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A Study of Hematological Profile and Vitamin B12 Levels in Chronic Kidney Disease Patients in a Tertiary Care Hospital

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Abstract: ***Background: Anemia is a major comorbidity of chronic kidney disease (CKD) and in patients with end stage renal disease (ESRD) on renal replacement therapy. Aims and Objectives: To study hematological profile and serum B12 levels in patients with chronic kidney disease in tertiary care hospital. Hospital based cross sectional study. Discussion: Among 50 patients 68% had Hb between 5-10gm% and 18% had Hb less than 5-10gm% and 18% had Hb less than 5gm%, 14% had more than 10%. serum ferritin levels value of less than 10 was observed in 7(14%) of patients and the remaining 43 (86%) had serum ferritin level in the normal range. 54% of patients had serum b12 levels less than 187 and the rest 46% had level between 187-883. Conclusion: This study shows that anemia is prevalent among CKD patients of which 86% had moderate degree of anemia which was the most frequent finding in both sexes and the degree of anemia was more severe in females as compared to males, most of the patients being elderly. Majority of the patients in our study revealed serum b12 deficiency which also caused elevated serum homocysteine levels in the patients.***

Keywords: CKD, Anemia, ferritin, vitamin B12

1. Introduction

Chronic Kidney Disease (CKD) is a worldwide public health problem. Indeed, the incidence and prevalence of CKD has increased in recent years in both developed and developing countries.

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. Currently, while effective, the cost burden of ESA is enormous. It is estimated that Medicare costs in the US for ESA are approximately two billion US dollars per year. Additionally, recent reports have shown that ESA are associated with strokes at high hemoglobin levels. While ESA address the deficiency in innate erythropoietin production, numerous other factors contribute to anemia as well as resistance to these agents in patients on dialysis. Inflammation, iron deficiency, chronic infections, bone marrow failure, and hyperparathyroidism are among these factors.

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". While intuitively, the diagnosis of B12 deficiency should be confirmed by serum B12 levels, this turns out to be neither sensitive nor specific for B12 deficiency. Serum homocysteine levels have superior sensitivity and specificity to serum B12 levels, but elevated methylmalonic acid (MMA) levels have been shown to be the most sensitive and specific marker in the general population.

Vegetarians are at risk of vitamin B12 and iron deficiency. The diagnosis can be confirmed with a peripheral smear showing hypersegmented neutrophils in addition to macrocytosis.

Chronic kidney disease (CKD) in an Indian cannot be assessed accurately. The approximate prevalence of CKD is 800 pmp and the incidence of ESRD is 150-200 pmp. The commonest cause of CKD is diabetic nephropathy.

The CKD burden is increasing rapidly worldwide. At the end of 2004, 1,78,3000 patients worldwide were receiving treatment for ESKD, of which 77% were on dialysis and 23% had a functioning renal transplant (RT) and this number is increasing at a rate of 7% every year. If the current situation prevails, the global ESRD population will exceed 2 million by 2020. The average incidence of ESKD in developing countries is 175 per million populations, which is lower than what is reported in the developed world. This has been attributed to racial and ethnic diversity, which is also reflected in the disparity in the incidence of ESRD between different populations within the developed nations.

The association of chronic renal failure (CRF) and anemia has been recognized since the early 19th century, first noted by Richard Bright in 1836 when he observed pallor in the development of Bright's disease. Nowadays, such a manifestation is regarded as one of the many components of the vast array of signs and symptoms present in the patients with CRF. Anemia is defined in terms of low levels of hematocrit or hemoglobin. Anemia of renal failure begins relatively early in the development of kidney disease. As progressive destruction of kidney tissue occurs, the degree of anemia increases. Although there is a large degree of

