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Prevalence of Vitamin B12 Deficiency among Haemodialysis Patients in Academy Charity Teaching Hospital, Khartoum, Sudan in 2019-2020

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ABSTRACT
Background: *Anemia is a major co-morbidity of chronic kidney disease (CKD) and in patients with end stage renal disease (ESRD) on renal replacement therapy. Patients with end-stage renal disease (ESRD) are at higher risk for nutritional deficiencies due to medication interactions, dietary restrictions and malnutrition. This suggests that vitamin B12 deficiency might be additional factors contributing in anemia.*
Methods and materials: *It was a hospital based cross sectional study conducted in Academy Charity Teaching Hospital, Khartoum, Sudan in 2019. Study included 80 patients suffering from chronic kidney disease undergoing haemodialysis in the nephrology unit. The 80 participants were selected purposively, each participant was asked for a verbal consent, and then each individual was asked about the questionnaire by the researcher. After 3 hours from each session of the haemodialysis, 2ml of blood sample was withdrawn from the machine by a nurse in the unit then immediately sent to the Laboratory for further investigations. Participants with vitamin B12 level below 190pg/ml were evaluated for deficiency.*
Results: *Out of total 80 subjects, 59% were males and 41% were females with a mean age of 50.89 years. Vitamin B12 deficiency was observed in 87% of chronic kidney disease patients. 58% of the participants with vitamin B12 deficiency suffered with neurological and haematological symptoms. As well as, there was a negative statistically significant association between years in haemodialysis and vitamin B12 Deficiency. There was also an indirect relationship between age and vitamin B12 level.*
Conclusion: *Present study showed high prevalence vitamin B12 deficiency in chronic kidney disease patients. Most of the patients had associated neurological and haematological symptoms. Hence all the treating nephrologists should anticipate the deficiency of vitamin B12 in CKD patients and take appropriate measures for its control.*
Keywords: *ESRD, end stage renal disease, chronic kidney disease, megaloblastic anemia, Vitamin deficiency, Vitamin B12 Levels, dialysis*

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I. INTRODUCTION AND LITERATURE REVIEW

1.1. INTRODUCTION

It is well established that chronic kidney disease (CKD) is a growing health burden in the world, associated with renal function decline accelerated in hypertension, diabetes, obesity and primary renal disorders [1]. Patients with end-stage renal disease (ESRD) are at higher risk for nutritional deficiencies due to medication interactions, dietary restrictions and malnutrition [2]. Furthermore, the dialysis procedure itself may lead to vitamin B deficiencies [3].

Rationale

Going through literature review, it was evident that end stage renal disease patients undergoing haemodialysis suffer from nutritional deficiencies due to dietary restriction in the community. The main goal was to determine the prevalence of vitamin B12 deficiency in haemodialysis patients and whether it has deleterious effect on haemodialysis patients.

1.2. LITEATURE REVIEW

Vitamin B12 is one of the water soluble vitamins that is also known as Cobalamin (Cbl) with normal range between 100- 200 nanograms per millilitre (190 - 950 picograms per milliliter (pg/ml), which is commonly found in animal products such as fish, meat, poultry, eggs, milk and others. The importance of vitamin B12 lays in its need in developing healthy neurological and haematological systems. The Deficiency of vitamin B12 can lead to haematological impairment in erythropoiesis, leading to macrocytic normochromic anemia. As well as it hinders the normal growth of myelin sheath of neurons causing impairment in its neural transmission [4].

Renal failure is impairment of the normal functions of the kidney which includes the disposal of excess electrolytes and metabolic by-products, as well as maintaining blood pressure, erythropoietin production which is needed for red blood cells production, and vitamin D activation [5]. Anemia is a major comorbidity of chronic kidney disease (CKD) and in patients with end stage renal disease (ESRD) on renal replacement therapy. Untreated dialysis patients were often symptomatic and dependent on blood transfusions with their innate morbidity until the advent of erythropoietin stimulating agents (ESA), which transformed anemia management in this population. ESA effectively increase hemoglobin and improve quality of life in patients on dialysis [6]. Renal failure can be managed mainly by haemodialysis and supplements; haemodialysis is a process of getting rid of toxins through semi permeable membrane from the blood to dialysis machine [7].

It was found that there is a weak correlation between vitamin B12 deficiency and haemodialysis patients, since they suffer from nutritional deficiency [8]. It was discovered that vitamin B12 deficiency in haemodialysis patients plays a role in erythropoietin resistance affecting the management of anemia [9]. As well as, vitamin B12 deficiency may have deleterious effects on end stage renal disease (ESRD) patients on maintenance haemodialysis, and may increase erythropoietin stimulating agent (ESA) resistance, yet little is known about its prevalence in this population [10].

