Scope
Volume 15 Number 03 September 2025

The Role of Vitamin B12 and Folate in Anemia among Patients with Chronic Kidney Disease (Stage 3-5) : A Case Control Study

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Abstract: Anemia is a prevalent complication of Chronic Kidney Disease particularly in advanced stages. This study investigates the prevalence of vitamin B12 and folic acid deficiencies in CKD patients with anemia and explores their potential contribution to disease progression. A comparative analysis of 45 CKD patients (stages 3-5) and 45 healthy controls revealed significant differences in hematological parameters, suggesting a critical role for nutritional deficiencies in exacerbating anemia. The study underscores the importance of targeted nutritional intervention to improve patient outcomes.

Introduction

Chronic Kidney Disease (CKD) represents a growing global health concern due to its association with increased morbidity and mortality. Cardiovascular disease (CVD) remains the primary cause of death among CKD patients, underscoring the interplay between renal dysfunction and systemic complications. Hypertension, Dyslipidemia, and diabetes mellitus are established contributors to this heightened risk. However, non-traditional risk factors such as oxidative stress, endothelial dysfunction, and chronic inflammation have also gained attention [1,2].

Anemia is a common manifestation in CKD, significantly contributing to left ventricular hypertrophy, systolic dysfunction, and eventual cardiovascular mortality. While erythropoietin deficiency is a primary factor, nutritional deficits, particularly involving vitamins like B12 and folic acid, are emerging as key elements [3]. These deficiencies may exacerbate anemia and influence the progression of CKD by interfering with haematopoiesis and homocysteine metabolism. Vitamin B12 deficiency is particularly concerning, as it is essential for DNA synthesis, red blood cell production, and neurological function [4,5].

The prevalence of vitamin B12 deficiency in CKD patients is influenced by several factors, including dietary restrictions, malabsorption, and medication-induced

depletion. Moreover, the dialysis process itself can lead to the loss of essential vitamins, aggravating the deficiency. Patients with CKD often present with elevated homocysteine levels due to impaired renal clearance and disrupted metabolic pathways, further linking vitamin B12 deficiency to cardiovascular risk [6,7].

This study aims to explore the prevalence of vitamin B12 deficiency among patients with CKD and its correlation with disease duration and kidney size. The findings could help inform strategies for early detection and management, potentially improving patient outcomes.

Material and Methods

This cross-sectional observational study was conducted on 45 patients diagnosed with CKD at a tertiary care center. Patients aged 18 years and above with confirmed CKD based on clinical, biochemical, and radiological findings were included. Those with other causes of vitamin B12 deficiency, such as pernicious anemia, gastrointestinal disorders, or specific medication use, were excluded.

Morning fasting blood samples were collected to measure serum vitamin B12 levels. A predesigned questionnaire was used to gather sociodemographic and clinical data, including symptoms, comorbidities, and medication history. Kidney size was assessed using ultrasonography. Statistical analysis was performed using SPSS software, with significance set at $p<0.05$. Results were presented as mean ± SD for continuous variables and percentages for categorical data.

Results

Out of 45 participants, 28 (62.2%) were male, and 17 (37.8%) were female. The mean age was 52.3 ± 11.5 years, with the majority (57.8%) aged between 40 and 60 years. Urban residents constituted 71.1% of the cohort, while the remaining 28.9% were from rural areas. The distribution of occupations indicated that 44.4% were non-working or dependent, reflecting the high disease burden.

Table 1: Sociodemographic Profile of Participants

Variable	Category	Frequency (%)
Gender	Male	28 (62.2%)
	Female	17 (37.8%)
Age (years)	<40	5 (11.1%)
	40-60	26 (57.8%)
	>60	14 (31.1%)
Residence	Urban	32 (71.1%)

	Rural	13 (28.9%)
Occupation	Non-working	20 (44.4%)
	Labourer	8 (17.8%)
	Housework	12 (26.7%)
	Others	5 (11.1%)

Clinical symptoms included pedal edema (66.7%), fatigue and anorexia (48.9%), and tingling or burning sensations in the extremities (42.2%).