interpatient variability, the hematocrit generally begins to fall when the plasma creatinine concentration is above 2 mg/dl and gets progressively lower as glomerular filtration rate declines further. A normocytic and normochromic red blood cell is a very common but not universal complication of CRF. While microcytic and hypochromic indices might suggest either iron deficiency or aluminium intoxication, macrocytic anemia due to folate and B12 deficiency can also occur in some CRF patients. On blood smears, occasional deformed, spiculated red cell (Burr cells) can be seen. The bone marrow shows erythroid hypoplasia profile of anemia in Chronic Renal Failure patients. Profile of anemia in Chronic Renal Failure patients with little or no interference with leukopoiesis or megakaryopoiesis. Although inadequate production of erythropoietin by kidney tissues is most important factor in the pathogenesis of anemia in CRF, it is not the only one. Other factors play a role in contributing to mild anemia that is often present despite the use of recombinant human erythropoietin. Chief among these factors are shortened erythrocyte survival, blood loss, iron and other nutritional deficiency, and perhaps the effect of uremic inhibitors on the bone marrow. Severe hyperparathyroidism can lead to myelofibrosis in some CRF patients, hence suggesting a direct suppressive effect on erythropoiesis. Non-renal, non-dialysis factors can also superimpose themselves on the anaemia of CRF. These include malignancy, drug-induced bleeding, infection and inflammation.

Aims and Objectives

To study hemtological profile and serum B12 levels in patients with chronic kidney disease in tertiary care hospital

2. Materials and Methods

Source of Data
The clinical study will be conducted on Chronic Kidney Disease patients in S.S. Institute of Medical Sciences and Research Centre, Davanagere.

Study Design
A hospital based Cross sectional study

Study Period and Duration
This study was conducted for a period of the period of 19 months from October 2015 to July 2017.

Place
The study was done under the Department of General Medicine, S.S. Institute of medical sciences & research centre, Davangere, Karnataka.

Sample Size
A total of 50 patients with clinical evidence of CKD fulfilling the inclusion criteria were included in the study.

Inclusion Criteria
All adults (above the age of 18 years) with Chronic Kidney Disease

Exclusion Criteria
- Patients with Acute Kidney Injury
- Patients on vit b12 therapy
- Chronic liver disease
- Chronic pancreatitis

Investigations
- Haemoglobin
- Peripheral smear
- Serum b12 levels
- Serum ferritin levels
- Serum homocysteine levels

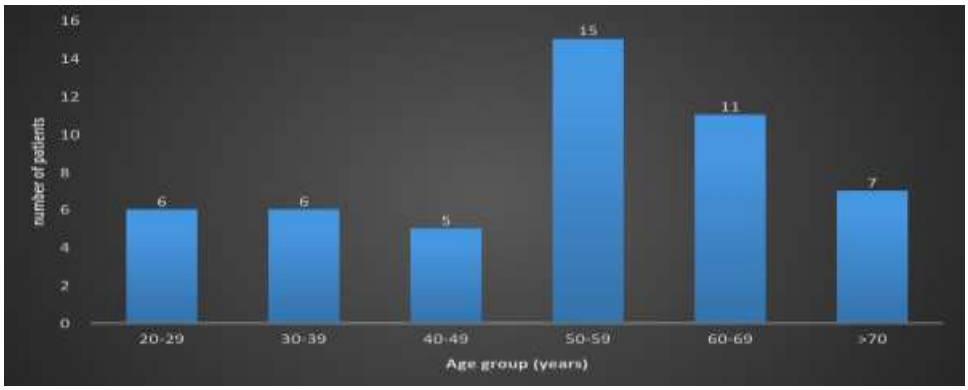
Sampling procedure:

Data Analysis
Statistical methods
The data collected is entered in Microsoft excel and analysed using SPSS version 21 software trial version. The data is expressed in frequencies, percentages, means and standard deviations. Results with p value <0.05 were considered as significant.

3. Results

Table 1: Table showing age distribution of the study group

Age Group	Frequency	Percentage
20-29	6	12.0
30-39	6	12.0
40-49	5	10.0
50-59	15	30.0
60-69	11	22.0
>70	7	14.0
Total	**50**	**100.0**

