

## A Study of Vitamin B12 Levels In Chronic Kidney Disease Patients In Tertiary Care Hospital

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### Abstract

#### INTRODUCTION

Chronic kidney <sup>disease</sup> is a growing health burden in the world, with an estimate of nearly 20 million affected. CKD is defined as either sustained reduction in kidney function with a glomerular filtration rate is less than 60ml/min/1.73 m<sup>2</sup> or evidence of kidney damage . Lack of erythropoietin , iron , deficiency anemia and shortened red cell lifespan are the major factor contributing to anemia in CRF. Another possibility is nutritional deficiency, vegetarian diet or deranged metabolism of vitamins in uremic patients

**OBJECTIVE :** To Define prevalence of Vitamin B12 deficiency in Chronic Kidney Disease (CKD) patients

#### MATERIALS AND METHOD

It is a hospital based cross sectional study conducted in Osmania General Hospital in January 2019. Study included 60 patients suffering from CKD disease who were taking treatment in hemodialysis nephrology unit. After taking informed consent, patients underwent history recording, clinical examination. Laboratory investigations included urine examination, blood sugar profile , renal function test and Serum vitamin B12. The individual venous blood, 3ml sample taken in red vacutainer and Analysed on ADVIA CENTAUR XPT siemens immunoassay analyzer for vit B12 levels by CMIA method .

**RESULT AND DISCUSSION:** Out of total 60 subjects, 42 were males and 18 were females with a mean age of 48.32 +/- 5.63 years. Vitamin B12 deficiency was observed in significant cases, p value < 0.005. This deficiency is caused by inadequate nutrition and loss through the haemodialysis procedure. Another possibility is deranged metabolism of vitamins in uremic patients. Similarly mean duration of CKD was also significantly associated with presence of Vitamin B12 deficiency.

**CONCLUSION:** Present study showed high prevalence of Vitamin B12 deficiency in CKD patients. Most of the patients had associated neurological, hematological and gastro-intestinal symptoms . Hence all the treating nephrologists should anticipate the deficiency of Vitamin B12 in CKD patients.

**KEY WORDS-** chronic kidney disease, dialysis, anemia, vitamin B12 deficiency

Date of Submission: 23-08-2019

Date of Acceptance: 07-09-2019

### I. Back ground

#### INTRODUCTION

Chronic kidney disease (CKD) is a global burden and its prevalence is rising exponentially(1,2). Chronic kidney disease is associated with increased morbidity and mortality and also with increased threat of cardiovascular disease, heart failure and increase healthcare expenditures(3,4).

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiological process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR < 60 mL/min per 1.73 m<sup>2</sup>). CKD as an abnormality of kidney structure or function regardless of cause or specific clinical presentation and proposed a staging system based on the level of GFR. The guideline also suggested a conceptual model for the natural history of CKD that often begins with initial kidney damage and progresses through the stages of CKD toward the outcome of kidney failure

In the total of world population, 5-7% of the population is affected by chronic kidney disease and is more common in developing countries(8). The overall prevalence of chronic kidney disease in India is 17.2% and prevalence of chronic kidney disease stages 1, 2, 3, 4 and 5 are 7%, 4.3%, 4.3%, 0.8% and 0.8%, respectively. Prevalence of vitamin B12 deficiency is at least 47% in Indian population

Anaemia has long been recognised as a feature of CKD. The anaemia of CKD is multifactorial. Anaemia is considered to be one of the most important factors responsible for the development of left ventricular hypertrophy, diastolic and later systolic dysfunction and cardiovascular disease, which is the single

most important contributor to the mortality in CKD [4]. Untreated dialysis patients were often symptomatic and dependent on blood transfusions with their innate morbidity

Severe Chronic Kidney Disease has an adverse effect on haematopoiesis. There is imbalance between haematopoiesis and increased destruction. The major defect appears to be one of like relative bone marrow failure. It may be circulating toxins like PTH (parathyroid hormone) that play major part and depress the marrow directly. Lack of erythropoietin, iron deficiency anaemia and shortened red cell lifespan are the major factors contributing to anaemia in CRF [5,6].

Another possibility is nutritional deficiency or deranged metabolism of vitamins in uremic patients. Many Patients with CKD show smear and megaloblastosis on examination of the bone marrow [7]. This suggests that Vitamin B12 & folic acid deficiency might be additional factors contributing to inadequate haematopoiesis in uraemia [8].