A study in New York proved that about 58% of the haemodialysis patients suffer from vitamin B12 deficiency [10]. In another study out of 60 patients 32 were found to be vitamin B12 deficient in Osmania General Hospital [11]. Out of total 50 patients of chronic kidney disease, 56% were also found to be vitamin B12 deficient in BharatiVidhyapeeth Deemed University Medical College, Pune, India [12].

1.3. STATEMENT OF RESEARCH PROBLEM

Low levels of vitamin B12 can affect erythropoietin activity, increase level of homocysteine which can result in cardiovascular complications and neurological deficit. As per study of Staten Island University Hospital in New York has established that about 58% of haemodialysis patients have vitamin B12 deficiency. In another study of Osmania general hospital 32 out of 60 patients were found to have vitamin B12 deficiency. Study of BharatiVidhyapeeth Deemed University Medical College, Pune, India showed 56% patients suffered from vitamin B12 deficiency. Little is known about the prevalence of vitamin B12 deficiency among patients undergoing haemodialysis in Sudan, and the potential impact that in terms of erythropoietin resistant anaemia.

II. OBJECTIVES

2.1 RESEARCH QUESTION

What is the prevalence of vitamin B12 deficiency among haemodialysis patients in Academy Charity Teaching Hospital?

2.2 GENERAL (PRIMARY) OBJECTIVE

To determine the prevalence of vitamin B12 deficiency among haemodialysis patients in Academy Charity Teaching Hospital.

2.3 SPECIFIC OBJECTIVES

1. To determine the number of haemodialysis patients suffering from vitamin B12 deficiency.
2. To determine the factors associated to vitamin B12 deficiency in haemodialysis patients.
3. To establish the relationship between vitamin B12 deficiency and haemodialysis.

III. MATERIAL AND METHODS

3.1 STUDY DESIGN

A facility-based descriptive cross-sectional study

3.2 STUDY AREA AND POPULATION

Haemodialysis patients in haemodialysis centre located in Academy Charity Teaching Hospital, Al Sahafa, Khartoum, Sudan. Statistics on number of staff of haemodialysis unit consist of 6 doctors and 18 nurses, 100 patients are under haemodialysis attending ACTH.

3.3 SAMPLING TECHNIQUE AND SAMPLE SIZE

Purposive sampling technique was used to select the study population. The estimated sample was calculated based on the formula $\mathbf{n=N/1+Nd^2}$ where:

n is the estimated sample size to be reached.

N is the total number of patients under haemodialysis (in and outpatients).

d is the degree of accuracy set at 0.05.

Based on this assumption, the estimated sample size of our research was 80 haemodialysis patients.

3.4 DATA COLLECTION, MANAGEMENT AND STATISTICAL ANALYSIS

The research tool primarily developed in English by the researcher (annex) was translated in Arabic to facilitate the understanding by the study participants. The research tool comprised two parts.

Part one was to collect information related to the characteristics of the participants (age, gender, and residence), the duration of being under haemodialysis, the diet of the participants, being under vitamin B12, iron and erythropoietin supplements, and the symptoms experienced.

Part two of the research tool was to record the results of blood testing as well as haemoglobin level recorded from medical records. The sample was withdrawn by a professional nurse from the haemodialysis machine at the last hour of the haemodialysis session, and then the samples was taken to the laboratory at Tamyaouz hospital for further investigation using B12 kit.

The type of B12 kit used was e411 which costs 33,000SDG with the caliber and control from SAMASU Company, all funded by the researcher. About 8-11 hours spent each day at the haemodialysis center for 2 weeks to collect the required samples, the 3rd week the results of the samples were given back to each patient.

The data collected was computerized through Epi-info 7, and analyzed through the statistical package for social sciences (SPSS 23). Firstly, the data was summarized graphically (frequency tables for estimating prevalence and graphics) and numerical (mean, standard deviation, median). The statistical analysis of the data included chi-square tests, correlation analysis and analysis of variance to find association between variables. All statistical tests was significant when $p < 0.05$.

3.5 ETHICAL CONSIDERATIONS

The research proposal was reviewed by the Research Committee of the Faculty of Medicine and Ethical approval was obtained from the management of Academy Charity Teaching Hospital. Authorization to implement the research was obtained from the Administration of ACTH.

A well –informed verbal consent was obtained from each of the study participants following clear and complete information of the research objectives including the blood sampling. The rights of the participants were ensured through their freedom to participate, deny, or withdraw at any time they may wish.

The confidentiality of the participants was ensured through the use of anonymous research tool and the data collected was not used for any other purpose other than the research objectives. The research was solely responsible of the data collected. The results of vitamin B12 level were communicated to the responsible doctor in order to act accordingly.

IV. RESULTS

The study carried out was done among haemodialysis patients in Academy Charity Teaching Hospital to assess their level of vitamin B12 and to assess the factors associated with vitamin B12 level.