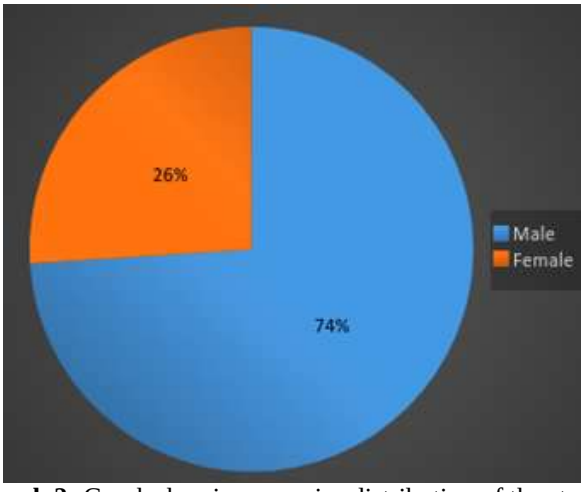


Graph 1: Graph showing Age distribution of the study group

In this study most of the patients were between age group of 50 to 70 yrs

Table 2: Table showing sex wise distribution of the study group

Gender	Frequency	Percentage
Male	37	74.0
Female	13	26.0
Total	**50**	**100.0**

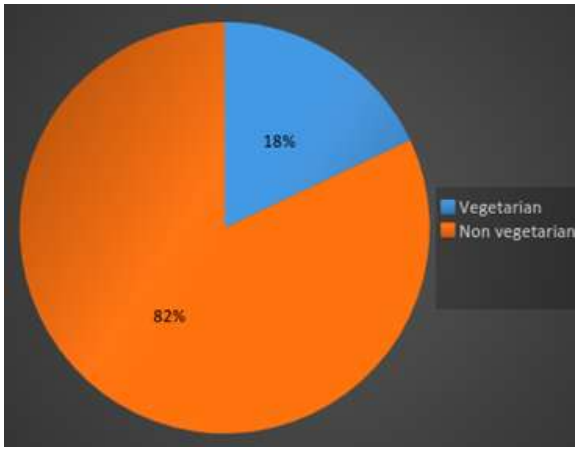


Graph 2: Graph showing sex wise distribution of the study group

In the present study, 37(74%) of patients were male and 13(26%) were female

Table 3: Table showing diet pattern of the study group

Diet Pattern	Frequency	Percentage
Vegetarian	9	18.0
Non vegetarian	41	82.0
Total	**50**	**100.0**

