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Original Research Article

Study of hematological profile in patients with chronic kidney disease

Gautam Panduranga*, Ugendhar Perla

Department of General Medicine, Mediciti Institute of Medical Sciences, Ghanpur, Telangana, India

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***Correspondence:**
Dr. Gautam Panduranga,
E-mail: gautampsetty@yahoo.com

ABSTRACT

Background: Chronic Kidney Disease (CKD) with its high prevalence, morbidity and mortality, has become an important public health problem. The incidence and prevalence of CKD is increasing worldwide, including India. CKD is associated with a variety of hematological abnormalities, include anaemia, infections and bleeding diathesis. Anaemia is the most consistent hematological abnormality and is associated with poor quality of life and poor cardiovascular outcomes.
Methods: A hospital based cross-sectional observational study was done to detect the prevalence of haematological abnormalities, correlation of anaemia with CKD stage and evaluation of iron deficiency. Newly diagnosed CKD (stages 3 to 5) patients were included in this study. Presence of anaemia (Hb%, haematocrit, MCV, peripheral smear), iron deficiency (TSAT, serum ferritin), thrombocytopenia, leucocyte count and coagulation abnormalities (PT, APTT) in different stages of CKD were studied.
Results: All the subjects in study group had anaemia which was normocytic and normochromic and of moderate degree in most patients. The severity of anaemia progressed with stage of the disease. Iron deficiency was significantly prevalent (52% in the study population, with transferrin saturation (TSAT) <20%). WBC count was not significantly altered. There was mild thrombocytopenia in a few patients. Bleeding time or other in vitro tests of platelet function were not measured. The coagulation parameters, PT and APTT, were not significantly altered.
Conclusions: All CKD patients should be screened for iron deficiency anaemia for its early treatment and to decrease morbidity.

Keywords: Anaemia in CKD, Chronic kidney disease, Haematological abnormalities in CKD, Iron deficiency anaemia, Transferrin saturation, Thrombocytopenia

INTRODUCTION

Chronic kidney disease is a major health problem throughout the world. Incidence and prevalence of chronic kidney disease is increasing worldwide. Renal dysfunction gives rise to a variety of hematological manifestations. Renal failure typically affects the red blood cells, leucocytes and platelets causing anaemia, increased incidence of infections and bleeding.

Anaemia was first linked to CKD over 170 years ago by Richard Bright. Anaemia has been shown to start appearing at GFR below 60ml/min, but more prevalent when it falls below 30ml/min (or stages 4 and 5 of CKD).[1,2] It affects nearly all patients with stage 5 CKD.[3] It is caused by the failure of renal excretory and endocrine function.

Anaemia in CKD is associated with reduced quality of life and increased cardiovascular disease, hospitalizations, cognitive impairment, and mortality.[3] Iron deficiency anaemia is common in CKD patients. Iron deficiency may be absolute, often due to poor dietary intake or sometimes occult bleeding, or functional, when there is an the imbalance between the iron requirements of the erythroid marrow and the actual iron supply.[4] Iron

deficiency leads to decreased formation of red cell hemoglobin and produces hypochromic microcytic type of anaemia. Early detection and treatment of iron deficiency is crucial in the treatment of anaemia and reducing morbidity. According to NKF-KDOQI guidelines absolute iron deficiency is defined as either TSAT <20% or serum ferritin <100 ng/ml.

Disturbances in the hemostasis are a common complication of CKD, mainly due to defective platelet function and anaemia. These have a major influence on the quality of life of patients. Uncorrected anaemia can be crippling to the patient who is already disabled. Early detection of anaemia and its etiology, and factors influencing platelet function and coagulation are very important for providing patient care in patients with CKD.

METHODS

The objective was to study the prevalence of hematological abnormalities including anaemia and thrombocytopenia in patients with CKD. Authors also evaluated iron deficiency in these patients and studied the correlation of anaemia with stage of CKD. The study was carried out in a tertiary hospital setting and it was a cross-sectional observation study done over a period of 18 months.