The most common causes of megaloblastosis are cobalamin (vitamin B12) and folate deficiencies. This deficiency is caused by: Inadequate nutrition and loss through the haemodialysis procedure. Most of the Indian population is vegetarian for cultural or religious reasons and even in the non-vegetarian population the amount of non-veg consumed contains less animal proteins than in typical western diet. The frequency of consumption of non-vegetarian food items is very low [9]

B12 deficiency is a well described etiology of anemia, classically producing megaloblastic anemia. It is likely due to inhibition of DNA synthesis, thought to be caused by the "methylfolate trap," or alternatively, the "formate starvation hypothesis".<sup>2</sup> While intuitively, the diagnosis of B12 deficiency should be confirmed by serum B12 levels Hence this study was undertaken to determine the contribution of Vitamin B12 deficiency to the overall picture of anaemia in Indian patients of CKD. We also attempted to study the contributory role of dietary factors to Vitamin B12 deficiency.

## **II. Material And Method**

It was a hospital based cross sectional study conducted in Osmania General Hospital in January 2019. Study included 60 patients suffering from CKD disease who were taking treatment in hemodialysis nephrology unit. After taking informed consent, patients underwent history recording, clinical examination. Laboratory investigations included urine examination, blood sugar profile, renal function test and Serum vitamin B12. Criteria used for Diagnosis of Chronic Kidney Disease (CKD):

. Glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m<sup>2</sup>

. Evidence of kidney damage (radiologic or pathologic findings)

Levels of urinary albumin excretion above 30 mg/day (or urinary albumin to creatinine ratios of 17 mg/g or higher for men or 25 mg/g or higher for women) on at least 2 measurements, regardless of the level of GFR. The individual venous blood, 3ml sample taken in red vacutainer and Analysed on ADVIA CENTAUR XPT siemens immunoassay analyzer for vitamin B12 levels by CMIA method

Vitamin B12 levels <200 pg/mL was considered deficient whereas B12 levels >350 pg/mL was considered normal. Blood levels of B12 between 100 and 350 pg/mL was considered indeterminate

### **INCLUSION CRITERIA**

Patients with established CKD, irrespective of etiology and maintenance on haemodialysis minimum duration 6 months. symptoms of uremia for 6 months or more. Elevated blood urea, creatinine  
Age – 40yrs to 70yrs

### **EXCLUSION CRITERIA**

Factors known to affect vitamin B12 stores, including: a history of hematological cancer, methotrexate use, alcohol ingestion of more than two drinks per day, vegetarian diet, previous gastric surgery, inflammatory bowel disease, pernicious anemia, recent blood transfusion, or patients receiving B12 supplementation and Patients on antimetabolites, antiviral drugs

## **III. Results**

Out of total 60 subjects, 42 were males and 18 were females with a mean age of 48.32 +/- 5.63 years. Duration of dialysis mean 1.2 +/- 0.5 yrs. urea mean 94 +/- 6 mg/dl, creatinine mean 5.8 +/- 2.3 mg/dl Vitamin B12 deficiency was observed in 36 cases, mean was 173.3 pg/ml, 24 cases have normal B12 levels mean 480.6 pg/ml. p value < 0.005 was taken as statistically significant. The result of the study also showed significant deficiency in CKD (p value < 0.005). This deficiency is caused by inadequate nutrition and loss through the

haemodialysis procedure. Another possibility is deranged metabolism of vitamins in uremic patients. Similarly mean duration of CKD was also significantly associated with presence of Vitamin B12 deficiency