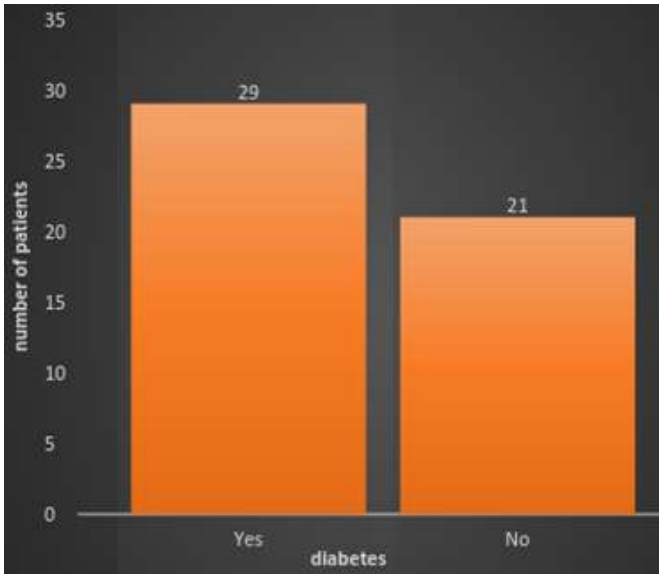


Graph - 3 Graph showing diet pattern of the study group

41 Patients (82%) are non-vegetarians
8 patients(18%) are vegetarians.

Table 4: Table showing the number of diabetics in the study group

Diabetes	Frequency	Percentage
Yes	29	58.0
No	21	42.0
Total	**50**	**100.0**

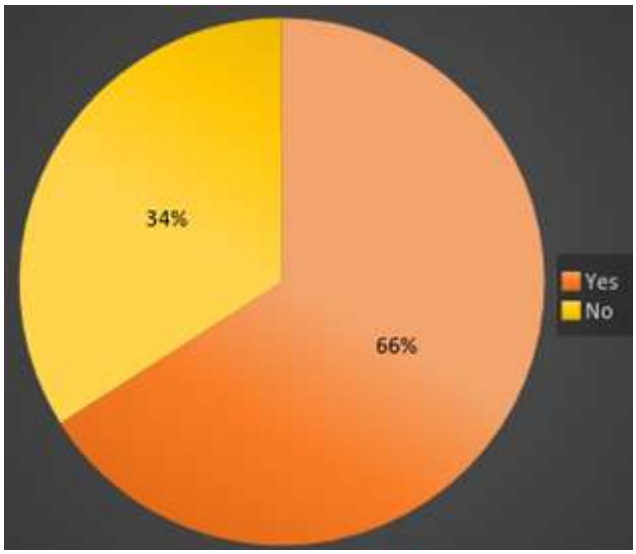


Graph 4: Graph showing the number of diabetics in the study group.

29 patients(58%) were diabetic
21 patients (42%) were non-diabetic

Table 5: Table showing blood transfusion of the study group(at least one transfusion in three months)

Blood Transfusion	Frequency	Percentage
Yes	33	66.0
No	17	34.0
Total	**50**	**100.0**

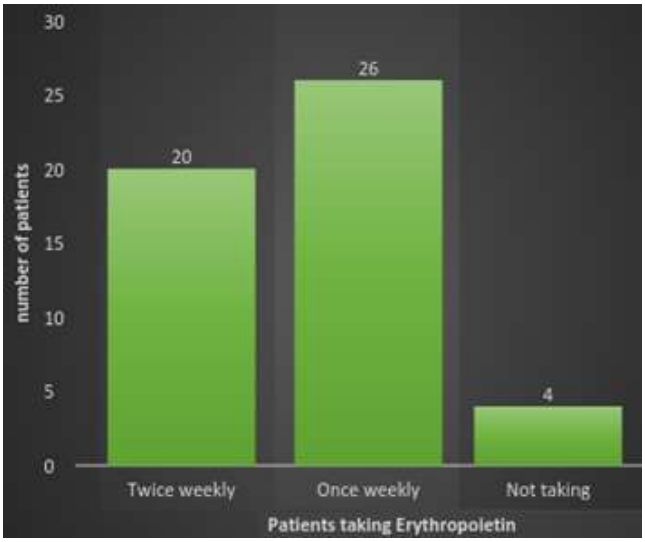


Graph 5: Graph showing blood transfusion of the study group (at least one transfusion in three months)

As depicted in the graph patients 33(66%) patients required blood transfusion atleast once in three months and 17 (34%) patients did not require blood transfusion in three months.

Table 6: Table showing patient taking injection erythropoietin of the study group

Patient taking Erythropoietin	Frequency	Percentage
Twice weekly	20	40.0
Once weekly	26	52.0
Not taking	4	8.0
Total	**50**	**100.0**

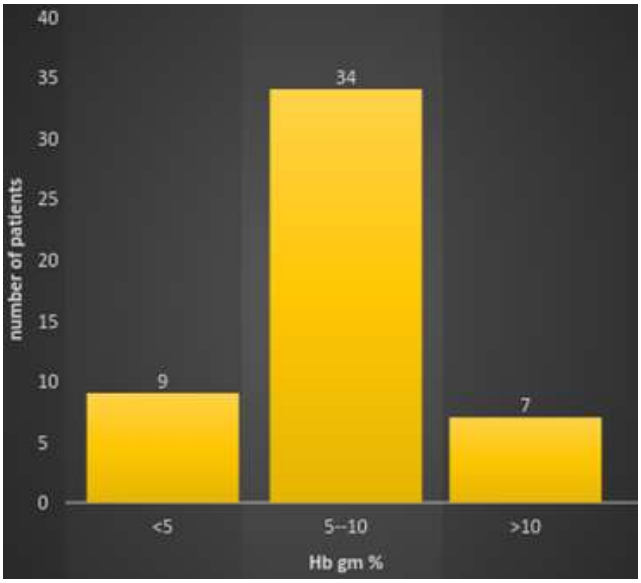


Graph 6: Graph showing patient taking injection erythropoietin of the study group

In our study 26 patients (52%) required erythropoietin injections once a week , 20(40%) patients required twice a week injections of erythropoietin and 4(8%) did not require erythropoietin injections in the study period.