The study included out-patients and in-patients of Nephrology department, both males and females, of age greater than 18 years, with diagnosis of Chronic Kidney Disease (stages III-V) based on elevation of serum creatinine (>1.5 mg/dL) for more than 3 months. Only newly diagnosed CKD patient (stages III III V) were included, before start of any intervention or treatment.

Exclusion criteria

Exclusion criteria included patients with other systemic illness without renal failure, pregnant women and those diagnosed with aplastic anaemia or haematological malignancy. Patients with End Stage Renal Disease (ESRD), treated with renal replacement therapy in the form of renal transplantation and those with history of blood transfusion during previous three months or history of oral or parenteral iron therapy during previous 3 months were also excluded from the study.

The study included 98 patients with newly diagnosed Chronic Kidney Disease stage III-V; patients fulfilled the criteria for definition of CKD as per KDIGO 2012 guidelines. Informed consent was taken from each participant (or nearest kin) in the study. The protocol was approved by Institutional Ethics Committee.

In addition to hematological and coagulation parameters and ultrasound imaging of abdomen, Iron profile was measured including Serum iron, TIBC, Ferritin and TSAT (transferrin saturation). True iron deficiency was defined according to National kidney foundation/kidney disease outcomes quality initiative guidelines (NKF-KDOQI): Either serum ferritin <100 ng/ml or TSAT <20%. In this study, TSAT <20% was considered as a marker of iron deficiency. All statistical analysis was done using SPSS software version 21.0.

RESULTS

This study included a total of 98 cases with chronic renal disease, the age group ranged from 22 to 80 years. Majority of cases were in the age group of >60 years (47 cases or 47.96%), the mean age being 57.35±11.95 years. The prevalence of CKD increases with increasing age because of age related decline in GFR. In present study majority of the study population were males (74 cases - 75.51%). Male gender is a risk factor for development of CKD.

In present study majority of the patients were in stage 5 (44 cases, 44.9% of total cases) and stage 4 (41 cases, 41.84%) (Figure 1).

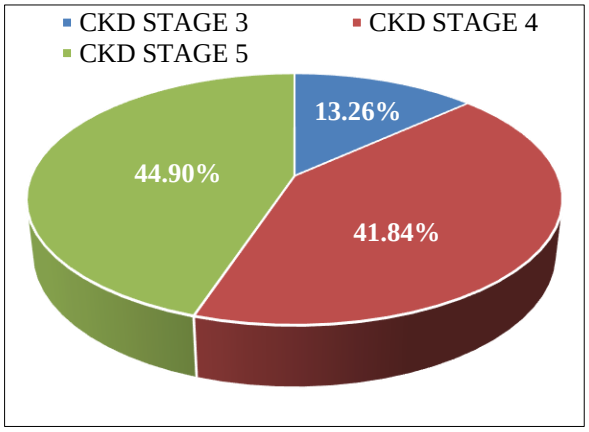


Figure 1: Stage wise distribution of study population.

Following KDIGO 2012 guidelines Anemia in CKD defined as Hb <13 gm/dl in males and Hb <12 gm/dl in females.

In present study all patients had anemia (100%) and Hemoglobin decreased with increasing stage of CKD. Severe anaemia (<7 gm %) (11cases) was seen in 1 out of 41 CKD stage 4 patients and 10 out of 44 CKD stage 5 patients (Table 1).

Table 1: Stage wise anaemia distribution.

HB (gm %)	CKD Stage 3	CKD Stage 4	CKD Stage 5
< 7 (severe anemia)	0	1(2.4%)	10(22.7%
7-11 (moderate)	11(84.6%)	38(92.7%)	33(75%)
>11 (mild)	2(15.4%)	2(4.9%)	1(2.3%)
Total	13(100%)	41(100%)	44(100%)

Leukocyte count

In present study total leucocyte count was normal in majority of the patients (77 cases -78.58%). Leucopenia was seen in 3 patients and leukocytosis was seen in 18 patients (18.36%).