Sociodemographic characteristic of the study population

1. Out of the 80 haemodialysis participants in the study it was found that the male gender was 59% showing predominance over the female gender who was 41%.

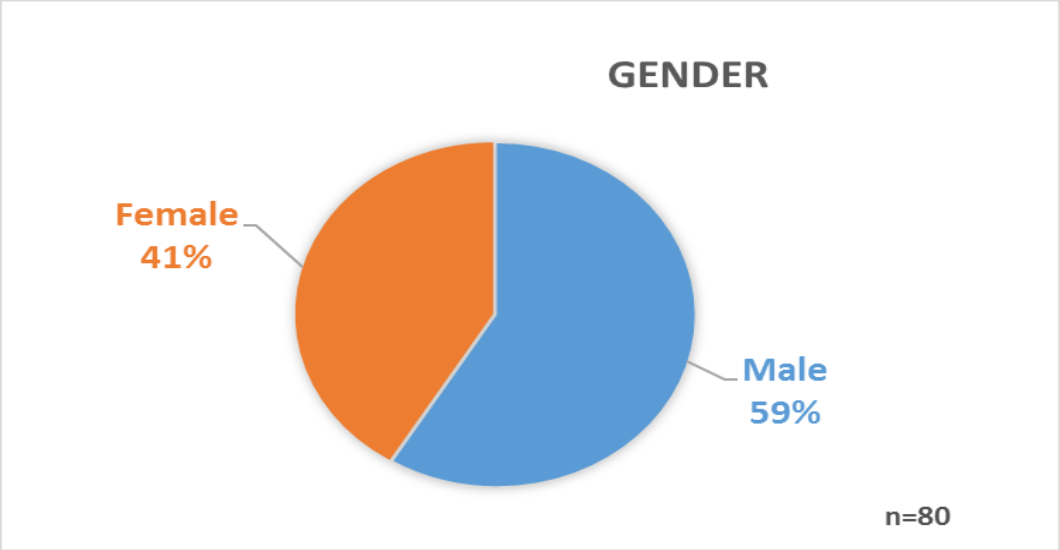

Figure 4.1: Distribution of the population based on gender

2. The curve shows the mean age in years was 50.89 and the standard deivation was 15.423.

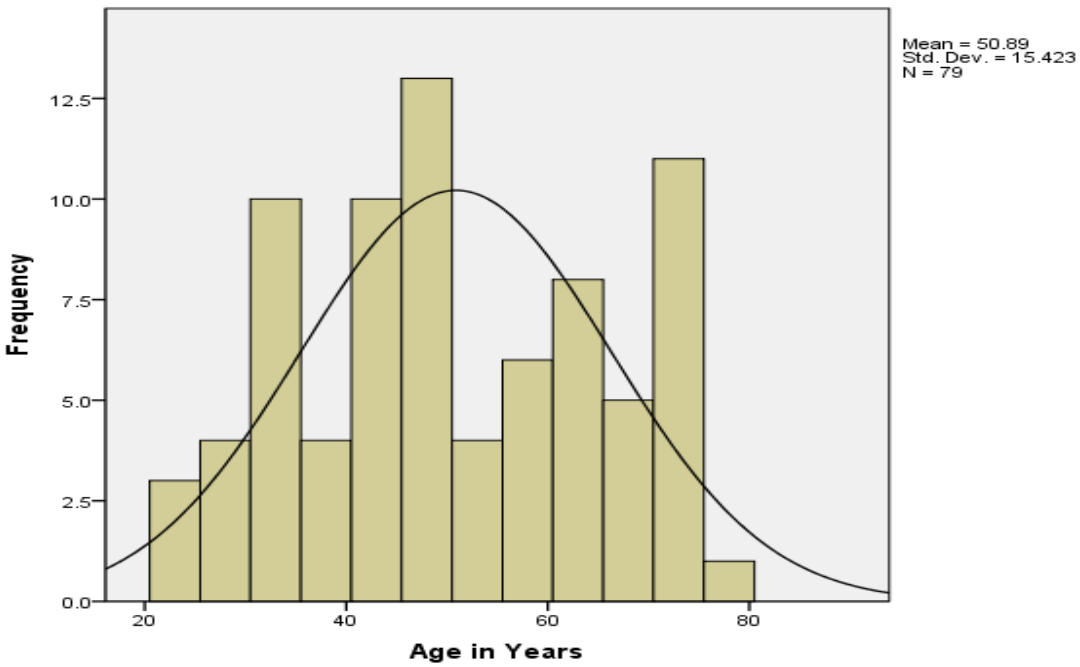

Figure 4.2: Age distribution curve of the study participants

3. The pie chart shows 85% of the participants who underwent haemodialysis live in Khartoum. 15% were compromised almost equally by residents of Nahr Alneel, Ksa, North Darfur, North kordofan, Northern State, and Aljazeerah.