Table 7: Table showing Hb gram % of the study group

Hb gm%	Frequency	Percentage
<5	9	18.0
5-10	34	68.0
>10	7	14.0
Total	**50**	**100.0**

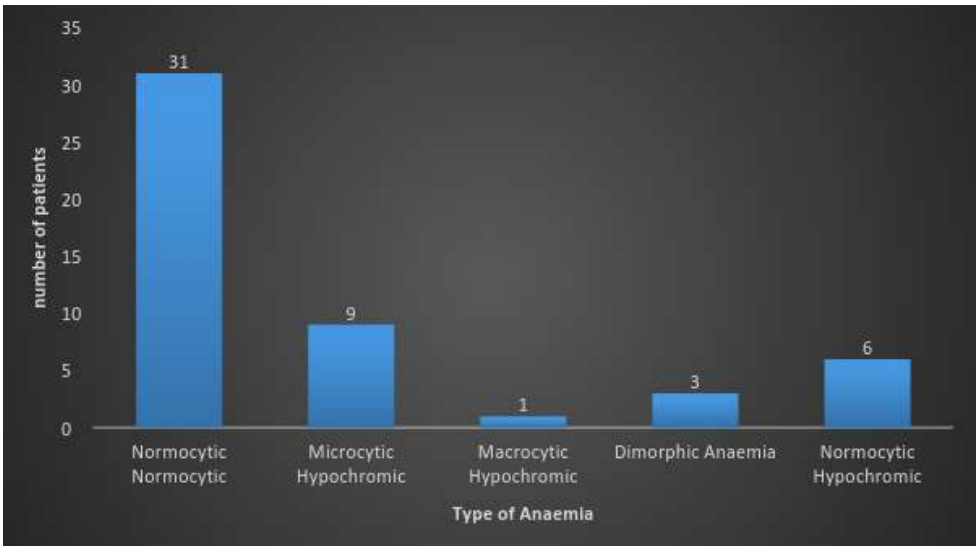


Graph 7: Graph showing Hb gram % of the study group

The haemoglobin value of less than 5gm% were found in 4 cases (8%) and 5-10gm% is 34 (68%) patients ,more than 10%gm% is 7 cases(14%).

Table 8: Table showing types of anaemia of the study group

Type of Anaemia	Frequency	Percentage
Normocytic Normochromic	31	62.0
Microcytic Hypochromic	9	18.0
Macrocytic Hypochromic	1	2.0
Dimorphic Anaemia	3	6.0
Normocytic Hypochromic	6	12.0
Total	**50**	**100.0**

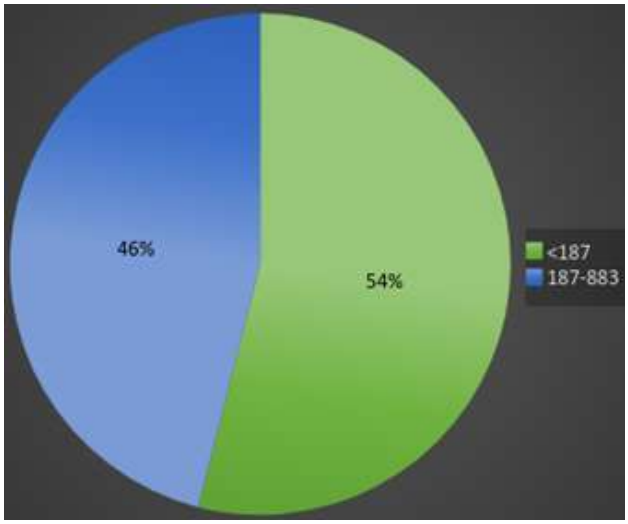


Graph 8: Graph showing types of anaemia of the study group

In our study about 31 patients (61%) are normocytic normochromic, 9 patients (18%) are microcytic hypochromic ,6 patients(12%) are normocytic hypochromic,3 patients(6%) are dimorphic anaemia and 1 patient (2%) are macrocytic hypochromic.

