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A Study on Hematological Profile in Chronic Kidney Disease

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Original Research Article

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Abstract: Kidney diseases rank 3rd amongst life threatening disease, after cancer and heart disease. Anemia is an constant complication of chronic kidney disease that significantly contributes to the symtoms and complications of the disease. Aim of the study is to study the hematological manifestations ofchronic kidney disease (CKD) and to correlate the hematological abnormality with the clinical stage.182 patients with chronic kidney disease admitted in Osmania general Hospital were included in the study for a period of 2 years. Patients in various stages of the disease were studied for various hematological parameters. CKD was seen across all age groups. Increased prevalence of CKD was seen in the age group of 41 - 50 years. Majority of patients at presentation were in stage V CKD. Hypertension (47.2%) was the leading cause of CKD, followed by diabetes. Ischemic heart disease was the most common associated illness seen in CKD. The mean hemoglobin in the present study was 7.99 +/- 1.2 g/dl. The fall in mean hemoglobin had an inverse correlation with the stage of CKD. The mean RBC count was 2.73 $x10^{12}$/l, with significant fall in the RBC count as the stage of CKD progressed. The mean absolute reticulocyte count also showed significant decline as the stage progressed.Chronic kidney disease is seen across all age groups with a malepreponderance. Hypertension is the most common cause of CKD. The anemia of CKD is a normocytic normochromic anemia. The fall in hemoglobin is due to low RBC count due to decreased erythropoiesis.
Keywords: Anemia, chronic kidney disease.

INTRODUCTION

BACKGROUND

Chronic kidney disease (CKD) is a major public health problem throughout the world [1]. The National Kidney Foundation in India states that, kidney diseases rank 3rd amongst life threatening disease, after cancer and heart disease. About 2,00,000 persons go into terminal kidney failure every year [2]. The major outcomes of chronic kidney disease, regardless of the specific diagnosis (i.e., type of kidney disease), include progression to kidney failure, complications from decreased kidney function, and development of cardiovascular disease [1]. Symptoms and overt signs of kidney disease are often absent until renal failure supervenes [3].Anemia is an almost constant complication of chronic kidney disease that significantly contributes to the symptoms and complications of the disease [4]. Anemia in CKD is primarily due to reduced production of erythropoietin in the kidney and secondarily to shortened red cell survival [19]. Due to its insidious onset, anemia associated with CKD is often asymptomatic and only picked upon routine blood analysis. Delayed diagnosis and treatment of anemia associated with chronic kidney disease may increase the risk of cardiovascular complications including coronary artery disease, left ventricular disorders and cardiac failure [5]. Due to the public health burden caused by renal anemia it is important to raise awareness of this condition and encourage early diagnosis and treatment [5].

The aim of the present study is to enumerate hematological manifestations of chronic kidney disease and to correlate the hematological abnormality with the clinical stage of chronic kidney disease.

METHODOLOGY

Patients with chronic kidney disease admitted in Osmania general hospital were included in the study for a period of 2years i.e. from June 2014 to May 2016. The clinical diagnosis of CKD was done based on serum creatinine for more than 3 months. Estimated Glomerular filtration Rate (eGFR) was calculated by MDRD (Modification of Diet in Renal Disease) equation ie,

GFR (mL/min/1.73 m^2) = 175 × $(Scr)^{-1.154}$ × $(Age)^{-0.203}$ × (0.742 if female) × (1.212 if African /American).

Based on eGFR, patients are categorized in various clinical stages of CKD as follows [6];

Table-1: Categorization of patients based on eGFR

GFR Categories (mL/min/1.73 m^2) Description and Range			
	G1	Normal or high	≥90
	G2	Mildly descreased	60–89
	G3a	Mildly to moderately decreased	45–59
	G3b	Moderately to severely decreased	30–44
	G4	Severely decreased	15–29
	G5	Kidney failure	<15

Patients in various stages of the disease were studied for clinical manifestations and hematological parameters. Detailed clinical history was collected from the patient and hospital records. After obtaining the informed written consent, blood was collected under aseptic precautions for investigations for assessment of hematological changes: Complete hemogram was done using SYSMEX-XT 1800i AUTOMATED 5-PART HEMATOLOGY ANALYZER. 21 hematological parameters obtained were HB, RBC, HCT, MCV, MCH, MCHC, RDW- SD, RDW-CV, WBC, NEUT%, LYMPH%, MONO%, EOSINO%, BASO%, NEUT#, LYMPH#, MONO#, EOSINO#, BASO#, PLT and MPV.