Mean Corpuscular Volume (MCV)

In present study Mean MCV was 85.10±7.47 (Table 2). Mean MCV was normal in all CKD stages. 20 out of 98 patients had low MCV (<80 fl), and 4 out of 98 patients had high MCV (>97fl).

Table 2: MCV distribution in CKD stages.

CKD stage	Number	Mean	SD	ANOVA (F)	p value
3	13	85.49	9.21	0.421	0.658 (NS)
4	41	84.28	7.63		
5	44	85.74	6.84		
Total	98	85.10	7.47		

p<0.05 statistically significant; NS: Not significant. MCV Biological reference: 80-97 femtolitres(fl).

Red Cell Distribution Width (RDW)

In present study Mean RDW was 15.84±2.11. Mean RDW increased from stage 3 to stage 5, this was not statistically significant. 67 out of 98 (34 out of 44 CKD stage 5, 26 out of CKD stage 4 and 7 out of CKD stage 3) patients had increased RDW.

Platelet count

In this study platelet count was normal in majority of the patients (77 cases-78.57%) (Table 3). Thrombocytopenia was seen in 19(19.39%) patients and Thrombocytosis was seen in 2(2.06%) patients.

Table 3: Platelet count distribution in study population.

Platelet count	Number	Percentage
<1.5 Lakhs/cumm	19	19.39%
1.5-4.5 lakhs/cumm	77	78.57%
>4.5 lakhs/cumm	2	2.04%

Platelet count Biological reference: 1.5- 4.5lakhs/cumm.

In present study although platelet count showed a decreasing trend with increasing stage of the disease, mean platelet count was normal in all CKD stages. Total mean platelet count was 2.24±0.97 (Table 4).

Serum iron

In present study serum iron levels were decreased with increasing of CKD stage but, mean Serum Iron was normal in all CKD stages. Total mean Serum Iron was 51.04±34.67 (Table 5).

Table 4: Platelet count distribution in CKD stages.

CKD Stage	Number	Mean	SD	ANOVA (F)	p value
3	13	2.46	1.03	1.006	0.369 (NS)
4	41	2.33	1.03		
5	44	2.09	0.90		
Total	98	2.24	0.97		

p<0.05 statistically significant. Platelet count Biological reference: 1.5-4.5 lakhs/cumm.

Table 5: Serum iron distribution in CKD stages.

CKD Stage	Number	Mean	SD	ANOVA (F)	p value
3	13	61.61	29.10	0.786	0.459 (NS)
4	41	51.09	41.79		
5	44	47.86	28.40		
Total	98	51.04	34.67		

p<0.05 statistically significant. Serum Iron Biological reference: 45-182.0µg/dl.

Ferritin and TIBC

In present study mean serum ferritin was 384.23±475.42. Mean serum ferritin levels increased with increasing of CKD stage. In present study mean serum TIBC (Total iron binding capacity) decreased in all CKD stages. Mean serum TIBC showed decreasing trend with increasing stage of CKD. Total mean serum TIBC was 227.99±59.96.

Table 6: TSAT distribution in study population.

		Number	Percentage
TSAT	Normal	43	43.88%
	Abnormal	55	56.12%

TSAT= Transferrin saturation. TSAT Biological reference: 20-50%

Table 7: TSAT (% saturation) distribution in CKD stages.

CKD stage	Number	Mean	SD	ANOVA (F)	p value
3	13	23.5	12.5	1.772	0.176 (NS)
4	41	18.7	11.4		
5	44	18.0	5.3		
Total	98	19.0	9.4		

p<0.05 statistically significant. TSAT Biological reference: 20-50%.

TSAT (Transferrin Saturation)

TSAT was decreased (<20%) in 55 cases (56.12%) (Table 6).

TSAT decreased with increasing stage of CKD. Total mean TSAT was 19.0±9.4 (Table 7).

Iron profile

According to NKF-KDOQI guidelines, presence of serum ferritin <100 ng/ml or TSAT <20% is defined as True iron deficiency. More than half of the patients had TSAT <20% (Table 8).