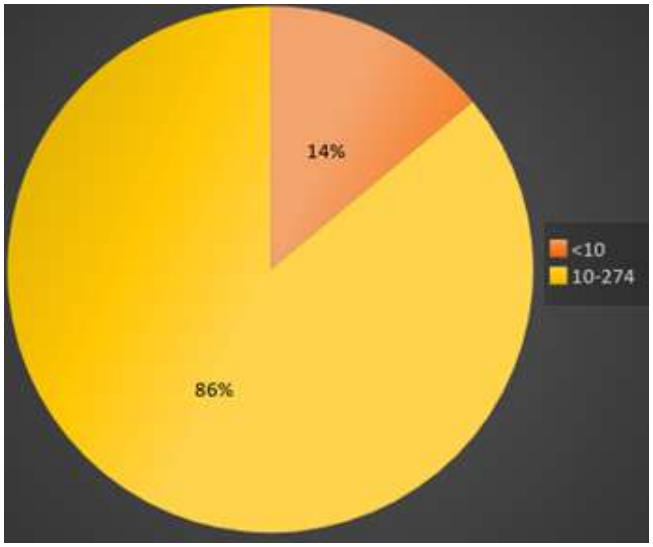
Table 9: Table showing serum B12 levels of the study group

Serum B12 Level	Frequency	Percentage
<187	27	54.0
187-883	23	46.0
Total	**50**	**100.0**



Graph 9: Graph showing serum B12 levels of the study group

In above table and graph serum b12 levels less than 187 are 27 patients (54%) and 23 patients (46%) are in between 187-883 in a total of 50 patients.



Graph 10: Graph showing serum ferritin levels of the study group

In this study it was observed that 43 patients (86%) serum ferritin levels are in the normal range and 7 patients(14%) are with deficiency of serum ferritin levels in a total of 50 patients.

Table 10: Table showing serum ferritin levels of the study group

Serum Ferritin levels	Frequency	Percentage
<10	7	14.0
10-274	43	86.0
Total	**50**	**100.0**

Table 15: Table showing association between types of anaemia and diet pattern

Type of anaemia	Diet Pattern		Total	Fisher's Exact Test value	p value
	Vegetarian	Non vegetarian			
Normocytic Normocytic	3(33.3%)	28(68.3%)	31(62.0%)	10.146	0.019
Microcytic Hypochromic	1(11.1%)	8(19.5%)	9(18.0%)		
Macrocytic Hypochromic	1(11.1%)	0(0.0%)	1(2.0%)		
Dimorphic Anaemia	2(22.2%)	1(2.4%)	3(6.0%)		
Normocytic Hypochromic	2(22.2%)	4(9.8%)	6(12.0%)		
Total	9(100%)	41(100%)	50(100%)		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 16: Table showing association between types of anaemia and diabetes

Type of anaemia	Diabetes		Total	Fisher's Exact Test value	p value
	Yes	No			
Normocytic Normochromic	16(55.2%)	15(71.4%)	31(62.0%)	4.049	0.363
Microcytic Hypochromic	6(20.7%)	3(14.3%)	9(18.0%)		
Macrocytic Hypochromic	0(0.0%)	1(4.8%)	1(2.0%)		
Dimorphic Anaemia	3(10.3%)	0(0.0%)	3(6.0%)		
Normocytic Hypochromic	4(13.8%)	4(9.8%)	6(12.0%)		
Total	29(100%)	21(100%)	50(100%)		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 17: Table showing association between types of anaemia and blood transfusion

Type of anaemia	Blood Transfusion		Total	Fisher's Exact Test value	p value
	Yes	No			
Normocytic Normocytic	21(63.6%)	10(58.8%)	31(62.0%)	3.549	0.481
Microcytic Hypochromic	5(15.2%)	4(23.5%)	9(18.0%)		
Macrocytic Hypochromic	0(0.0%)	1(5.9%)	1(2.0%)		
Dimorphic Anaemia	3(9.1%)	0(0.0%)	3(6.0%)		
Normocytic Hypochromic	4(12.1%)	2(11.8%)	6(12.0%)		
Total	**33(100%)**	**17(100%)**	**50(100%)**		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 18: Table showing association between types of anaemia and serum ferritin levels