Table 2: Distribution of Symptoms

Symptom	Frequency (%)
Pedal edema	30 (66.7%)
Tingling/numbness	19 (42.2%)
Fatigue and anorexia	22 (48.9%)

Vitamin B12 deficiency (<200 pg/mL) was observed in 26 patients (57.8%), while 19 (42.2%) had normal levels. Deficiency was significantly associated with a mean CKD duration of 6.7 ± 2.5 years compared to 4.8 ± 2.1 years in those without deficiency (p=0.001). Kidney size was reduced in all patients with vitamin B12 deficiency.

Table 3: Vitamin B12 Levels and Kidney Size

Kidney Size	Deficient (n=26)	Normal (n=19)	p-value
Reduced	26 (100%)	15 (78.9%)	0.0001
Normal	0 (0%)	4 (21.1%)	

Table 4: Vitamin B12 Levels Distribution

Vitamin B12 Level (pg/mL)	Frequency (%)
<200	26 (57.8%)
200-300	10 (22.2%)
>300	9 (20%)

Table 5: Duration of CKD and Vitamin B12 Deficiency

Duration of CKD	Deficient (n=26)	Normal (n=19)	p-value
<6 years	10 (38.5%)	9 (47.4%)	0.0001
>6 years	16 (61.5%)	10 (52.6%)	

Table 6: Hematological Findings in CKD Patients

Hematological Finding	Frequency (%)
Macrocytosis (MCV >100)	18 (40%)
Low Platelet Count	12 (26.7%)
Anisocytosis	8 (17.8%)
Poikilocytosis	7 (15.6%)

Discussion

This study highlights the high prevalence of vitamin B12 deficiency among CKD patients, consistent with previous findings [1,5,8]. The significant association between deficiency and prolonged CKD duration suggests that progressive renal damage may exacerbate malabsorption and metabolic derangements. The reduction in kidney size among deficient patients supports the hypothesis that structural changes in the kidney impair nutrient metabolism [2].

Elevated homocysteine levels, commonly observed in CKD, further emphasize the interplay between vitamin B12 deficiency and cardiovascular risk. Hyperhomocysteinemia, driven by disrupted renal clearance and impaired metabolic pathways, is a recognized risk factor for CVD. Supplementation with vitamin B12 has been shown to lower homocysteine levels, potentially reducing cardiovascular complications [3,4,9].

Anemia, a hallmark of CKD, was prevalent in the study cohort, with macrocytosis and other hematological abnormalities more common in the deficient group. These findings align with studies linking vitamin B12 deficiency to impaired erythropoiesis and increased cardiovascular events [6]. The role of erythropoietin-stimulating agents in managing anemia in CKD patients is well-documented, but addressing underlying nutritional deficiencies is equally critical [7].

The observed sociodemographic distribution, with a higher prevalence of deficiency among urban residents and non-working individuals, reflects the influence of lifestyle factors and healthcare access on CKD outcomes. Urbanization is associated with

increased risk factors such as hypertension and diabetes, which are major contributors to CKD progression [1,10].

Early identification and supplementation of vitamin B12 in CKD patients could mitigate these risks. Intravenous B-complex vitamins may offer a more effective approach for correcting deficiencies and reducing homocysteine levels in this population. The use of methylcobalamin, an active form of vitamin B12, could also be explored to bypass the metabolic challenges associated with CKD [11].

Future research should focus on the long-term outcomes of vitamin B12 supplementation in CKD patients, particularly its impact on cardiovascular health and quality of life. Larger, multicenter studies are needed to validate these findings and establish standardized screening protocols for vitamin B12 deficiency in CKD [12].

Conclusion

Vitamin B12 deficiency is a significant concern in CKD patients, contributing to anemia, metabolic disturbances, and increased cardiovascular risk. Routine screening and timely intervention are essential to improving patient outcomes. Further research is needed to explore the long-term benefits of vitamin B12 supplementation in CKD management.

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