Table 8: Iron profile in study population.

Iron marker	Number(percentage)
TSAT<20%	55 (56.12%)
Serum ferritin <100ng/mL	23 (23.47%)
TSAT<20% and Ferritin<100ng/mL	20 (20.4%)
TSAT>20% and Ferritin>100ng/mL	40 (40.8%)

True iron deficiency

In this study, presence of TSAT <20% was taken as true iron deficiency. 6 out of 13 CKD stage 3 patients, 25 out of 41 CKD stage 4 patients and 24 out of 44 CKD stage 5 patients had TSAT <20 % (Fig 2).

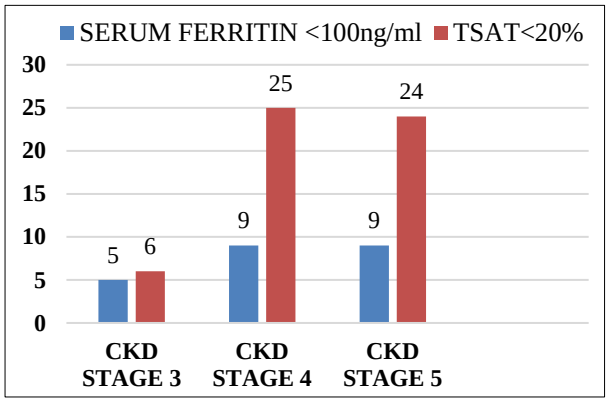
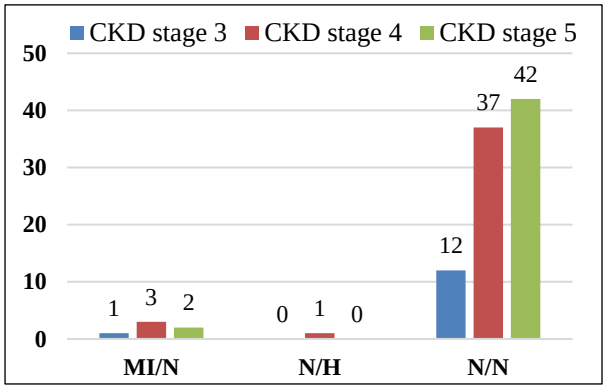


Figure 2: True iron deficiency based on CKD stages.



MI/N= microcytic normochromic
N/N=normocytic normochromic
N/H=normocytic hypochromic

Figure 3: Peripheral smear and CKD stages.

Coagulation parameters

In present study mean Prothrombin time marginally elevated (12.89±1.74), but it was not statistically significant. In present study Total mean a PTT was 29.36±4.64, which was in normal range.

Peripheral smear

In present study normocytic normochromic type of anaemia was seen in 91 out of 98 patients. Normocytic normochromic anaemia was most common type of anaemia in all stages of CKD patients (Figure 3).

DISCUSSION

Renal dysfunction gives rise to a variety of hematological manifestations. Renal failure typically affects the red blood cells, leucocytes and platelets causing anaemia, increased incidence of infections and bleeding. All the patients were anemic as defined by WHO criteria. This was similar to study done by Chakravarti et al, 20175 in which 100% subjects were anaemic. The mean hemoglobin was 8.80±1.48. In present study Anaemia was graded as mild (Hb% >11 gm%), moderate (7-11 gm %) and severe (<7 gm %). Moderate grade anaemia was most common in all stages of CKD (82 cases-83.6%). This is consistent with studies done by Dewan et al, (50% cases) and Chakravarti et al, (55.26%).[5,6] The mean hemoglobin decreased from stage 3(9.87) to stage 5(8.37) and this correlation was statistically significant (p=0.004).

