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VITAMIN B 12 LEVELS IN THE PATIENTS WITH CHRONIC RENAL DISEASE

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ABSTRACT

Background: Vitamin B12 deficiency is regarded as a dangerous condition that can cause a variety of neurological symptoms, especially if it is not effectively treated or identified. Deranged metabolism, nutritional deficiencies from dietary restrictions, and consequent vitamin loss during dialysis are the main reasons of vitamin B12 insufficiency in patients with chronic renal disease.

Aim: Comparing the levels of active and total vitamin B12 in Indian participants with chronic renal illness was the goal of the current investigation.

Methods: During the specified study period, 248 subjects—156 men and 92 women—between the ages of 18 and 60 who reported to the Institute's Department of Biochemistry were included in the study. Using chemiluminescent microparticle immunoassay, the active and total levels of vitamin B12 in each participant were measured.

Results: Thirteen percent of the final sample size of 214 participants exhibited deficiencies in both active B12 and total B12 levels, out of the 248 subjects, 34 of whom had chronic renal disease and were omitted from the study for various reasons. Active and total vitamin B12 levels showed a considerable positive connection ($p < 0.01$), with mean active levels of 67.3 ± 32.73 pmol/L and total levels of 604.83 ± 495 pg/mL in 214 participants. Significant vitamin B12 deficiency was found in participants who had been receiving hemodialysis for longer than three years.

Conclusion: measurement and diagnosis of vitamin B12 insufficiency can be aided by the evaluation of active B12 levels, which can also serve as a possible biomarker and indicator for determining vitamin B12 deficiency in individuals with chronic renal illness.

Keywords: active B12, chronic renal disease, Hyperhomocysteinemia, vitamin B12

INTRODUCTION

Individuals with chronic kidney disease (CKD) are more likely to experience vitamin and mineral deficiencies, which can result in comorbidities such as anemia, metabolic imbalances, and cardiovascular disease. Previous research has shown that poor vitamin B12 metabolism is becoming a non-traditional risk factor for negative outcomes linked to chronic renal disease. This has sparked interest in learning more about how vitamin B12 may improve clinical outcomes. While TC-II, also known as transcobalamin, is the main carrier for cellular transport of vitamin B12, which is essential for vitamin B12 entry into the tissues, cobalamin, also known as vitamin B12, is a water-soluble metal enzyme that is necessary for the critical reaction of methyl transferase.¹

Transcobalamin has a strong affinity for free vitamin B12 and releases it into tissues and bone marrow. HoloTC (holotranscobalamin) or active B12 is the name given to this complex, which aids in differentiating it from complexes of transcobalamin I and III that firmly bind the vitamin without releasing it into the tissues. However, individuals with chronic kidney disease (CKD) exhibit elevated transcobalamin levels, decreased vitamin B12 absorption, and a substantial physiological shortage of vitamin B12.²

Additionally, because of decreased TC-II absorption in the proximal tubule and increased TC-II loss in the urine, uremia patients may have a functional vitamin B12 shortage. Another factor leading to vitamin B12 insufficiency is hormonal dysregulation and metabolic changes brought on by deranged metabolism in patients with chronic renal disease. All of these abnormalities can lead to a paradoxical rise in homocysteine levels in cells, which is a modifiable risk factor for heart disease.³

Subjects with vitamin B12 deficiency have hyperhomocysteinemia right away, which has also been shown to be a significant risk factor for cardiovascular illnesses in patients with chronic kidney disease. Therefore, early identification of vitamin B12 insufficiency is essential for improved outcomes in patients with chronic renal disease. According to data from earlier research, levels of active B12 can accurately depict the state of functional vitamin B12 and may be a more reliable predictor of vitamin B12 status than total B12 levels. Therefore, in individuals with chronic renal illness, it may be more important to measure active B12 levels than total B12 levels.⁴

Therefore, comparing the effectiveness and identifying the levels of active B12 and total B12 as clinical biomarkers as a clinical method for evaluating vitamin B12 deficiency in individuals with chronic renal disease were the goals of the current investigation.

MATERIALS AND METHODS

As a clinical method for evaluating vitamin B12 deficiency in patients with chronic renal disease, the current cross-sectional study sought to compare the effectiveness of measuring active B12 and total B12 levels as clinical biomarkers. The study participants came from the Institute's Department of Biochemistry. Prior to their involvement in the study, all subjects gave their written and verbal informed consent.