Type of anaemia	Serum ferritin level		Total	Fisher's Exact Test value	p value
	<10	10 – 274			
Normocytic Normocytic	6(85.7%)	25(58.1%)	31(62.0%)	2.743	0.616
Microcytic Hypochromic	0(0.0%)	9(20.9%)	9(18.0%)		
Macrocytic Hypochromic	0(0.0%)	1(2.3%)	1(2.0%)		
Dimorphic Anaemia	0(0.0%)	3(7.0%)	3(6.0%)		
Normocytic Hypochromic	1(14.3%)	5(11.6%)	6(12.0%)		
Total	**7(100%)**	**43(100%)**	**50(100%)**		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 19: Table showing association between types of anaemia and patients taking injection erythropoietin

Type of anaemia	Patient taking erythropoietin			Total	Fisher's Exact Test value	p value
	Once	twice	Not once			
Normocytic Normocytic	12(60.0%)	15(57.7%)	4(100%)	31(62.0%)	4.525	0.945
Microcytic Hypochromic	5(25.0%)	4(15.4%)	0(0.0%)	9(18.0%)		
Macrocytic Hypochromic	0(0.0%)	1(3.8%)	0(0.0%)	1(2.0%)		
Dimorphic Anaemia	1(5.0%)	2(7.7%)	0(0.0%)	3(6.0%)		
Normocytic Hypochromic	2(10.0%)	4(15.4%)	0(0.0%)	6(12.0%)		
Total	**20(100%)**	**26(100%)**	**4(100%)**	**50 (100%)**		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 20: Table showing association between serum B12 levels and diet pattern

Serum B12 Level	Diet Pattern		Total	Fisher's Exact Test value	p value
	Vegetarian	Non Vegetarian			
<187	6(66.7%)	21(51.2%)	27(54.0%)	0.709	0.479
187 – 883	3(33.3%)	20(48.8%)	23(46.0%)		
Total	**9(100%)**	**41(100%)**	**50(100%)**		

p value calculated by fisher's exact test, p <0.05 considered as significant

Table 21: Table showing association between serum B12 levels and diabetes

Serum B12 Level	Diabetes		Total	χ^2 value	p value
	Yes	No			
<187	18(62.1%)	9(42.9%)	27(54.0%)	1.810	0.179
187 – 883	11(37.9%)	12(57.1%)	23(46.0%)		
Total	29(100%)	21(100%)	50(100%)		

p value calculated by chi square test, p <0.05 considered as significant

Table 22: Table showing association between serum B12 levels and homocysteine levels

Serum B12 Level	Homocysteine Level		Total	χ^2 value	p value
	<30	30 – 100			
<187	20(55.6%)	7(50.0%)	27(54.0%)	0.125	0.723
187 – 883	16(44.4%)	7(50.0%)	23(46.0%)		
Total	36(100%)	14(100%)	50(100%)		

p value calculated by chi square test, p <0.05 considered as significant

Table 23: Table showing association between serum ferritin levels and blood transfusion

Serum Ferritin Level	Blood Transfusion		Total	χ^2 value	p value
	Yes	**No**			
<10	6(18.2%)	1(5.9%)	7(14.0%)	1.410	0.398
10 – 274	27(81.8%)	16(94.1%)	43(86.0%)		
Total	**33(100%)**	**17(100%)**	**50(100%)**		

p value calculated by chi square test, p <0.05 considered as significant

4. Discussion

Anaemia is a common complication among patients with CKD .Early detection and treatment of anaemia would potentially improve quality of life and reduce burden of care.

In our study we took 50 patients of CKD between the age group 20 and 80 years.

37 male and 13 female patients with CKD .out of them 41 were taking non vegetarians and 9 were taking strict vegetarians food substance since their childhood period .These patients are chosen as to exclude some common conditions .It is a cross sectional study.

Our study showed a rise in the prevalence of CKD as the age increased. It is rare before the age of 20yrs and the prevalence of CKD was more in the age group between 50-69(52%)

Our study revealed that most patients had diabetes 29 patients (58%) and 21 patients (42%)were non diabetic .

Our study showed that a significant number of patients 33 patients(66%) required blood transfusion and 17 patients(34%) did not require blood transfusion.