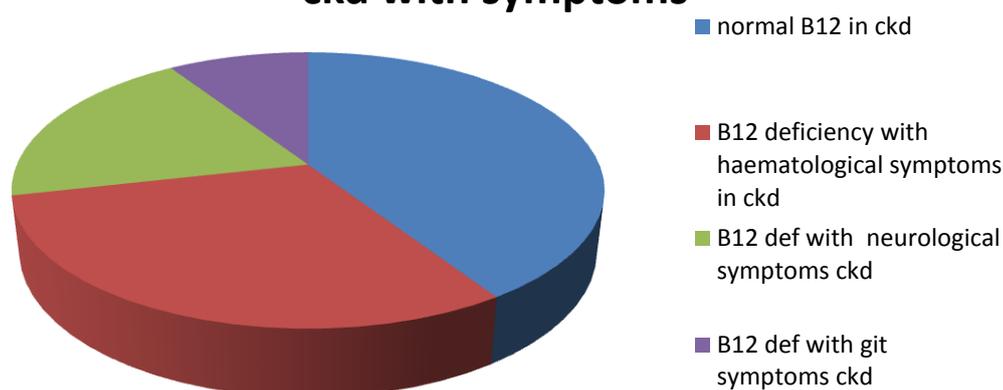
**Table No 1 Results In Ckd**

Vitamin B12	N	%
NORMAL	24	40
DEFECIENT	36	60
TOTAL	60	100

**Table no 2**

VARIABLES	In CKD	Mean	SD	P-VALUE
Vitamin B12 normal	24	480.6	+/- 8.4	
Vitamin B12 deficient	36	173.3	+/- 6.7	<0.005

**pie diagram showing B12 deficiency in ckd with symptoms**



**IV. Discussion**

Vitamin B12 (B12) is a water-soluble vitamin that plays a key role in the normal function of the nervous

system and blood formation along with serving as a cofactor for the formation of methionine from homocysteine [11]. Normally, B12 is released from dietary protein in the stomach and binds to intrinsic factor (IF). The B12-IF complex is absorbed in the ileum via the cubilin receptor [11]. Defects in cubilin, a proximal tubular membrane protein, have been associated with both megaloblastic anemia and tubular proteinuria [11-14]. Cubilin also acts to reabsorb the majority of filtered albumin from the urine and recently, genome-wide association studies have identified SNPs in CUBN in association with albuminuria [15] and B12 levels [16, 17].

Vitamin B12 deficiency was observed in 60% of CKD patients in present study. Similar results were observed by Kartik et al., who observed macrocytosis in 54% of patients of CKD [18]. Other authors also reported similar findings [19-21]. The potential mechanism for the same can be explained as: Vitamin B12 in the blood is primarily protein-bound. Approximately 20% of circulating B12 is bound to holotranscobalamin (TC2) with the remainder to haptocorrin. TC2-bound B12 is the biologically active form as B12 bound to haptocorrin cannot be taken up into cells. A congenital form of megaloblastic anemia has been described in infants lacking TC2 despite normal total B12 levels. The kidney plays an important role in TC2 metabolism. TC2 is filtered at the glomerulus and is reabsorbed in the proximal tubule by megalin. B12 is then returned to the blood bound to newly synthesized TC2. Thus, defects in protein reabsorption in the proximal tubule could lead to a loss of biologically active TC2 in the urine [22].

B12 deficiency has not been well studied in CKD and dialysis patients. Dialysis patients generally have poor nutritional intake, predisposing them to B12 deficiency. In addition, foods that are high in B12 typically contain high concentrations of electrolytes harmful to dialysis patients, limiting them to low B12 foods. Furthermore, B12 is a classic middle size molecule, which is cleared well with modern high flux dialyzers, providing an additional reason for hemodialysis (HD) patients to be B12 deficient

B12 deficiency is associated with anemia and neurological disorders. In present study a significant association was observed between presence of neurological symptoms (like tingling, numbness, loss of balance,

weakness) and presence of vitamin B12 deficiency in CKD Patients. Similar results were observed by various other authors [23].

In present study we also observed that mean duration of CKD was significantly associated with presence of Vitamin B12 deficiency in patients. The landmark study by Obrador et al. [24]

Furthermore, although anemia is not as common in earlier stages of chronic kidney disease, patients with stage III disease have a prevalence of concurrent anemia of 5.2%, whereas those with stage IV disease have a prevalence of concurrent anemia of 44.1% [25]. There is also a greater prevalence of anemia of chronic kidney disease in those older than 60 years, as compared to those aged between 46 and 60 years. This is probably secondary to the greater rate of chronic kidney disease in older individuals, as well as the lower estimated glomerular filtration rates (GFRs) that are associated with aging.

## V. Conclusion

Present study showed high prevalence of Vitamin B12 deficiency in CKD patients. Out of 50 patients 40% had associated neurological, 50% hematological and 20% gastro-intestinal symptoms. Should take appropriate measures for its control.

## VI. Recommendations

Vitamin B12 supplementation should be considered in CKD patients as a part of treatment to prevent the complications associated with its deficiency. We also recommend further large scale prospective studies to validate our findings.

## Acknowledgement

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors/ editors/ publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

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Dr.KattaVani. "A Study of Vitamin B12 Levels In Chronic Kidney Disease Patients In Tertiary Care Hospital." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 9, 2019, pp 10-14.