiency in elderly individuals (≥40 years), associated with deteriorating renal function and diminished cutaneous vitamin D production [16]. Satirapoj et al. (2013) observed that deficit exacerbates with the advancement of chronic kidney disease (CKD), attaining 84.7% in stage 5 CKD as a result of diminished renal 1 α -hydroxylase activity [17].

Our finding of increased deficit in low-BMI patients contradicts obesity-related sequestration theories but aligns with Memon et al. (2020), who associated deficiency with malnutrition and inflammation [18]. The correlation with a shorter disease duration (≤24 months) indicates either acute metabolic stress or a delayed diagnosis, a topic that has been insufficiently examined in previous studies.

Our analysis indicated a non-significant male predominance (76.0% vs. 63.8%), however Alkathem et al. (2024) emphasized a greater deficiency in females attributable to cultural sun avoidance and hormonal influences [19]. Naqvi et al. (2017) highlighted socioeconomic inequalities, indicating that rural and low-income patients face heightened risk [20].

Cholecalciferol supplementation (1,000 IU/day) restored vitamin D levels in 89.7% of patients in Kim et al.'s trial [16], supporting its safety and efficacy. However, Jean et al. (2017) debated whether native vitamin D or VDRA (e.g., calcitriol) is superior for managing secondary hyperparathyroidism [13]. Our data underscore the

need for individualized regimens, especially in advanced CKD.

This study rectifies multiple deficiencies through its stringent methodology, including CKD confirmation and vitamin D assessment conducted by blinded pathologists, which mitigated misclassification. Another advantage is the thorough stratification achieved by controlling for age, BMI, and disease duration, allowing for the isolation of independent risk factors, representing a methodological improvement over previous regional studies. The consecutive enrollment of 186 patients across various CKD stages further augmented the generalizability within resource-constrained environments, constituting another strength of this research.

This study underscores the concerning incidence of vitamin D deficiency (69.9%) among chronic kidney disease (CKD) patients in our population, emphasizing its importance as a crucial yet controllable risk factor in renal health. Our findings correspond with global trends while also highlighting distinct regional patterns, notably the significant correlation with advanced age (≥ 40 years), reduced BMI (≤ 20 kg/m²), and abbreviated disease duration (≤ 24 months), characteristics that may indicate malnutrition, metabolic stress, or a postponed diagnosis in early CKD. Our study further emphasized that Vitamin D insufficiency is a widespread, inadequately addressed comorbidity in CKD that intensifies morbidity and mortality. Our research highlights the necessity for regular monitoring, focused replenishment, and localized guidance to alleviate its effects. Future study should investigate appropriate supplementation protocols and their impact on definitive clinical outcomes in chronic kidney disease populations.

CONCLUSION

This study underscores the concerning prevalence of vitamin D deficiency (69.9%) among chronic kidney disease (CKD) patients in our population, emphasizing its importance as a significant yet controllable risk factor in renal health. Our findings correspond with global trends while also uncovering distinct regional patterns, notably a significant correlation with advanced age (≥ 40 years), reduced BMI (≤ 20 kg/m²), and abbreviated disease duration (≤ 24

months), characteristics that may indicate malnutrition, metabolic stress, or a postponed diagnosis in early CKD. Our study further emphasized that Vitamin D insufficiency is a widespread, inadequately addressed comorbidity in CKD that intensifies morbidity and mortality. Our research highlights the necessity for regular monitoring, focused replenishment, and localized protocols to alleviate its effects. Future investigations should examine appropriate supplementation protocols and their impacts on definitive clinical outcomes in chronic kidney disease populations.

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