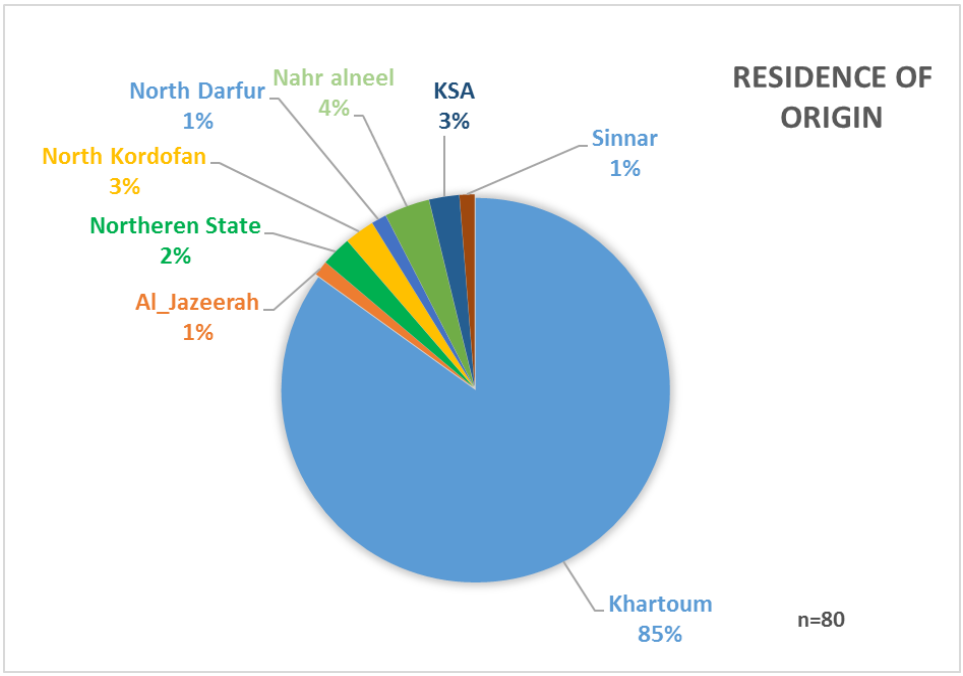

Figure 4.3: Distribution of the population based on their residence

The Prevalnce of vitamin B12 defieceny among haemodialysis patients

The figure shows that 87% of patients undergoing haemodialysis have vitamin B12 deficiency.

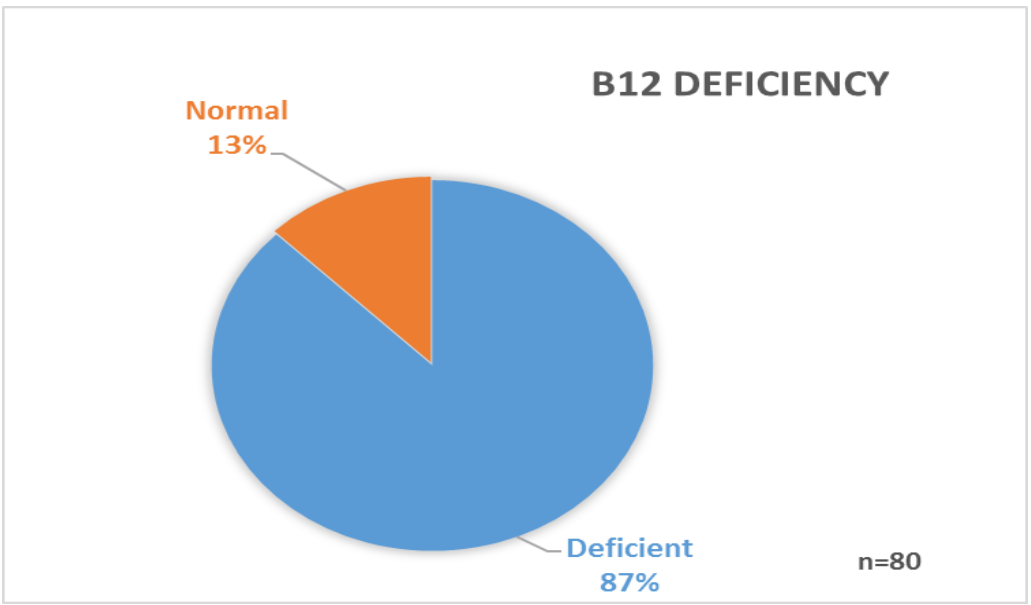

Figure 4.4: The prevalnce of vitamin B12 deficiency

Screening of symptoms related to vitamin B12 level

Interpretation: 58% of people with vitamin B12 deficiency suffer from weakness, tiredness, or lightheadedness compared to 40% who suffer from the same symptoms, but with normal vitamin B12 levels.