INCLUSION CRITERIA

- Patients of chronic kidney disease with stage I –V disease.
- Patients with end stage renal failure on hemodialysis and peritoneal dialysis.

EXCLUSION CRITERIA

- Pregnancy.
- Patients on end stage renal disease treated with renal transplantation.
- History of blood transfusion during last three months.

RESULTS

182 patients with chronic kidney disease were included in the present study. Among the study population 110 (60.4%) patients were male and 72(39.6 %) were female. The age of the study population ranged from 9 months to 80 years, with the mean age being 44.9 ± 15.22 years. Majority of the patients belonged to the age group of 40 - 50 years (Table-1). Majority of the patients (66%) in the study were in stage V CKD, followed by stage IV (23%), stage III (8%) and stage II (3%) (Figure-1). No cases of stage I were seen. Hypertension was the leading cause of CKD (72 cases) followed by diabetes (55 cases) (Figure-2). Least common causes were Lupus nephritis, chronic glomerulonephritis, Chronic infective disease and cystic kidney disease. The most common presenting symptoms were generalized weakness, anorexia, pedal edema, facial puffiness and dyspnoea. Ischemic heart disease was the most frequent illness associated with CKD. Pallor and signs of volume overload (Pedal edema, pulmonary edema and ascites) were frequently seen in CKD. Volume overload state is most frequently seen in stage V CKD. In the present study haemoglobin values ranged from 4.0g/dl to 15.0 g/dl, with a mean haemoglobin of 7.99 ± 1.2 g/dl (Table-2). There is fall in hemoglobin level with progression of CKD (Table-3). The RBC count ranged from 1.74 to 6.45 $x10^{12}$/l with a mean of 2 .73 ± 0.91 $x10^{12}$, and there was fall in RBC count as the stage progressed. RDW-CV was increased in 37 cases of CKD and normal in the rest. Table 4 shows the distribution of RDW-CV in various stages of CKD. RDW-CV ranged from 11.2 - 22.6, with a mean of 15.8 ± 2.1. The Red cell distribution width increased as the stage progresses. The most frequent peripheral smear picture seen was Normocytic normochromic anemia (61 cases), followed by Normocytic hypochromic anemia (42 cases). Microcytic anemia was seen in 23 cases and dimorphic blood picture was seen in 36 cases (Figure-3).

The predominant poikilocytes seen on the peripheral smear in CKD were the burr cells. Other poikilocytes like pencil shaped cells, elliptocytes, fragment cells were seen occasionally with severe degree of anemia. The WBC count ranged from 3.2 –

29.0 x10^9/l, with a mean value of 10.8 ± 5.9 x10^9/l. Neutrophilia was common across all stages of CKD seen in 19.2% cases in stage III, 35 % in stage IV and 44.8% cases in stage V. The platelet count ranged from 101 - 474 x10^9/l, with a mean value of 202 ± 0.89 x10^9/l (Figure-4). Eight cases had uremic bleeding on presentation. All 8 cases presented with mucosal bleeding. Majority of cases of uremic bleeding were in stage V. The absolute reticulocyte count ranged from 18.8 – 100.4 x10^9/l, with a mean ARC of 30.0 ± 18.8x10^9/l. (Figure -5). There is fall in ARC with progression of the stage of CKD. Majority of patients had grade 3 renal parenchymal changes and were in stage V CKD. Most of patients with CKD had proteinuria and microalbuminuria.

Table-2: Age and gender distribution

Age (years)	Male	Female	Total
0 – 10	1	0	1
10 – 20	4	2	6
20 – 30	15	10	25
30 – 40	17	13	30
40 – 50	28	25	**53**
50 – 60	30	12	42
60 – 70	10	7	17
70 – 80	2	3	5

