ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 5, Issue – 5, September – October - 2022, Page No. : 130 - 137

Vitamin B12 Profile in Patients of Chronic Kidney Disease

[1]Dr. Pratik Kucha, Consultant General Medicine

[2]Dr. Avinash Sharma, Senior Resident, Department of Emergency Medicine, Government Medical College Surat, India

[3]Dr. Chirag D. Patel, Senior Resident, Department of General Medicine, Government Medical College Surat, India

Corresponding Author: Dr. Chirag D. Patel, Senior Resident, Department of General Medicine, Government Medical College Surat, India

How to citation this article: Dr. Pratik Kucha, Dr. Avinash Sharma, Dr. Chirag D. Patel, "Vitamin B12 Profile in Patients of Chronic Kidney Disease", IJMACR- September – October - 2022, Vol – 5, Issue - 5, P. No. 130 – 137.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Chronic kidney disease is characterized by the presence of an abnormality of kidney structure or function (or both) present for at least 3 months. Only 3% to 5% of all patients with ESRD in India get some form of renal replacement therapy. Thus, planning for prevention of CKD on a long-term basis is the only practical solution for India.

Anaemia has long been recognized 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. The most common causes of megaloblastosis are cobalamin (vitamin B12) and folate deficiencies. Various studies carried out on Asian Indians with normal renal function show that they have low levels of Vitamin B12 and high levels of homocysteine and methylmalonic acid.

Methodology: Patients with chronic kidney disease presented and admitted at General Medicine department was spread over one and half year from January 2019 to August 2020 after applying inclusion and exclusion criteria. After collection of data, the data entry forms were checked for their completeness and missing and incomprehensible data was rechecked from the respective participant profile. Data entry was done in MS Excel data sheet.

Result: Majority of the age group was in the range of 41-60 years about 50 % due to several risk factors varies with age such Diabetes, Hypertension. Symptoms of volume overload like Dyspnea, Puffiness of face, abdominal distension was found most common in CKD patients. It was observed that 34 cases had Vitamin B12 deficiency while 16 cases did not had had Vitamin B12 deficiency. In the present study subjects, out of 50, 31 were male while remaining 19 were female. It was observed that among the Vitamin B12

deficient group, 24 cases were male and 10 cases were female while among the Vitamin B12 normal group, 07 cases were male and 09 cases were female. Vitamin B12 deficiency is found in 68% of patients.

Conclusion: There is high prevalence of Vitamin B12 deficiency in CKD patients. Hence, Serum Vitamin B12 level testing should be recommended routinely in patients with chronic kidney disease.

Keywords: Chronic kidney disease, Vitamin B12, Anemia.

Introduction

Chronic Kidney Disease (CKD) is a growing health burden in the world, with estimates of nearly 20 million affected (1). CKD is defined as either sustained reduction in kidney function with a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m2 or evidence of kidney damage (2). Although kidney damage may be defined by radiologic or pathologic findings, it is diagnosed most frequently by the presence of micro albuminuria. Levels of urinary albumin excretion above 30 mg/day (or urinary albumin to creatinine ratio of 17 mg/g or higher for men or 25 mg/g or higher for women) on at least 2 measurements are consistent with CKD, regardless of the level of GFR (3).

Anaemia has long been recognized 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).

Severe Chronic Kidney Disease has an adverse effect on haematopoiesis. There is imbalance between haematopoiesis and increased destruction. Many Patients with CKD show megaloblastosis on examination of the bone marrow. This suggests that Vitamin B12& folic acid deficiency might be additional factors contributing to inadequate haematopoiesis in uraemia. The most common causes of megaloblastosis are cobalamin (vitamin B12) and folate deficiencies. Various studies carried out on Asian Indians with normal renal function show that they have low levels of Vitamin B12 and high levels of homocysteine and methylmalonic acid. The major defect appears to be one of like relative bone marrow failure. Lack of erythropoietin, Iron deficiency anaemia and shortened red cell lifespan are the major factors contributing to anaemia in CRF (5, 6).