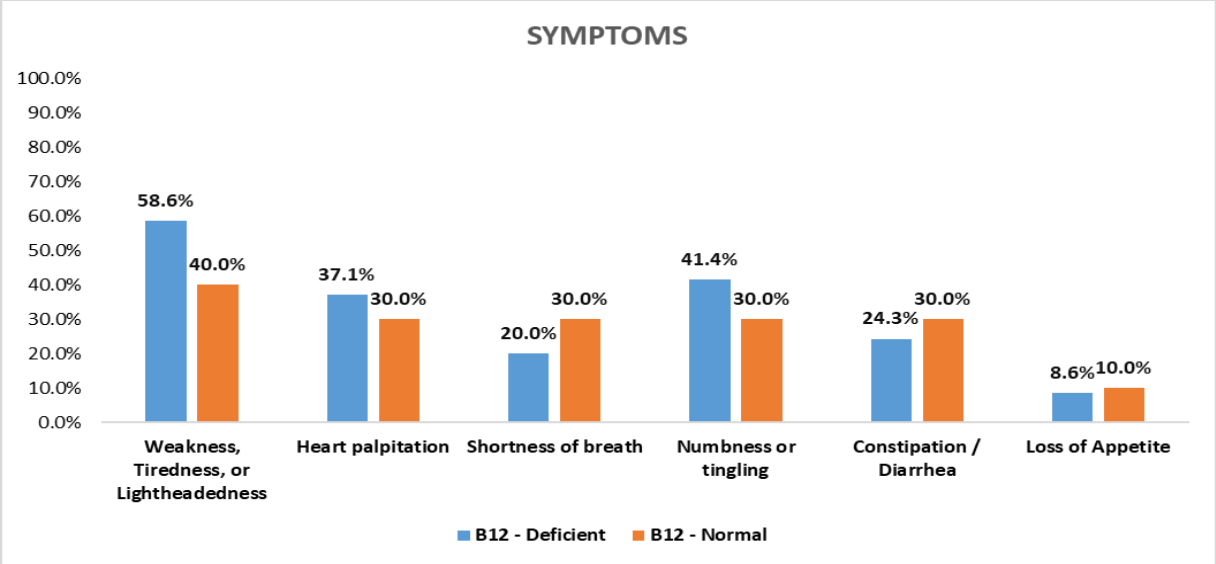

Figure 4.5: Screening of symptoms related to vitamin B12 level

Classification of patients based on supplement intake

The figure shows the participants on vitamin B12 supplements were found to be 3.8%, while 96.3% were not on vitamin B12 suppliments. 60% were on iron supplements, while 40% were not on iron. However, All the particpants were on erythropoietin.

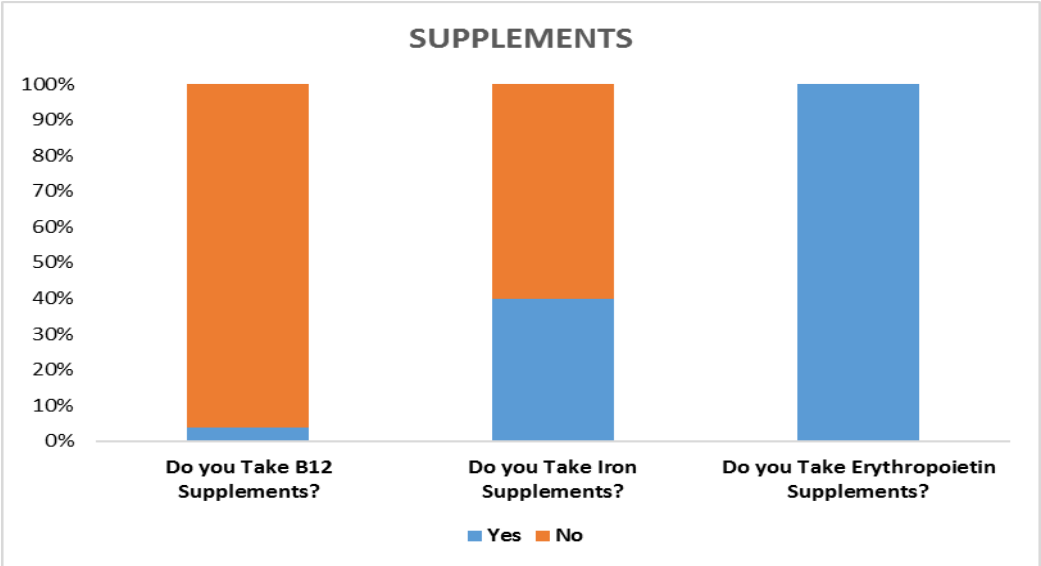

Figure 4.6: Classification of patients based on supplement

Descriptive statistics

The table shows the maximum age in years was 80 and minimum was 23, the mean age was 50.89, the median was 48, the mode was 43, and standard deviation was 15.42. While for the duration of haemodialysis the maximum duration of haemodialysis was 14 years and minimum was 0.25 (3months), the mean was 4.0956, and standard deviation was 3.19.