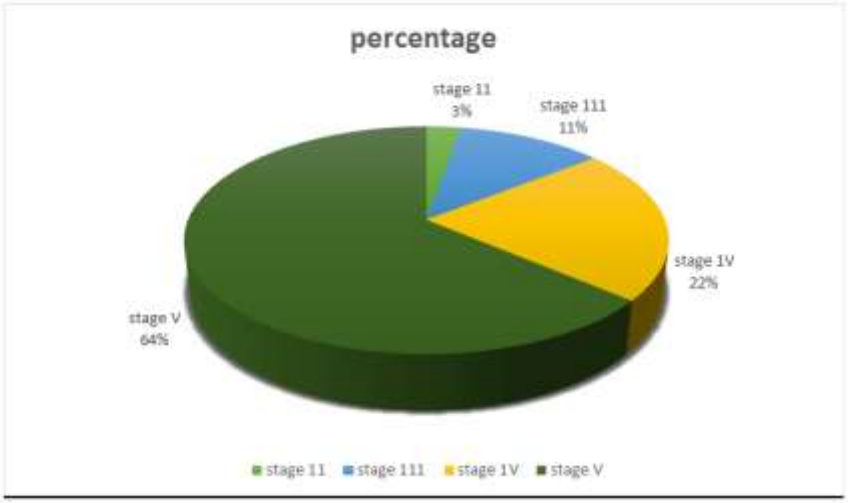

Fig-1: Percentage distribution of various stages of CKD

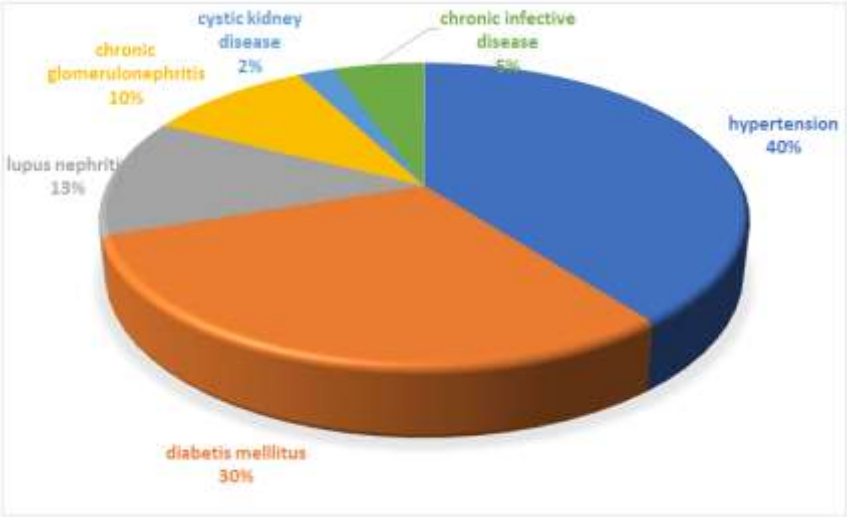

Fig-2: Etiological distributionin CKD

Table-3: Hemoglobin distribution in CKD

Hemoglobin (g/dl)	Number of cases	Percentage
<4	0	0.0%
4.1-6	23	12.7%
6.1-8	58	31.9%
8.1-10	40	21.9%
10.1-12	32	17.6%
12.1-14	27	14.8%
>14.1	2	1.1%

Table-4: Distribution of Hemoglobin in various stages of CKD

Hemoglobin	Stage II	Stage III	Stage IV	Stage V
(g/dl)				
4.1-6	0	0	8	15
6.1-8	0	0	13	45
8.1-10	0	1	8	31
10.1-12	0	5	15	12
12.1-14	1	17	9	0
>14.1	0	1	0	1
Mean SD	12.3± 0.0	12.2±1.4	10.4 ± 1.6	7.9 ± 1.7