According to the KDOQI criteria, the study first screened 248 participants with chronic kidney disease, 156 of whom were male and 92 of whom were female. The participants ranged in age from 18 to 60 years, with a mean age of 42 years.⁵ Chronic kidney disease (CKD) was defined as kidney damage lasting at least three months, as shown by anomalies in the kidney's structure or function, whether or not kidney damage was present, and whether or not the GFR was lower than 60 mL/min/1.73 m². Using eGFR values determined from the CKDEPI (CKD epidemiology collaboration) equation, the participants were further separated into stages in accordance with KDOQI standards (Table 1).

Following an initial evaluation that included clinical information and medical history, all participants were enrolled. All of the necessary information was obtained from the pupils' lab and medical records. Participants who had regular B12 testing and were in different stages of chronic kidney disease (CKD) met the study's inclusion requirements.

The study's exclusion criteria included participants receiving multivitamin therapy or supplements that could alter their vitamin B12 levels, participants under the age of 18, participants who had undergone a transplant, cardiovascular events, known cancers, acute illnesses, or acute kidney injuries.

Following the manufacturer's instructions, the research participants' serum levels of active B12 and total vitamin B12 were measured in each participant. The CMIA (Chemiluminescent Microparticle Immunoassay) method was used to measure the levels of vitamin B12 and active B12 in the reportable ranges of 148–2000 pg/ml and 5–128 pmol/L. RLUs (relative light units) were used to evaluate the chemiluminescent reaction.

Cutoff values were defined as >300 pg/mL as normal, 200-300 pg/mL as borderline, and <200 pg/mL as deficient based on literature data and conventional clinical concentration.^{7,8} Deficient levels of active B12 were defined as less than 35 pmol/L.

ANOVA, the chi-square test, the student's t-test, Fisher's exact test, the Mann Whitney U test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) were used to statistically evaluate the gathered data. When the p-value was less than 0.05, the significance level was taken into account.

RESULTS

248 participants, 156 men and 92 women, between the ages of 18 and 60, who reported to the Institute's Department of Biochemistry during the study period were evaluated in this study.

Using chemiluminescent microparticle immunoassay, the active and total levels of vitamin B12 were measured in each participant. According to KDOQI recommendations, the included CKD participants were split into five stages of CKD. Of the 248 participants, 12 had active B12 levels greater than 128 pmol/L and 22 had total B12 levels greater than 2000 pg/dl. Thirteen percent (n=28) of the 214 participants had both active and total B12 deficiencies.

36 individuals were in stage 1, 32 in stage 2, 46 in stage 3, 34 in stage 4, and 66 in stage 5, according to the demographic and illness features of patients with various CKD staging. In stages 1, 2, 3, 4, and 5 CKD, the patient's mean age was 41.2±13.2, 38.6±8.05, 50.6±16.2, 43.5±12.0, and 47.4±14.7 years, respectively.

In stage 1, 2, 3, 4, and 5 CKD, the corresponding active B12 levels were 73.84±31.32, 68.45±32.29, 64.25±31.47, 7.67±26.17, and 50.25±36.87 pmol/mL. In stage 1, 2, 3, 4, and 5 CKD, the corresponding total B12 levels were 590.2±460.5, 536.3±434.3, 620.3±498, 798.4±561.3, and 534.4±505.2 pg/mL. In stage 1, 2, 3, 4, and 5 CKD, the corresponding creatinine levels were 1.09±0.32, 2.22±0.85, 3.72±1.19, 7.69±2.70, and 8.44±4.10 (Table 2).

According to the study's findings, 42 participants had vitamin B12 levels between 200 and 300 pg/mL, which was regarded as a case of borderline deficiency. The remaining participants had B12 levels over 300 pg/mL, which was regarded as a normal level. On the other hand, the study participants' mean folate concentration was 7.14±3.36 ng/ml, which was within the normal range. The average values of vitamin B12 in 214 participants were 67.3±32.73 pmol/L for active B12 and 604.83±495 pg/mL for total B12 (Table 3).