For the vitamin B12 level the maximum level was 273 and the minimum level was 52, the mean was 148.88, the median was 154.5, the mode was 112, and standard deviation was 45.14. For the haemoglobin level the maximum level was 18.5 and the minimum level was 5.2, the mean value was 9.67, the median was 9.25, the mode was 8.6, and standard deviation was 2.06.

Table 4.1a: Descriptiive statisitics of Age, duration of haemodialysis, Vitamin B12 level and Haemoglobin level

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age in Years	79	23	80	50.89	15.423
For How long have you been undergoing haemodialysis?	80	.25	14.00	4.0956	3.19074
Vitamin B12 pg/ml	80	52.00	273.00	148.8750	45.14067
Haemoglobin g/dl	76	5.20	18.50	9.6658	2.06395

Table 4.1b: Descriptiive statisitics of Age, duration of haemodialysis, Vitamin B12 level and Haemoglobin level

Statistics

		Age in Years	Vitamin B12 pg/ml	Haemoglobin g/dl
N	Valid	79	80	76
	Missing	1	0	4
Mean		50.89	148.8750	9.6658
Median		48.00	154.5000	9.2500
Mode		43	112.00[a]	8.60
Std. Deviation		15.423	45.14067	2.06395

a. Multiple modes exist. The smallest value is shown

The Figure shows the mean of vitamin B12 level among the particpants was 148.88pg/ml and the standard deviation was 45.13.

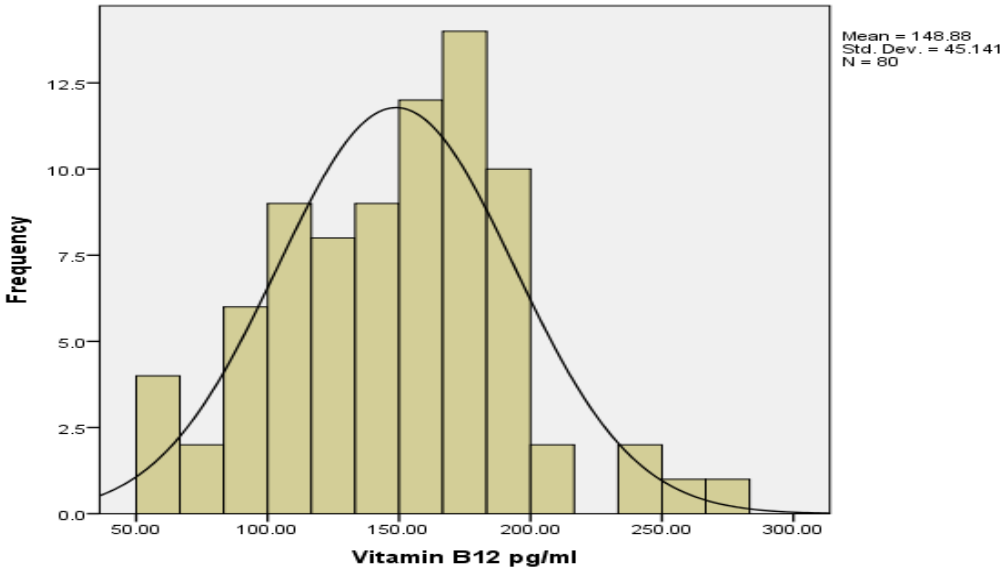

Figure 4.7: Vitamin B12 level distribution curve of the study participant

The figure shows the mean haemoglobin level was 9.67g/dl and standard deviation was 2.064.