Most of the patients in our study required injection erythropoietin once in a week basis that is 52% ,40% patients required it twice weekly and 8% of individual did not require erythropoietin.

Anaemia was evident in our study among 50 patients 68% had Hb between 5-10gm% and 18% had Hb less than 5-10gm% and 18% had Hb less than 5gm%,14% had more than 10%.

The demographic health survey of Tanzania in 2010 revealed that a majority of the patients (40%) had a high prevalence of anemia among women in the age group of 15-49 yrs.

The prevalence of anemia in this study was higher than values obtained elsewhere. McClellan et al5, in a large scale cross sectional multicentre survey done in USA involving 5,222 patients and using 12g/dl as definition of anemia reported an overall prevalence of anemia of 47.75% and progression of anemia from 26.7% in stage 3 to 75.5% in stage 5.

Suega et al in Indonesia and Afshar et al in Iran, reported the prevalence rate of anemia in predialysis patients 73.1% and 75.0% respectively and Africa a Nigerian studies documented 77.5% and 87% prevalence of anemia in CKD patients[2,3]

This high prevalence of anemia among CKD patients in this study may be accounted for by the disproportionately high number of patients with advanced CKD (78.0%) in whom the mean hemoglobin was 7.8 g/dl. These findings should alert clinicians that majority of patients with Chronic Kidney diseases who are referred at SSIMS & RC hospital as tertiary hospital have advanced CKD contributing to presence of severe anemia and progression to end stage renal disease.

It is also possible that the high prevalence of anemia might be explained partly by other causes peculiar to environment including poor nutrition and parasitic infestations majority of patients are normocytic normochromic accounting for 62%.

In our study serum b12 levels varied between 187-883 IU.The cut off serum b12 level for data analysis was taken as 187 IU among which 54% of patients had serum b12 levels less than 187 and the rest 46% had level between 187-883.

Ketut S et al explored the profile of anemia among CKD patients and reported similar results in which two cases had low level of serum folic acid and all cases had normal level of serum vitamin B12. This result verifies that, folic acid and vitamin B12 were not important contributing factors to anemia in this study.

In our study serum ferritin levels value of less than 10 was observed in 7(14%) of patients and the remaining 43 (86%) had serum ferritin level in the normal range.

Our study showed that mild Hyper-homocysteinemia was observed in 72% of patients in our study followed by 28% moderate homocysteinemia. Gender wise distribution revealed males are more hyper-homocystenaemic (74%) of patients.

In our study hyper-homocysteinemia was more common among non-vegetarians 41(82%) patients (70.7%).

In our study comparison between the type of anaemia and diet pattern in which most of them are non-vegetarians(82%) which is statistically significant p value(<0.05).

In our study comparison between the type of anaemia and diabetes ,most of them are normocytic normochromic (62%) and diabetic people which is not statistically significant.

In our study group comparison between the type of anaemia and blood transfusion out of 50 patients 33 patients underwent blood transfusion not statistically significant.

In our study comparison between serum b12 levels and diet pattern 54% of patients were with vitamin b12 deficiency which is not statistically significant.

In our study association between the serum ferritin levels and blood transfusion not statistically significant.

5. Conclusion

CKD affects millions of people worldwide and is a major cause of ill health among the elderly population. This study shows that anemia is prevalent among CKD patients of which 86% had moderate degree of anemia which was the most frequent finding in both sexes and the degree of anemia was more severe in females as compared to males, most of the patients being elderly.

Majority of the patients in our study revealed serum b12 deficiency which also caused elevated serum homocysteine levels in the patients.

Anemia in chronic kidney disease develops gradually over time as CKD progresses through its stages and add's to the morbidity in patients.

The most common type of anaemia in CKD was found to be normocytic normochromic anaemia. Anemia was more common among non-vegetarian's in our study group unlike previous studies[4].

Diabetes and diabetic nephropathy was found to be a contributing factor in the development of Chronic kidney disease among our study population. However there is no significance between the type of anemia and diabetes among the patients.

Majority of the patients of CKD with anemia may require blood transfusion for correction of anemia atleast once or more during their period of illness, thus warranting their admission to a healthcare facility with adequate blood banks and blood transfusion facilities for management.

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