In present study majority of patients (92.86%) had normocytic normochromic type of anaemia which was followed by microcytic hypochromic anaemia (6.12%). This was similar to the studies done by Chakravarti et al, (77.19% of N/N) and Dewan et al, (96.87%N/N). Hematocrit was decreased in all stages.[5,6]

Iron studies

In present study all patients were anemic. On evaluation of iron status it was found that 51 out of 98 patients had low serum iron levels (<45 µg/dl), because majority of study population were in CKD stage 4 and 5. Mean serum iron was 51.04±34.67 which was similar to the study done by Mambatta et al, in which mean serum iron was 59.62±25.91 (Table 9).[7]

True iron deficiency

Following national kidney foundation/kidney disease outcomes quality initiative guidelines (NKF-KDOQI), either serum ferritin <100 ng/ml or TSAT <20% means true iron deficiency. In present study 55 (56.12%) out of 98 patients had TSAT <20%, which was high comparable to other studies as shown in (Table 10). True iron deficiency was therefore seen in a significant proportion of patients (more than half of the patients).

Table 9: Comparison of iron studies.

	Present study	Mambatta et al,[7]	GC Reddy et al,[11]
Serum iron	51.04±34.67	59.62±25.91	66±7.0
Serum ferritin	384.23±475.42	423.12±388.61	207±28
TSAT	19.06±9.44	23.94±11.58	30±3.0
TIBC	227.99±59.96	260.97±63.31	234±12

Table 10: Comparison of true iron deficiency (based on TSAT).

Study	True Iron deficiency anaemia (TSAT <20%)
Present study	56.12%
Deori et al,[8]	26%
Lukaszyke et al,[9]	17%
Sang-Ryu et al,[10]	14%

TSAT=transferrin saturation

Leucocytes and platelets

There doesn't seem to be any significant change in leukocyte count in CKD patients. Few patients with leucocytosis (18 out of 98 patients) may have had concurrent infection which was not studied. In this study mean platelet count was 2.24±0 (Table 11).

Platelet count was normal in majority of patients (77 cases - 78.57%). Thrombocytopenia was seen in 19 out of 98 patients (19.39%). Similar to the study done by M Huang et al, mean platelet count decreased from stage 3 to stage 5, but this correlation was not statistically significant.[12]

Table 11: Comparison of platelet count.

CKD stage	Platelet count(Mean±SD)	
	Present study	M Huang et al,[12]
Stage 3	2.46±1.03	2.14±0.65
Stage 4	2.33±1.03	2.14±0.52
Stage 5	2.09±0.90	1.95±0.58

Coagulation parameters

In this study mean Prothrombin time was near normal (12.89±1.74). and mean aPTT was 29.36±4.64 (normal).

CONCLUSION

A hospital based cross-sectional observational study was done to detect the prevalence of haematological abnormalities, correlation of anaemia with CKD stage and evaluation of iron deficiency. Newly diagnosed CKD (stages 3 to 5) patients were included in this study. Presence of anaemia (Hb%, haematocrit, MCV, peripheral smear), iron deficiency (TSAT, serum ferritin), thrombocytopenia, leucocyte count and coagulation abnormalities (PT, APTT) in different stages of CKD were studied.

It was found that all the subjects in the study group had anaemia. The anaemia in CKD patients was normocytic and normochromic and of moderate degree in most of the patients. The severity of anaemia progressed with stage of the disease. Iron deficiency was significantly prevalent (52% in the study population, with transferrin saturation (TSAT) <20%). Hence, all CKD patients should be screened for iron deficiency anaemia for its early treatment and to improve the quality of life.

Total WBC count was not significantly altered. There was mild thrombocytopenia in a few patients. Bleeding time or other in vitro tests of platelet function were not measured in this study. The coagulation parameters, PT and APTT, were not significantly altered.

It was a hospital-based study and sample size being small, it does not represent the general population. Measurement of reticulocyte count, serum folate and B12 levels and testing for occult blood in stool would have made the evaluation of anaemia more comprehensive. In CKD, platelet dysfunction is the cause of bleeding diathesis and tests of platelet function include bleeding time and other in vitro tests. However, bleeding time is rarely done any longer due to poor standardization, accuracy, reproducibility, and ability to predict bleeding risk. Further studies with newer tests of platelet function would be very valuable.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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