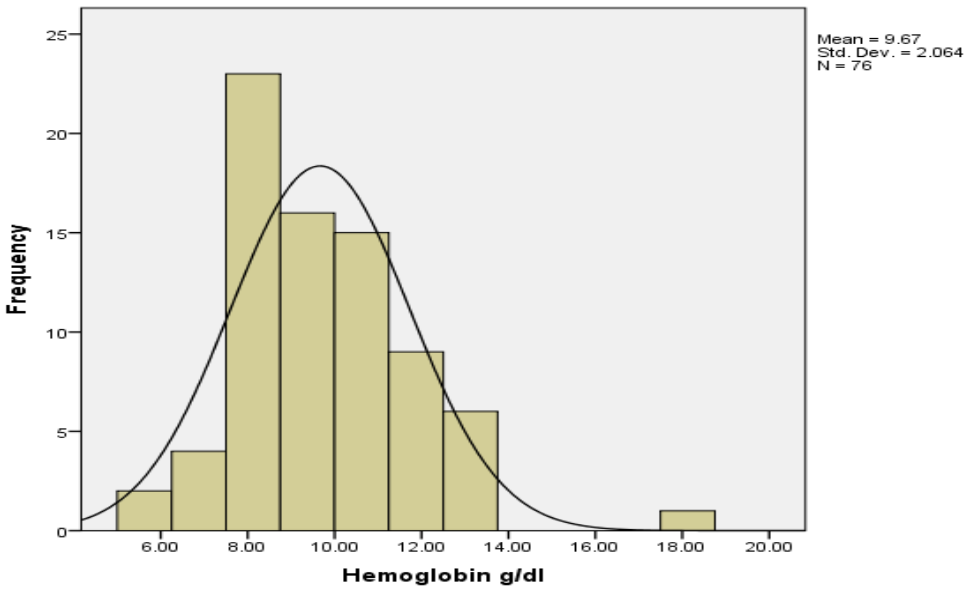

Figure 4.8: Haemoglobin distribution curve of the study participant

The duration of haemodialysis according to vitamin B12 level

The figure of bar chart shows those who underwent haemodialysis for less than 5 years with vitamin B12 deficiency were 46 particpants, while those with normal vitamin B12 level were 8 participant. Those who underwent for 5-10 years with vitamin B12 deficiency were found to be 19 particpant, while those with normal level are 2 particpiants. However those who underwent for 10-15 years with deficieny of vitamin B12 are found to be 5 particpants.

The result shows that those who underwent haemodialysis for less than 5 years are more deficiecnt compared to those who underwent for more than 5 years.

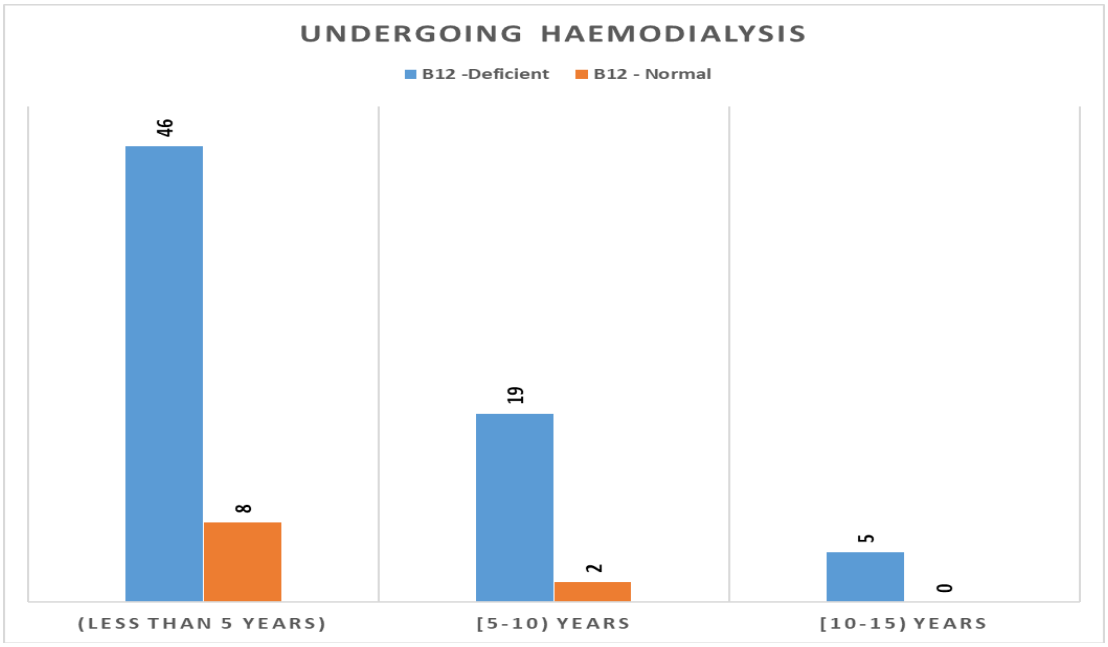

Figure 4.9: Duration of haemodialysis according to vitamin B12 level

The association between vitamin B12 rich food and vitamin B12 level

There was no statistically significant association between the vitamin B12 deficiency, and food consumed in the groups who consumes or doesn't consume each food product under the question [test used: Chi Test of Association]

Table 4.2: The association between vitamin B12 rich food and vitamin B12 level

CROSS TABULATION (vitamin B12 Deficiency and Food Consumption)