Many Patients with CKD show megaloblastosis on examination of the bonemarrow. This suggests that Vitamin B12 & folic acid deficiency might be additional factors contributing to inadequate haematopoiesis in uraemia. Patients with CKD are at higher risk for nutritional deficiencies due to medication interactions, dietary restrictions and malnutrition. Furthermore, the dialysis procedure itself may lead to vitamin B deficiency, especially in the case of folate where its molecular size renders it capable of being cleared during Hemodialysis (HD). As folate is not stored in the body in large amounts, deficiency can develop within a few weeks (7).

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. (8)

Material and Method

Study design: Cross sectional study

Study setting: Tertiary Care Hospital.

Study Participants: All patients of ckd who were attending the Tertiary care hospital.

Inclusion criteria

1 Indoor patients / patients admitted in Dialysis unit of our tertiary care hospital.

2 Known case of chronic kidney disease

3 Willing to participate in the study

Exclusion criteria

1 < 18 years.

2 Any evidence of other factors that leads to Vitamin B12 deficiency anemia like Ilea Resection, Gastrectomy.

3 Known case of Pernicious Anaemia.

Sample size: 50

Procedure

Case of CKD, meeting the inclusion criteria

↓

Enrolled after informed written consent

↓

Detailed evaluation

↓

Entered in Patient's Proforma

↓

Serum Vitamin B12 Level

↓

Findings documented

↓

Correlation B12 deficiency with duration of CKD.

Result and Discussion

Table 1: Sex Distribution of the patients

Sex	No. of Patients	Percentage
Male	31	62
Female	19	38
Total Patients	50	100

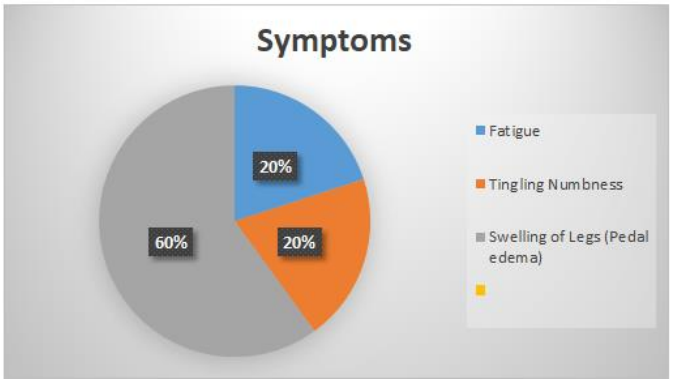
Among the 50 patients included in the study, 31 (62%) were males and 19 (38%) were females.

Table 2: Age Distribution of Patients

Age Group(Years)	Total	Percentage
<40	5	10
40-60	20	40
>60	25	50
Total	50	100

The above table shows the age distribution of cases. It was seen that 5 (10%) cases were less than 40 years, 20 (40%) cases were between 40- 60 years and 25 (50%) cases were above 60 years of age.

Figure 1: Distribution of cases according to Symptoms Frequency Percentage



The above table shows distribution of cases according to symptoms of chronic kidney disease. It was observed that 30 (60%) cases had Swelling of Legs (Pedal edema), 10 (20%) cases had Tingling Numbness and 10 (20%) cases had fatigue.

Table 3: Distribution of cases according MCV

MCV	Frequency	Percent
Raised	27	54%
Normal	23	46%
Total	50	100%

The above table shows distribution of cases according to MCV. It was observed that 27 (54 %) cases had raised MCV and 23 (46%) cases had normal MCV.

Table 4: Distribution according to Kidney size

Kidney size	Frequency	Percent
Reduced	45	90
Normal	5	10
Total	50	100

The above table shows distribution of cases according to kidney size. It was observed that 45 (90%) cases had reduced kidney size while 5 (10.0) cases had normal kidney size.