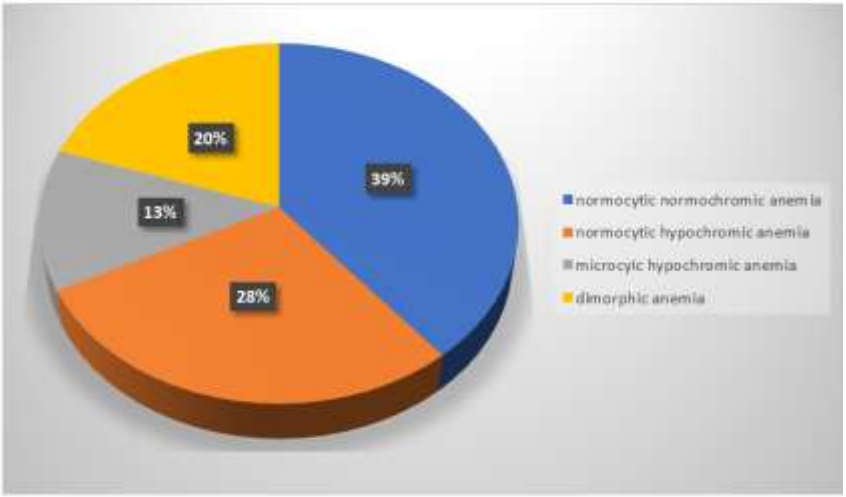

Fig-3: Peripheral smear picture in CKD

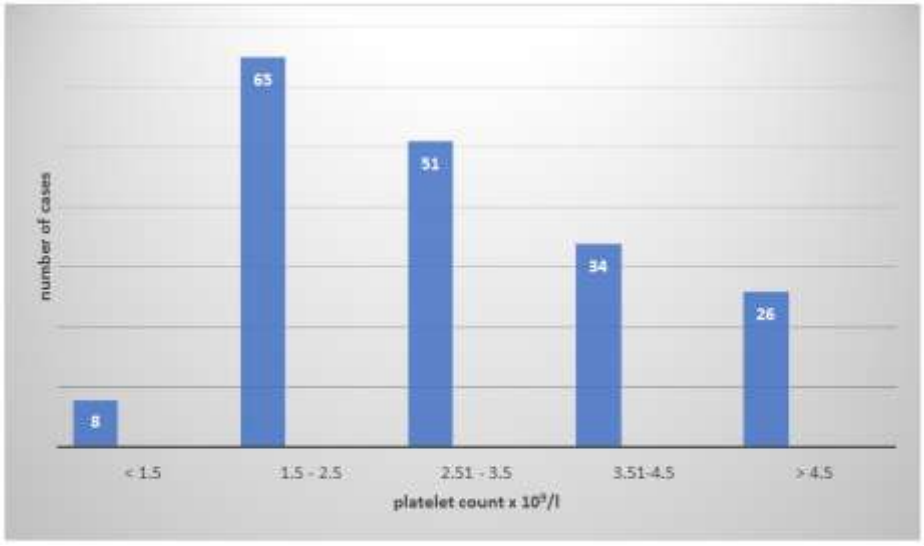

Fig-4: Distribution of Platelet count in CKD

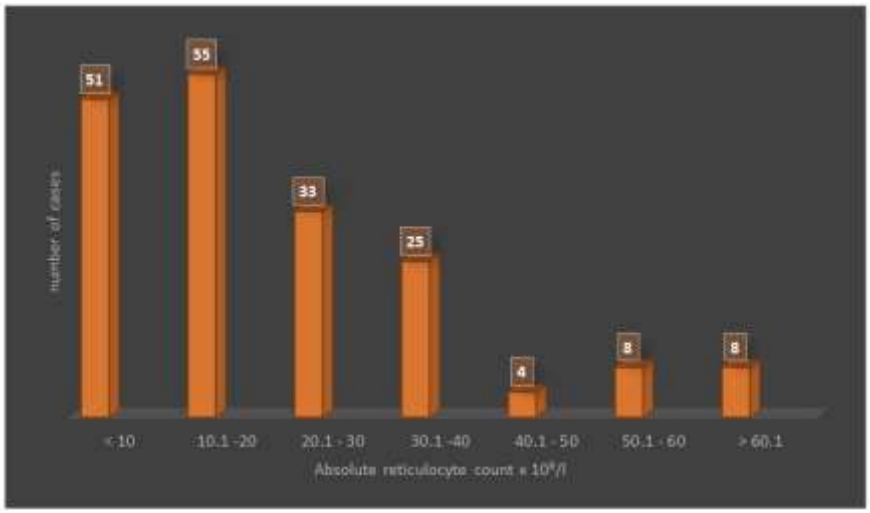

Fig-5: Distribution of Absolute reticulocyte count

DISCUSSION

Chronic kidney disease is progressive renal disease characterised by various manifestations and haematological abnormalities. The present study shows mean age falling in the 5th decade which is similar to the study by Talwar *et al*., [7] done in India. Studies by Anees *et al*., [8] Sardenberg *et al*., [10] and Moranne *et al*., [9] report higher mean age. The present study agrees with all the other studies in terms of increased male preponderance, which is attributed to the high prevalence of risk factors for CKD in males. The present study shows an increased prevalence of CKD patients in stage V. This is because of the fact that the present study is a hospital based study and hospitalisation occurs more in stage V as a result of complications and co-morbidities. Moranne *et al*., [9] and Agarwal *et al*., [11] observed an increased prevalence in stage III and IV.