Food	Liver		Chicken		Fish and Tuna		Beef		Milk & Dairy Products		Eggs	
Consumed	B12 - Deficient	B12 - Normal	B12 - Deficient	B12 - Normal	B12 - Deficient	B12 - Normal	B12 - Deficient	B12 - Normal	B12 - Deficient	B12 - Normal	B12 - Deficient	B12 - Normal
Yes	48	6	60	9	51	7	51	9	62	10	60	9
	88.9%	11.1%	87.0%	13.0%	87.9%	12.1%	85.0%	15.0%	86.1%	13.9%	87.0%	13.0%
No	22	4	10	1	19	3	19	1	8	0	10	1
	84.6%	15.4%	90.9%	9.1%	86.4%	13.6%	95.0%	5.0%	100.0%	0.0%	90.9%	9.1%
P value	0.720		1		1		0.437		0.586		1	

Correlation

1. There was no statistically significant association between vitamin B12 deficiency, and the groups who were under supplements or those who were not on supplements [test used: Chi Test of Association]

Table 4.3: The association between vitamin B12 deficiency and supplements intake

Supplements?	B12		Iron		Erythropoietin	
	Yes	No	Yes	No	Yes	No
B12 - Deficient	3 (4.3%)	67 (95.7%)	26 (37.1%)	44 (62.9%)	70 (100%)	0 (0%)
B12 - Normal	0 (0%)	10 (100%)	6 (60%)	4 (40%)	10 (100%)	0 (0%)
P- Value	1		0.187		No comparison	

2. R= -.265 , P value=.018, there was a weak negative statistically significant correlation between years in haemodialysis and vitamin B12 deficiency [negative means: as years in haemodialysis increases the vitamin B12 Level decreases]

Table 4.4: Correlation between years in haemodialysis and vitamin B12 level

		Vitamin B12 pg/ml	For How long have you been undergoing haemodialysis?
Vitamin B12 pg/ml	Pearson Correlation	1	-.265*
	Sig. (2-tailed)		.018
	N	80	80

*. Correlation is significant at the 0.05 level (2-tailed).

3. R= -.304 , P value=.006, there was a weak negative statistically significant correlation between age and vitamin B12 level, which means the older the patient the more likely he has lower vitamin B12 level.

Table 4.5: Correlation between Age and Vitamin B12 level

Correlations

		Age in Years	Vitamin B12 pg/ml
Age in Years	Pearson Correlation	1	-.304**
	Sig. (2-tailed)		.006
	N	79	79

**. Correlation is significant at the 0.05 level (2-tailed).

V. DISCUSSION AND CONCLUSIONS

5.1. DISCUSSION

End stage renal disease populations are well known for their continuous health complications. One of the most of the common complication is anemia, but yet little is known about whether certain deficiencies can be the cause of their chronic anemia.

The study attempted to assess the prevalence of vitamin B12 deficiency among haemodialysis patients in Academy Charity Teaching Hospital in Khartoum in 2019.

The sample sizes of 80 participants were selected purposively, each received a questionnaire and blood sample was withdrawn from the haemodialysis machine. Out of the 80 participants 59% were male and 41% were female with a mean age of 50.89years. About 85% of the participants are originally from Khartoum the rest were from rural areas or neighboring countries.

While assessing throughout the study it was found that the mean duration of haemodialysis was 4.1 years. About 3.8% are on vitamin B12 supplementation, 60% are on iron supplements and 100% are on erythropoietin.

Vitamin B12 deficiency was observed in 87% of CKD patients in present study, and the mean level was 148.88pg/ml which is below the normal range (190- 950 pg/ml). It was found that 58% of those with vitamin B12 deficiency suffer from weakness, tiredness or lightheadedness. Although, they have poor nutrition and restricted diet there was a no association between vitamin B12 rich food intake and vitamin B12 deficiency.

It was also observed that those who underwent haemodialysis less than 5 years have higher prevalence of vitamin B12 deficiency compared to those underwent for more than 5 years, indicating a weakly negative correlation. It might be due to those who are new to heamodialysis their body was not well adapted to the losses and restricted diet. While on the other hand those who underwent for more than 5 years their body was already adapted to the changes.

In addition, there was a weak indirect relationship between age and vitamin B12 level, which mean as the age increases the vitamin B12 level decreases.

The mean haemoglobin was 9.67g/dl indicating most patients were anemic even though 60% were on iron and all of the patients were on erythropoietin.

It was found that the prevalence of vitamin B12 deficiency in Sudan was the highest compared to the previous studies that took place in New York which showed 58% patients, in India Osmania general hospital which showed 53.3% patients and in India, Pune study which showed 56%.

5.2. CONCLUSIONS

Study showed high prevalence vitamin B12 deficiency in chronic kidney disease patients. 58% of the patients had associated neurological and haematological symptoms. Hence all the treating nephrologists should anticipate the deficiency of vitamin B12 in chronic kidney disease patients and take appropriate measures for its control.

5.3. RECOMMENDATIONS

Vitamin B12 supplementation should be considered in chronic kidney disease patients as part of treatment protocol to prevent the complications associated with its deficiency. We also recommend further larger scale prospective studies to validate our findings.

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