Table 5: Distribution of cases according to Vitamin B12 deficiency

Vitamin B12 deficiency	Frequency	Percent
Present	34	68%
Absent	16	32%
Total	50	100%

The above table shows distribution of cases according to Vitamin B12 deficiency. It was observed that 34(68%) cases had Vitamin B12 deficiency while 16(32%) cases did not had had Vitamin B12 deficiency

Table 6: Distribution of quantitative variables among the two groups Variables B12 No. Mean Std. Deviation P- value

Variable	B12	No.	Mean	Std. Deviation	P- value
Age	Deficient	34	54.02	11.157	
	Normal	16	54.72	7.608	0.753
Hemoglobin	Deficient	34	8.62	2.125	
	Normal	16	9.02	1.631	0.369
Blood Urea	Deficient	34	55.1	18.407	
	Normal	16	57.06	27.314	0.703
Serum Creatinine	Deficient	34	3.64	2.184	
	Normal	16	4.54	3.232	0.14
Serum Uric acid	Deficient	34	5.32	1.773	
	Normal	16	5.83	1.755	0.205
Serum K+	Deficient	34	5.26	0.765	
	Normal	16	5.34	1.129	0.694
Serum LDH	Deficient	34	60.884	8.88	
	Normal	16	59.148	10.296	0.391

The above table shows details of the mean comparison of Age, Hb, Blood Urea, Serum Creatinine, Serum Uric acid, Serum K+, LDH and Duration of CKD among the Vitamin B12 Deficient and Normal Group. There is no significant difference between the mean Age, Hb, Blood Urea, Serum Creatinine, Serum Uric acid, Serum K+, LDH among the Vitamin B12 deficient and normal group, whereas significant difference observed in mean duration of CKD among the Vitamin B12 Deficient and Normal Group which is statistically significant. The mean duration of CKD is more in B12 deficient group as compared to Normal Group.

Table 7: Comparison of Vitamin B12 deficiency with Age

Age (in years)	Deficient Vit B12		Normal Vit B12		Total
	No.	%	No.	%	No.
<40	6	17.64	1	6.25	7
40-60	16	47.05	10	62.5	26
>60	12	35.29	5	31.25	17
Total	34	100	16	100	50

The above table shows Comparison of Vitamin B12 deficiency with age. It was observed that among the

Vitamin B12 deficient group, 6 (17%) cases were less than 40 years, 16 (47%) cases were between 40-60 years and 12 (35%) cases were above 60 years of age while among the Vitamin B12 normal group, 1 (6.0%) cases were less than 40 years, 10 (62%) cases were between 40-60 years and 5 (31%) cases were above 60 years of age.

Table 8: Comparison of Vitamin B12 deficiency with family history of CKD

Family history of CKD	Deficiency of Vit B12		Normal Vit B12		Total	
	No.	%	No.	%	No.	%
Present	3	8.5	2	12	5	10
Absent	31	91.5	14	88	45	90
Total	34	100	16	100	50	100

The above table shows Comparison of Vitamin B12 deficiency with family history of CKD. It was observed that among the Vitamin B12 deficient group, 3(8.5%) cases had family history of chronic kidney disease was present and in 31 (91.5%) cases family history of chronic kidney disease was absent while among the Vitamin B12 normal group, 2 (12%) cases had family history of chronic kidney disease was present.

Table 9: Comparison of Vitamin B12 deficiency with tingling& numbness

Tingling numbness	Deficient Vit B12		Normal Vit B12		Total	
	No.	%	No.	%	No.	%
Present	14	41.7	6	37.5	20	45
Absent	20	59.3	10	62.5	30	55
Total	34	100	16	100	50	100

p-value by Fisher's Exact Test is 0.945

The above table shows Comparison of Vitamin B12 deficiency with tingling numbness. It was observed that among the Vitamin B12 deficient group, 14 (41.7) cases had tingling numbness and 20 (59.3) cases did not have tingling numbness while among the Vitamin B12 normal group, 06 (37.5) cases had tingling numbness and 10 (62.5) cases did not had tingling numbness.