Additionally, a positive association with a p-value of less than 0.01 was seen in the Pearson correlation analysis between total and active vitamin B12 levels. The effects of dialysis for vitamin B12 deficiency showed that subjects with CKD and those receiving hemodialysis for longer than three years had significantly lower levels of active B12 and total vitamin B12 than those receiving dialysis for less than three years. This difference was statistically significant, with $p < 0.01$ at 95% CI (Table 4).

DISCUSSION

Twelve patients with active B12 levels greater than 128 pmol/L and 22 subjects with total B12 levels greater than 2000 pg/dl were eliminated from the study out of a total of 248 subjects. Thirteen percent (n=28) of the final 214 individuals exhibited both active and total B12 deficiencies. The current study's study design was similar to that of earlier research by Nexo E et al. (2002) and Heinz J et al. (2010), where the authors also reported a study design similar to the current study.

According to the study findings, 36 participants were in stage 1, 32 in stage 2, 46 in stage 3, 34 in stage 4, and 66 in stage 5 for demographic and clinical features among study participants with varying stages of CKD. In stage 1, 2, 3, 4, and 5 CKD, the study participants' mean ages were 41.2±13.2, 38.6±8.05, 50.6±16.2, 43.5±12.0, and 47.4±14.7 years, respectively. In stage 1, 2, 3, 4, and 5 CKD, the corresponding active B12 levels were 73.84±31.32, 68.45±32.29, 64.25±31.47, 7.67±26.17, and 50.25±36.87 pmol/mL.

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42 study participants had vitamin B12 levels between 200 and 300 pg/mL, which was regarded as a case of borderline deficiency. The remaining patients had B12 levels over 300 pg/mL, which was regarded as a normal level. In contrast, all study participants had a mean folate concentration of 7.14±3.36 ng/ml, which was within the normal range. The mean values of vitamin B12 in 214 participants were 67.3±32.73 pmol/L for active B12 and 604.83±495 pg/mL for total B12. These results were consistent with those of Ikizler TA et al. (2020) and Juszczak AB et al. (2021), whose vitamin B12 and folate values were similar to those of the current investigation.

The study's findings also revealed a positive correlation ($p < 0.01$) between total and active vitamin B12 levels in the Pearson correlation analysis. The effects of dialysis for vitamin B12 deficiency showed that subjects with chronic kidney disease (CKD) and those receiving hemodialysis for longer than three years had significantly lower levels of active B12 and total vitamin B12 than those receiving dialysis for less than three years. This difference was statistically significant ($p < 0.01$ at 95% CI). These findings were consistent with those of Das B et al. (2015) and Siddappa MN et al. (16) in 2020, where the current study's findings were similar to those of the authors' investigations.

CONCLUSION

Taking into account its limitations, the current study comes to the conclusion that measuring active B12 levels can aid in measuring vitamin B12 levels, diagnosing vitamin B12 deficiency, and serving as a potential biomarker and indicator for determining whether a subject has chronic renal disease.

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Stages	CKD stage	GFR
Stage 1	Normal/high GFR	>90mL/min
Stage 2	Mild CKD	60-89 mL/min
Stage 3	Moderate CKD	30-59 mL/min
Stage 4	Severe CKD	15-29 mL/min
Stage 5	End-stage CKD	<15 mL/min

Table 1: Staging criteria for chronic renal disease based on GFR in study subjects

Parameters	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Number (n)	36	32	46	34	66
Mean age (years)	41.2±13.2	38.6±8.05	50.6±16.2	43.5±12.0	47.4±14.7
Active B12	73.84±31.32	68.45±32.29	64.25±31.47	7.67±26.17	50.25±36.87
Total B12	590.2±460.5	536.3±434.3	620.3±498	798.4±561.3	534.4±505.2
Creatinine	1.09±0.32	2.22±0.85	3.72±1.19	7.69±2.70	8.44±4.10

Table 2: Demographic and disease characteristics in study subjects with different CKD staging

Mean range	Active B12	Total vitamin B12	Folate
Range	8.1-123	144-1985	3.2-16.1
Mean ± S. D	67.3±32.73	604.83±495	7.14-3.36

Table 3: Comparison in folate, active B12, and total B12 levels in study subjects

Dialysis duration	<3 years	>3 years
Number of subjects (n)	56	34
Active vitamin B12	66.22±35.76	54.23±30.54
Total vitamin B12	549.22±323.2	509.39±413.5

Table 4: Comparison of active B12 and total Vitamin B12 levels to the dialysis duration in study subjects