Table-5: Comparison of stage prevalence in CKD

	Morranne *et al.*, 2009 [9]	Agarwal *et al.*, 2011 [11]	Present study
Stage I	0%	1%	0%
Stage II	12%	3%	3%
Stage III	**48%**	51%	8%
Stage IV	31%	**38%**	23%
Stage V	9%	6%	**66%**

Hypertension was the leading cause of CKD among the study group, constituting 40% (72 cases). Diabetes as a cause was seen in 55 cases.

Table-6: Comparison of etiological distributions in CKD

Etiology	Drueke *et al.*, 2006 [12]	Dash *et al.*, 2006 [13]	Anees *et al.*, 2009 [15]	Morranne *et al.*, 2009 [9]	TimothyHM*etal.*, 2010 [14]	Present study
Diabetes	20%	29.7%	67.6%	10%	30%	30%
Hypertension	23%	14%	9.7%	10%	69%	40%
CGN	24%	19.3%	16.8%	55%	-	10%
Cystic diseases	12%	8.4%	-	0%	-	2%

Pallor is frequently seen in CKD as a result of fall in hemoglobin. The present study showed the prevalence of pallor in 69% cases as compared to Talwar *et al*., [7] which had a high prevalence of 96%.

In the present study, the degree of pallor had a significant correlation with the stage of CKD. CKD is associated with anemia in a majority of patients. The mean hemoglobin in the present study in 7.8g/dl/. Talwar *et al*., [7] and Singh *et al.*, [16] observed lower hemoglobin.

Study done by Agarwal *et al.*, [11] observed a higher hemoglobin value in the CKD population in the US.

Hemoglobin levels fall with the progression of the stages in CKD. The present study demonstrated a significant fall in hemoglobin as the stage progresses. This fall in hemoglobin is statistically significant and correlated well with the stage of CKD.

Study by Khanam *et al*., [17] showed a gradual fall in the hemoglobin levels in CKD as the stage progress. But the mean hemoglobin was lower in each stage when compared to the present study.

The present study demonstrated that the average RBC count is low in CKD. The RBC indices are within the normal range. The present study agrees with studies by Talwar *et al*., [7] and Singh *et al*., [16] which also showed low RBC count and normal RBC indices. The fall in RBC significantly correlates with the stage of CKD, with lower counts observes as the stage progresses.

The absolute reticulocyte count in the present study is lower than normal with a mean of 30.0 ± $18.8x10^9$/l. The fall in ARC increases gradually as the stage progresses. Not many studies have evaluated reticulocyte parameters in renal failure. In the present study, normocytic normochromic picture was the predominant finding in the peripheral smear and the anemia also being of the normocytic normochromic type in the majority.

There were 23 cases of microcytic anemia in the present study. A study which was conducted by Talwar *et al*., [7] observed microcytic hypochromic anaemia in most of the patients of chronic renal failure. Arun S *et al*., [18] studies revealed normocytic normochromic anaemia. Good number of poikilocytes was observed in the present study. Most frequently seen poikilocytes are burr cells, tear drop cells, acanthocytes, pencil shaped cells, fragmented cells and elliptocytes. The mean platelet count in CKD in the present study is normal.

CONCLUSION

CKD is seen across all age groups with increased prevalence in the age group 41- 50 years, with male predominance. Majority of patients presenting at stage V CKD.

Hypertension and diabetes are the most common causes of CKD in adults. Volume overload is a frequent presentation of CKD. Anemia is a common complication of CKD, seen with increasing prevalence as the stage progresses. The mean hemoglobin in the present study was 7.99 +/- 1.2 g/dl. The fall in mean hemoglobin had an inverse correlation with the stage of CKD. The fall in haemoglobin is due to the low RBC count as a result of decreased erythropoiesis. The anemia in CKD is predominantly of normocytic normochromic type. Mucosal bleeding is the most frequent bleeding tendency seen in CKD. Renal anemia is a public health burden and it is important to raise the awareness of this condition and encourage early diagnosis and treatment to decrease the comorbidity due to ischemic heart diseases.

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