Table 10: Comparison of Vitamin B12 deficiency with macrocytes

Macrocytes	Deficient Vit B12		Normal Vit B12		Total	
	No.	%	No.	%	No.	%
Present	30	88.4	8	50	38	76
Absent	4	12.6	8	50	12	24
Total	34	100	16	100	50	100

P-value by Fisher's Exact Test is 0.001

The above table shows Comparison of Vitamin B12 deficiency with macrocytes. It was observed that among the Vitamin B12 deficient group, 30 (88.4) cases had macrocytes and 4 (12.6) cases did not have macrocytes while among the Vitamin B12 normal group, 8 (50%) cases had macrocytes and 8 (50%) cases did not had macrocytes.

Table 11: Comparison of Vitamin B12 deficiency with Kidney size

Kidney size	Deficient Vit B12		Normal Vit B12		Total	
	No.	%	No.	%	No.	%
Reduce	34	100	12	75	46	90
Normal	0	0	4	25	4	10
Total	34	100	16	100	50	100

P-value by Fisher's Exact Test is 0.001 The above table shows Comparison of Vitamin B12 deficiency with Kidney size. It was observed that among the Vitamin B12 deficient group, 34 (100%) cases had reduced Kidney size while among the Vitamin B12 normal group, 12(75%) cases had reduced Kidney size and 4(25%) cases had normal Kidney size.

Table12: Comparison of Vitamin B12 deficiency with duration of CKD

Duration of CKD	Deficient Vit B12		Normal Vit B12		Total	
	No.	%	No.	%	No.	%
<6 years	22	64.7	11	68.75	33	66
>6 years	12	35.29	5	31.34	17	44
Total	34	100	16	100	50	100

P-value by Chi-Square Test is 0.06

The above table shows Comparison of Vitamin B12 deficiency with duration of CKD. It was observed that among the Vitamin B12 deficient group, 22 (64.7%) cases have <6 years duration of CKD and 12 (35.29%) cases have >6 years duration of CKD while among the Vitamin B12 normal group, 11 (68.75%) cases have <6 years duration of CKD and 05 (31.4%) cases have >6 years duration of CKD.

Discussion

In the present study, the mean hemoglobin of the participants in Vitamin B12 deficient group was 8.62 ± 2.125 and Vitamin B12 normal group was 9.02 ± 1.631. The association between mean hemoglobin of participants among both groups was statistically insignificant. Anemia is a common manifestation of CKD and the prevalence of anemia increases as the eGFR declines (9). Anemia is associated with a poorer quality of life and the rapid decline of renal function, as well as cardiovascular mortality (10). Anemia is mainly caused by insufficient kidney EPO production and a deficiency of the available iron to support ongoing erythropoiesis in CKD patients. However, several different factors including inflammation, malnutrition, and metabolic disease, have been considered to contribute to the anemia of CKD. Besides, previous studies have demonstrated that people with diabetes were more likely to have anemia compared to those without diabetes(11). Furthermore, anemia was more frequently present in a diabetic population with albuminuria compared to those without albuminuria. To date, several studies have demonstrated that albuminuria is a strong and independent predictor for the progression of kidney disease, development of cardiovascular disease, and mortality (12). Erythropoietin production/secretion declines with advancing renal failure in all cases of CKD, regardless of cause, hence the similarity in prevalence across the different settings. Anaemia in CKD has been associated with poorer cardiovascular outcomes, including heart failure, LVH and increased rates of morbidity and mortality (13). Some authors have proposed that significant losses of transferrin in heavy proteinuria resulted in iron-deficiency anemia (14). Others have suggested that endothelial dysfunction and microvascular damage in the renal tubulointerstitium which were thought to be the pathogenesis of albuminuria, can lead to the impairment of EPO production and release. Tubulointerstitial injury is a major feature of diabetic nephropathy and also reflects influences in other forms of renal disease(15). Unal et al. found that anemia was frequent among kidney transplant recipients with microalbuminuria and they suggested that a tubulointerstitial injury of chronic allograft nephropathy leads to erythropoietin deficiency, which starts even before significant deterioration of excretory renal function has occurred (16). In addition, a recent study demonstrated that a low hemoglobin level predicted the progression or development of albuminuria in those with type 2 diabetes (17). The authors proposed that the leakage of protein which is thought to be an important contributor to progressive tubulointerstitial injury, may cause ineffective erythropoiesis in renal tubulointerstitium. Indeed, further experimental studies are needed to explore the delicate interaction mechanisms between impaired endothelial function and erythropoiesis. Based on these findings, we surmised that anemia is an upcoming early marker of microvascular damage and tubulointerstitial injury, can precede declining renal

function, similar to albuminuria. However, this issue should be confirmed by further studies on the serial correlation between changes in renal function and hemoglobin level.

Conclusion

There is high prevalence of Vitamin B12 deficiency in CKD patients. Hence, Serum Vitamin B12 level testing should be recommended routinely in patients with chronic kidney disease and all the treating Nephrologists/Physicians should anticipate the deficiency of Vitamin B12 in CKD patients and take appropriate measures to prevent associated neurological, hematological and gastro-intestinal symptom.

References

1 Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139: 13

2 J.Goddard,A.N.Turner, A.D.Cumming, L.H.Stewart :Davidson's Principle andPractice of Medicine, 20th edition :485-49

3 Cockcroft DW,Gault MH: Prediction of creatinine clearance from serum creatinine.Nephron1976;16:31-41

4 Babitt JL, Lin HY. Mechanisms of anemia in CKD. Journal of the American Society of Nephrology. 2012 Oct1;23(10):1631-4

5 Penington D.G.-Anaemia and polycythemia with renal disease- Postgraduate Journal 1962; 38:497-50

6 Koch K.M., Cook J. D,Finch C.A: Anaemia of regular haeodialysis patients and its treatment:Nephron1974;12:405-419

7 Clase CM, Ki V, Holden RM. Water-soluble vitamins in people with low glomerular filtration rate or on dialysis: a review. Semin Dial 2013; 26:546–56

8 Refsum H, Yajnik C.S., GadkariM et al- Hyperhomocysteinemia and elevated methylmalonic acid indicate a high prevalence of cobalamine deficiency in Asian Indians - Am. J. Cli. Nutrition 2001; 74:233-24

9 Mondo CK, Otim MA, Akol G, Musoke R, Orem J. The prevalence and distribution of non-communicable diseases and their risk factors in Kasese district, Uganda. Cardiovasc J Afr 2013; 24:52–57

10 Astor BC, Muntner P, Levin A, Eustace JA, Coresh J. Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988– 1994). Archives of internal medicine. 2002; 162(12):1401–8. Epub2002/06/22.

11 Babazono T, Hanai K, Suzuki K, Kiuchi Y, Inoue A, Tanaka M, et al. Lower haemoglobin level and subsequent decline in kidney function in type 2 diabetic adults without clinical albuminuria. Diabetologia. 2006; 49(6):1387–93. Epub2006/04/14.

12 ThomasMC,MacIsaacRJ,TsalamandrisC,PowerD,Jerums G.Unrecogn ized Anemia in Patients With Diabetes A cross-sectional survey. Diabetes care. 2003; 26(4):1164–9

13 Levey AS, de Jong PE, Coresh J, El Nahas M, Astor BC, Matsushita K, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney international. 2011; 80(1):17–28. Epub 2010/12/15.

14 Astor BC, Arnett DK, Brown A, Coresh J. Association of kidney function and hemoglobin with left ventricular morphology among African Americans: the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis 2004; 43:836.

15 Prinsen BH, de Sain-van der Velden MG, Kaysen GA, Straver HW, van Rijn HJ, Stellaard F, et al.

Transferrin synthesis is increased in nephrotic patients insufficiently to replace urinary losses. Journal of the American Society of Nephrology: JASN. 2001; 12(5):1017–25. Epub2001/04/24

16 Gilbert RE, Cooper ME. The tubulointerstitium in progressive diabetic kidney disease: more than an aftermath of glomerular injury? Kidney international. 1999; 56(5):1627– 37

17 Unal A, Kocyigit I, Arikan T, Sipahioglu MH, Tokgoz B, Oymak O. Microalbuminuria is associated with high prevalence of anemia in renal transplant recipients. Transplantation proceedings. 2013; 45(3):949–52.